From Research to Action: Breaking New Ground

September 7-9, 2007
Westin Bonaventure Hotel
Los Angeles

Sponsored by the
California Breast Cancer Research Program

CALIFORNIA
Breast Cancer
Research Program

General Symposium Information

CALIFORNIA
Breast
Cancer
Research
PROGRAM

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Contents

DIRECTOR'S WELCOME

To Pause and Reflect, to Engage and Inspire

It's time again to pause and reflect on the progress made by our funded investigators and overall within breast cancer research. "From Research to Action: Breaking New Ground" gives us the chance to see the accomplishments that people are making against breast cancer, to interact directly with each other, and to launch ourselves into the next two years with renewed vigor and enthusiasm.

Plenary sessions and workshops will discuss a broad range of the most important topics currently under investigation in breast cancer research and identify other potentially fruitful areas to explore. These discussions are designed to be friendly to a lay audience in order to increase participation in the discussions.

Be sure to browse the exhibit area, where you'll find displays of some of the latest research results presented by our funded researchers, an art exhibition, and valuable information and resources offered by nonprofit organizations.

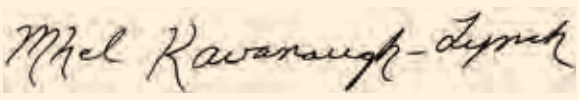
Art and science stand side by side at our symposium, because we see how art bridges the gap between complex fact and intuitive understanding. Artists create tangible expressions of research questions; we fund the research that addresses the issues expressed in art. Art inspires science, and science inspires art.

We are making tremendous progress on our Special Research Initiatives, and symposium attendees will have the opportunity to hear from—and speak with—several of our steering committee members. Sandra Steingraber is our keynote speaker this year, and Olufunmilayo I (Funmi) Olopade and David R. Williams will be speaking in our evening plenary session, "Racial and Ethnic Disparities in Breast Cancer" on Friday, September 7. Because all of our SRI steering committee members are or have been involved in the CBCRP, they understand and share our mission and our stakeholders' vision.

Constructive input helps us remain flexible and continue as one of the top-rated breast cancer research programs. We encourage and appreciate public input and feedback about our Program at any time, but there is something truly special about the face-to-face opportunities that arise during our symposium. The immediate value of having a conversation, sharing a moment, and exchanging ideas creates new opportunities for growth and brings together our diverse attendees to share priorities, needs, and research findings.

The symposium offers a chance for all of us to pause, reflect, and see where we can make advances against breast cancer. It's a chance to acknowledge both the progress our researchers have made and the impact that breast cancer still has on our lives. It's a personal opportunity for me to become recharged in our mission of eradicating breast cancer. We come together with enthusiasm and intensity in order to create new hope and optimism for a future without breast cancer.

Mhel Kavanaugh-Lynch, M.D., M.P.H.
Director, California Breast Cancer Research Program



CONTINUING MEDICAL EDUCATION CREDITS

Accreditation

The Office of Continuing Medical Education, David Geffen School of Medicine at UCLA, is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

The Office of Continuing Medical Education, David Geffen School of Medicine at UCLA designates this educational activity for a maximum of 12 AMA PRA Category 1 Credit(s)TM. Physicians should only claim credit commensurate with the extent of their participation in the activity.

Disclosure Statement

The FDA has issued a concept paper which classifies commercial support of scientific and educational programs as promotional unless it can be affirmed that the program is "truly independent" and free of commercial influence. In addition to independence, the FDA requires that non-promotional, commercially supported education be objective, balanced, and scientifically rigorous. The policy further states that all potential conflicts of interest of the CME staff and faculty be fully disclosed to the program's participants. In addition, Accreditation Council for Continuing Medical Education policy now mandates that the provider adequately manages all identified potential conflicts of interest prior to the program. We, at UCLA, fully endorse the letter and spirit of these concepts.

CME Credit

Registered Nurses: The California State Board of Registered Nursing accepts Category 1 hours toward renewal. On the BRN license renewal form, report the number of hours you attended (up to 12 hours of credit) and fill in "CME Category 1" instead of BRN provider number.

If you wish to receive CME credit for participation in accredited sessions, be sure to complete and sign a "CME Address Verification Form" and return it with payment prior to leaving the conference. These forms are available at the Registration Desk.

The fee for processing CME credit is $25. Payment may be made by credit card (Visa, Mastercard, and Discover) or by check, made payable to UC Regents.

The following sessions are eligible for CME credits:

Friday, September 7, 2007

Workshop 1 – Breast Cancer 101

Workshop 2 – Breast Cancer Prevention Strategies

Workshop 3 – Special Topics involving Young Women with Breast Cancer

Workshop 4 – Estrogen and Breast Cancer

Workshop 5 – Complementary and Alternative Medicine

Saturday, September 8, 2007

Plenary Session – New Directions in Breast Cancer Treatment

Breakout Session 1: Services and Support for the Underserved

Breakout Session 2: Emerging Topics in Breast Cancer Biology

Breakout Session 3: Exploring Breast Cancer Risk

Breakout Session 4: Improving Breast Cancer Diagnosis and Therapy

STATE OF CALIFORNIA ASSEMBLY BILL 1195: CULTURAL COMPETENCY

Effective July 1, 2006, California State Assembly Bill 1195 requires that all continuing medical education activities include curriculum in the subjects of cultural and linguistic competency in the practice of medicine. In compliance with this mandate, the following information is being provided: (1) a review and explanation of relevant federal and state laws and regulations regarding linguistic access (see paragraphs below) and (2) a list of cultural and linguistic competency resources.

Brief Review of Federal and State Law Regarding Linguistic Access and Services for Limited English Proficient Persons

Prepared for the UC CME Consortium by the UC Office of General Counsel

I. Purpose

This document is intended to satisfy the requirements set forth in California Business and Professions code 2190.1. California law requires physicians to obtain training in cultural and linguistic competency as part of their continuing medical education and professional development programs. This document and the accompanying attachments are intended to provide physicians with an overview of federal and state laws regarding linguistic access and services for limited English proficient ("LEP") persons. The document is not comprehensive and there may be additional federal and state laws governing the manner in which physicians and healthcare providers render services for disabled, hearing impaired, or other protected categories. We recommend that physicians review the CMA California Physician's Legal Handbook for a comprehensive review of laws affecting a physician's medical practice in California.

II. Federal Law—Federal Civil Rights Act of 1964, Executive Order 13166, August 11, 2000, and Department of Health and Human Services ("HHS") Regulations and LEP Guidance

The Federal Civil Rights Act of 1964, as amended, and HHS regulations require recipients of federal financial assistance to take reasonable steps to ensure that LEP persons have meaningful access to federally funded programs and services. HHS recently issued revised guidance documents for Recipients to ensure that they understand their obligations to provide language assistance services to LEP persons. A copy of HHS's summary document titled "Guidance for Federal Financial Assistance Recipients Regarding Title VI and the Prohibition Against National Origin Discrimination Affecting Limited English Proficient Persons—Summary" is attached for your review. Additional in-depth guidance is available at HHS's website at http://www.hhs.gov/ocr/lep/.

As noted above, Recipients generally must provide meaningful access to their programs and services for LEP persons. The rule, however, is a flexible one and HHS recognizes that "reasonable steps" may differ depending on the Recipient's size and scope of services. HHS advised that Recipients, in designing an LEP program, should conduct an individualized assessment balancing four factors, including: (i) the number or proportion of LEP persons eligible to be served by the Recipient; (ii) the frequency with which LEP individuals come into contact with the Recipient's program; (iii) the nature and importance of the program, activity or service provided by the Recipient; and (iv) the resources available to the Recipient and the costs of interpreting and translation services.

Based on the Recipient's analysis, the Recipient should then design an LEP plan based on five recommended steps, including: (i) identifying LEP individuals who may need assistance; (ii) identifying language assistance measures; (iii) training staff; (iv) providing notice to LEP persons; and (v) monitoring and updating the LEP plan.

A Recipient's LEP plan likely will include translating vital documents and providing either on-site interpreters or telephone interpreter services, or using shared interpreting services with other Recipients. Recipients may take other reasonable steps, such as hiring bilingual staff who are competent in the skills required for medical translation, hiring staff interpreters, or contracting with outside public or private agencies that provide interpreter services.

III. California Law—Dymally-Alatorre Bilingual Services Act

The California legislature enacted the California's Dymally-Alatorre Bilingual Services Act (Govt. Code 7290 et seq.) in order to ensure that California residents would appropriately receive services from public agencies regardless of the person's English language skills. The Act generally requires state and local public agencies to provide interpreter and written document translation services in a manner that will ensure that LEP individuals have access to important government services. Agencies may employ bilingual staff, and translate documents into additional languages representing the clientele served by the agency. Public agencies also must conduct a needs assessment survey every two years documenting the items listed in Government Code section 7299.4, and develop an implementation plan every year that documents compliance with the Act. A copy of this law may be found at the following url: http://www.spb.ca.gov/bilingual/dymallyact.htm.

UNIVERSITY OF CALIFORNIA (UCCME) CULTURAL AND LINGUISTIC COMPETENCY RESOURCES

June 2006

A) Major Resources

1. University of California-Center for the Health Professions
http://futurehealth.ucsf.edu/TheNetwork/Default.aspx?tabid=387

2. Kaiser Permanente National Diversity Department
http://kphci.org/resources/links.html

3. The Office of Minority Health
http://www.omhrc.gov

4. California Academy of Family Physicians
http://www.familydocs.org/multicultural_health.php

5. Institute for Medical Quality
http://www.imq.org

6. On-line dictionary providing translations into 25 different languages

http://www.ectaco.com/English-Multilanguage-Dictionary/

7. Foreign Language Assessment Guide (F.L.A.G.), Produced by Medi-Flag Corporation
http://www.medi-flag.com

B) Hospital Care

1. National Association of Public Hospitals and Health Systems. "Serving Diverse Communities in Safety Net Hospitals and Health Systems," The Safety Net 2003; 17(3): Fall.
http://www.naph.org/Template.cfm?Section=The_Safety_Net_Archive&template=/ContentManagement/ContentDisplay.cfm&ContentID=3407

2. Andrulis DP. "Study of How Urban Hospitals Address Sociocultural Barriers to Health Care Access":
http://www.rwjf.org/portfolios/resources/grantsreport.jsp?filename=023299s.htm&iaid=133

C) Ambulatory Care

1. Center for the Health Care Professions- Towards Culturally Competent Care: Toolbox for Teaching Communication Strategies
http://futurehealth.ucsf.edu/TheNetwork/Default.aspx?tabid=290

2. National Center for Cultural Competence, Georgetown University. "Self-Assessment Checklist for Personnel Providing Primary Health Care Services"

http://gucchd.georgetown.edu/nccc/documents/Checklist%20PHC.pdf

3. National Initiative for Children's Healthcare Quality (NICHQ), Improving Cultural Competency in Children's Health Care: Expanding Perspectives
http://www.nichq.org/NR/rdonlyres/5B534B7B-0C38-4ACD-8996-EBB0C4CB2245/0/NICHQ_CulturalCompetencyFINAL.pdf

4. "Cultural Positivity – Culturally Competent Care For Diverse Populations"
http://www.gvhc.org/

D) Managed Care

1. "National Standards For Culturally And Linguistically Appropriate Services In

Health Care Executive Summary"
http://www.omhrc.gov/assets/pdf/checked/executive.pdf

2. America's Health Insurance Plans (AHIP), Center for Policy and Research.
"Innovations in Medicaid Managed Care," March, 2005.
http://www.ahip.org/content/default.aspx?docid=8414

E) Caring for Individuals with Limited English Proficiency

1. Center for the Health Professions-Common Sentences in Multiple Languages (ICE) Tool for Office Staff
http://futurehealth.ucsf.edu/TheNetwork/Portals/3/CommonSentences.pdf

2. National Council on Interpreting in Health Care
http://www.ncihc.org

3. Addressing Language Access in Your Practice Toolkit, California Academy of Family Physicians
http://www.familydocs.org/multicultural_health.php

4. Hablamos Juntos: Improving Patient-Provider Communication for Latinos
http://www.hablamosjuntos.org

5. Process of Inquiry: Communicating in a Multicultural Environment, Georgetown University National Center for Cultural Competence
http://www.nccccurricula.info/

6. Cross-Cultural Communication in Health Care: Building Organizational Capacity
http://www.hrsa.gov/reimbursement/broadcast/default.htm

F) Health Literacy

1. AMA/AMA Foundation's Health Literacy toolkits, videos, partnerships
http://www.ama-assn.org/ama/pub/category/8115.html

2. Weiss BD. Health Literacy: A Manual for Clinicians Chicago: American Medical Association Foundation, 2003

3. Schwartzberg, JG, VanGeest JB, Wang CC: Understanding Health Literacy: Implications for Medicine and Public Health. Chicago, IL: American Medical Association Pres., 2004

G) Movies, Videos, and CD-ROM Resources

1. Alexander M. Cinemeducation: An Innovative Approach to Teaching Multi-Cultural Diversity in Medicine. Annals of Behavioral Science and Medical Education 1995; 2(1):23-28.

2. Communicating Effectively Through an Interpreter (1998) (Available from the Cross Cultural Health Care Program, 270 South Hanford Street, Suite 100, Seattle, Washington 98134; Phone (206)-860-0329; Website www.xculture.org).

3. The Bilingual Medical Interview I (1987) and The Bilingual Medical Interview II: The Geriatric Interview, Section of General Internal Medicine, Boston City Hospital, in collaboration with the Department of Interpreter Services and the Boston Area Health Education Center (Available from the BAHEC, 818 Harrison Ave., Boston, MA 02118; Phone (617) 534-5258).

4. The Kaiser Permanente/California Endowment Clinical Cultural Competency Video Series. In 2000, Kaiser Permanente, with funding from The California Endowment, embarked on a project to create "trigger" videos as teaching tools for training healthcare professionals in cultural competence. These now completed videos comprise three sets, each with accompanying

facilitator's guide and contextual materials. Each set costs $35.00 or $105 for all 20. The scenarios are from eight to fourteen minutes long.

5. Quality Care for Diverse Populations. Video/CD-ROM/Facilitator's Guide.
Contributors: K. Bullock, L.G. Epstein, E.L. Lewis, R.C. Like, J.E. South Paul, C. Stroebel, et al) This educational program includes five video vignettes depicting simulated physician-patient visits in an office setting as a means to explore ethnic and sociocultural issues found in today's diverse health care environment. Produced by the American Academy of Family Physicians (AAFP), with partial funding by the Bureau of Primary Health Care, Health Resources and Services Administration, June 2002. (Available from the American Academy of Family Physicians, AAFP Order Dept., 11400 Tomahawk Creek Parkway, Leawood, KS 66211; Phone (800) 944-0000; Fax (913) 906-6075; http://www.aafp.org/x13887.xml).

6. Community Voices: Exploring Cross-Cultural Care Through Cancer. Video and Facilitator's Guide by Jennie Greene, MS & Kim Newell, MD (Available from the Harvard Center for Cancer Prevention, Harvard School of Public Health, 665 Huntington Avenue, Bldg 2, Rm 105, Boston, MA 02115; Phone (617) 432-0038; Fax: (617)-432-1722; hccp@hsph.harvard.edu , or Fanlight Productions, www.fanlight.com).

7. Worlds Apart. A Four-Part Series on Cross-Cultural Healthcare. By Maren Grainger-Monsen, MD, and Julia Haslett, Stanford University, Center for Biomedical Ethics (available from Fanlight Productions, www.fanlight.com)

8. The Angry Heart: The Impact of Racism on Heart Disease Among African-Americans, Jay Fedigan. (Available from Fanlight Productions, http://www.fanlight.com).

9. The Culture of Emotions: A Cultural Competence and Diversity Training Program . Harriet Koskoff, Producer/Co-Coordinator, 415 Noe Street, #5, San Francisco , CA 94114 ; Phone 415-864-0927; Fax 415-621-8969 (Available from Fanlight Productions, www.fanlight.com).

10. Ohio Department of Health and Medical College of Ohio. Cultural Competence in Breast Cancer Care (CD-ROM), 2000.

H) Continuing Education Programs

1. Office of Minority Health
A Family Physician's Guide to Culturally Competent Care
http://cccm.thinkculturalhealth.org

2. Quality Interactions: A Patient-Based Approach to Cross-Cultural Care
Manhattan Cross Cultural Group and Critical Measures
http://www.criticalmeasures.net/cross_cultural/elearning.htm

3. Delivering Culturally Effective Care for Patients with Diabetes
Medical Directions - The Virtual Lecture Hall and Department of Family Medicine, University of Arizona College of Medicine at the Arizona Health Sciences Center
http://www.vlh.com/shared/courses/course_info.cfm?courseno=1786

4. Communicating Through Health Care Interpreters
Medical Directions - The Virtual Lecture Hall and Rush University Medical Center
http://www.vlh.com/shared/courses/course_info.cfm?courseno=1705

5. Culture and Health Care: An E-Learning Course (based on Cultural Sensitivity: A Guidebook for Physicians and HealthCare) Doctors in Touch (DIT)
http://www.doctorsintouch.com/courses_for_CME_credit.htm

6. Quality Care for Diverse Populations. Video/CD-ROM/Facilitator's Guide.
Contributors:
K. Bullock, L.G. Epstein, E.L. Lewis, R.C. Like, J.E. South Paul, C. Stroebel, et al) This educational program includes five video vignettes depicting simulated physician-patient visits in an office setting as a means to explore ethnic and sociocultural issues found in today's diverse health care environment. Produced by the American Academy of Family Physicians (AAFP), with partial funding by the Bureau of Primary Health Care, Health Resources and Services Administration, June 2002. (Available from the American Academy of Family Physicians, AAFP Order Dept., 11400 Tomahawk Creek Parkway, Leawood, KS 66211; Phone (800)-944-0000; Fax (913)-906-6075; http://www.aafp.org/x13887.xml).

7. Cultural Competency Challenge CD-ROM Educational Program (AAOS Product #02735). American Academy of Orthopaedic Surgeons, 6300 North River Road, Rosemont, IL 60018-4262; http://www.aaos.org/challenge).

8. Cross-Cultural Health Care: Case Studies Pediatric Pulmonary Centers: A Collaborative Web Site of the MCH Training Network;
http://ppc.mchtraining.net/custom_pages/national_ccce

9. Measuring Health Disparities, Interactive CD-ROM. John Lynch, PhD, and Sam Harper, PhD, McGill University. Produced by the Michigan Public Health Training Center (MPHTC);
http://measuringhealthdisparities.org

I) Recent Articles and References on Cultural and Linguistic Competency

1. Brach C, Fraser I, and Paez K. "Crossing the Language Chasm," Health Affairs 2005 (March); 24(2):424-434.

2. Betancourt, J.R., Green, A.R., Carillo, J.E. et al. (2005). Cultural competency and health care disparities: Key perspectives and trends. Health Affairs, 24(2), 499-505.

3. Brach, C., Fraser, I., Paez, K. (2005). Crossing the language chasm: An in-depth analysis of

what language-assistance programs look like in practice. Health Affairs, 24(2), 424-434.

4. Betancourt J.R., Green A.R., Carrillo J.E., et al. (2003). Defining cultural competence: A practical framework for addressing racial/ethnic disparities in health and health care. Public Health Reports, 118(4), 293-302.

5. AB 801 Assembly Bill – Chaptered. Official California Legislative Information website. http://www.leginfo.ca.gov/pub/03-04/bill/asm/ab_0801- 850/ab_801_bill _ 20030925 _ chaptered.html (cited 7 Nov. 2005).

6. AB 1195 Assembly Bill—Chaptered. Official California Legislative Information website. http://www.leginfo.ca.gov/pub/bill/asm/ab_1151-1200/ab_1195_bill_20051004_chaptered.html (cited 7 Nov. 2005).

7. Youdelman M, Perkins J. "Providing Language Interpretation Services in Health Care Setting: Examples from the Field," National Health Law Program, May 2002

8. Youdelman M, Perkins J. "Providing Language Services in Small Health Care Provider Settings" Examples from the Field," National Health Law Program, April 2005
(The latter two reports can be obtained at http://www.cmwf.org or http://www.healthlaw.org).

Compiled by:
The University of California, Continuing Medical Education Consortium

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For questions, please call Gwenn Welsch, UC CME Website Coordinator at (916)734-5773 or email gwenn.welsch@ucdmc.ucdavis.edu.

FINANCIAL DISCLOSURES

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Disclosure Declaration: The following speaker has indicated an affiliation with organizations that have interests related to the content of this program and has managed these conflicts. This is pointed out to you so that you may form your own judgments about the presentation with full disclosure of the facts.

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GSK—Medical Advisor & Speaker

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Commercial: GlaxoSmithKline, Cellgate, Genentech—Research Grant
CellBiosciences/Affymetrix—Research Collaboration

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Eli Lilly—Research support
Genentech—Speaker's Bureau
Novartis—Speaker's Bureau & consultant
Organon—Consultant, research support
Sanofi Aventis—Consultant

The following faculty members have **indicated** that they **do not have an affiliation** with organizations, which have interests related to the content of this program:

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Anuja Mendiratta	Center for Environmental Health
Moon Chen, Ph.D., M.P.H.	University of California, Davis
Beverly Burns, M.S., Lac.	Charlotte Maxwell Complementary Clinic

WORKING TOGETHER TO MAKE THE SYMPOSIUM HEALTHIER

The CBCRP has carefully evaluated its meeting logistics and identified ways to conserve and recycle, and to promote good health. Together we can make this event informative, healthy, and environmentally friendly.

What the CBCRP is Doing:

- Sponsoring free yoga and exercise classes on Friday and Saturday
- Making the symposium a non-smoking event
- Providing healthy food options at every meal and food break (fruit and vegetables, water)
- Serving organic produce when possible (based on market availability and cost)
- Reducing use of the plastic products in our food service
- Minimizing the use of individual food and beverage containers
- Producing all symposium materials on recycled chlorine-free paper using soy-based ink
- Providing conference bags made from Polylactide (a biodegradable material derived from corn starch or sugarcane, a renewable resource) rather than petroleum
- Encouraging a fragrance free symposium
- Providing symposium materials (bags, pens) on a voluntary rather than automatic basis. You want one, you take one

What the Westin Bonaventure is Doing:

- Recycling Program—the hotel recycles grease and cardboard
- Towel and sheet reuse program
- Not replacing consumable amenities daily unless they are gone
- No Styrofoam use
- Use of cloth napkins whenever possible
- Use of cleaning products that do not introduce toxins into the air or water. Environmentally friendly cleaning products are used throughout the hotel

What You Can Do:

- Bring refillable containers for water and coffee
- Join us at the yoga and exercise classes
- Take full advantage of recycling receptacles
- Remember to recycle your name badge
- Consider attending meetings “fragrance-free”
- If you’re staying at the Westin Bonaventure, conserve water and energy by not having your sheets and towels serviced every day

We thank the Westin Bonaventure and you for helping to make this symposium a healthier one.

Travel Information

Westin Bonaventure Hotel

404 South Figueroa Street
Los Angeles, California 90071
Tel: 866 716-8132
Fax: 213 612-4800

Directions to the Westin Bonaventure Hotel

From East

From either I-10 or Highway 60, follow the signs into downtown Los Angeles. Take 110 South and exit onto Wilshire Boulevard. Turn left onto Wilshire Boulevard and continue to Figueroa Street. Turn left onto Figueroa Street and proceed to 4th Street. Turn right onto 4th Street, then turn right onto Flower Street and proceed to the hotel.

From North

Take either Interstate 405, Highway 101, or Interstate 5 and follow the signs into downtown Los Angeles. Then take 110 South and exit onto Wilshire Boulevard. Turn left onto Wilshire Boulevard, and then turn left onto Figueroa Street. Turn right onto 4th Street, then turn right onto Flower Street and proceed to the hotel.

From West

From I-10 or Interstate 105, take 110 North and exit onto 3rd Street. Turn right onto 3rd Street and proceed to Flower Street. Turn right onto Flower Street and proceed 1 block to the hotel.

From South

Take I-405 North to 110 North. Exit onto 3rd Street and turn right. Turn right onto Flower Street and drive 1 block to the hotel. The hotel is located on the right.

Transit Information

Taxi transportation is available from LAX airport to the Westin Bonaventure

Limo/Super Shuttle: 213 688-0444

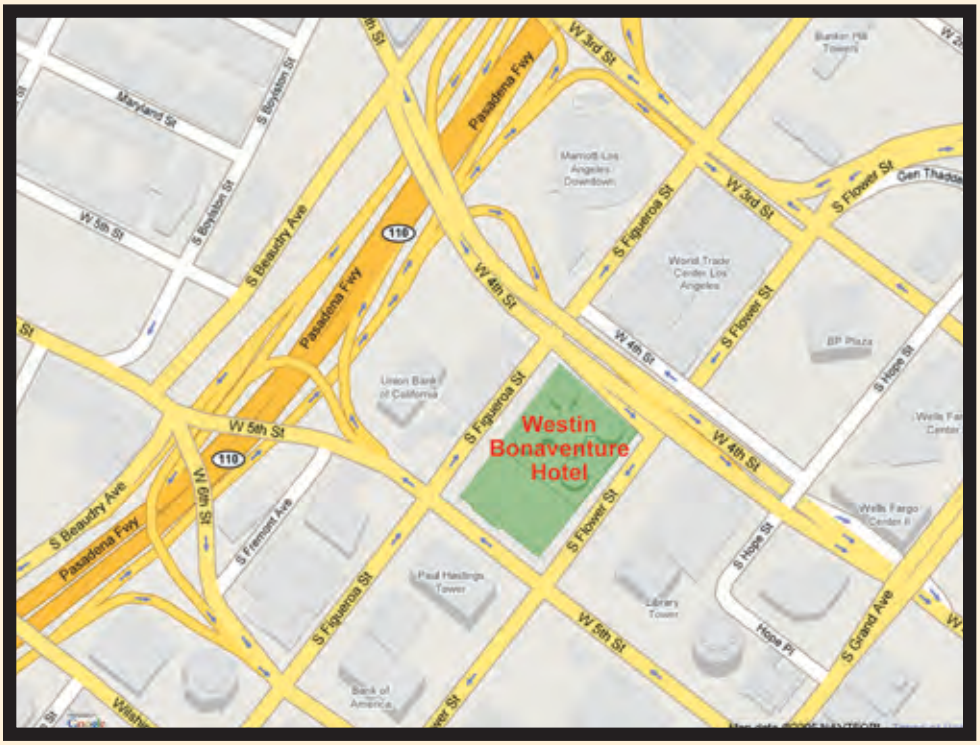
Rail or Subway: Union Station–3 miles

Bus or Other Transportation: Metro/Subway Station–2 blocks

Transportation from City Center to hotel is available

Please note that fees may apply to above transportation.

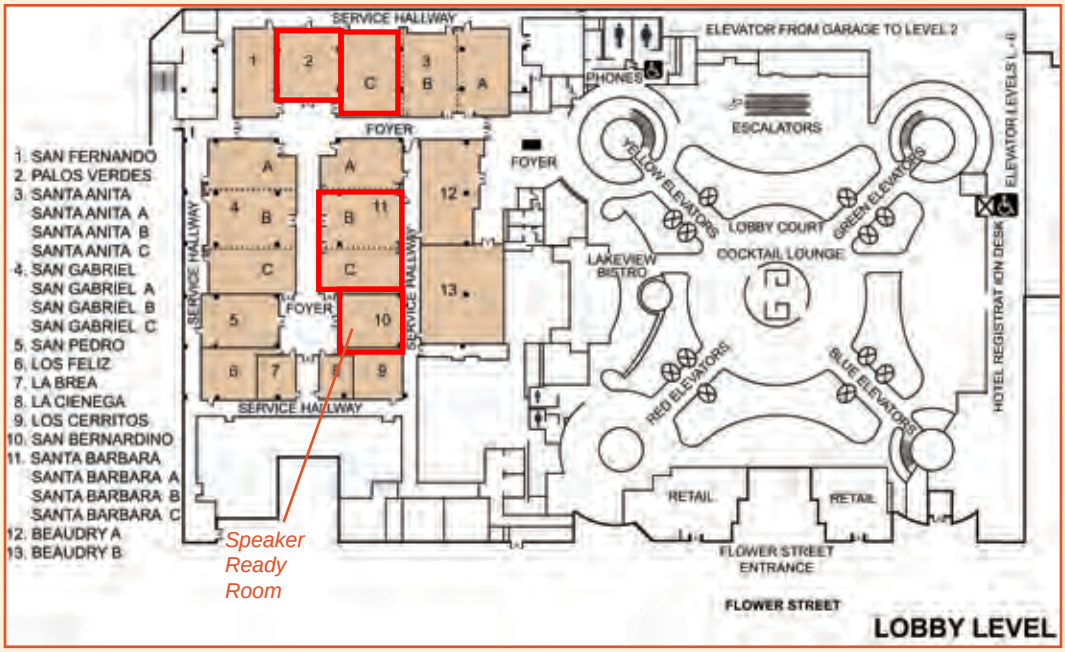
Symposium Location



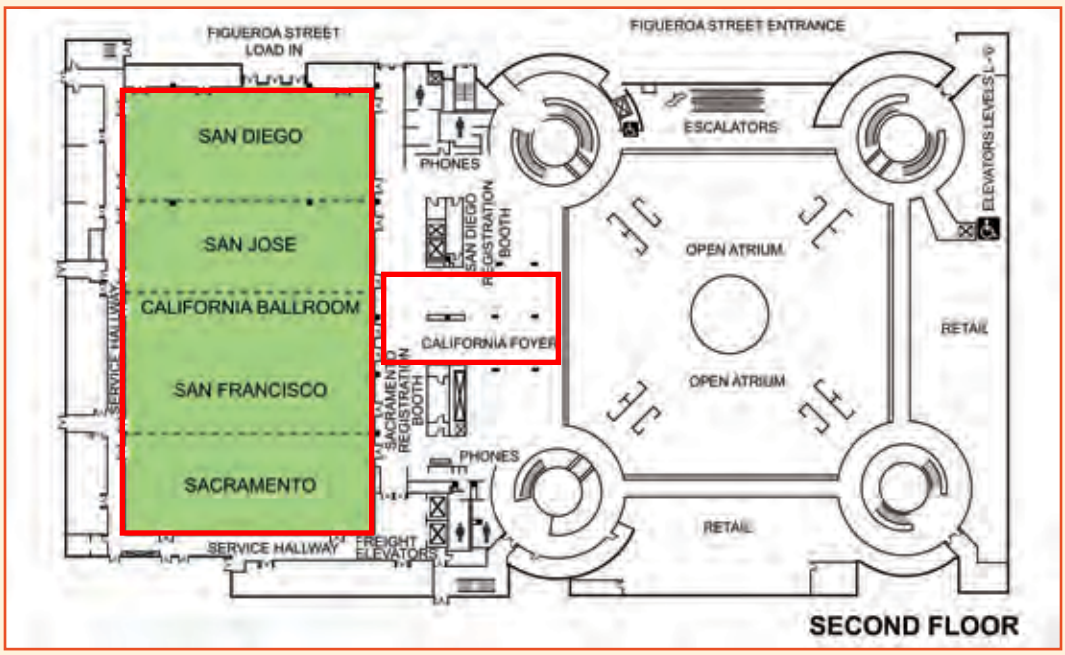
SYMPOSIUM AT A GLANCE

Time	Event	Location
Friday, September 7, 2007		
6:15am – 7:15am	Yoga	Palos Verdes
6:15am – 7:15am	Morning Exercise Session	Santa Anita C
7:00am – 6:00pm	Registration	California Foyer
7:00am – 9:00am	Continental Breakfast	Pasadena
7:45am – 8:00am	Welcome	San Diego
8:00am – 9:00pm	Art Exhibition	Pasadena
8:00am – 8:00pm	Poster Viewing	Pasadena
8:00am – 10:00am	**Workshop 1—Breast Cancer 101**	San Jose
8:00am – 10:00am	**Plenary Poster Discussion**	San Diego
10:00am – 10:30am	Break	Pasadena
10:30am – 12:30pm	**Workshop 2—Breast Cancer Prevention Strategies**	San Diego
10:30am – 12:30pm	**Workshop 3—Special Topics Involving Young Women with Breast Cancer**	San Jose
12:30pm – 1:30pm	Lunch	Pasadena
1:30pm – 3:30pm	**Workshop 4—Estrogen, Progesterone, and Breast Cancer**	San Diego
1:30pm – 3:30pm	**Workshop 5—Complementary and Alternative Medicine**	San Jose
3:30pm – 4:30pm	Break	Pasadena
4:30pm – 5:30pm	**Plenary Session: Racial and Ethnic Disparities in Breast Cancer**	San Diego
5:30pm – 6:30pm	**CBCRP Listens–Special Research Initiatives (SRI): Environmental and Disparities Research Funding Initiative**	San Diego
6:30pm – 9:00pm	**Reception**	Sacramento/San Francisco
Saturday, September 8, 2007		
6:15am – 7:15am	Yoga	Palos Verdes
6:15am – 7:00am	Morning Exercise Session	Santa Anita C
7:00am – 2:00pm	Registration	California Foyer
7:00am – 8:00am	Meet the Experts	Pasadena
7:00am – 9:00am	Breakfast	Pasadena
7:00am – 8:00am	**Workshop 6—Navigating the CBCRP Application Process**	San Diego
8:00am – 5:30pm	Poster Viewing	Pasadena
8:15am – 8:30am	Welcome	Sacramento/ San Francisco
8:30am – 10:30am	**Plenary Session: New Directions in Breast Cancer Treatment**	Sacramento/ San Francisco
10:30am – 11:00am	Break	Pasadena
11:00am – 12:30pm	**Concurrent Breakout Sessions**	
	1) Services and Support for the Underserved	San Diego
	2) Emerging Topics in Breast Cancer Biology	San Jose
12:30pm – 2:00pm	**Lunch (Keynote Address and Awards)**	Sacramento/ San Francisco
2:00pm – 3:30pm	**Concurrent Breakout Sessions**	
	3) Exploring Breast Cancer Risk	San Diego
	4) Improving Breast Cancer Diagnosis and Therapy	San Jose
3:30pm – 5:30pm	Poster Presentation with Advocate Guides	Pasadena
5:30pm – 6:00pm	Closing Ceremonies	Pasadena
Sunday, September 9, 2007		
8:00am – 10:00am	Registration	Santa Barbara Foyer
8:00am – 9:00am	Breakfast	Santa Barbara C
9:00am – 12:00pm	**Workshop 7—Community Research Collaboration Session**	Santa Barbara B

WESTIN BONAVENTURE HOTEL FLOOR PLAN

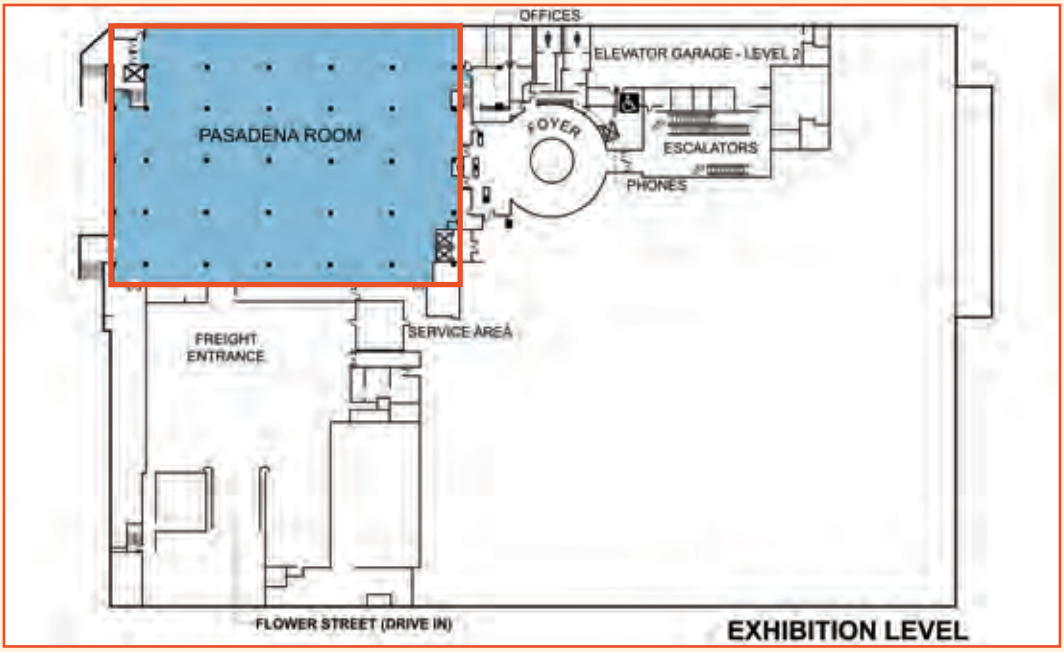


Symposium activity areas shown in red.



WESTIN BONAVENTURE HOTEL FLOOR PLAN

Symposium activity areas shown in red.



Program
Friday, September 7, 2007

Friday, September 7, 2007

NEED TO STRETCH?

The CBCRP is offering free yoga and cardio classes for all conference attendees. Class sizes will be limited to the first 50 attendees.

The Art of Hatha Yoga
Palos Verdes Room, Friday and Saturday, 6:15am - 7:15am
Instructor: Purusha Hickson

It is designed to awaken and strengthen the body, clear the mind, and open the heart; so that we are more receptive to receiving the many blessings of the day!

A.M. Cardio Arobics
Santa Anita C, Friday and Saturday, 6:15am - 7:15am
Instructor: Doug Jones

Wun Hop Kuen Do—"combination fist fighting art style"—was invented by Sigung Al Dacascos, and is a branch of Kajukenbo. Developed around 1948, the Kajukenbo system was the first original American mixed martial art form. Both Wun Hop Kuen Do and Kajukenbo utilize approximately 70% Kung-Fu, 20% Karate, and 10% Judo and Jujitsu.

WELCOME and PLENARY POSTER SESSIONS

Welcome (7:45am – 8:00am) | San Diego

Mhel Kavanaugh-Lynch, M.D., M.P.H., Director,
California Breast Cancer Research Program

Plenary Poster Discussion (8:00am – 10:00am) | San Diego

Selected CBCRP investigators will give oral presentations of their posters.

Moderator:
Gordon Parry, Ph.D.
Monogram Biosciences and California Breast Cancer Research Program Council

Poster Presenters:

A-18
Underserved Women with Breast Cancer at the End of Life: A CBPR Pilot Study
Shelley Adler, Ph.D., University of California, San Francisco /Charlotte Maxwell

B-03
Body Size and Premenopausal Breast Cancer Risk in a Multiethnic Population
Esther John, Ph.D., Northern California Cancer Center

B-06
Diabetes and Risk of Breast Cancer in Asian American Women
Anna H. Wu, Ph.D., University of Southern California

C-06
Identifying Metastatic Breast Cells from Peripheral Blood
Kristin Kulp, Ph.D., Lawrence Livermore National Laboratory

C-07
Identifying Targeted Treatments for Wound-like Breast Cancers
Howard Chang, M.D, Ph.D., Stanford University

D-03
Angiogenesis in the Progression of Premalignant Breast Ductal Proliferations
Philip Carpenter, Ph.D., University of California, Irvine

PROGRAM

Workshop 1 – Breast Cancer 101 (8:00am – 10:00am) | San Jose

Leader: *M. Ellen Mahoney, M.D., F.A.C.S.,* Community Breast Health Project

The workshop will teach the fundamentals of breast cancer basic science and clinical outcomes to symposium attendees who do not have a background in scientific research.

The history of breast cancer treatment will be presented, along with the rationale for the way the field has developed in the laboratory and at the bedside to date. Concepts of molecular oncology, genetics, epidemiology, and the scientific basis for treatment choices will be explored and explained. The workshop is designed for participants who know about the clinical aspects of breast cancer decision-making, but who may not understand the nuances of the science so far. This material is being presented at the beginning of the symposium in order to set the stage for the enhanced understanding of the material being presented in subsequent sessions. The scientific basis for research funded by the CBCRP will become clearer, and the future direction of the field more understandable.

Researchers in the basic sciences who are unfamiliar with the clinical aspects of breast cancer may also find the workshop useful in demonstrating where and how principles of molecular oncology are used in medical practice.

Workshop 2 – Breast Cancer Prevention Strategies (10:30am – 12:30pm) | San Diego

The workshop will explore behaviors and exposures to that may affect the risk of developing breast cancer. The contributions of environmental influences, exercise, diet, smoking, and hormones will be discussed.

Leader: *Marilie Gammon, Ph.D.,* University of North Carolina

Speakers:

Peggy Reynolds, Ph.D., Northern California Cancer Center

Anna H. Wu, Ph.D., University of Southern California

Lawrence H. Kushi, Sc.D., Kaiser Permanente

Workshop 3 – Special Topics Involving Young Women with Breast Cancer (10:30am – 12:30pm) | San Jose

The workshop will explore the ways in which breast cause and treatment in pre-menopausal women may differ from post-menopausal women. The workshop will address questions such as: Should treatments, most of which have been tested in post-menopausal women, be specifically designed for younger women? What additional considerations should be taken into account when treating pre-menopausal women?

Leader: *John S. Link, M.D.,* Breastlink Medical Group, Inc

Speakers:

James R. Waisman, M.D., Breastlink Medical Group, Inc

Carey A. Cullinane, M.D., M.P.H., Long Beach Memorial Medical Center

Heather Himelwright, Cancer Patient Insurance Advocates

Workshop 4 – Estrogen, Progesterone, and Breast Cancer (1:30pm – 3:30pm) | San Diego

Estrogen has long been correlated with breast cancer, but our lack of understanding of its true role is underlined by the Women's Health Study, where estrogen alone has been shown to be safer than estrogen with progesterone. This workshop would review what we know and what we still need to learn about estrogen and breast cancer.

Leader: Adrian Lee, Ph.D., Baylor College of Medicine

Speakers:

Rowan Chlebowski, MD, Ph.D., University of California, Los Angeles

Leena Hilakivi-Clarke, Ph.D., Georgetown University

Eva Lee, Ph.D., University of California, Irvine

Workshop 5–Complementary and Alternative Medicine (1:30pm – 3:30pm) | San Jose

This session will include a discussion of what is being used, how we can go about testing their effectiveness, and guarantee the current and future quality assurance of complementary and alternative medicine.

Leader: *Beverly Burns, M.S., L.Ac.,* Charlotte Maxwell Complementary Clinic and Osher Center for Integrative Medicine

CBCRP LISTENS

Don’t Miss Out!

Attend the CBCRP Listens Session Friday 5:30pm–6:30pm in the San Diego room

- Learn more about recent changes to grant funding and new program initiatives
- CBCRP Director and Advisory Council Members will be on hand to hear your questions and comments
- Take this chance to talk with the people charting the future of the California Breast Cancer Research Program

PLENARY SESSION—RACIAL AND ETHNIC DISPARITIES IN BREAST CANCER

4:30pm–5:30pm | San Diego

Speakers:

Nature, Nurture and Breast Cancer
Olufunmilayo (Funmi) Olopade, M.D., F.A.C.P., University of Chicago Medical Center

The Social Context of Breast Cancer: Evidence, Challenges and Implications
David R. Williams, Ph.D., Harvard School of Public Health

Olufunmilayo (Funmi) Olopade, M.D., F.A.C.P.

Olufunmilayo I (Funmi) Olopade, M.D., Walter L. Palmer Distinguished Service Professor of Medicine, directs a multidisciplinary clinical and laboratory research program at the University of Chicago Medical Center. Dr. Olopade is internationally renowned for her expertise in cancer genetics and has published extensively in the area of genetics of breast cancer predisposition. Dr. Olopade received her medical degree with distinction from the University of Ibadan in Nigeria. She came to the U.S. as a resident in internal medicine at Cook County Hospital, Chicago, where she was named Chief Medical Resident. Dr. Olopade completed her postdoctoral fellowship training in the joint section of Hematology/Oncology at the University of Chicago and was appointed to the faculty in 1991. Dr. Olopade is the recipient of numerous honors and awards including the ASCO Young Investigator award, the James S. McDonnell Foundation Scholar award, the Doris Duke Distinguished Clinical Scientist award, and a 2005 MacArthur Fellowship "genius" grant.

David R. Williams, Ph.D.

David R. Williams, Ph.D., is the Norman Professor of Public Health at the Harvard School of Public Health and a Professor of African American Studies and Sociology at Harvard University. His prior academic appointments were at the University of Michigan (14 Years) and Yale University (6 years). His research expertise includes socioeconomic and racial differences in health and the ways in which religious involvement can affect health. The award-winning author of more than 130 scholarly papers in scientific journals and edited collections, he has been involved in developing federal health policy, testified before Congress, and been featured in national print media and on national television.

CBCRP Listens–Special Research Initiatives (SRI): Environmental and Disparities Research Funding Initiative (5:30pm – 6:30pm) | San Diego

Join members of the SRI Steering Committee and CBCRP Advisory Council in discussing potential research initiatives to answer questions about and find solutions to the environmental causes of breast cancer and the unequal burden of the disease. Participants are invited to share thoughts with and get to know the people who are charting the future of the CBCRP.

PROGRAM

Evening Networking Reception (6:30pm – 9:00pm)
Sacramento/San Francisco

The symposium will be attended by researchers, advocates, patients, and healthcare providers, all with common interests in defeating breast cancer. The reception will provide an opportunity for groups with varied backgrounds to come together and share experiences.

ART EXHIBITION

8:00am–9:00pm Friday / 8:00am–6:00pm Saturday | Pasadena Room

Curatorial Statement

This year's biennial exhibition weaves together a diversity of experiences that reflect the far-reaching impact of breast cancer. Each voice underscores the importance of advancing our understanding of this disease—from its causes and prevention to effective and accessible treatments. Works range from the political to the personal, from the celebration of life to the processing of profound loss. Some of the participants are seasoned, award-winning artists while others have newly discovered the transformative power of art, employing it as a vehicle for healing and growth. Each unique perspective embodies extraordinary vision and courage. These individuals represent a much larger chorus of voices, and by bringing them to the forefront of the symposium, we bring into focus the reason behind our commitment to finding better ways to prevent, treat, and cure breast cancer.

—Catherine Saiki

Artist Biographies

African-American Breast Cancer Task Group

The African-American Breast Cancer Task Group responded to an urgent need to reach African American women with early detection, screening, survivorship and community resource information. The calendar project, "Celebrate! Reflections Beyond Surviving," is a breast cancer education project designed to encourage and inspire African American women to perform monthly breast self-exams, to have annual clinical breast exams or mammograms, and to access community services. The calendar features African American breast cancer survivors who are role models, leading active, productive, and healthy lives because of early detection and access to community resources. Ardella Carter is one such inspiration, at 100 years of age, she continues to be proactive about her health care. After undergoing a mastectomy of her right breast at the age of 57, Mrs. Carter recognized there was a problem with her left side 19 years ago. "I knew there was something wrong—at my age, you know, I knew something was wrong. But it didn't have a lump, so they did an x-ray. X-ray didn't show it either but still I insisted on [having a mastectomy]. So they removed it and it was cancer." The calendar also pays tribute to extraordinary women who have lost their lives to the disease. Such women have included Faith Fancher, a leader whose courageous fight for life extended beyond herself to include women who continue to benefit from her steadfast commitment to raising awareness, tireless advocacy, and fundraising efforts benefiting low-income women with breast cancer.

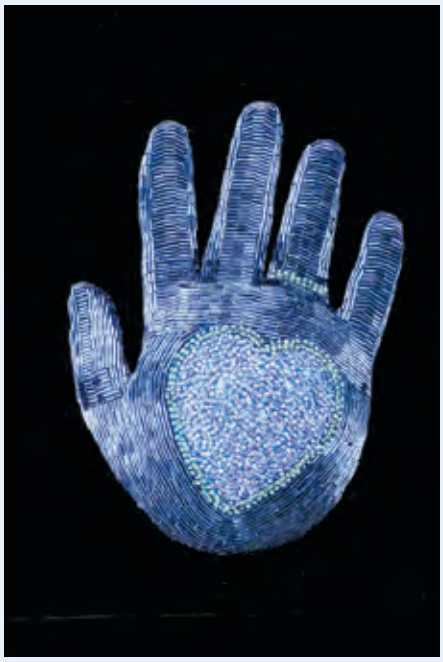
Prayer, Stefanie J. Atkinson

Stefanie J. Atkinson

Stefanie Atkinson is a professional photographer with a background in motion graphic design and art direction for television and film. She is the recipient of an Emmy Award and numerous Broadcast Design Association awards. These photographs were selected from a series entitled Bravery, a project that Stefanie embarked on to document the experiences of young women diagnosed with breast cancer. Her work conveys the strength of her subjects as they wrestle with the uncertainties of living with the disease. Young women living with the ambiguity of breast cancer face a host of daunting challenges: from deciding whether or not to become a parent or talking about their illness with young children, to coping with dramatic physical changes that may cut to the core of their sexuality and self-image, including mastectomy, early menopause and baldness. Common threads run through their stories: threads of bravery, hope, strength, faith, and determination.

CBCRP (donated by various artists)
The Art of Healing

Unique pieces of wearable Breast Art are on display, and worn by survivors attending the symposium. The artwork, worn over places of trauma, represents a symbol of courage and life. By creating and wearing these works of art, new doors of self-expression are opened and affirmation is given to the artist. Frankie Hansbearry, a participating artist this year, created *Heart and Hand.* The work of art was created in the shape of a hand, painstakingly adorned with intricate beadwork, to express self-nurturing and vulnerability. Hansbearry mused that while the sculpture was an exercise in patience (it is meticulously covered with a design using brilliant, indigo-blue beads) it was a piece that evolved on its own.

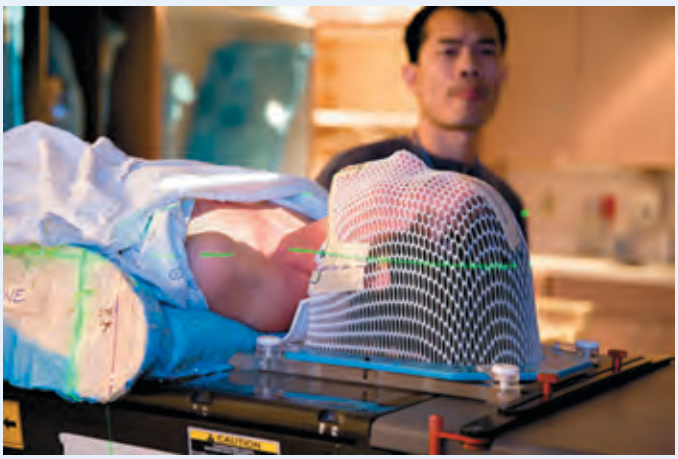


Heart and Hand, Frankie Hansbearry

Jane Bresnick

In 2004, Jane Bresnick was diagnosed with stage I, invasive breast cancer at the age of 40. She underwent a lumpectomy, eight rounds of dose-dense chemotherapy and radiation. In the summer of 2005 she learned her cancer had returned and that, in addition to chemotherapy, she would undergo 42 sessions of radiation.

Teacher Warrior is a film about taking that terrifying experience and turning it into a heroic one. The double life of teaching kindergarteners in the classroom, followed by afternoons spent on the radiation table for eight and a half weeks was a difficult and surreal experience for Jane. The first step in preparing for her radiation was the creation of a face-fitted mask. The purpose of the mask was to secure her head to the radiation table, limiting any movement, while undergoing the 42 treatments. “While I could barely see anything from under the mask, I was desperate to be seen. I brought the support of friends with me to my appointments, calling it a “party”, brought in my own music and made myself as active a participant as I could. My friends photographed and videotaped me so that I could eventually see myself. I made this film to show how I conquered my fear, and empowered myself through this very difficult treatment. It is a story, one of many, of my survival. When I watch it, and when others watch it, I know that it’s true. I hope it inspires strength, compassion, and understanding in those who witness this intimate experience.”



Mask, Jane Bresnick *Photo courtesy of Lynnly Labovitz*

ART EXHIBITION

Allegra Davis Burke

These pieces were inspired by the loss of friend to breast cancer. Allegra's work explores the fallacy of many revolving "truths" we are taught about a disease we ultimately, and sadly, have little understanding of. In *Skirting The Issues,* Allegra tackles a number of roots linked to breast cancer—lack of adequate health care for socio-economically disadvantaged individuals and the glut of fast food that afflicts our nation. She beckons people to step closer in order to read the small script stitched into the skirt, all with the intention of asking individuals to take a closer look. With *How Many Are Enough?* she questions how many more women must lose their breasts and lives before we have better means of detection and more effective treatments. Allegra works with reclaimed materials and hopes to artistically speak for those whose voices often go unheard.

Claudia Damon

"I have named my watercolor *The Journey*. My daughter Amy, mother of two beautiful little girls, was thrown a real curve on her life's path. With a very loving husband and lots of support surrounding her, I have always felt she was still facing a journey by herself. She is the one who faced the treatments. She never once complained about anything—she just focused on getting through the treatments and trying to make things as normal as possible for her family. She made others feel comfortable by answering any questions about her cancer and the treatments. Will things really ever be back to normal? What must she be thinking when there is news of another celebrity's cancer returning? With Amy, it's just showing that happy smile and loving every day. Every time I look at my watercolor it truly reminds me of the journey that she has faced head-on—not looking back but just focusing on life after the treatments."

Ilene Danse

Plant Seeds of Music, Grow Feet That Dance, Five Years Cured, *Ilene Danse*

These three works of art were selected from a larger series of sculptures commemorating the journey of Ilene Danse from a diagnosis of breast cancer to the present. "These three works concern Taxol's unwanted effects on the feet: the frustration of onychomycosis of the toenails, the never ending battle to cure this resistant condition and the joy of healing from it. Taxol-induced disease of the toenails was described by one erudite oncologist as 'that crud.' *Taxol, (My Very Worst Case of Athlete's Foot)* represents the heartbreak of trying to live with 'cruddy toenails.' *Plant Seeds of Music, Grow Feet that Dance* reflects the positive attitude, attentive hygiene, and therapeutic regimens that cured it. *Free Bird,* at last, after five years my heart is light and I can wear sandals in public."

ART EXHIBITION

Amelia Davis

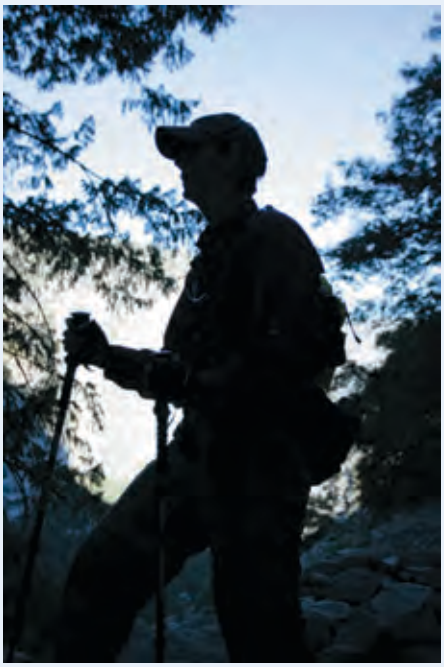
Amelia Davis is a professional photographer based in San Francisco. Her work has been featured in magazines, textbooks, and numerous solo and group exhibitions. *The First Look* is a bold collection of portraits of, and essays by, women living postoperatively with breast cancer. It has won two awards since it was published in 2000. Davis embarked upon the project in honor of her mother's journey through breast cancer treatment. The photographs, capturing the resilience of the human spirit, empower women facing surgery with a direct and honest look at life after diagnosis.

Sylvia Colette Gehres

Sylvia Colette Gehres started her first life-drawing class two years before breast cancer diagnosis. Despite undergoing a series of treatments—a lumpectomy followed shortly by a mastectomy, then chemotherapy and radiation—she remained committed to creating her art. It was during support meetings at The Wellness Community that she realized art was her true passion. She is grateful that these years have provided her with the needed time to create these works of art. She acknowledges that, in a strange way, cancer was the catalyst for the gift of art in her life. Gehres has since exhibited nationally, as well as internationally, participating in shows as far reaching as Hong Kong.

Jason Doiy

Jason Doiy is currently the photo editor for *The Recorder*—his photos have been published in the *San Francisco Chronicle,* the *San Francisco Bay Guardian, Associated Press, Forbes,* and *Business Week* among others. Jason initially met Deb Mosley, the co-founder of Bay Area Young Survivors, when he was on assignment for *The Recorder* that was chronicling Deb's first fundraiser: a triathlon she trained for and completed that raised $42,000 for Bay Area breast cancer organizations. He was subsequently invited to join BAYS on their second fundraising event, a 17 mile hike up and down Half Dome. "I am amazed at the tenacity of Deb Mosley as she continues to climb, as though the cancer has no effect. I am gasping for air and I look up to find her waiting for me, urging me to climb on. When I finally reach the top of Half Dome, Deb is all smiles. She can't stop talking about what to tackle next… It is my hope that these photos can somehow capture her determination, not only to challenge herself but to raise money for breast cancer research."

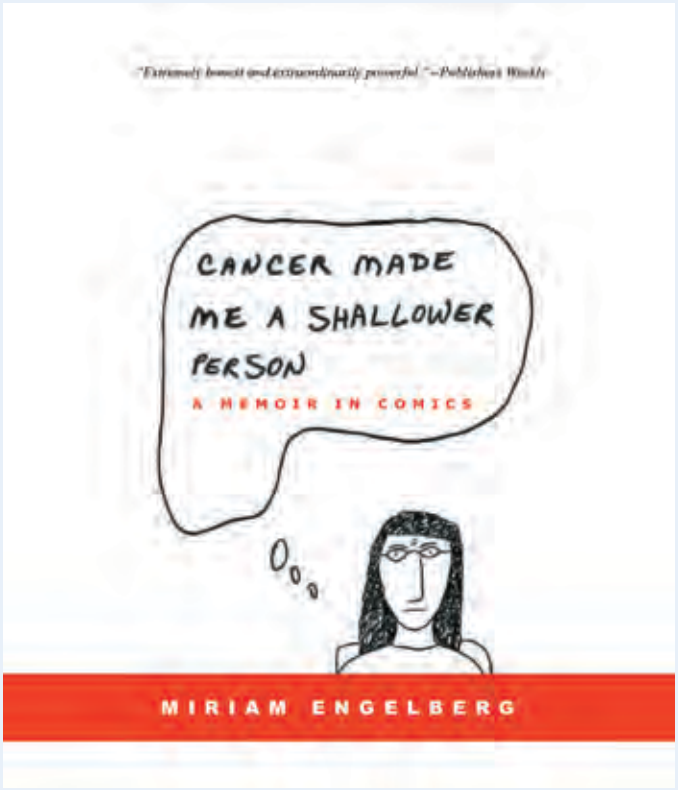


Portrait of Deb Mosley, Half Dome, Jason Doiy

ART EXHIBITION

Miriam Engelberg

Miriam Engelberg was 43 when she was diagnosed with breast cancer. Like anyone faced with a life-altering personal trauma, she sought out a coping mechanism. While fellow patients championed the benefits of support groups and hypnotherapy, Engelberg found her greatest comfort in drawing, her lifelong passion. These cartoons are excerpts pulled from her highly acclaimed, irreverently humorous book, *Cancer Made Me A Shallower Person: A Memoir in Comics*. Miriam passed away on October 17th, 2006, due to complications from breast cancer. Her artwork has generously been loaned to this exhibition by her husband, Jim Gormley, and their son Aaron.



Cancer Made Me A Shallower Person: A Memoir in Comics, Miriam Engelberg

Peter Essick

For the past 20 years, Peter Essick has worked as a freelance photojournalist. His primary client is the *National Geographic* magazine. He has produced more than 30 stories for the magazine on numerous topics—including the impact of everyday environmental toxins on the body. This particular photo was taken at Chevron's Richmond Oil Refinery, one of the largest oil refineries in the United States. The refinery spans 2,900 acres, has over 5,000 miles of pipeline, and is dotted with tanks that can hold up to 15 million barrels of gasoline, crude oil, jet and diesel fuel as well as other chemicals produced by the refinery. All three women in this photo, Marleen Quint, Wanna Wright, and Etta Lundy, live in Richmond and have been diagnosed with breast cancer. They are working together to force the oil refinery to reduce "flaring" of excess gases. Essick's award-winning photographs have been included in numerous exhibitions around the world and in April 2005, *Outdoor Photographer* magazine did a feature story about his efforts to photograph the effects of global warming. These photos were also seen on The Oprah Show, This Morning with George Stephanopolis, and in the movie, *An Inconvenient Truth.*

Richmond Oil Refinery, Peter Essick (interior portrait of Quint courtesy of Amelia Davis)

ART EXHIBITION

Jeanne Giles Hackney

The Circle Project was created to bring awareness to issues particular to young women diagnosed with breast cancer. To that end, Jeanne's project brings the viewer's attention to all of the people in a young breast cancer patient's life—the constellation of those around her who are deeply affected by the diagnosis. Among the many issues confronting young women with this diagnosis is the possibility of infertility that can accompany treatment options—alternately, she may be facing this diagnosis with young children to consider. Jeanne underwent surgery, chemotherapy, and radiation treatments for breast cancer at the age of 37. "How many lives does a breast cancer diagnosis touch? It touches the circle of all the people a woman loves. Look around this circle. Do you see yourself?"

Lynnly Labovitz

"My interests as a photographer began at age eight and have spanned everything from editorial and documentary to fine art, portraiture, and landscape. It has been my vocation and avocation—in short, a compulsion and yearning to connect with the world around me. In recent months my world has become seemingly very small; defined by my battle with metastasized breast cancer. The usual freedom to haul gear and work on an assortment of projects has been frequently curtailed by hospital stays, medications, and bouts of sleeplessness. But within that seemingly small world there is still my camera. Contemplating my own fragility and mortality has moved me to reach out for my camera and try again to see and connect with the world around me—looking for small miracles in an unfurled sunflower or a vibrant piece of fruit—looking for signs of life in myself often in the darkness of night. My foray into digital storytelling grew in response to living with the unpredictability of metastatic disease—realizing that rather than knowing what happens next, I often just get to show up and see what happens. The expected is often unexpected and what may seem predictable is often unpredictable."

Michelle Mansour

Michelle Mansour's work is an investigation of the interior world of the body. Fluctuating between the miniscule and the grandiose, she looks for wonder in the unknown, the invisible, and the uncontrollable. Her interest in this body of work stems in part from her mother's diagnosis with cancer, and is further informed by growing up in a family of science and health care practitioners. The repetitive process of painting and manipulating physical materials allows her to feel somewhat empowered over life situations that are ultimately beyond her control. While the subject matter suggests the seemingly inevitable possibility of illness and disease, the paintings serve as meditations on the exquisite and delicate balance of the natural world.

Julie Moll

Julie Moll was diagnosed with breast cancer at age the age of 40. At the time of her diagnosis, Julie was serving as the Deputy City Attorney for the City and County of San Francisco. Her sons were two, four and seven years old. "At first, I was preoccupied with how to talk with them about what was happening—about my surgery and chemotherapy, and especially about losing my hair. I wanted to keep their lives as normal and joyful as possible, and I didn't want them to be afraid of or embarrassed by the changes in my appearance. In the end, it was the three of them that kept my life normal and full of humor. They adapted quickly to all the changes in our lives, and they amazed me with their sweet affection for my bald head."

Deborah Mosley

Deb Mosley was first diagnosed with breast cancer in early 2000, at the age of 31. In 2003, when she was 35, she learned that her cancer had returned and had spread to her liver and bones. In response to the lack of support for young women diagnosed with breast cancer, Deb co-founded Bay Area Young Survivors (BAYS) with her friend, Angela Padilla. BAYS is a sup-

port and action group for young women living with breast cancer. Since 2004, Deb has created fundraisers around her participation in a triathlon in 2004, BAYS' trek to the top of Half Dome in 2005 and BAYS' descent to the bottom of the Grand Canyon in 2006. By doing so, she and the women of BAYS have raised over $130,000 for Bay Area breast cancer organizations.

In this video, Deb speaks candidly about her experience trekking to the top of Half Dome with six other BAYS women in 2005. They hiked more than 18 miles in just over 12 hours—up and down almost 5,000 feet of elevation in a single day. In making what they called, "The Climb of Our Lives," Deb says, "I am driven to take my body beyond certain physical limits that people may be tempted to apply to me because of my diagnosis. By doing so, I hope to challenge the way we think—I hope to challenge the way I am tempted to think—about what it means to live with metastatic disease. Equally important is the fact that every time I endure, I come face to face with the depth of my ability to persevere and I am reminded of my body's incredible resilience."

Art Myers

In addition to being a fine art photographer, Art Myers is a physician specializing in preventative medicine and public health. Although largely self-taught in photography, he has studied in workshops with Annie Liebovitz, Arnold Newman, Larry Fink, Sally Mann, and Joyce Tenneson, among others. An award winning and nationally exhibiting artist, Myers draws inspiration from the loss of his sister to breast cancer as well as from his wife's subsequent diagnosis with the disease. This series addresses the resilience of a woman's beauty, strength, and femaleness in all of its complexity, even after the transforming experience of breast cancer.

Josie Rodriguez

Eskimo Legend, Josie Rodriguez

Josie holds tightly to her heart the intrinsic healing power involved in the creation of art. *Nancy's Altar* was made after the loss of a close friend to breast cancer. It is a memorial that reflects her love for her, incorporating the flowers that Nancy loved, the Milagros and prayer card from her memorial. Josie, who believes that art in many forms can heal the spirit, created an encaustic assemblage *Eskimo Legend* with the words "Perhaps they are not stars in the sky, but rather openings where loved ones shine down to let us know they are happy" written on the side of the box and floating on top of the paper embedded in the box. Names of loved ones are printed inside a tiny book on the side of the golden box—in their memory. *Spheres of Influence* was made from styrofoam balls, printed strips of mulberry paper dipped in and surrounded with wax. Josie wanted to remember and honor those people in her life, those who had died and those still living who had greatly influenced her—poets, friends, political and world leaders, family, educators. Every time a name was adhered to the sphere, "it was like a silent prayer or meditation" Josie said.

Joanne Beaule Ruggles

Implorante VII, Joanne Beaule Ruggles

Joanne Ruggles was diagnosed with breast cancer on February 27, 2004. Having lost her sister at the age of 35 to the disease, she was consumed with fear. Throughout her chemotherapy treatments and surgeries, she painted, finding emotional relief and a physical respite in the act of painting. She tackled questions surrounding her diagnosis: "Why did this terrible event happen to me? How could I survive it? What kind of creator would let this occur?" Cognizant that finding the answers was not her goal, Joanne allowed herself to examine the issues in all of their complexity—to feel them intensely. In a series ultimately titled The Stone of Hope, her works move from expressions of rage to resignation; they explore death and express hope for life; they question why and they accept the incomprehensible with faith. Ultimately, they provided her the opportunity to document her breast cancer journey and to tell her story.

Barry Toranto and Verna Wefald

Verna was diagnosed with Stage III breast cancer when she was 36 weeks pregnant. She gave birth to a healthy baby girl earlier than planned, by C-section, on January 19, 2006. Two weeks later she began four months of chemotherapy—followed by a double mastectomy and radiation. Verna hired Barry Toranto, a local photographer, to document her experience. Keenly aware that she would never see her breasts again, she wanted to memorialize her body before undergoing the surgery. It took her nearly six months before she could look at the photos. "It was sad, but I was also grateful that I had a record of who I used to be. At that point, I realized that the person I was looking at was gone and that I needed to honor and accept the person I have become. So, I called Barry and asked him to come back. He came back in January, very close to the anniversary of my diagnosis. When I first met Barry, I was bald, had breasts and was a mother of a 5 month old baby. When he came back I had hair, no breasts, and my baby was a toddler. I would never have done photos like these if I hadn't been diagnosed with breast cancer. Having these memories and honoring my new self has helped me heal."

Jillian Wefald

Jillian was almost 16 and staying with her then 41-year old aunt, Verna Wefald (and her family) last summer while she took a class at the San Francisco Institute of Art. Her aunt was undergoing treatment for Stage III breast cancer. This painting was created in response to having witnessed her aunt undergoing treatments that included chemotherapy as well as a double mastectomy. The brutal reality of the treatments is juxtaposed with symbols of hope. "You hold out hope because the expression of the woman is one of peace, rather than anguish—you sense that she is at peace and will prevail. I certainly hope that my aunt Verna will see the beauty and hope through my art. Of course I love Verna more than words can say. My only hope is for the best recovery possible for her and for her to have a peaceful happy life."

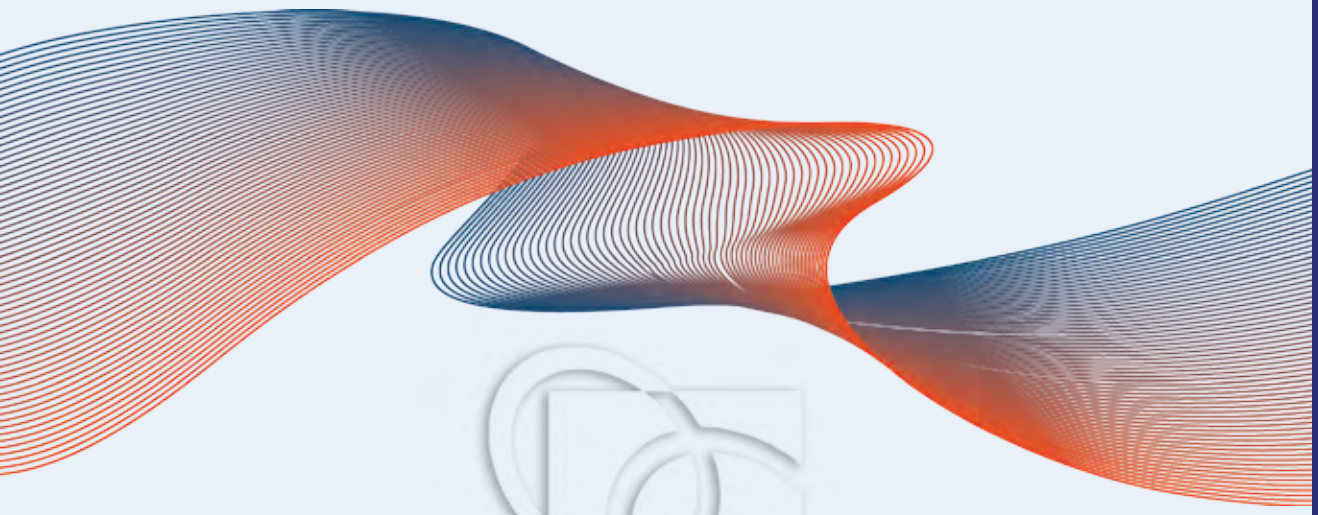
ART EXHIBITION

Kathrine Worel

Born and raised in the Bay Area, Kathrine Worel lived and studied in England, Spain, and Italy before attending the San Francisco Art Institute and settling in Oakland, CA. Worel's practice as an artist and curator is deeply influenced by her desire to discover and/or create connections—visual, linguistic, or metaphorical within formal artistic and social structures. She consciously uses beauty and pleasure as decoys to lure viewers into deeper waters where they are confronted with issues of mortality, dislocation, and longing. She has created sculptures, site specific sound installations, social interventions, and video installations here and in Europe. *Touch/Icon* is intended to embody the tensions between types of touch. In the video, flesh is manipulated and massaged, when the flesh is discovered to be a breast the immediate association is auto-erotic stimulation. This paradigm shifts however when the action slowly reveals itself to be a breast self-examination—shifting the implication of touch from seeking pleasure to seeking danger—turning one's body into an "other" or object, something over which the self no longer has knowledge or control.

FEEDBACK. EVALUATE. IMPROVE. RESPOND.

TELL US WHAT YOU THINK!



Within a few days, you will receive an email from us with a link to a brief online survey to help us evaluate this meeting and make improvements for the future. If you don't have email, stop by the CBCRP booth and we'll give you a paper version of the survey.

Thank you in advance for providing us with valuable feedback.

The CBCRP staff

EXHIBITOR SHOWCASE

Pasadena Exhibit Hall

Nonprofit groups from around California will share practical knowledge about what you can do to confront breast cancer in your community.

American Cancer Society, California Division

The American Cancer Society is dedicated to eliminating cancer as a major health problem by saving lives, diminishing suffering, and preventing cancer through research, education, advocacy and service.

Breast Cancer Action

Breast Cancer Action carries the voices of people affected by breast cancer to inspire and compel the changes necessary to end the breast cancer epidemic.

Breast Cancer Fund

In response to the public health crisis of breast cancer, the Breast Cancer Fund identifies and advocates for elimination of the environmental and other preventable causes of the disease.

California Breast Cancer Organizations (CABCO)

CABCO is a coalition of eight organizations from throughout California. The mission of CABCO is to work toward the eradication of breast cancer through education and advocacy.

California Breast Cancer Research Program

The California Breast Cancer Research Program (CBCRP) was established pursuant to passage by the California Legislature of the 1993 Breast Cancer Act. The program is responsible for administering funding for breast cancer research in the State of California, and its mission is to eliminate breast cancer by leading innovation in research, communication, and collaboration in the California scientific and lay communities.

California Cancer Registry

The California Cancer Registry (CCR) is California's statewide population-based cancer surveillance system. The CCR collects information about all cancers diagnosed in California.

California Health Collaborative

The Collaborative is committed to addressing the health needs of Californians who have limited access to resources affecting their well-being. Those who face barriers related to culture and language, geography, and financial resources are of particular focus. With a vision of serving the underserved throughout the state, the Collaborative's principal service area is Central and far Northern California.

California Partnership for Long-Term Care

The mission of the California Partnership for Long-Term Care is to increase the number of middle-income Californians who have quality long-term care insurance that prevents or delays their dependence on Medi-Cal.

Charlotte Maxwell Complementary Clinic

Charlotte Maxwell Complementary Clinic (CMCC) is a state licensed holistic health clinic that provides free complementary alternative medicine treatments to low-income women with cancer.

Forum Medical Group

Provides free mammograms to low-income women, who are 40 years of age and older, live in California, do not have insurance, and have not had a mammogram in at least one year.

Guam Communications Network, Inc.

A multi-service Chamorro community-based agency headquartered in Long Beach, California. Our mission is to facilitate increased public awareness of the issues concerning the Chamorro people and culture through education, coalition building, and advocacy.

Health Education Council/Cancer Detection Programs

We are dedicated to promoting quality of life and community norms which include the prevention of diseases; the right to a healthy environment; respect for individual rights, cultural traditions, ethnic and linguistic diversity, shared community responsibility, and involvement; and innovative and visionary responses which meet the unique needs of the populations we serve.

Hoag Cancer Center Breast Cancer Program

Hoag Cancer Center was built with one fundamental principle in mind: providing state-of-the-art cancer care in a comforting, patient-friendly setting.

NCI Cancer Information Services
The National Cancer Institute coordinates the National Cancer Program, which conducts and supports research, training, health information dissemination, and other programs with respect to the cause, diagnosis, prevention, and treatment of cancer, rehabilitation from cancer, and the continuing care of cancer patients and the families of cancer patients.

Partnered for Progress
The Los Angeles County Regional Cancer Detection Partnership is contributing to the battle against breast cancer by promoting our community's infrastructure to respond to the increased need for breast cancer education, advocacy and early detection services.

Pink-Link
Pink-Link is a nonprofit organization which provides an online support resource for women affected by breast cancer. On our website: www.pink-link.org, women can connect with other women with similar breast cancer issues using the search capabilities of our innovative online database. Our members can create a personal journal, to keep family and friends updated about their treatment and get help from our on-staff professionals regarding nutrition, exercise, and alternative medicine. All services provided on our website are completely free.

Sisters Network Inc., SF Chapter
SNI's outreach initiatives strives to promote the importance of breast health through personal empowerment, support, breast education programs, resources, information, and research through its strong affiliate chapter base.

The Bay Area Breast Cancer and The Environment Research Center (BABCERC)
The BABCERC is one of four national centers funded by NIEHS and NCI to research environmental risks of breast cancer by focusing on mammary gland development during puberty. The research at each center includes a laboratory study, an epidemiology study, and a community-based outreach and translation Core (COTC). The joint research being conducted by the centers is based on the hypothesis that environmental exposures during mammary gland development may impact the breast in ways that can after the risk of breast cancer in later life.

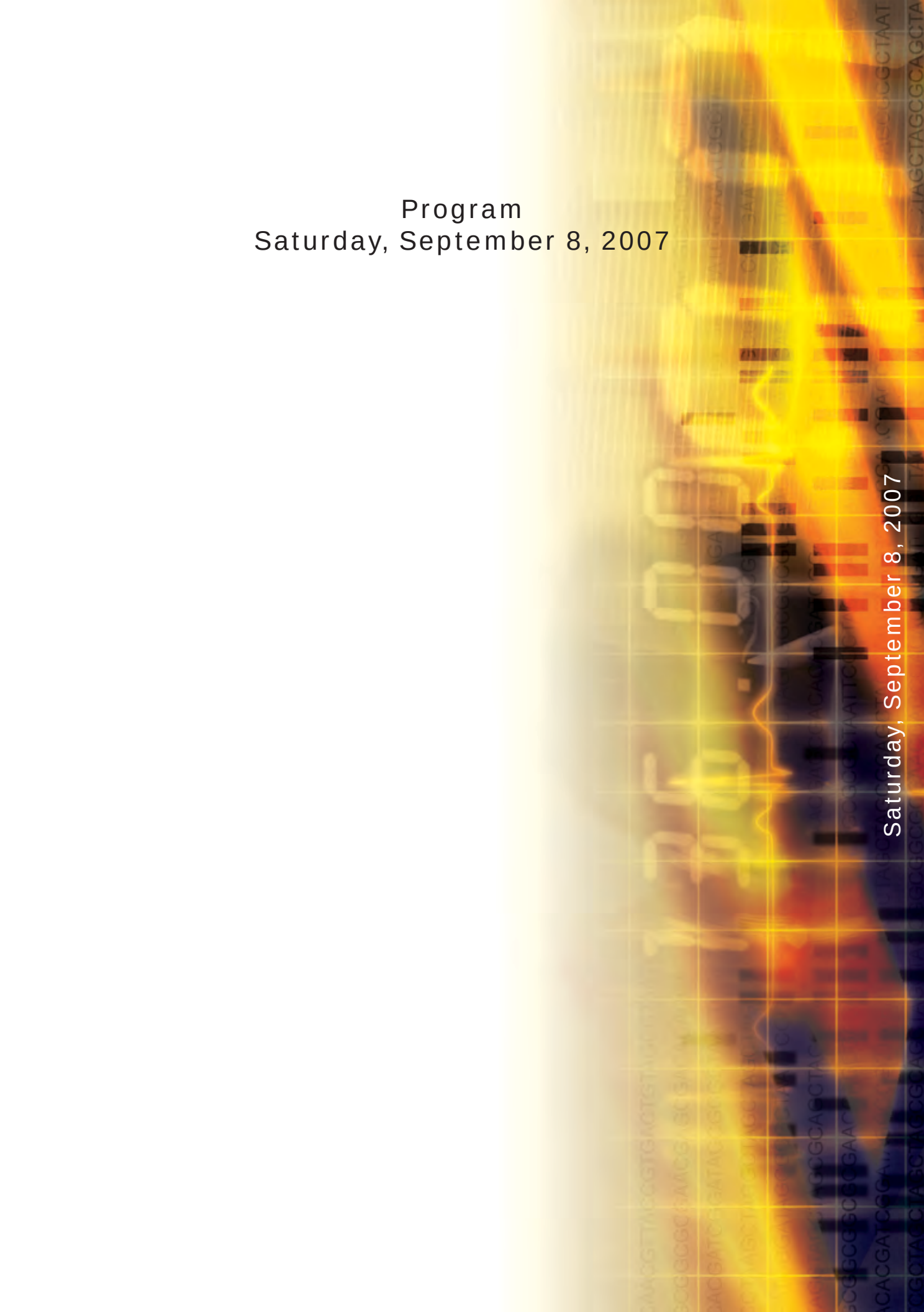
Tobacco-Related Disease Program
The mission of the Tobacco-Related Diseases Program (TRDRP) is to support research that focuses on the prevention, causes, and treatment of tobacco-related disease and the reduction of the human and economic costs of tobacco use in California.

Women of Color Breast Cancer Survivor's Support Project
Our mission is to:
- Provide psychosocial support for you and your loved ones
- Provide crisis intervention for you and your loved ones
- Provide breast health education to community members at large
- Offer knowledge focused on early detection
- Commit to effecting public policy
- Commit to social change regarding breast health awareness
- Support culturally sensitive research
- Lobby on both state and federal levels for breast cancer legislation

Women's Cancer Resource Center, Oakland
To empower women with cancer to be active and informed consumers and survivors; to provide community for women with cancer and their supporters; to educate the general community about cancer; and to be actively involved in the struggle for a life-affirming, cancer-free society.

Zero Breast Cancer
Zero Breast Cancer is a nonprofit organization dedicated to finding the causes of breast cancer through community participation in the research process. We focus on identifying environmental factors and the role they play in the development of breast cancer at all stages of life.

Program
Saturday, September 8, 2007



MEET THE EXPERTS BREAKFAST SESSION

7:00am–8:00am | Pasadena Exhibit Hall

Symposium attendees will be able to join highly interactive discussions about breast cancer topics that have implications for performing research and living with the disease. Informal small group discussions will be led by experts in the field.

Steve Artandi, Ph.D.

Cell Death and Senescence

Steve Artandi is an assistant professor of medicine at Stanford University. His research interests encompass the relationship of cell regeneration and death mechanisms to breast cancer development. Dr. Artandi will lead a discussion on how exploration of the cell life cycle can lead to insights in breast cancer progression.

Dorothy (Dee) Bainton, M.D.

Academic Careers for New Investigators

Dee Bainton was the Vice Chancellor for Academic Affairs of the University of California, San Francisco from 1994–2004. In her post, she was responsible for the planning and review of all teaching programs at UCSF. She oversaw the Registrar and Student Academic Affairs and Academic Personnel academic units, among others. She will lead a discussion of how to make the most of academic career opportunities.

Christopher Benz, M.D.

New Drug Development for Treatment

Chris Benz is the director of the Cancer and Developmental Therapeutics Program at the Buck Institute for Age Research. Dr. Benz is internationally recognized for his research and expertise in breast cancer. He is a practicing oncologist at UCSF's Carol Franc Buck Breast Care Center and is actively involved in designing treatments for aggressive forms of breast cancer. Dr. Benz will lead a discussion on the development of new treatments for breast cancer, particularly molecularly targeted and personalized therapies.

Teresa Burgess, Ph.D.

Breast Cancer Research Careers in Industry

Terri Burgess is a Director in Oncology Research at Amgen, Inc. She joined Amgen, Inc. as an entry level Research Scientist in 1992, where she undertook both basic and applied cell biological research. Since joining the Oncology Research Department in 2001, she has identified novel, molecularly targeted drug candidates and guided them into clinical development. Currently Terri leads a successful team of 12 scientists within the Oncology Research program where projects range from the discovery stage up to Phase 2. Dr. Burgess will lead a discussion of how to make the most of career opportunities in industry.

Anna Cluxton, MBA

Advocacy for Young Women with Breast Cancer

Anna Cluxton was diagnosed with breast cancer at the age of 32. She sits on the National Board of Directors for the Young Survival Coalition, co-founded and chairs the Central Ohio Chapter, and chairs the Survivorship Committee for Ohio Partners in Cancer Control. She works as Research Project Manager for the Patient Navigator Research Program at the Ohio State University. Ms. Cluxton

will lead a discussion on how advocacy can inform research, impact service delivery, and turn issues of concern to communities into action, particularly for young women with breast cancer.

Marion (Mhel) Kavanaugh-Lynch, M.D., M.P.H.

CBCRP Future Directions

Mhel Kavanaugh-Lynch has served as director of the CBCRP for over a decade. She will be available to discuss the ongoing projects, funding opportunities, and future directions of the CBCRP, or any other issues related to the program.

Marilie Gammon, Ph.D.

Modifiable Risk Factors and Breast Cancer

Marilie Gammon is a professor of epidemiology at the University of North Carolina. Dr. Gammon's current research focuses on the identification of risk factors related to the incidence and survival of breast cancer, particularly estrogen-related factors that are potentially modifiable (e.g., physical activity, obesity, and environmental exposures, including polycyclic aromatic hydrocarbons and active and passive cigarette smoking). Dr. Gammon will lead a discussion about the modifiable breast cancer risk factors identified to date.

Carmen Ortiz, Ph.D.

Breast Cancer English-limited Support Groups

Carmen Ortiz, an experienced psychologist and breast cancer survivor, has served as Director of the Círculo de Vida support program in San Francisco since 1995. Dr. Ortiz specializes in Spanish-language support group development and community outreach planning. She developed and implemented both a hospital based support program for newly diagnosed Latinas at San Francisco General and an in-home support program for Latinas in the terminal phase of their illness. Dr. Ortiz will lead a discussion on how to form an effective breast cancer support network.

Peggy Reynolds, Ph.D.

Environment and Breast Cancer

Peggy Reynolds is a senior research scientist at the Northern California Cancer Center. She has conducted a number of cancer epidemiology studies, with a particular focus on environmental risk factors. Dr. Reynolds has served as the principal investigator for a study of regional variations in breast cancer in California, a study of body burden levels of endocrine disruptors in breast cancer patients, a study of breast cancer in young women, and a study of breast cancer incidence in flight attendants. Dr. Reynolds will lead a discussion on environmental factors that are suspected in breast cancer.

Workshop 6–Navigating the CBCRP Application Process (7:00am – 8:00am) | San Diego

Improve your chances of success by gaining insight into the CBCRP application review and funding process. This workshop session will include an overview of CBCRP award types for 2008, our research priority issues, how applications are peer reviewed, and how funding decisions are made by our advisory council. Data from the past several years will be presented. There will be time for questions and answers.

Leader: *Laurence Fitzgerald, Ph.D., Manager,* CBCRP Core Funding

WELCOME

8:15am–8:30am | Sacramento/San Francisco

Mistress of Ceremonies:

Holly J. Mitchell

CEO, Crystal Stairs, Inc.

Speaker

Mhel Kavanaugh-Lynch, M.D., M.P.H.

Director, California Breast Cancer Research Program

Angela Padilla

Chair, California Breast Cancer Research Program Advisory Council, 2007-2008

Holly J. Mitchell, **CEO**

Crystal Stairs, Inc.

Holly Mitchell is the Chief Executive Officer (CEO) of Crystal Stairs, one of the largest private nonprofit child care development agencies in California facilitating care to approximately 25,000 children on a daily basis. Her team has championed a public affairs agenda that has significantly increased Crystal Stairs' profile among government agencies, local media, and other community-based organizations while also increasing the visibility of child care as a critical public policy issue.

Ms. Mitchell's public policy expertise has enabled Crystal Stairs to increase its voice in child care policy making throughout the state. In addition to being invited by various members of the California Legislature to provide expert testimony before policy and budget committees, she has received statewide honors and recognition from the National Women's Political Caucus—Westside Chapter, the Los Angeles County Black Employees Association, and Black Women for Political Action (BWOPA), among others. Since 2003, Holly has served with other nationally recognized leaders on the selection panel for Good Housekeeping Magazine's Annual Women in Government Award.

In addition to her duties at Crystal Stairs, Ms. Mitchell is active in other child care and human services related organizations. These include her leadership roles on the California Resource and Referral Network, and the Children's Health Sub-committee of the State Department of Health Services' California Health Information Survey (CHIS). Ms. Mitchell also serves as Chair on the California State Commission on the Status of Women. She has also served on numerous other boards and committees, including the Governor's Women's Health Advisory Council and the University of California's Breast Cancer Research Council. In 2005, Los Angeles Mayor Antonio R. Villaraigosa appointed Ms. Mitchell to serve as a Los Angeles City Commissioner on the Commission for Children, Youth, and their Families.

Ms. Mitchell's public advocacy career began in the office of State Senator Diane Watson, where she advised members of the legislature on issues related to quality child care as a policy analyst for the Senate Health and Human Services Committee. Before joining Crystal Stairs, Ms. Mitchell was a Legislative Advocate for the Western Center on Law and Poverty where she coordinated with other advocates on health policy issues affecting low-income communities. Prior to this, she was the Executive Director of the California Black Women's Health Project where she interfaced with community-based agencies, policy makers, government agencies, grant makers, and health care professionals on current trends and data on the status of women's health.

Ms. Mitchell is the proud mother of 7-year old Ryan.

PLENARY SESSION—NEW DIRECTIONS IN BREAST CANCER TREATMENT

8:30am–10:30am | Sacramento/San Francisco

The panel will discuss the implications of the dramatic changes that have been taking place in the arena of breast cancer treatment, particularly the shift from anatomically-based approaches of diagnosis and treatment to genetic-based approaches. They will describe the current status of breast cancer treatment, the revolutionary new directions that the field is taking, and the caveats we need to consider as new treatments are developed.

Moderator:

Crystal D. Crawford, Esq., California Black Women's Health Project, California Breast Cancer Research Council

Panelists:

Joe W. Gray, Ph.D., Life Sciences Division Director, Associate Laboratory Director for Life & Environmental Science

Max Wicha, M.D., Professor, University of Michigan

Musa Mayer, Author and Advocate for Women with Advance Breast Cancer

Marisa Weiss, M.D., Director and Founder, Breast Cancer.org

PLENARY SESSION SPEAKERS

Crystal D. Crawford, Esq.

Crystal Crawford serves as CEO of the California Black Women's Health Project, where she performs legislative, educational, and policy advocacy to improve the health status of African American women and girls. Throughout her career, she has combined legal and policy approaches to civil rights and social justice issues.

Ms. Crawford earned her J.D. from New York University Law School, where she served as an editor of the Journal of International Law & Politics, a Hays-Weber Civil Rights Fellow, and Chairperson of the Black Law Students Association.

Ms. Crawford gained litigation experience as an associate with premier corporate law firms in Los Angeles, Boston, and New York, and then turned her attention to the nonprofit sector, serving as Legal Director of the Alliance for Children's Rights. Crystal serves on a variety of boards and councils including Health Access, VIP Mentors, and California's Women's Health Council.

Joe W. Gray, Ph.D.

Dr. Gray is the director of the Life Sciences division of the Lawrence Berkeley National Laboratory, professor of Laboratory Medicine and Radiation Oncology at the University of California, San Francisco, and a principal investigator and co-leader of the Breast Oncology Program and Breast SPORE at UCSF. He has been making advances in developing better ways to identify ways to tailor existing therapies to individuals and how best to target new therapies. Using gene expression signatures as biomarkers, Dr. Gray and his colleagues have developed a system to evaluate drug response comprised of a panel of 50 breast cancer cell lines. "Individuals respond differently to different therapeutics because there are substantial differences in the spectrum of genetic, biological and epigenetic characteristics between breast cancers," he says, "although some recurrent abnormality patterns are emerging that define breast cancer subtypes.

PLENARY SESSION SPEAKERS

Max Wicha, M.D.

Dr. Max Wicha is a physician scientist whose entire career has been devoted to the treatment of women with breast cancer and the study of basic biology of the normal breast and breast cancer. He received his MD degree from Stanford University and after training in internal medicine at the University of Chicago, went to the National Cancer Institute where he trained in medical oncology. It was at that time that he began his research into the study of the factors that control development of the normal breast and breast cancer. In 1980, he went to the University of Michigan where he has spent his entire career. Dr. Wicha was the founding Director of the University of Michigan Comprehensive Cancer Center in 1987, a position which he still maintains. He holds the Distinguished Professor of Oncology Chair at the University of Michigan. Dr. Wicha is a practicing medical oncologist whose medical practice is exclusively devoted to women with breast cancer. Over the years his laboratory has made important contributions towards the study of the biology of normal breast development and breast cancer. These studies have included the elucidation of the role of extra cellular matrix in mammary development and pathways that control apoptosis during mammary involution and breast cancer development. Most recently his laboratory has been a pioneer in the study of stem cells in the normal human breast and breast cancer. These studies have included the development of new techniques for the isolation and culture of human mammary stem cells. Dr. Wicha's group was part of the team that first described stem cells in human breast cancer. This was the first description of tumor stem cells in any solid malignancy. These findings have fundamental importance for understanding the origins of breast cancer and significant implications for breast cancer prevention and therapy.

Musa Mayer

Musa Mayer is an 18-year survivor, advocate, and author of three books on breast cancer. Her articles on breast cancer and advocacy frequently appear in magazines, newsletters, websites, and medical journals. She frequently speaks and consults on many advocacy and survivorship issues, and on advanced and metastatic breast cancer. As a teacher, Ms. Mayer has served as both a faculty member and advocate mentor at the National Breast Cancer Coalition's science training program, Project LEAD. In addition to doing peer review for the California Breast Cancer Research Program, in 2003 she prepared a position paper for the CBCRP entitled "Treatment and Outcomes for High-Risk and Metastatic Breast Cancer in California: An Inquiry into Disparities and Research Needs." As an independent advocate, Ms. Mayer has worked with national and local breast cancer organizations, and has been a frequent keynote and plenary speaker at many conferences. Providing daily information and support online for women with advanced (metastatic) breast cancer on the largest Internet mailing list of its kind at www.bcmets.org has informed Ms. Mayer's work as a Patient Consultant for the FDA's Cancer Drug Development Program, and a voting Patient Representative to the Oncologic Drugs Advisory Committee.

Ms. Mayer has recently completed work on an online training course for advocates for the U.S. Cochrane Center, entitled, “Understanding Evidence-Based Healthcare: A Foundation for Action,” to be released in the fall of 2007. She is a consumer reviewer for the Cochrane Collaboration. Other recent projects include a needs assessment survey of women with advanced breast cancer for Living Beyond Breast Cancer, presented at the 2005 San Antonio Breast Cancer Symposium and at the American Psychosocial Oncology Society 2007 conference. Ms. Mayer currently serves on the Institute of Medicine Forum on Drug Discovery, Development and Translation. Her web resource for women with advanced breast cancer can be found at www.AdvancedBC.org.

Marisa Weiss, M.D.

Marisa C. Weiss, M.D., is founder, president, and guiding force behind breastcancer.org, providing over 8 million visitors per year with medically reviewed breast health and breast cancer information. An active breast cancer oncologist for 20 years, Dr. Weiss is a visionary advocate for her innovative and steadfast approach to informing, empowering, and treating breast cancer patients.

Dr. Weiss is also Director of Breast Radiation Oncology and Director of Breast Health Outreach at Lankenau Hospital, part of the Main Line Health Hospitals of the Thomas Jefferson University Health System in the Philadelphia area. For over a decade, she has been a respected medical voice in the media. She is a regular ABC News contributor, and has appeared frequently on CNN House Call and NBC Today Show’s Special Breast Cancer Series. She is regularly quoted in print outlets, including *USA Today, The Wall Street Journal, The New York Times,* and *Associated Press*. She is a medical source for magazine articles and radio interviews, including *Ladies Home Journal, Self, More, People, Redbook,* NPR, CNN Radio, ABC Radio, and Cosmopolitan radio.

Dr. Weiss co-authored *Living Beyond Breast Cancer,* and is founder and past president of Living Beyond Breast Cancer, a national nonprofit education and support organization. Dr. Weiss is a regular keynote speaker at international women’s health conferences and a frequent contributor to online conferences through WebMD and breastcancer.org.

In 2005, Dr. Weiss was named Doctor of the Year by Philadelphia Magazine, and has received several awards, including 2003 Professor of Survivorship Award from the Susan G. Komen Foundation. She serves on the professional advisory board of Mommy’s Light Lives On, American Society of Clinical Oncology, and the American Society of Therapeutic Radiation Oncology. Dr. Weiss is a past board member of the National Breast Cancer Coalition and served in the National Cancer Institute Director’s Consumer Liaison Group from 1997-2007.

CONCURRENT BREAKOUT SESSIONS

11:00am–12:30pm

Session 1–Services and Support for the Underserved | San Diego

Breast cancer is a disease that touches every California community, but the availability of treatment and support services varies wildly. The presentations in this session will show how researchers are identifying and finding ways to overcome barriers to breast health services and information due to ethnic, racial, or even geographical differences.

Moderators:

Sora Park Tanjasiri, Dr.P.H., M.P.H., California State University, Fullerton

Mary Ann Kreshka, Northern Sierra Rural Health Network

Speakers:

A Breast Cancer Educational Program for Samoans

Shiraz Mishra, Ph.D., University of Maryland

Pat Luce, National Office of Samoan Affairs

Promoting Patient Participation in Treatment Decisions in Rural Northern California

Jeff Belkora, Ph.D., University of California, San Francisco

Sara O'Donnell, Mendocino Cancer Resource Center

Addressing Disparities in Breast Cancer Mortality

Rebecca Smith-Bindman, Ph.D., University of California, San Francisco

Session 2–Emerging Topics in Breast Cancer Biology | San Jose

The breast is populated by a variety of different types of cells, each with its own job. By investigating how these different types of cells influence each other's behavior and change as cancer develops, we should be able to devise ways to intervene in the process. Presentations in this session will describe our understanding of breast aging, the genes that are mutated in breast cancer, and mechanism of how tumor cells spread to other parts of the body.

Moderators:

Klaus Porzig, M.D., South Bay Oncology Hematology and California Breast Cancer Research Council

Vernal Branch, The Virginia Breast Cancer Foundation

Speakers:

Early Genetic Changes in Mammary Stem Cells

Steve Artandi, Ph.D., Stanford University

The Role of Cellular Environment in Breast Cancer Progression and Metastasis

Kristiina Vuori, M.D, Ph.D., The Burnham Institute for Medical Research

Using Microarrays to Find Novel Breast Cancer Genes

Jonathan Pollack, M.D., Ph.D., Stanford University

DID YOU KNOW....

The CBCRP has a special place on our website just for your comments, suggestions, and feedback?

It's called CBCRP Listens!

Follow the link on the home page and let us know what you think!

www.CABreastCancer.org

The staff and advisory council carefully review all comments.

We appreciate your input!

KEYNOTE LUNCHEON

12:30pm–2:00pm | Sacramento/San Francisco

Mistress of Ceremonies:
Holly J. Mitchell, CEO Crystal Stairs, Inc.

Achievement Award:
M. Ellen Mahoney, M.D., F.A.C.S.

Presented by Mhel Kavanaugh-Lynch, M.D., M.P.H., Director, California Breast Cancer Research Program

Cornelius L. Hopper Poster Award Presentations:
Cornelius Hopper, M.D., Vice President, Emeritus, University of California, Office of the President, Office of Health Affairs

Charles Gruder, Ph.D., Director, Special Research Programs, University of California, Office of the President

Mhel Kavanaugh-Lynch, M.D., M.P.H., Director, California Breast Cancer Research Program

Keynote Address:
And from Action to Research: the Reciprocity of Breast Cancer Activism and Breast Cancer Research from Rachel Carson to Today

Sandra Steingraber, Ph.D.

KEYNOTE LUNCHEON

Photo copyright: Frank DiMeo/Cornell University Photography

Sandra Steingraber, Ph.D.

Ecologist, author, and cancer survivor, Sandra Steingraber is an internationally recognized expert on the environmental links to cancer and reproductive health. An enthusiastic and sought-after public speaker, Steingraber has keynoted conferences on human health and the environment throughout the United States and Canada and has been invited to lecture at many universities, medical schools, and teaching hospitals—including Harvard, Yale, Cornell, and the Woods Hole Oceanographic Institute. She is recognized for her ability to serve as a two-way translator between scientists and activists.

In her book *Living Downstream: An Ecologist Looks at Cancer and the Environment,* she presents cancer as a human rights issue. The book was the first to combine data on toxic releases with data from U.S. cancer registries. It garnered widespread praise from international media. *Living Downstream* has been recently optioned for a documentary film. Her new book, *Having Faith: An Ecologist's Journey to Motherhood,* reveals the alarming extent to which environmental hazards now threaten each crucial stage of infant development. Dr. Steingraber received a Hero Award from the Breast Cancer Fund in 2006, and also lectures widely at conferences, universities, medical schools, and teaching hospitals.

M. Ellen Mahoney, M.D.

Ellen's exceptional care for breast cancer patients and contributions to breast cancer research and to the California Breast Cancer Research Program are many, varied, and ceaseless. She is a practicing breast surgeon and an outspoken advocate for breast cancer patients. Besides her medical practice in Arcata, Dr. Mahoney is a Clinical Assistant Professor of Surgery at Stanford University. She is the co-founder of the Community Breast Health Project in Palo Alto. Her work there resulted in extensive knowledge of current breast cancer literature and of the questions and problems faced by patients and families. She has used this knowledge to support other nonprofit breast cancer organizations, including the Breast Cancer Fund and the Humboldt Community Breast Health Project.

She helps Susan Love M.D. in the maintenance of the Personal Guidance service on www.susanlovemd.com. Her goal is that all patients have the latest concepts and knowledge available in language they can understand. She describes herself as "passionate about the need to improve our knowledge about breast cancer and our care of all whose lives are affected by this disease."

CONCURRENT BREAKOUT SESSIONS

2:00pm–3:30pm

Session 3–Exploring Breast Cancer Risk | San Diego

Understanding the risks associated with developing breast cancer may direct us toward effective preventive strategies. The presentations in this session will explore how breast density, milk production, and environmental factors influence breast physiology and ultimately affect breast cancer risk.

Moderators:

Celia Byrne, Ph.D. Georgetown University

Ana Teresa Garcia, Kohala Family Health Center

Speakers:

Breast Density as a Risk Factor for Cancer

Karla Kerlikowske, M.S., M.D., University of California, San Francisco

Measuring Estrogen Receptor Changes Due to Environmental Exposures

Christopher Benz, M.D., Buck Institute of Aging Research

Protection against Breast Cancer by Prolactin in Milk

Ameae Walker, Ph.D., University of California, Riverside

Session 4–Improving Breast Cancer Diagnosis and Therapy | San Jose

The ultimate goal for breast cancer treatment is to make it as non-toxic to normal cells as possible, while still efficiently killing tumor cells. The method for achieving this goal is to identify which tumors will respond to specific therapies and treat them accordingly. The presentations in this session will describe how researchers are learning to recognize tumor cells in the blood, identify which tumors will respond to specific treatments, and develop new therapies from natural products.

Moderators:

Abenaa Brewster, M.D., MD Anderson Cancer Center

Anna Cluxton, Young Survival Coalition

Speakers:

Markers for Predicting Response to Therapy

Michael F. Press, M.D., Ph.D., University of Southern California

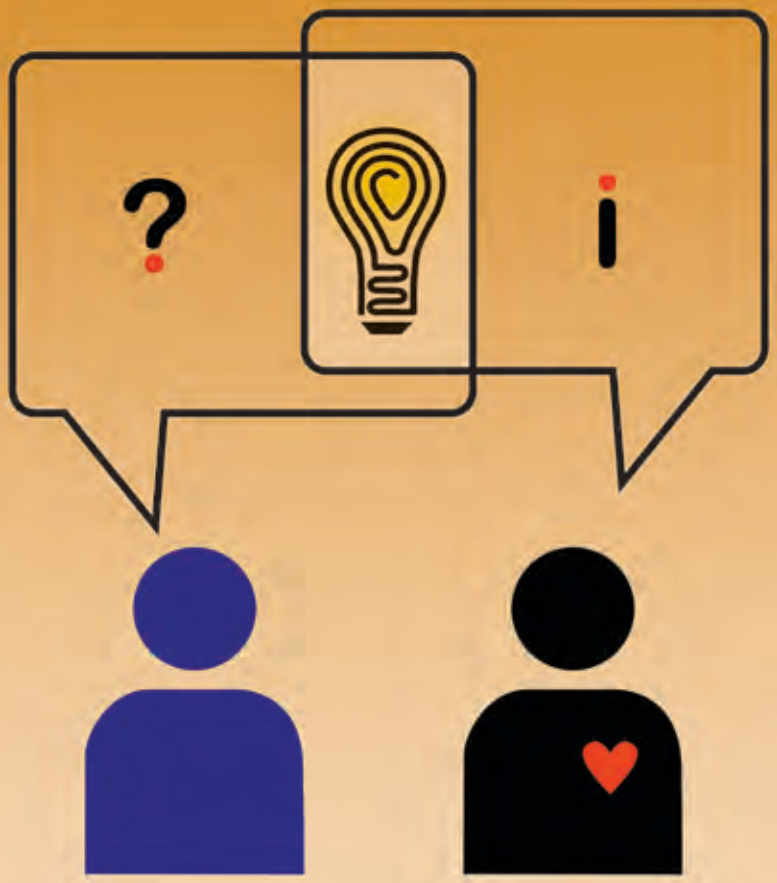
New Approaches to Detecting and Characterizing Circulating Tumor Cells

Stefanie Jeffrey, M.D., Stanford University

Developing Chemotherapy from Herbs

Michael J. Campbell, Ph.D., University of California, San Francisco

Need help understanding poster presentations?



If so, Advocate Guides have come from around the country to help. All of the Advocate Guides at the "From Research to Action: Breaking New Ground" symposium have reviewed grant applications for the CBCRP and other organizations and will bridge the language barrier between scientists and the general public.

Advocate Guides will:

- lead you through the poster sessions
- orient you to the concept of poster displays of scientific projects
- facilitate discussions between poster presenters and poster viewers

POSTER PRESENTATIONS WITH ADVOCATE GUIDES

3:30pm–5:30pm | Pasadena Exhibit Hall

CBCRP investigators will display their research results in the form of posters. Posters will be available for viewing all day, but will be attended by researchers from 3:30pm – 5:30pm. Advocate guides will be available during this session to lead groups through the posters and to facilitate discussions between scientists and audience.

CBCRP investigators will attend their posters at the following viewing times:

3:30pm – 4:30pm	Sessions A and B
4:30pm – 5:30pm	Sessions C and D

Advocate Guides:

Sandy Blank	Florida Breast Cancer Resource Network	Deerfield Beach, FL
Susan Cohen	New York Breast Cancer Network	New York, NY
Margaree Crosby	Clemson University	Greenville, SC
Roberta Gelb	SHARE	New York, NY
Pat Haugen	National Breast Cancer Coalition	Sioux Falls, SD
Karen Jacobs	Women's Cancer Resource Center	Berkeley, CA
Anne-Marie Kunzler	National Breast Cancer Coalition	New York, NY
Kathleen Livingston	Inflammatory Breast Cancer Research Foundation	Waterford, MI
Ginny Mason	Inflammatory Breast Cancer Research Foundation	Goshen, IN
Selma J. Morris	Grady Breast Health Initiative	Atlanta, GA
Sylvia Garcia Rickard	Utah Breast Cancer Network	Sandy, UT
Susan Samson	California Advocate	Berkeley, CA

POSTER SESSION A

3:30pm–4:30pm | Pasadena Exhibit Hall

Community Impact

A-01
Access and Barriers to Breast Health and Care for Slavic Immigrant Women
Debora Paterniti and Roman Romaso

A-02
Cognitive Behavioral Therapy for Insomnia in Breast Cancer Survivors
Lavinia Fiorentino

A-03
Conducting Breast Health and Breast Cancer Research Among Deaf and Hard-of-Hearing Women: Meeting the Challenges
Heidi Kleiger and Barbara Berman

A-04
Cost-Effectiveness of Breast MRI Screening by Cancer Risk
Allison Kurian

A-05
Developing a Tailored Community-based Health Navigation Curriculum to Reduce Breast Cancer Disparities for Southeast Asian American Women
Mary Anne Foo and Marjorie Kagawa-Singer
Presenter: Tu-Uyen Nguyen

A-06
Does a Peer Navigator Improve Quality of Life at Diagnosis?
David Spiegel and Carolyn Bliss-Isberg
Presenter: Janine Giese-Davis

A-07
Effect of Light on Fatigue in Women with Breast Cancer
Sonia Ancoli-Israel

A-08
Informal and Formal Social Support Needs of Samoan Breast Cancer Survivors
Sora Tanjasiri and Sala Mataalii

A-09
Physician Communication Challenges and New Approaches to Breast Cancer Care
Leah Karliner

A-10
Physician Financial Incentives in Breast Cancer Care: Results from the Los Angeles Women's Health Study
Katherine Kahn
Presenter: Diana Tisnado

A-11
Psychosocial Support Services for Latinas with Breast Cancer
Anna Napoles-Springer and Carmen Ortiz

A-12
Quality of Life of Young Breast Cancer Survivors at Five and Ten Years Post-Diagnosis
Joan R. Bloom

A-13
Reconstructive Breast Surgery in Medically Underserved Women with Breast Cancer: The Role of Patient-Physician Communication
Rose Maly

A-14
Social and Religious Support in Older Racial/Ethnic Minority Women with Newly Diagnosed Breast Cancer
Yoshiko Umezawa

A-15
Social Capital, Social Support, and Long-term Quality of Life
Dana Petersen

A-16
South Asian Women and Breast Cancer: What Are Their Needs?
Beth Glenn, Roshan Bastani, and Zul Surani

A-17
Physician Use of Health Professionals and Support Staff in Caring for a Population-based Cohort: Results from the Los Angeles Women's (LAW) Study
Katherine L. Kahn
Presenter: Danielle Rose

A-18
Underserved Women with Breast Cancer at the End of Life: A CBPR Pilot Study
Shelley Adler and Beverly Burns

A-19
Factors Influencing Breast Cancer Screening in Older Thai Women
Bulaporn Natipagon-Shah and Mary Jo Clark

A-20
Fresno Breast Cancer Navigation Pilot Program
John Capitman, Mary Wallace, and John Zweifler
Presenter: Matilda Ruwe

A-21
Addressing Cultural and Tribal Issues
Marlene von Friederichs-Fitzwater and Linda Navarro

POSTER SESSION B

3:30pm–4:30pm | Pasadena Exhibit Hall

Cause and Prevention

B-01
Anti-aromatase Activity of Phytochemicals in White Button Mushrooms
Shiuan Chen

B-10
Grape Seed Extract is an Aromatase Inhibitor and a Suppressor of Aromatase Expression
Shiuan Chen

B-02
Assessment of Recurrent Genomic Aberrations Linked to Ethnicity
Koei Chin

B-03
Body Size and Premenopausal Breast Cancer Risk in a Multiethnic Population
Esther John

B-05
Development of Data Linkage Strategies to Study Early Life Exposures and Breast Cancer in Young California Women
Peggy Reynolds
Presenter: Susan Hurley

B-06
Diabetes and Risk of Breast Cancer in Asian American Women
Anna Wu

B-16
Tamoxifen, Soy, and Lifestyle Factors in Asian American Women With Breast Cancer
Anna Wu

B-07
Differential Effects of the Isothiocyanate Sulforaphane on Breast Cancer and Normal Human Mammary Epithelial Cells
Olga Azarenko

B-08
EPHA2 Expression is Associated with Breast Cancer Risk
Richard Neve

B-09
Grape Seed Extract as a Natural Aromatase Inhibitor
Melanie Palomares

B-11
Grapefruit Intake and Risk of Breast Cancer in Postmenopausal Women
Malcolm C. Pike
Presenter: Kristine Monroe

B-12
Hereditary Breast Cancer and Novel Hispanic BRCA Mutations: A Recurring BRCA1 Genomic Rearrangement in High-risk Hispanic Families
Jeffrey Weitzel

B-13
Leptin-Receptor Gene Polymorphisms and Body Composition among African American, Caucasian, and Hispanic Women
Catherine Carpenter

B-14
Oral Contraceptives, Reproductive Factors, BRCA1 and Breast Cancer
Giske Ursin

B-18
Uncovering Novel Post-translational Modifications in Human Breast Cancer Estrogen Receptor
Christopher Benz
Presenter: David Britton

B-19
Elucidating the Mechanism by which the Dietary Indole I3C Can Inhibit Breast Cancer by Regulation of Estrogen Receptor-Alpha
Crystal Marconett

POSTER SESSION C

4:30pm–5:30pm | Pasadena Exhibit Hall

Detection, Prognosis, and Treatment

C-01
Activity Probes for Monitoring Cytochrome P450 Induction and Drug interactions in Vivo
Benjamin Cravatt
Presenter: Aaron Wright

C-02
Alteration of Topoisomerase II-alpha Gene in Human Breast Cancer and its Association with Responsiveness to Anthracycline-based Chemotherapy
Michael Press

C-03
BreastCancerTrials.org: Evaluation of a Pilot Clinical Trial Matching Service
John Park
Presenter: Ellyn Cohen

C-04
Development of Small Molecule for Hsp70
Chung-Wai Shiau

C-05
Factors Influencing Mammography Screening among Thai Immigrant Women
Mary Jo Clark and Bulaporn Natipagon-Shah

C-06
Identifying Metastatic Breast Cells from Peripheral Blood
Kristen Kulp

C-07
Identifying Targeted Treatments for Wound-like Breast Cancers
Howard Chang

C-08
Increasing mammography screening for Latinas with diabetes
Stergios Roussos and Christine Noguera

C-09
MR Imaging of Benign, Pre-malignant and Pre-invasive Breast Lesions: Can They Be Differentiated?
Min-Ying Su
Presenter: Chung-Ho Chen

C-10
Multi-modality Imaging for Breast Cancer
Gultekin Gulsen

C-11
Brominated Flame Retardants (PBDEs) in Breast Adipose of Women with and without breast Cancer
Myrto Petreas

C-12
Breast Tumor Responses to Novel TGF-beta Inhibitors
Kelly Harradine

C-13
Cannabidiol as a Novel Inhibitor of ID-1 Gene Expression in Aggressive Breast Cancer Cells
Sean McAllister

C-14
Differential Optical Mammography
Gregory Faris and Christopher Comstock

C-15
Determinants of Response to Microtubule Stabilizing Drugs
Tatana Spikacova

C-16
Augmenting Immune Responses against Breast Cancer with IL-15 Cytokine Complexes
Ananda Goldrath
Presenter: Mark Rubinstein

C-17
Early Breast Cancer Detection Using 3D Ultrasound Tomography
Thomas Nelson

C-18
Lymphangiogenesis Predictions in Normal Lymph Nodes
Barbara Garmy-Susini

C-19
Real Time 3D Ultrasound Image Guidance
Michael Bax

C-20
Vaccine for Cancer and Infectious Disease
Albert Deisseroth

POSTER SESSION D

4:30pm–5:30pm | Pasadena Exhibit Hall

Normal and Tumor Biology

D-01
A Mass Spectrometric approach to BRCA1 Function
Peter Kaiser
Presenter: David Meierhofer

D-02
Analysis of MicroRNA Expression in Breast Cancer Stem Cells
Yohei Shimono

D-03
Angiogenesis in the Progression of Premalignant Breast Ductal Proliferations
Min-Ying Su
Presenter: Philip Carpenter

D-04
Breast Cancer Studies in a 3-D Cell Culture System
Kristiina Vuori
Presenter: Amy Howes

D-05
Classification of BRCA1 and BRCA2 Variants
Giske Ursin
Presenter: Eunjung Lee

D-06
Comparative Metabolic Profiling of Breast Cancer
Chen Yang

D-07
Discovery and Characterization of Novel Mutation Pathways in Eukaryotes
Ewa Lis
Presenter: Floyd Romesberg

D-08
Essential Role of CSN5 in Breast Cancer Progression
Adam Adler

D-09
High Resolution Imaging of the Dynamic Tumor Cell-vascular Interface in Transparent Zebrafish
Konstantin Stoletov

D-10
Inflammation Alters Transcription by the Estrogen Receptor in Breast Cancer
Eliot Bourk

D-11
LMO4 Can Interact with Smad Proteins and Modulate Transforming Growth Factor-beta Signaling in Epithelial Cells
Xiaoman Xu

D-12
LMO4 Controls Cell Proliferation and Apoptosis of Mammary Epithelial Cells by Regulating Expression of the BMP7 Gene
Zhengquan Yu

D-13
Mammary Invasion and Remodeling Occurs via a Novel Activated Epithelial State
Andrew Ewald

D-14
Oxidative Stress Pathways Highlighted in Tumor Cell Immortalization
Shanaz H. Dairkee
Presenter: Aejaz Sayeed

D-15
Structural Characterization of Aromatase
Yanyan Hong

D-16
Targeting Up-regulated Notch Signaling in Inflammatory Breast Cancer
Sanford Barsky

D-17
The Identification and Modification of Rad51 Recombinase Inhibitors and their Applications in Inhibiting Breast Tumor Growth
Jiewen Zhu

D-18
The Identification of an Enzyme that Regulates Ether Lipid Signaling Pathways in Cancer
Ben Cravatt
Presenter: Sherry Niessen

D-19
The Importance of the MAPK Pathway During Mammary Gland Development
Jimmie Fata

D-20
The Role of Slit Family Guidance Cues in Breast: Adhesive Factors and Tumor Suppressors
Lindsay Hinck

D-21
Twist Activation in Breast Cancer Metastasis
Jing Yang

D-23
At the Interface of Lipid Metabolism and Receptor Signaling: Lipid Rafts and the (De)regulation of ERBB2
Ralf Landgraf

CLOSING CEREMONIES

5:30pm–6:00pm | Pasadena Exhibit Hall

Raffle

(Must be present to win)

We would like to thank the following companies and individuals for donating prizes:

Encore Plus Printing

Freeman Decorating Services

Target Stores

See's Candies

Macy's

RRR Travel

Westin Bonaventure

CHOOSE TO HELP

Contribute to the California Breast Cancer Research Fund on line 55 of your State income tax form 540.
Simple, effective, and automatically tax deductible.

Learn more at www.endbreastcancer.org

Your contributions are already making a difference. California Breast Cancer Research Fund grants have:

- Found extremely early genetic changes that can be used to eliminate cancer cells before they become tumors
- Shown that extracts from white button mushrooms decrease estrogen production, which can block tumor growth
- Identified ways to empower breast cancer patients within the health care system

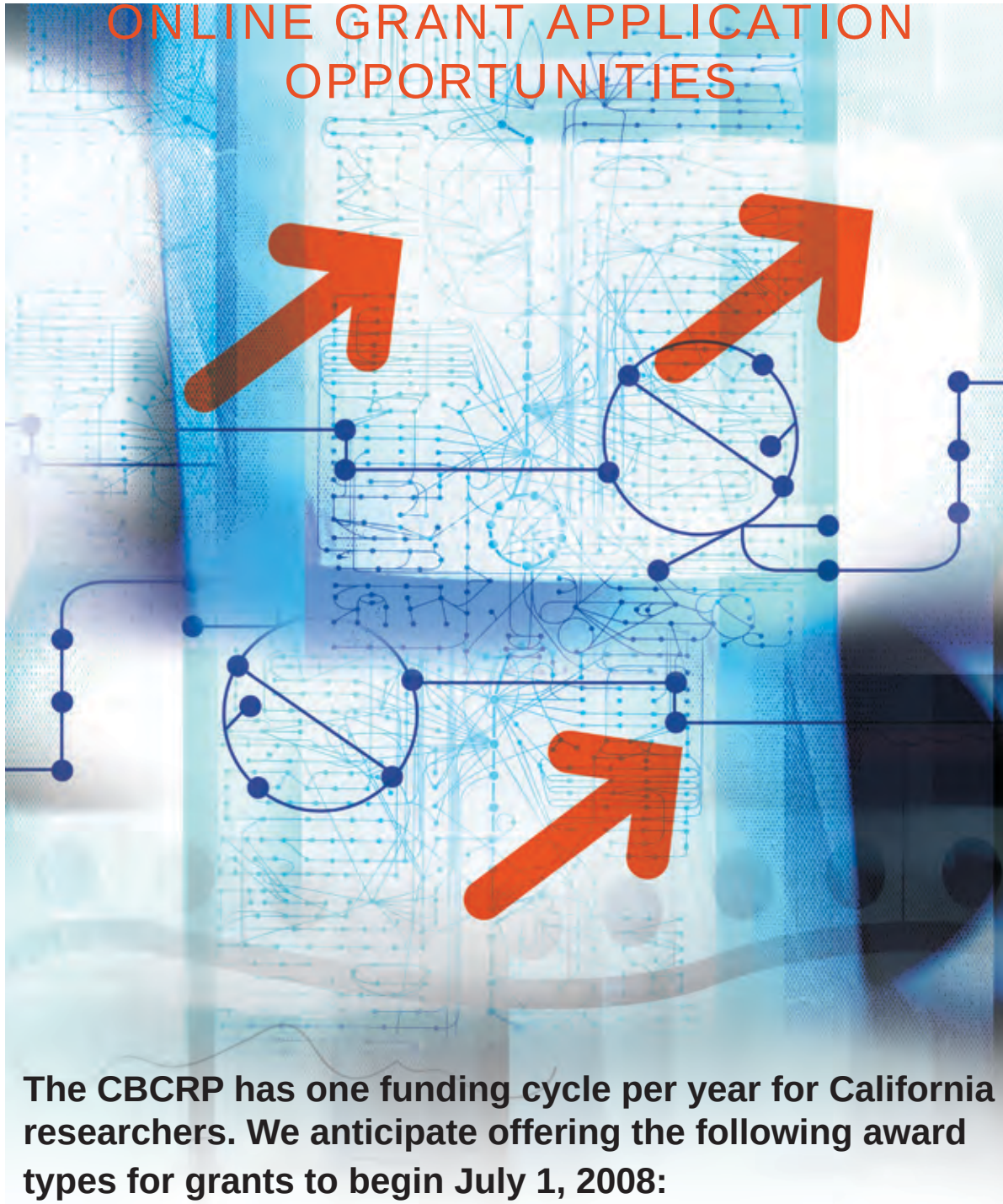
But we still need your help to conquer the disease.
You can see a full list of grants supported by California Breast Cancer Fund contributions on our website at:

www.endbreastcancer.org/awardsList.php.

CALIFORNIA
Breast Cancer
Research Program

300 Lakeside Drive, 6th floor | Oakland, CA 94612-3550 | Toll-free: 888 313-2277 | E-mail: taxcheck@cabreastcancer.org

ONLINE GRANT APPLICATION OPPORTUNITIES



The CBCRP has one funding cycle per year for California researchers. We anticipate offering the following award types for grants to begin July 1, 2008:

- **Translational Research Award**
- **Community Research Collaborations (CRC)**
- **Dissertation, Postdoctoral Fellowship, and IDEA (regular and junior investigator)**
- **IDEA-competitive renewal**
- **CRC (Pilot, Full, and Implementation & Development [I&D])**
- **Joining Forces Conference Award**

Program
Sunday, September 9, 2007

Sunday, September 9, 2007

PROGRAM

Registration (8:00 – 10:00) | Santa Barbara Foyer
Breakfast (8:00am–9:00am) | Santa Barbara C

Workshop 7–Community Research Collaboration (9:00am–12:00pm)
Santa Barbara B

Breast cancer is a disease that touches every California community, but the availability of detection, treatment, and support services varies widely. The presentations in this session will show how CBCRP researchers are identifying breast cancer disparities and finding ways to overcome barriers to breast health services and information due to ethnic, racial, or even geographical differences.

All interested researchers and community members are encouraged to attend!

Leader:
Marj Plumb, Dr.P.H., M.N.A., Plumbline Coaching and Consulting, Inc.

Theories of Community Identity and Group Dynamics

Marj will give a brief overview of the role and meaning of "community" in CBPR and will offer recommendations on how to operationalize the community partner so that all levels of community are involved and engaging their full experience, skill, and knowledge. Marj will also give a brief overview of group dynamics theories and suggest ways that CRC teams can improve their relationships and communication.

Speakers:
Scientific Rigor with Hard to Reach Populations

Cheryl will highlight challenges and successful strategies to achieve scientifically meaningful results in a hard to reach, rural population where recruitment difficulties are an issue. She will discuss the tension between meeting scientific standards for recruitment and how to realistically recruit participants in a hard to reach geographic area.

Cheryl Koopman, Ph.D., Stanford University

Collaborative Data Analysis

Steve will talk about how equal participation from community and research partners in the data analysis stage can pose a challenge in a collaborative partnership. He will discuss successful tools to increase capacity among community partners to take an equal role in analyzing data.

Steve Kaye, Ph.D., University of California, San Francisco

Community IRBs

Mary Anne will discuss the benefits of using a community IRB to oversee CRC research projects. She'll discuss the process for developing an IRB; including appropriate board members; and how the IRB provides oversight during the CRC project.

Mary Anne Foo, M.P.H., CHES, Orange County Asian Pacific Islander Community Alliance (OCAPICA)

Integration of Community

Broad community involvement in the research project is an essential part of CBPR. Lola will talk about integrating members of the community into research projects so that these studies are truly participatory and beneficial to the community at large.

Lola Sablan Santos, Guam Communications Network

ABOUT THE CBCRP

The Breast Cancer Research Program

The mission of the CBCRP is to eliminate breast cancer by leading innovation in research, communication, and collaboration in the California scientific and lay communities.

- The CBCRP is one of the top-rated research funders in the nation and is administered by the University of California, Office of the President
- The CBCRP is funded through a portion of the tobacco tax, voluntary tax check-off on personal income tax forms, and individual contributions
- The tax check-off, included on the personal income tax form since 1993, has drawn over $5 million for breast cancer research
- Ninety-five percent of our revenue goes directly to funding research and education efforts
- The revenue is used to make grants for California scientists and community researchers to find better ways to prevent, treat and cure breast cancer
- Since 1994, the California CBCRP has awarded over $181 million for 761 grants to 92 California research institutions and community organizations. The CBCRP supports innovative breast cancer research—like cow viruses, Tibetan herbs, snake venom—that might otherwise go unfunded. With continued investment, the CBCRP will work to find better ways to prevent, treat, and cure breast cancer

Breast Cancer Research Advisory Council Members

To continue to fund innovative research, the California Breast Cancer Research Program (CBCRP) must rely on its advisory committee. The committee, the Breast Cancer Research Advisory Council (BCRC) is responsible for tracking the trends and opportunities for progress that arise in the breast cancer community, making funding recommendations, and planning future directions of the CBCRP. The BCRC is made up of 15 people selected to represent those affected by breast cancer and the institutions that can help find a solution.

2006-2007 Breast Cancer Research Council

Chair, Lisa Wanzor, *advocate*

Vice Chair, Amy Kyle, Ph.D., M.P.H., *scientist/clinician*

Moon S. Chen, Jr., Ph.D., M.P.H., *scientist/clinician*
Crystal Crawford, Esq., *advocate*
Diane Griffiths, a*dvocate*
Anuja Mendiratta, *nonprofit health organization representative*
Angela Lucia Padilla, Esq., *advocate*
Gordon Parry, Ph.D., *private industry representative*
Mark Pegram, M.D., *scientist/clinician*
Klaus Porzig, M.D., *medical specialist*
Catherine Quinn, *nonprofit health organization representative*
Maria Wetzel, *advocate*

Symposium Planning Committee

Moon S, Chen, Jr., Ph.D., M.P.H., University of California, Davis
Crystal Crawford, Esq., CEO, California Black Women's Health Project
Jim Ford, M.D., Stanford University
Angela Padilla, Advocate, Bay Area Young Survivors (BAYS)
Gordon Parry, Ph.D., Senior Director, Oncology, Monogram Biosciences
Mark Pegram, M.D., University of California, Los Angeles
Kim Pierce, University of California, Los Angeles
Klaus Porzig, M.D., Director of Cancer Research, South Bay Oncology Hematology
Catherine Quinn, Executive Director, California Health Collaborative
Maria Wetzel, Cancer Resource Centers of Mendocino County

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Katherine McKenzie, Ph.D.
Lisa Mininfield
Eric Noguchi
Joyce Price
Walter Price, Dr.P.H.
Catherine Thomsen, M.P.H.

Abstracts Section

Session A: Community Impact

Access and Barriers to Breast Health and Care for Slavic Immigrant Women

Principal Investigators:
Debora Paterniti and Roman Romaso

University of California, Davis, and Slavic Assistance Center

Abstract #: A-01

Our project is aimed at understanding the breast health and cancer experience of Slavic women so that we may develop a program for Slavic community-based health educators who will have the skills and training materials to help women in their community to understand breast health, to access screening, and to seek care for breast cancer. Our primary research question is: How do Slavic immigrant women come to understand breast health and breast cancer (i.e., what is their experience)? We believe that the best way to understand the breast health and breast cancer experience of Slavic women is by talking with Slavic women about their experiences. We have conducted six focus groups made up of first and second generation Slavic women from Sacramento and Yolo counties. We asked women questions relating to their experience with breast cancer, how they understand breast health, and about the problems they face related to getting health care. Community members have been involved throughout the project by participating in town hall meetings and focus group discussions. During the town hall meetings, community members reviewed the focus group results and provided feedback on our findings. We will describe Slavic women's current understandings of breast health and barriers to care and care seeking to design a health educator program by and for Slavic women. Our presentation identifies Slavic immigrant women's understandings of breast health and care as well as barriers to care, screening, and treatment. Information from focus group data and community-based input has helped our team design a preliminary community health education training program by and for Slavic women. We will assess the acceptability of this training program in a second phase of focus groups.

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Cognitive Behavioral Therapy for Insomnia in Breast Cancer Survivors

Principal Investigator:
Lavinia Fiorentino

University of California, San Diego

Abstract #: A-02

Introduction: Survivors of breast cancer often suffer from insomnia. Sleep problems and correlated symptoms can last for years after the end of treatment. The present data are from an ongoing study testing the effects of a cognitive behavioral treatment for insomnia (CBT-I) on sleep, depression, anxiety, and quality of life in breast cancer survivors

Methods: The study is a 12-week randomized controlled crossover design, with participants being randomized to either 6 weeks of CBT-I followed by 6 weeks of follow up (i.e., group 1), or six weeks of treatment as usual (TAU) followed by six weeks of CBT-I (i.e., group 2). Self-reports of insomnia (Insomnia Severity Index: ISI) and quality of sleep (Pittsburgh Sleep Quality Index: PSQI) are assessed at baseline, 6 weeks, and 12 weeks. The CBT-I treatment is administered in 6 individual one-hour weekly sessions. The following data describe the results of the first four participants who have completed all assessments of the study protocol. Of these, 1 participant was randomized initially to CBT-I, and 3 were randomized to TAU followed by CBT-I.

Results: All 4 participants (mean age=57 years, SD=9, range=46-67) had reduced levels of insomnia and sleep disruption comparing baseline (ISI: mean=18.2, SD=3.9, range=13-22; PSQI: mean=13.5, SD=2.4, range=11-16) to after the CBT-I (ISI: mean=5.7, SD=3.9, range=2-11; PSQI: mean=5.2, SD=2.9, range=3-9). In addition, the 3 participants in group 2 did not improve during the 6 weeks of TAU (ISI: mean=18.3, SD=1.5, range=17-20; PSQI: mean=13.3, SD=2.5, range=11-16). The participant randomized to initial CBT-I continued improving during the follow up (ISI: score=0, PSQI=1).

Discussion: Although these data are very preliminary, breast cancer survivors appear to benefit from CBT-I. After 6 sessions of CBT-I all 4 participants reported having no insomnia and better sleep quality. A larger sample size, currently being recruited, will permit statistical analysis of these differences.

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Session A: Community Impact

Conducting Breast Health and Breast Cancer Research Among Deaf and Hard-of-Hearing Women: Meeting the Challenges

Principal Investigator:
Heidi Kleiger and Barbara Berman

Greater Los Angeles Agency on Deafness, Inc., and University of California, Los Angeles

Abstract #: A-03

Deaf and hard-of-hearing (deaf/hh) women are invisible in the research that has shaped breast health and breast cancer educational interventions There exists cultural, social, and communication barriers, which prevent d/hh women from accessing public information about breast health and breast cancer. We describe here a program of research, unique in the nation, funded by California Breast Cancer Research Program (CBCRP) and by the Susan G. Komen Breast Cancer Foundation, focused on developing and testing an effective program tailored for this population. The goals of our research are to: (1) produce a comprehensive multimedia tailored breast cancer program for deaf/hh women that spans to elements of the breast cancer control continuum and that focuses on empowering deaf/hh women to take the steps needed to ensure that they receive much needed breast health and breast cancer information and services; (2) evaluate the effect of the program on: breast cancer screening behavior, knowledge and awareness of breast health and breast cancer, and on lifestyle behaviors and physician communication relating to breast health, through a demonstration project and a randomized controlled trial (RCT); and (3) disseminate study findings to the deaf/hh community, health care providers, and others serving the deaf/hh throughout California and the nation.

We report here on the community-academic partnership forged to conduct this research which includes the Greater Los Angeles Agency on Deafness (GLAD), the Division of Cancer Prevention and Control Research (UCLA), an Advisory Committee of deaf/hh community members, and expert consultants; including two of the nation's few Deaf physicians. We describe: why this program of research is needed; the steps taken to craft culturally and linguistically appropriate program content to serve a general population of deaf/hh women and those who are breast cancer survivors; elements of the intervention (small group sessions, signed/captioned/voice over DVD, written materials); recruitment strategies; data collection instrumentation and procedures; and our assessment plan which involves 240 deaf/hh women 40+ years of age (at least 200 women with a high school or less education, and 20 deaf/hh breast cancer survivors). We examine cultural considerations relevant to conducting research in this underserved and understudied population, consider challenges faced in developing and implementing our study, and describe the steps taken to address potential barriers to this much needed research.

.....

Cost-effectiveness of Breast MRI Screening by Cancer Risk

Principal Investigator:
Allison W. Kurian

Stanford University School of Medicine

Co-Investigators:
Bronislava M. Sigal, Ph.D., Bruce L. Daniel, M.D., Debra M. Ikeda, M.D., Frank E. Stockdale, M.D., Ph.D., Alan M. Garber, M.D., Ph.D., Sylvia K. Plevritis Ph.D. (research mentor)

Abstract #: A-04

Goal: To evaluate the effectiveness (measured in terms of breast cancer mortality reduction) and cost-effectiveness (measured as a ratio of cost versus effectiveness) of screening women with breast magnetic resonance imaging (MRI), incorporating women's preferences and adjusting to a woman's individual level of risk.

Background: Breast MRI is increasingly used as a screening tool for breast cancer, but no study has yet shown that it decreases mortality. Although breast MRI has been shown to detect tumors when they are smaller, MRI is more costly than mammography and can lead to a higher rate of breast biopsies, causing patients anxiety and discomfort. Screening breast MRI is likely to be of greatest benefit to women at increased risk of breast cancer for whom standard screening mammography performs poorly.

Methods: We adapted a previously developed computer simulation model of breast cancer screening with mammography to reproduce the natural history of breast cancer in women at high risk due to BRCA1/2 mutations. We incorporated the use of screening breast MRI into this simulation model, and estimated the impact on breast cancer mortality and cost-effectiveness. Simultaneously, we performed a questionnaire-based study of high-risk women's preferences for breast MRI screening versus the alternative of prophylactic mastectomy.

Results: Adding annual screening breast MRI to mammography in BRCA1/2 mutation carriers is estimated to yield a 23% relative reduc-

tion in breast cancer mortality, and a cost per quality-adjusted life year gained of $55,420 in BRCA1 and $130,695 in BRCA2 mutation carriers ages 35-54. These cost-effectiveness ratios are similar to those of widely accepted interventions in breast cancer management. Further model analyses suggest that MRI will add less benefit to screening women at lower breast cancer risk. High-risk women were more likely to choose breast screening over prophylactic mastectomy if they were older (mean age 47 versus 40) and had no prior breast cancer.

Potential Impact and Future Research: Our research produced estimates of the breast cancer mortality reduction and cost-effectiveness of MRI screening in BRCA1/2 mutation carriers, which were published in the Journal of the American Medical Association and cited in the recent American Cancer Society guidelines on screening breast MRI. In ongoing work, we are evaluating the impact of breast cancer-risk modifying characteristics and interventions, such as prophylactic oophorectomy, on the life expectancies of high-risk women who must choose between MRI-based breast screening or prophylactic mastectomy.

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Developing a Tailored Community-based Health Navigation Curriculum to Reduce Breast Cancer Disparities for Southeast Asian American Women

Principal Investigators:
Mary Anne Foo and Marjorie Kagawa-Singer

Orange County Asian Pacific Islander Community Alliance and University of California, Los Angeles

Poster Presenter:
Tu-Uyen Nguyen

Co-Investigators:
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Abstract #: A-05

The goal of our research project is to examine, from the perspective of patients, navigators, and medical health system providers, the specific aspects of current community-based patient navigation efforts that influence and support Southeast Asian women at different stages of the cancer spectrum to obtain breast health care and services. We plan to use the pilot study findings to develop and refine a patient breast health navigation curriculum and model that can be tailored to the community needs and resources of Southeast Asian women in California as well as other underserved, uninsured, low-income, and limited-English proficient immigrant and refugee communities.

Our study involves qualitative focus groups and interviews with 100-120 Cambodian, Laotian, Thai, and Vietnamese patients, 8-14 navigators, and 16-24 providers to identify and document the essential elements they feel are needed for an effective, community-based patient health navigation program. At the symposium, we will present the preliminary results and findings from the project. We plan to focus on how navigation strategies are tailored for women at different stages of the cancer continuum, highlighting important community and cultural issues that may differ across the four Southeast Asian groups. We will also discuss ways in which trust, credibility, and respect are established by the health navigators and how different types of social support roles, interpersonal relationships, and social networks may affect navigation. All of these components are important elements that we anticipate will need to be included in a training curriculum for community-based patient health navigators.

In recent years, there has been increasing emphasis on the importance of community health workers and navigators in helping women access and navigate services across the cancer care continuum, from screening through diagnosis, treatment, and recovery. By looking at the specific barriers, facilitators, and lessons learned from our previous community-based health navigation programs, we hope our work will contribute new and useful strategies for designing cost-effective and culturally relevant breast cancer prevention and control programs that take into account the unique environmental and social characteristics of underserved communities.

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Does a Peer Navigator Improve Quality of Life at Diagnosis?

Principal Investigators:
David Spiegel and Caroline Bliss-Isberg

Stanford University School of Medicine and WomenCARE

Poster Presenter:
Janine Giese-Davis

Co-Investigators:
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Abstract #: A-06
This study evaluated whether matching a woman newly diagnosed with breast cancer for 3 to 6 months after diagnosis with a trained volunteer who is herself a breast cancer survivor improves quality of life over the first year post-diagnosis. Women indicate the greatest needs for counseling at the time of initial diagnosis for primary breast cancer. However, this is the time when a woman, overwhelmed by shock and trauma, is least likely to absorb information provided or seek new sources of information. An informed peer navigator with carefully trained communication skills can judge the level of information to disclose and pace that information in a way that can be easily absorbed and understood. She will also provide support. WomenCARE, a well-established Santa Cruz agency providing free support services for women with cancer, and the Psychosocial Treatment Lab at Stanford conducted a randomized clinical trial of peer navigation.

In our study, Navigators and Sojourners (newly diagnosed women) were matched on things that were important to them. We assigned half of the women (by a process similar to a coin toss) to our peer navigator program and half to a group that receives standard medical care but no peer navigator. All women who joined our study, regardless of the group to which they were assigned, received an extra consultation with a nurse specialist who reviews the cancer resources available to the woman in Santa Cruz County. This meeting was tailored to the woman's individual diagnosis and situation.

Since the beginning of this study, we trained 36 Navigators. In addition 104 newly diagnosed women were randomized (52 receiving a match with a Navigator). We found that the women receiving a Navigator significantly increased on marital satisfaction while those in the control group decreased (p=.02), and greater breast-cancer-specific quality of life (p=.01). Women receiving a Navigator who were highly distressed at study entry also experienced a significantly greater reduction in anxiety (p=.03), distress (p=.04). However, those not matched with a Navigator who were low on Post-Traumatic Growth at baseline significantly increased to a greater extent than did those matched.

This first randomized clinical trial of an extensive peer counseling program demonstrates that being matched with a Peer Navigator appeared to mitigate the distress newly diagnosed women often experience as they are undergoing treatment for breast cancer. It is also clear that not having a peer counselor may stimulate women to perhaps put more thought and energy into self-motivated growth post-diagnosis.

We believe that this evidence indicates that this program is important and its dissemination may improve the quality of similar informal programs, stimulate the formation of more programs, and provide evidence to support health policy changes. This could lead to effective peer navigation programs throughout California.

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Effect of Light on Fatigue in Women with Breast Cancer

Principal Investigator:
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University of California, San Diego

Co-Investigators:
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Abstract #: A-07
Background: Studies have shown that women with breast cancer undergoing chemotherapy report disturbed sleep. Studies have also suggested that these women have very little bright light exposure, yet it is known that bright light may improve sleep. This study examined whether increasing exposure to bright light will improve fatigue in women with breast cancer. Methods: 11 women (mean age=50.3 yrs, SD=8.4, range: 35-70 yrs) diagnosed with stage I-III breast cancer, scheduled to receive at least 4 cycles of adjuvant or neoadjuvant anthracycline-based chemotherapy participated. Sleep quality was assessed with the Pittsburgh Sleep Quality Index (PSQI) and

objective measures of sleep were assessed with 72-hours of actigraphy (Ambulatory Monitoring, Inc. and Respironics) at baseline (pre-chemotherapy) and during the last week of cycle 4 (C4). An actigraph is a device worn on the wrist which measure sleep/wake patterns. Participants were randomized into two treatment groups: bright white light (BWL) and dim red light (DRL). Both groups were instructed to self-administer light therapy for 30 minutes every morning throughout 4 cycles of chemotherapy.

Results: In the BWL group, total sleep time (TST) increased by 41 min (SD=69), while wake time during the night stayed approximately the same. In the DRL group TST decreased by 32 minutes (SD=30), while wake time increased by 27 minutes (SD=39). Subjectively, PSQI sleep latency subscale for BWL was reduced from 2.6 (SD=3.0, range=0-5) at baseline to 1.9 (SD=2.3, range=0-6) at C4, while for DRL, mean sleep latency increased from 2.7 (SD=2.5, range=0-5) at baseline to 3.0 (SD=3.0, range=0-6) at C4. PSQI total score for BWL decreased from 12.0 (SD=4.7, range=7-19) at baseline to 10.9 (SD=4.2, range=5-16) at C4 while for DRL it decreased from 8.3 (SD=3.1, range=5-11) at baseline to 7.7 (SD=5.1, range=2-12) at C4.

Conclusions: Preliminary results suggest that bright white light may increase the number of hours of sleep in women undergoing chemotherapy, as well as decreasing the amount of time it takes to fall asleep and improving sleep quality.

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Informal and Formal Social Support Needs of Samoan Breast Cancer Survivors

Principal Investigators:
Sora Park Tanjasiri and Sala Mataalii

California State University, Fullerton and Samoan Nurses Association

Abstract #: A-08

There are over 50,000 Samoans in California. While Samaoan and other Pacific Islander women have high rates of breast cancer incidence and mortality, there are few studies of their survivorship and social support needs after diagnosis. This 18-month pilot CRC study is a collaboration between two groups: the Samoan National Nurses Association (Sala Mataalii, Co-PI) and California State University, Fullerton (Sora Tanjasiri, Co-PI). The aim of the study is to explore the social support needs of Samoan breast cancer survivors from two groups: one who have participated in SNNA's support group program, and who have not participatedin the program. In addition, two of each survivors family members or friends (i.e., supporters) will also be invited to participate in order to understand their roles in providing social support to the survivor. Over the past year, the collaborative has undertaken the acivities: 1) convened the members of our Community Advisory Council to guide development of our methods and interview guides, 2) conducted two focus groups with community leaders to identify the social support issues to be explored with survivors, 3) finalized indepth interview guides for survivors and their supporters; 4) identified and trained three nurses from SNNA in recruitment and consent processes, qualitative interviewing skills, and conducting the qualitative interviews; 5) transcribed and translated interviews; 6) conducted data analyses using Atlas.ti software; and 7) presented preliminary results to research staff and Community Advisory Council members for feedback and discussion. Long term goals include the sharing of all data analyses with study participants and the larger community, and preparing a larger, three-year study to evaluate the effects of SNNA's support groups on the lives of Samoan survivors.

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Physician Communication Challenges and New Approaches to Breast Cancer Care

Principal Investigator:
Leah Karliner

University of California, San Francisco

Co-Investigators:
L.S. Karliner, E.S. Hwang, MD MPH, C. P. Kaplan, PhD

Abstract #: A-09

Background: Breast cancer doctors face the ongoing task of both incorporating new approaches to care into their practice and communicating about these approaches with their patients.

Objective: To assess the specific challenges surgeons and medical oncologists encounter when communicating with their breast cancer patients about prognosis, treatment and new options of care.

Methods: We mailed surveys to a representative sample of physicians (1250; 661 surgeons, 588 medical oncologists), randomly selected from the American Medical Assosciation Physician Masterfile.

Preliminary Data: To date, 254 physicians have responded. Of these, 119 (47%) were surgeons,

135 (53%) medical oncologists; 191 (76%) were men; 169 (67%) were in solo/group private practice; 188 (74%) were graduates of medical schools. In general, physicians found communicating with breast cancer patients most challenging when the woman has preformed ideas about what is acceptable or unacceptable treatment (80%), desires under-treatment (52%), or has trouble understanding how population-based statistics apply to her (49%). More respondents found it difficult to discuss treatment options and prognosis with women when they were non-English speaking than when they either had a low level of education or were from a different culture than the physician. When considering a new approach/technique in breast cancer care, both surgeons and medical oncologists were most excited about being able to offer their patients additional choices (82%) and the most up to date advances (79%). Surgeons and medical oncologists were equally and most frequently concerned about the potential unknown long-term side effects of the new approach/technique (72%).

Conclusions/Implications: Our preliminary results suggest that both surgeons and oncologists are excited about new approaches/techniques to care, but they are also worried about how implementation of these in their practice may lead to unknown long-term harm. Breast cancer physicians experience communication challenges in discussing treatment and prognosis, particularly when the patient enters the encounter with pre-existing ideas about limits to her treatment. Lastly, language barriers present a particular challenge for physicians. The results lay the foundation for the development of specific communication interventions which will most assist physicians in communicating with their breast cancer patients.

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Physician Financial Incentives in Breast Cancer Care: Results from the Los Angeles Women's Health Study

Principal Investigator:
Katherine Kahn

University of California, Los Angeles

Poster Presenter:
Diana Tisnado

Abstract #: A-10

Objectives Health care quality is of concern nationally, and health care structural arrangements have been evolving rapidly to respond to increasing financial pressures and demands to enhance quality. These changes have been shown to impact primary care delivery, yet little is known about how evolving organizational and financial arrangements affect the delivery of breast cancer care. We sought to better understand how physicians characterize their own financial incentives to perform various practices and services.

Methods: Cross-sectional, observational study of physician self-reported financial arrangements from a 2004 survey of breast cancer care providers. We surveyed medical oncologists (n=111), radiation oncologists (n=66) and surgeons (n=171) practicing in Los Angeles County, identified by a population-based cohort of women with newly diagnosed breast cancer identified by the cancer registry (76% physician response rate, n=348). Physicians were asked to describe their overall, individual financial incentives with respect to selected clinical practices and services pertinent to breast cancer care (n=8 for medical oncologists, 6 for radiation oncologists, 3 for surgeons). For example, medical oncologists were asked to describe their individual financial incentives regarding the use of office-based parenteral chemotherapy. Respondents were asked to indicate whether on balance, incentives favor reducing the practice or service, expanding it, or neither. We examined the prevalence of self-reported incentives to reduce or expand each practice or service. Descriptive analyses were weighted for physician survey non-response.

Principle Findings: Self-reports of implicit financial incentives to reduce or expand practices or services varied by specialty type and item. For example, among medical oncologists, rates of incentives either to reduce or expand practices or services ranged from 42% for office-based chemotherapy to 16% for use of in-dwelling venous catheter. Among radiation oncologists, rates ranged from 21% for CT-based treatment planning to 14% for stereotactic radiosurgery. Among surgeons, rates ranged from 11% for hospitaliza-

tion to 6% for patient enrollment in clinical trials. Among medical oncologists who reported any incentives, incentives to expand services were reported for 4 out of 8 items (e.g., office-based chemotherapy) and incentives to reduce services were reported for 2 of 8 items (e.g., referral to other cancer care providers). Among radiation oncologists who reported any incentives, 4 of 6 services examined were associated with incentives to expand services. Among surgeons who reported any incentives, incentives were equally likely to be associated with service reduction (e.g., hospitalization) as with more service use (e.g., clinical trial enrollment).

Conclusions: The majority of physicians delivering specific cancer treatments in Los Angeles County reported perceiving no overall personal financial incentives to reduce or expand the practices or services studied. However, notable proportions of physicians did report financial incentives either to reduce or expand performance of certain practices and services. Of these items, incentives were more often reported to favor expanding the practice or service. Further research is needed to determine whether such incentives change breast cancer care and outcomes, and what if any associations exist between implicit financial incentives (e.g., capitation or fee-for-service reimbursements) and performance on quality indicators.

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Psychosocial Support Services for Latinas with Breast Cancer

Principal Investigators:
Anna Napoles-Springer and Carmen Ortiz

University of California, San Francisco and Circulo de Vida

Abstract #: A-11

Background: Latina breast cancer patients infrequently use cancer support services, even though they may be at higher risk of psychosocial problems than White women. This under-use has not been well-studied.

Goals: To identify factors that influence whether Spanish-speaking Latinas with breast cancer seek psychosocial cancer support services, their psychosocial needs, and the implications of these findings for the development of a peer support counselor (PSC) program for this population.

Methods: In this collaborative pilot study by the academic partner, UCSF, and the community partner, Círculo de Vida (a community-based cancer support center for Latinos; CDV), we conducted a telephone survey of 89 Spanish-speaking Latino cancer patients referred to CDV (including people who did and did not accept services); about 70% were Latinas with breast cancer with less than a high school education. We completed semi-structured interviews with 29 Latina breast cancer survivors who had and had not used support services (most were diagnosed within two years of the interview), and 17 interviews with community advocates working with Latinas with breast cancer (patient navigators, cancer support and education specialists, oncology social workers).

Results: We found that the greatest barriers to use of support services in this population were: lack of transportation, lack of familiarity with the nature of support services, and being unaware that services were available in their local area. For women who had used support services, the most frequently mentioned benefits were, in order of importance: 1) the ability to discuss cancer related issues with a fellow cancer survivor; 2) support and compassion received; and 3) information on cancer and its treatment. The two dominant psychosocial needs in the period following diagnosis were help with coping with an intense fear that they were dying, and information to address their sense of powerlessness. Community advocates identified four key areas that are critical for addressing the psychosocial needs of this population that would need to be integrated into a peer support intervention: 1) the provision of simple information in Spanish on breast cancer, treatments, treatment side effects, and management of side effects; 2) knowledge of community resources; 3) cultural sensitivity; and 4) patient empowerment. With systematic input from community members, survivors, and professionals, we wrote a resource manual for community organizations on developing a PSC program, and pilot-tested a PSC training program. Working with a large group of community organizations, community advocates, and Spanish-speaking Latina breast cancer survivors, we submitted an application for a full CBCRP CRC award to test the effectiveness of a PSC intervention for Spanish-speaking Latinas newly diagnosed with breast cancer.

Implications: Using a randomized, controlled trial design, the proposed study will test a social-cognitive theory-based, peer-delivered intervention that has been adapted for use with Spanish-speaking Latinas with breast cancer based on the results of our pilot study and the CDV PSC model. If proven effective, this program could serve as a model to meet the psychosocial needs of other vulnerable women diagnosed with breast cancer.

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Quality of Life of Young Breast Cancer Survivors at Five and Ten Years Post-Diagnosis

Principal Investigator:
Joan R. Bloom

University of California, Berkeley

Abstract #: A-12

Background: Our study of young breast cancer survivors (age 50 or younger at diagnosis) at five years post-diagnosis reported lingering effects of treatment that include arm and chest problems, weight gain, sexual difficulties, problems with health and life insurance and fears for the future. Younger women treated with chemotherapy are at increased risk for early menopause and the development of age-related chronic health conditions as well.

Goals of Research: This research will determine the extent to which women who were young at diagnosis and are now ten year survivors of breast cancer, experience 1) more intense concerns than women of the same age, ethnicity and education who have not had cancer with respect to (a) physical well-being (e.g. arm and chest problems, weight gain, and development of chronic health conditions); (b) psychological well-being (e.g. mood distress, fears for the future, body image); (c) social well-being (e.g. communication problems, sexual problems, work-related concerns); and (d) spiritual well-being; and 2) more intense concerns than they did as five year survivors in the physical and social domains and fewer concerns in the psychological domain of quality of life.

Methods: The sample includes a) 443 young breast cancer survivors interviewed who were diagnosed with breast cancer at age 50 or under who are now ten year survivors and are cancer free, 311 were also interviewed at their five year anniversary; and b) 390 women without a history of cancer who are friends of the survivors and recruited by them. The study participants were surveyed regarding their backgrounds (e.g. current age, education, family size, whether they are married, etc.), quality of life in four domains (physical, psychological, social, and spiritual) and chronic health conditions. Analysis of the data includes descriptive statistics (frequencies and counts) of the measures, comparisons between the groups (10 year survivors and their age-matched friends as well as comparisons between their self-reports at five and ten years following their breast cancer daignosis.

Results: Preliminary results for the second question indicate that 87% of this cohort were 50+ at interview. As expected, they reported poorer general health, decreases in physical well-being, sexual activity and increases in the number of chronic conditions than they did as five year survivors. No differences were found for mental well-being or for social support. However, at ten years the women reported poorer self-esteem than at five years; this finding was not expected.

Impact on breast cancer: This is the first population-based cohort study of the impact of breast cancer and its treatment on ten year breast cancer survivors who were diagnosed at age 50 or younger, a segment of the population that is increasing both in number and in life expectancy. Findings from the study will provide valuable information to survivors and their providers regarding the relative impacts of aging and breast cancer treatment on their health as well as points of intervention for the health care system that will be able to reduce the physical side effects of treatment and improve quality of life.

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Reconstructive Breast Surgery in Medically Underserved Women with Breast Cancer: The Role of Patient-Physician Communication

Principal Investigator:
Rose Maly

University of California, Los Angeles

Co-Investigators:
Rose C. Maly, MD, MSPH, Yihang Liu, MD, MS, Allison L. Diamant, MD, MSPH, Amardeep Thind, MD, PhD

Abstract #: A-13

Background: Breast reconstruction (BR) can improve mastectomy patients' psychological outcomes and social functioning, but may be underutilized in low-income, medically underserved women. Lack of information has been suggested as one of the barriers for these women in choosing BR. Effective interactive patient-physician communication may perpetuate or moderate the BR disparity in this vulnerable population.

Objectives: To assess the impact of the patient-physician communication on rates of receipt or planned BR in low income mastectomy women.

Methods: A cross-sectional survey was conducted for low-income women in California who were enrolled in either the federal or the Medi-Cal Breast and Cervical Cancer Treatment Program (BCCTP), aged 18 years and older, and newly diagnosed with breast cancer between 2003 and 2005. A

subset of 327 mastectomy women with non-metastatic disease from a cohort of 924 English- and Spanish-speaking women (61% overall response rate) was identified for the current study. Of these 55% were Latina, 29% white, 5% African-American, and 11% were Asian American. The outcome measured was patient's report of receipt or planned BR. The impact on BR of patient-physician communication, in the form of information-giving by physicians and patient perceived self-efficacy in patient-physician interactions (PEPPI), was assessed, holding a wide range of other potential factors constant.

Results: The overall rate of receipt of/planned BR was 37%. Latinas and Asian Americans were significantly less likely to receive BR (unadjusted odds ratios (OR) =.50, p=.007; OR=.17, p<.001, respectively). Greater physician interactive information-giving and greater patient perceived self-efficacy positively predicted breast reconstruction (adjusted odds ratio (AOR)=1.11, p=0.047; AOR=1.04, p=0.006, respectively), regardless of age, race, education, comorbidity (presence of other significant diseases), body image, interview language, and care in a cancer center. In contrast, older age and Asian/Pacific Island race/ethnicity negatively predicted receipt of BR (AOR=0.92, P<0.001; AOR=0.13, P<0.001, respectively), while the impact of Latina ethnicity disappeared after patient-physician communication was considered.

Conclusion: Patient-physician communication appears to be among the most powerful determinants of BR in low-income, medically underserved women with breast cancer. Of ethnic minority women, Asian American women were less likely to receive BR. However, communication appeared to moderate the negative effect of Latina ethnicity on BR.

Potential Impact on Breast Cancer Patients: Intervening on provider information-giving and patients' self-efficacy in interacting with physicians could result in BR rates more consistent with patient preferences and in improved quality of life in this vulnerable population. This may be particularly true for low-income Latinas, regardless of their preferred language.

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Social and Religious Support in Older Racial/Ethnic Minority Women with Newly Diagnosed Breast Cancer

Principal Investigator:
Yoshiko Umezawa

University of California, Los Angeles

Abstract #: A-14

Background: Support from family and religious community may serve as a vital, immediately available resource for older Latina and African American women with breast cancer (BC) to enhance their quality of life. While sources of support may vary by ethnic groups, BC care typically addresses the individual patient alone or patient-partner pair, without acknowledging the role of cultural diversity in social support. Provider insensitivity to these differences may hinder the development of trusting partnerships between the patient, family, and providers, which may further exacerbate disparities in BC treatment and survival.

Specific Aims: To understand the role of social and religious support in older racial/ethnic minority women with BC.

1) To explain racial/ethnic differences in patterns of social and religious support resources and support-seeking behaviors;

2) To explain racial/ethnic differences in the impact of a new diagnosis of, and treatment for, BC on members of the patient's social network and the patient's reciprocal concerns about this impact;

3) To examine whether racial/ethnic differences in social support during the office visit affect medical communications.

Methodology: The data are derived from a population-based, consecutive survey of 99 Latina, 66 African American, and 92 white women (total: 257 women), aged 55 years or older, newly diagnosed with breast cancer between January and July 2001 in LA County.

Results: Social and Religious Support. Minority women, especially Latinas, were more likely than whites to receive support from children. Women who received less support form partner and children received more support from other family members or friends. Compared to whites, both African Americans and Latinas perceived greater support from religious beliefs; African Americans also perceived greater support from religious community.

Impact of BC on Patient's Network Members: Latinas, especially less-acculturated Latinas,

reported greater impact of BC on their network members compared to whites. Less-acculturated Latinas also reported greater worries about being a burden on their network members. However, Latinas were no less likely than whites to refrain from seeking support. African Americans were no different from whites in the impact in any of these regards.

Medical Communications: Patients received more information from doctors if their companions asked questions.

Conclusions: Contrary to the conventional research framework that presupposes partner as the single most important source of support, children and religion were particularly important sources of support for older minority women with BC. Other family members or friends may be a more flexible source of support who play a complementary role to partner and children. Network members of less-acculturated Latinas may experience extensive care-giving strain, likely originating from family-centered cultural values. Finally, companion's participation during the office visit may enhance medical communications.

Implications: This study informs healthcare policy-makers and providers about at-risk populations of women with BC who experience inadequate social support. The examination of the role of companion during medical visits also gives the scientific basis for the development of partnerships between patient, family, and providers. These culturally sensitive efforts will contribute to decreasing the unequal burden of BC.

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Social Capital, Social Support, and Long-term Quality of Life

Principal Investigator:
Dana Petersen

University of California, Berkeley

Abstract #: A-15

Which matters more: Who you know or where you live? This study seeks to clarify this question, and explores why some long-term breast cancer survivors experience high levels of quality of life while others report physical and mental concerns long after treatment. It is important to discover the reasons why some breast cancer survivors recover more fully and remain healthy while others do not so that public health researchers and practitioners can promote the well-being of all survivors.

The goal of this study is to identify social characteristics of the San Francisco Bay Area neighborhoods in which survivors live that positively affect the quality of their lives. Specifically, the project examines whether differences in survivors' quality of life are predicated by the amount of social capital available in a survivor's neighborhood and/or the amount of social support a survivor receives. Social capital is defined as the degree of social cohesion, interaction, trust, reciprocity, and sense of mutual obligation experienced among members of a neighborhood. Social support is defined as the number of confidants and social connections a survivor has.

Information regarding socio-demographic backgrounds, available social support, perceptions of neighborhood social capital, and quality of life was collected through telephone interviews with approximately 400 ten-year breast cancer survivors. Information about the availability of voluntary and social organizations in women's neighborhoods was also collected. Descriptive statistics are complete.

Findings from this study could provide the basis to promote the development of new public health interventions, public health policy and neighborhood vitalization activities that increase the social capital of neighborhoods. Findings could also be used to support the production of social capital through community-building activities and other infrastructure investments. Community-based activities, programs, interventions and policies may offer support for long-term breast cancer survivors, enhance their quality of life, and diminish some of their functional difficulties.

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South Asian Women and Breast Cancer: What Are Their Needs?

Principal Investigators:
Beth Glenn, Roshan Bastani, and Zul Surani

University of California, Los Angeles and South Asian Cancer Foundation

Abstract #: A-16

Background: Breast cancer is a growing problem among South Asian women in the United States. While increasing numbers of South Asian women are diagnosed with breast cancer every year; few published studies have examined the unique needs of this population. The goal of this study is to conduct semi-structured qualitative interviews to capture information about the needs and experiences of these women.

Method: South Asian women with a previous diagnosis of breast cancer were asked to participate in individual interviews. All interviews were

audiotaped and transcribed. Content analysis was conducted to identify relevant themes pertaining to ten conceptual domains (e.g., spiritual, social, access to medical care, role functioning, cultural beliefs).

Results: Eight South Asian women were recruited from the community to serve as interviewers. Interviewers speak English and a variety of South Asian languages including Hindi, Bengali, Urdu, and Sinhalese among others. Our goal is to conduct interviews with 40 South Asian women. Approximately 75% of planned interviews have been completed. Participant recruitment has been the primary challenge faced by this study. A number of strategies have been employed including advertisements in ethnic print media and outreach at cultural events, health fairs, and religious settings. Study staff have found that many survivors are interested in contributing to research but are hesitant to participate due to the ongoing stigma of breast cancer in the community. Results of interviews conducted to date suggest that cancer continues to be a taboo subject within the community. Related to access to care participants have reported a wide range of experiences with some women having optimal care while others reported difficulties in access related to insurance coverage. There were also a range of experiences pertaining to social support with some women feeling very strongly supported by family and community members to those feeling alienated by the South Asian community due to their cancer status. Furthermore, findings suggest that the women in our sample also had a range of attitudes towards the role of spirituality and religion throughout their breast cancer experience. While some found their religious or spiritual beliefs to be a strong comfort, others felt that religious or spiritual principles negatively impacted their breast cancer experience. Most participants suggested that in-person assistance provided by cancer survivors near the time of diagnosis and throughout the treatment process would be beneficial.

Discussion: Results suggest that the stigma of breast cancer in the community plays a significant role in the experiences of South Asian women related to social and psychological functioning. South Asian survivors may be important components of interventions to help these women adjust to their disease and reduce the negative impact of social stigma.

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Physician Use of Health Professionals and Support Staff in Caring for a Population-based Cohort: Results from the Los Angeles Women's (LAW) Study

Principal Investigator:
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Poster Presenter:

Danielle Rose

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Diana Tisnado, PhD, MPP, Jennifer Malin, MD, PhD, May Lin Tao, MD, Patricia Ganz, MD, Katherine Kahn, MD

Abstract #: A-17

Research objective: Understanding whether physicians, nurses, paraprofessionals, or support staff complete prevalent tasks during patient visits with physicians could reveal useful insights into variations in care and outcomes. Physicians vary in the strategies they use to assure the delivery of high quality care at the lowest costs. Some physicians delegate tasks, while others complete the tasks themselves to optimize efficiency. Little is known about the clinical epidemiology of how office tasks are completed and how variations in who completes these tasks influence patient care and outcomes.

Study design: Using a cross-sectional survey, we queried physicians associated with a population-based cohort of women with incident breast cancer in Los Angeles County. We asked "Who usually performs clinically relevant tasks in your office setting?" (e.g., who: documents medication use, takes vital signs, monitors catheter use, monitors patient signs/symptoms, administers treatment ,monitors patient's progress). Response options were: themselves, other health professionals (RN, LVN, administrative staff or no set policy).

We present the proportion of tasks (n=8) reported as performed by physicians themselves. We tested for bivariate and multivariate associations with physician age, gender, specialty, practice setting (county or medical school; HMO; solo practice; single specialty group, multispecialty group) and large practice size (>=50 physicians). Analyses were weighted for survey non-response and controlled for clustering at the office level.

Population studied: We surveyed all medical oncologists, radiation oncologists, and surgeons practicing in Los Angeles County identified by a

population-based cohort of women with breast cancer retrieved from the cancer registry (76% response rate, n=348).

Principal findings: Of eight tasks studied, we noted substantial variations in physician report of completing tasks themselves: Physicians reported completing 0 tasks (5%), 1-2 tasks (23%), 3-4 tasks (34%), 5-6 tasks (32%), and 7-8 (6%) of 8 tasks. In bivariate analyses, older physicians reported performing a higher proportion of tasks ($p<0.01$); radiation oncologists and surgeons reported performing more tasks compared to medical oncologists ($p<0.001$). Physicians in large practices reported performing fewer tasks ($p<0.05$). In multivariable analyses, radiation oncologists and surgeons were more likely to report performing a higher proportion of tasks compared to medical oncologists ($p<0.001$). Physicians in single specialty groups were associated with a smaller proportion of tasks compared to physicians in solo practice ($p<0.001$).

Conclusions: Significant specialty and practice setting differences exist in the proportion of tasks reported as performed by cancer physicians themselves, as compared with by their designees. Physicians in solo practice appear less likely to delegate tasks compared to other physicians. Medical oncologists appear more likely to delegate tasks compared to other cancer specialists. In multivariate regression, large practice size did not appear to predict proportion of work done by physicians.

Implications for policy, delivery or practice: Understanding variations in practice style and predictors of those variations are the first step in understanding how structure influences care and outcomes. Next steps include linking these data to patient-level data to determine if differences in tasks performed by physicians as compared with their designee influences care or outcomes.

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Underserved Women with Breast Cancer at the End of Life: A CBPR Pilot Study

Principal Investigators:
Shelley Adler and Beverly Burns

University of California, San Francisco and Charlotte Maxwell Complementary Clinic

Co-Investigators:
Kendra Stone (CMCC); Tekeshe Mekonnen (UCSF); Marjorie Kagawa Singer, PhD (UCLA); Judith Luce, MD (San Francisco General Hospital)

Abstract #: A-18

This one-year qualitative pilot study examines the ways in which underserved women with metastatic breast cancer and the diverse individuals who provide their care approach and understand end-of-life issues. The burden of cancer morbidity and mortality is disproportionately borne by low-income women, particularly women of color, but the majority of end-of-life research in the United States to date has focused primarily on white European American, middle class patients in hospitals or extended care facilities. Symptoms relating to psychological distress and existential concerns are even more prevalent than pain and other physical symptoms among those with life-limiting conditions. This pilot study represents an equal partnership between UCSF and the Charlotte Maxwell Complementary Clinic (CMCC)—a state-licensed health clinic providing free complementary and alternative medicine (CAM) treatments to low-income women with cancer.

Semistructured interviews and participant observation were conducted with 10 networks (40 participants) of multiethnic women (CMCC clients, ages 35-59), diagnosed with metastatic breast cancer (3 interviews); the patients' main informal care givers (2 interviews); the patients' main CAM practitioners (1 interview); and the patients' main physicians (1 interview)

Digitally-recorded interviews addressed (a) beliefs, values, and goals regarding the end-of-life transition and (b) quality of communication on end-of-life issues

Qualitative team-based analysis of themes in interview transcripts and field notes using Atlas.ti. Our CBPR pilot study established the strength and mutual benefit of our community-research collaboration and pointed to two areas of community interest regarding future work.

We will (a) design a narrative method, an "ethical will," intended to improve the quality of CMCC clients' end of life by reducing suffering through enhancing meaning and (b) develop a community

peer-based system to support women through the process of completing a Five Wishes booklet (a document that provides a legally binding plan for the way an individual wishes to be cared for during serious illness).

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Factors Influencing Breast Cancer Screening among Older Thai Women

Principal Investigators:
Bulaporn Natipagon-Shah and Mary Jo Clark

Thai Health and Information Services, Inc., and University of San Diego

Abstract #: A-19

Introduction: Asian women have lower rates of breast cancer but higher mortality rates than other racial/ethnic groups due to late diagnosis. Little information has been obtained regarding breast cancer screening in subsets of Asian women such as Thai immigrant women.

Aim of the study: To identify factors that influence mammography screening among Thai immigrant women in Southern California.

Methodology: Focus groups were conducted with Thai immigrant women in Los Angeles and San Diego counties to identify factors that influence participation in mammography screening. Focus group findings were then used to construct a telephone survey questionnaire to determine the extent to which identified factors were present in the Thai population.

Innovative elements and community involvement: Members of the Thai community helped to identify factors influencing mammography use by Thai women. They also validated the researchers' interpretation of the focus group findings and used those findings to construct a telephone survey questionnaire to examine the extent of identified factors in the population. The women also served as a source of contacts for obtaining telephone survey interview participants. Findings of both portions of the study will be used by community members to design subsequent interventions to promote mammography screening in this ethnic population.

Findings: Factors in each of six dimensions of health were found to influence mammography screening in this cultural population. For example, age (a biophysical factor) was found to influence women's beliefs about their chances of developing breast cancer. Similarly, cultural beliefs in karma and family and work responsibilities, both sociocultural factors, limited participation in screening activities.

Potential impact: Knowledge of the extent of the identified factors in the Thai population will help us design programs to improve mammography screening and early diagnosis of breast cancer screening in this population and subsequently to reduce breast cancer mortality rates.

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Fresno Breast Cancer Navigator Pilot Program

Principal Investigators:
John Capitman, Mary Wallace, and John Zweifler

California State University, Fresno Foundation; Central Valley Health Policy Institute; and University of California, San Francisco

Poster Presenter:
Mathilda Ruwe

Abstract #: A-20

Introduction: Breast cancer care involves several complicated steps, which contribute to disparities in care and outcome. A Breast Cancer Navigator (BCN) service offers a practical solution to overcome the barriers to receiving adequate and timely care. However, designs that provide maximum benefits are unknown. Evaluating complex systems requires multiple stakeholder inputs and involves several phases. This study assesses the feasibility of a BCN intervention and addresses phase I-II of a four-stage design.
Presentation goals are to share experience on:

- Program development process (developing culturally relevant materials and recruiting culturally appropriate program staff)
- Community and research partnership development
- Preliminary findings from retrospective and qualitative studies

Methods
Design: This is a process evaluation using a quasi-experiment design; targeting women receiving care at a safety-net hospital who have a suspicious breast lesion or are undergoing treatment. We utilized community participatory research approach and culturally adapted breast cancer navigator model. Phase-I established community and research partnerships, developed culturally relevant materials and recruited program staff and identified service components/barriers. Phase II determined and evaluated components of the BCN program that would provide maximum benefits.

Data sources: chart review (n=150), survivor interviews (n=15), patient interview and care audit (n=72), community and provider consultations.

Factors Examined: The chart review examined a) completion and b) timing of treatment/diagnosis and c) barriers to completing care. The process evaluation focused on Feasibility of best BCN design in terms of a) clinical, and b) community service needs, c) BCN capacity and d) program acceptability. Furthermore, we examined the role health insurance status and race/ethnicity.

Findings: We found great need for culturally adapted material and community involvement in the breast cancer health care process. Our experience has been overall positive and rewarding. However, we found that developing a culturally relevant material and recruiting culturally appropriate program staff requires tremendous efforts and resources. Furthermore, work involving multiple stake holders in developing and evaluating a complex program required on-going negotiation of roles and compromises. Based on the retrospective chart review and the survivors interviews we expect that women of color will have harder time navigating the health care system and face greater social economic barriers. Moreover, we also anticipate finding that women who are UN/underinsured face harder time navigating the health care system.

Conclusion: There are multiple barriers to receiving timely BC diagnosis/treatment; the best possible BCN service will require enhancement of both clinical and social services.

The need for additional and external resources necessitates evaluation of extent of need and optimal design to facilitate quality of care and return on investment.

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Addressing Cultural and Tribal Issues in Breast Cancer

Principal Investigator:
Marlene von Friederichs-Fitzwater and Linda Navarro

University of California, Davis, and Turtle Health Foundation

Abstract #: A-21

Building on a holistic theme of "connecting to nativeness," the UC Davis Cancer Center and the Turtle Health Foundation, Inc., an American Indian nonprofit, are partnering in a pilot study to determine the usefulness of a culturally-sensitive, interactive, multimedia DVD, for use on standard DVD players and TV sets, to increase awareness and knowledge of breast health and breast cancer risk reduction among American Indian women. The principles of indigenous healing (nutrition, exercise/movement, music, spirituality, etc.) have been integrated with Western medicine information in the development and testing of an educational/information intervention on breast health and breast cancer risk reduction in a program entitled the "Mother's Wisdom Breast Health Program." The misperceptions and fears about breast cancer among American Indian women have been addressed by focusing on breast health and a return to traditional healthy lifestyles. This study also acknowledges differences in literacy levels by limiting the amount of text used.

An American Indian Advisory Council of 12 women from eight tribes will guide the project and oversee the testing and evaluation of the Program through American Indian health organizations, tribal councils, and tribal health clinics.

American Indian women will be invited to screenings where they will watch the DVD on a TV monitor and also have an opportunity to test it on laptop computers. They will complete pre- and post-viewing surveys including an evaluation of the program and results will compiled, analyzed and shared through journals, professional meetings, tribal health meetings and the media. The results will also provide the data for further research to determine if increasing awareness and knowledge of breast health and breast cancer risk reduction results in lifestyle changes and screening behaviors.

Our hypothesis is that American Indian women will be receptive to an educational intervention that is culturally sensitive, interactive and visual, thus, such an intervention will increase their awareness of breast health and breast cancer risk reduction. Future studies will examine whether such interventions actually change screening behaviors of American Indian women. Specifically, the research questions we are seeking to answer with this proposed project are:

What specific strategies and methods work in integrating traditional health and disease beliefs and values with Western medicine in an educational intervention to increase awareness of breast health and breast cancer risk reduction among American Indian women?

Will one educational intervention model of breast health and breast cancer risk reduction work across several American Indian tribes in California?

Is a DVD format a viable delivery channel for breast health and breast cancer risk reduction information for American Indian women?

So little is known about risk reduction strategies to prevent the incidence of cancer and mortality throughout Indian Country, making this pilot

study timely with high translational potential if successful.

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Anti-aromatase Activity of Phytochemicals in White Button Mushrooms

Principal Investigator:
Shiuan Chen

Beckman Research Institute of the City of Hope

Abstract #: B-01

White button mushrooms (Agaricus bisporous) are a potential breast cancer chemopreventive agent, as they suppress aromatase activity and estrogen biosynthesis. Therefore, we evaluated the activity of mushroom extracts in the estrogen receptor positive/aromatase positive MCF-7aro cell line in vitro and in vivo. Mushroom extract decreased testosterone-induced cell proliferation in MCF-7aro cells but had no effect on the MCF-10A, a non-tumorigenic cell line. Most potent mushroom chemicals are soluble in ethyl acetate (EA). The major active compounds found in the EA fraction are unsaturated fatty acids such as linoleic, linolenic and conjugated linoleic acids. The interaction of linoleic acid and conjugated linoleic acid (CLA) with aromatase mutants expressed in CHO cells showed that these fatty acids inhibit aromatase with similar potency and that mutations at the active site regions affect its interaction with these two fatty acids.

While these results suggest that these two compounds bind to the active site of aromatase, inhibition kinetic analysis indicates that they are non-competitive inhibitors with respect to androstenedione. Since only CLA was found to inhibit the testosterone-dependent proliferation of MCF-7aro cells, the physiologically relevant aromatase inhibitors in mushrooms are most likely CLA and its derivatives. The in vivo action of mushroom chemicals was demonstrated using nude mice injected with MCF-7aro cells. The studies showed that mushroom extract decreased both tumor cell proliferation and tumor weight with no effect on rate of apoptosis. Therefore, our studies illustrate the anti-cancer activity in vitro and in vivo of mushroom extract and its major fatty acid constituents.

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Assessment of Recurrent Genomic Aberrations Linked to Ethnicity

Principal Investigator:
Koei Chin

University of California, San Francisco

Abstract #: B-02

The incidence of breast cancer in African American women is about 20% lower than that in Caucasians, and the 5-year disease specific survival rate in African Americans is also about 20% lower than in Caucasians. Some the differences in incidence and survival may be explained by socio-economic factors. However, these factors are unlikely to explain why reasons breast tumors in African American tend to be more frequently poorly differentiated and estrogen receptor-negative that tumors in Caucasian women.

The goal of this project is to identify genes in the regions that recurrently exhibit copy number aberrations and deregulation of their expression contributing to the poor prognosis in African American women with breast cancer. The correlation between gene copy number and gene expression will be assessed to identify candidate genes that may be driving the differences in breast tumors between African American and Caucasian women. These analyses may suggest models of the molecular mechanisms that result in higher mortality with poor-differentiation and negative ER status in breast cancers in African-American women. It is important to understand the mechanisms of how these abnormalities occur and how genes are associated with functions that drive the development of breast cancer pathophysiology.

We analyzed ~120 breast tumors in African American women and ~110 breast tumors in Caucasian women for genome copy number abnormalities using array-based comparative genomic hybridization (array CGH) and for gene expression using GeneChip (U133A, High Throughput System, Affymetrix). The samples were collected from the University of California, San Francisco and the University of Alabama at Birmingham. We assessed the recurrent abnormalities of genome copy numbers and deregulated gene expression to identify genomic events that might contribute to cancer pathophysiology. The genomic loci that exhibit recurrent genome copy number aberrations (CNAs) in African American women are similar to genome CNAs in Caucasian women. These are briefly copy number gains of chromosomes 1q, 8p11-12, 8q, 10p, 11q13-14, 12q13-14, 17q11-12, 17q21-24, 20q13 and copy number losses of 1p, 3p, 8p, 13q, 16q, 17p. Also we found coamplification of 8q24 and 20q13 and

coamplification of 11q12-14, 12q13-14, 17q11-12 and 17q21-24 which regions include ERBB2, MYC, CCND1 and MDM2. The results suggest there are some differences at the level of genome copy number and at the extent of high-level copy number gains between breast cancers in African American and Caucasian women. Most samples from African Americans and Caucasians were successfully segregated into three genomic subtypes (1q /16q, amplifying and comples) by unsupervised hierarchical clustering for genome copy number.

We will explore the detail of combined analyses of genome copy number and gene expression and present the significance of our study for breast cancers in African American women.

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Body Size and Premenopausal Breast Cancer Risk in a Multiethnic Population

Principal Investigator:
Esther John

Northern California Cancer Center

Co-Investigators:
Esther M. John, Meera Sangaramoorthy, Jocelyn Koo, Northern California Cancer Center

Abstract #: B-03

Background: There is increasing epidemiologic evidence that hormone-related factors may be more strongly associated with estrogen receptor (ER) and progesterone receptor (PR) positive breast cancer than ER- and PR- tumors. The data for obesity and other body size measures are limited and inconsistent, particularly in young women. Few studies have assessed associations with body size in non-white women who not only have a higher prevalence of obesity and abdominal adiposity, but also are more likely to be diagnosed with ER- and PR- tumors. We examined obesity, weight gain, and body fat distribution in relation to premenopausal breast cancer defined by hormone receptor status in a large population-based case-control study in Latina (L), African American (AA) and non-Hispanic white (W) women.

Methods: Breast cancer cases aged ≥35 years and diagnosed from 1995-2002 were identified through the SEER cancer registry of the San Francisco Bay area; controls were identified through random-digit dialing. For premenopausal women, interview data, anthropometric measurements, and information on estrogen receptor (ER) and progesterone receptor (PR) status (for cases) were available for 564 cases (L: 313, AA: 127, W: 124) and 812 controls (L: 486, AA: 160, W: 166). Associations with body size measures were assessed estimating odds ratios (OR) and 95% confidence intervals (CI) by unconditional logistic regression, adjusting for age, education, family history of breast cancer, personal history of benign breast disease, parity, breast-feeding, physical activity, alcohol consumption, and caloric intake. Associations were assessed for breast cancer defined by joint ER and PR status and specific racial/ethnic groups.

Results: Among controls, the prevalence of obesity (BMI ≥30) was highest in African Americans (41%), intermediate in Latinas (36%), and lowest in Whites (20%). Similar differences by race/ethnicity were seen for current weight, weight gain since the 20s, waist and hip circumference, and waist-to hip ratio, a measure of abdominal adiposity. Height was associated with increased breast cancer risk (quartile 4 vs. quartile 1: OR=1.76, CI=1.23-2.52) and the association did not vary by hormone receptor status or race/ethnicity. For other body size measures, inverse associations were limited to ER+PR+ tumors (n=306). Consistent with other studies, significant trends of decreasing risk were associated with increases in BMI (≥30 vs. <25: OR=0.41, CI=0.28-0.60), current weight (Q4 vs. Q1: OR=0.40, CI=0.25-0.62), weight in the 20s (Q4 vs. Q1: OR=0.71, CI=0.48-1.05), and weight gain (>20 vs ≤3 kg: OR=0.33, CI=0.20-0.53). Furthermore, risk reductions were of similar magnitude in the three racial/ethnic groups. For ER+PR+ tumors, we also found inverse associations with measured waist (Q4 vs. Q1: OR=0.64, CI=0.42-0.98) and waist-to-hip ratio (Q4 vs. Q1: OR=0.69, CI=0.45-1.06). However, after adjustment for current BMI, no significant trends of decreased risk remained.

Conclusions: These findings support other epidemiologic studies in mostly white women that high current weight, BMI and weight gain are inversely associated with breast cancer risk in premenopausal women. Risk reductions were limited to women with ER+PR+ tumors, and were similar in Latina, African American and White women. Since ER/PR status differs by race/ethnicity, the consideration of hormone receptor status may be important when assessing racial/ethnic differences in risk factor profiles.

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Development of Data Linkage Strategies to Study Early Life Exposures and Breast Cancer in Young California Women

Principal Investigator:
Peggy Reynolds

Northern California Cancer Center

Poster Presenter:
Susan Hurley

Abstract #: B-05

Background: Evidence is emerging for the importance of pre- and peri-natal environmental exposures in the etiology of adult-onset diseases, including breast cancer. Such factors, however, are extremely difficult to study given that such exposures are impossible, or nearly impossible to self-report. Consequently, the development of methods to link adult health outcome data, birth data, and historical socioeconomic (SES) and environmental contaminant data, could prove extremely useful in studying such exposures.

Objective: As part of a larger case-control study aimed at evaluating the association between breast cancer risk and early-life exposures, the purpose of this analysis is to evaluate the feasibility of linking female breast cancer cases to California birth records.

Methods: All cases of breast cancer diagnosed in California women, 1988-2003 who were born 1960-1969 were identified from the California Cancer Registry (CCR). A group of women with other cancer diagnoses (i.e., non-reproductive cancers and non-smoking-related cancers) were similarly selected to serve as controls. Linkage of female cancer cases to their birth records is complicated by name changes due to marriage and incomplete data on birthplace available in the CCR. The CCR has a maiden name available for only 15% of married women diagnosed with breast cancer. Birthplace is available for less than 60% of the cases. In order to maximize the success of our CCR linkage to birth records, we have gathered marriage data both from the state and from 11 of the 12 largest counties in California. These data are being linked to the CCR data to harvest additional maiden name and birthplace information in order to improve the success of our linkage to birth records, thereby increasing our study's sample size.

Results: Linkages of the CCR to the marriage and birth data are currently underway. Initial linkage of cases listed as never married or married with a maiden name available in the CCR resulted in an overall match rate of approximately 41%, with success considerably higher (63%) among those records with a California birthplace listed in the CCR. After augmenting CCR records with additional information on maiden name and birthplace from linkages to the marriage files, we have increased the number of cases linked to a birth record (and therefore eligible for our case-control study) by more than 50%.

Conclusions: Preliminary results suggest that augmenting CCR data with county and statewide marriage data is useful for improving our ability to link female cancer cases to California birth records, thereby enhancing our ability to study early life exposures in breast cancer etiology.

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Diabetes and Risk of Breast Cancer in Asian American Women

Principal Investigator:
Anna H. Wu

University of Southern California

Co-Investigators:
Anna H. Wu, Mimi C. Yu, Chiu-Chen Tseng, Frank Z. Stanczyk, Malcolm C. Pike

Abstract #: B-06

The role of diabetes in the etiology of breast cancer in Asian Americans is not known. We investigated the relation between diabetes and breast cancer risk in a population-based case-control study in Los Angeles County that included 1,248 Asian American women with incident, histologically confirmed breast cancer and 1,148 control women, who were frequency matched to cases on age, Asian ethnicity and neighborhood of residence. The relation between history of diabetes and serum concentrations of estrogens, androgens and sex hormone-binding globulin (SHBG) was investigated in 212 postmenopausal control women.

A history of diabetes was statistically significantly associated with breast cancer risk (odds ratio (OR)=1.68, 95% confidence interval (CI)=1.15-2.47) after adjusting for reproductive and other factors. This increased risk was unchanged after further adjustment for body mass index (BMI) and waist-hip ratio (WHR). We found a stronger diabetes-breast cancer association in women with lower BMI (<=22.7) (adjusted OR= 3.50, P=0.011) than those with higher BMI (>22.7) (adjusted OR=1.39, P=0.23) but this difference in ORs was not statistically significant. Our results also show that the diabetes-breast cancer association was observed only in low/intermediate soy consumers (OR=2.48, P=0.0008) but not among

high soy consumers (OR=0.75, P=0.41) (P interaction =0.014). Controls who were diabetic showed significantly lower SHBG (20%) (P=0.02) but higher free testosterone levels (26%) (P=0.08) than women without such a history after adjusting for BMI and WHR. Our results support the hypothesis that diabetes may have a role in the development of breast cancer, influencing risk via both sex hormone and insulin pathways.

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Differential Effects of the Isothiocyanate Sulforaphane on Breast Cancer and Normal Human Mammary Epithelial Cells

Principal Investigator:
Olga Azarenko

University of California, Santa Barbara

Abstract #: B-07

Isothiocyanates (ITCs) are important anticarcinogenic phytochemicals abundant in cruciferous vegetables, such as broccoli, broccoli sprouts, cabbage, and cauliflower. Recent studies have revealed that ITCs exert cytotoxic effects on various cancer cell lines through the inhibition of cell growth, induction of cell cycle arrest and activation of cell death, and that some ITCs might be selective exclusively towards cancer cells.

In this study we compared the effects of major ITC, sulforaphane (SFN) on breast cancer (MCF7) and normal human mammary epithelial cells (HMEpC). We determined that SFN inhibited cell proliferation ~2-fold more potently in MCF7 than in HMEpC cells (IC50 SFN: 9 mM and 19 mM, respectively). We also found that ³15 mM SFN blocked MCF7 cells in prometaphase stage of mitosis by disrupting spindle formation and preventing proper chromosome segregation. Interestingly, SFN did not induce mitotic arrest in HMEpC cells at these concentrations; however, some aberrant mitotic spindles with abnormal chromosome segregation were observed. Cell cycle analysis by flow cytometry confirmed that SFN induced G2/M phase delay in MCF7 cells (15 mM SFN, 24 h: 46 ± 1.5 % in G2/M vs. 29 ± 1.3 % in controls), while the cell cycle of HMEpC cells was not affected. Furthermore, SFN induced microtubule depolymerization in interphase MCF7 and HMEpC cells in a concentration dependent manner. MCF7 cell growth inhibition was accompanied by a significant time- and dose-dependent induction of apoptosis. Surprisingly, high concentrations of SFN (>15 mM, 24h) significantly reduced the viability of HMEpC cells. Our results indicate that low concentrations of SFN may trigger cell cycle arrest in mitosis by perturbing normal microtubule polymerization and suppressing microtubule dynamic instability, leading to apoptosis in MCF7 cells. However, high concentrations of SFN also inhibited proliferation of HMEpC cells and disrupted cytoplasmic microtubule polymerization without blocking cells in mitosis.

These results indicate that high concentrations of SFN are active in both normal and cancerous cells. Further experiments are under way to elucidate the mechanisms of action of SFN on human breast cancer cells vs. normal human mammary epithelial cells. Our data lead to important questions regarding proper implementation and suitability of isothiocyanates and SFN in particular in cancer chemoprevention.

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EPHA2 Expression is Associated with Breast Cancer Risk

Principal Investigator:
Richard Neve

Lawrence Berkeley National Laboratory

Co-Investigators:
Richard M. Neve[1,2], Madhu Macrae[1], Rick Baehner[1], Karen Chew[1], Frank McCormick[1] and Joe W Gray[1,2].

[1]Life Sciences Division, Lawrence Berkeley National Laboratory, [2]Department of Laboratory Medicine and Comprehensive Cancer Center, University of California, San Francisco

Abstract #: B-08

Metastases, rather than primary tumors, are responsible for most breast cancer related deaths. To understand the pathogenesis of this disease we need to identify genes which are directly involved in the process of metastasis. Our laboratory has identified a cell surface sensor, or receptor, (EPHA2) that is strongly associated with metastasis in the breast. We present data on the mechanisms by which this receptor controls normal and malignant biology of the breast.

We sought to evaluate the biologic role of EPHA2 with respect to tumor cell invasion. We have looked at EPHA2 biology using functional assays to asses the invasive potential of the cells. All the EPHA2-positive cells exhibited an aggressive morphology, in agreement with our published measurements of invasion. In contrast, cells lacking EPHA2 formed more differentiated structures, either grape-like strings of cells or disorganized acini-like structures. By applying recombinant EFNA1 (B61, the ligand for EPHA2) or using RNAi

to "knock-down" EPHA2 receptor levels in each cell line in 3D we show EPHA2 is required to maintain invasive morphology in most of the cell lines tested.

Furthermore, using co-culture assays we show that presentation of EFNA1 by a neighboring cell is sufficient to restrict highly invasive EPHA2-positive tumor cells to islands of growth with distinct borders and more differentiated morphology.

In addition we will present data showing that another cell surface receptor, ERBB3, is found reciprocally expressed with EPHA2 in breast tumors and acts to suppress cell invasion. We have evidence that reciprocal levels of EPHA2 and ERBB3 define distinct biologically and clinically relevant breast tumor subsets reflective of invasiveness and clinical outcome. The clinical implications are that EPHA2 and ERBB3 may have utility as diagnostic markers as well as representing distinct therapeutic targets.

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Grape Seed Extract as a Natural Aromatase Inhibitor

Principal Investigator:
Melanie Palomares

Beckman Research Institute of the City of Hope

Co-Investigators:
Melanie R. Palomares, M.D., M.S.; Sheryl Phung, M.S.; Elizabeth T. Eng, Ph.D.; Ikuko Kijima, M.S.; Timothy W. Synold, Pharm.D.; Shiuan Chen, Ph.D.

Abstract #: B-09
Suppression of estrogen through inhibition the enzyme aromatase is thought to have potential for breast cancer risk reduction. While pharmaceutical agents have an established role in breast cancer treatment, foods and dietary compounds are now also being explored for cancer prevention. The purpose of this research is to screen foods for aromatase inhibitory activity, identify the chemicals responsible for that activity, perform preclinical studies evaluating the ability of a food extract to inhibit aromatase-mediated cancer development, and translate promising natural aromatase inhibitors into clinical trials.

Our laboratory tested seven fruit juices and found that juice from red grapes was the most effective in inhibiting aromatase activity. We subsequently found that extracts of red grape juice and wine suppressed aromatase in a dose-dependent manner. We demonstrated that the extracts also suppressed proliferation of an aromatase over-expressing, estrogen receptor-positive breast cancer cell line, MCF-7aro. Furthermore, oral administration of the extract completely halted aromatase-induced hyperplasia in a mouse model of aromatase-mediated breast cancer. We then showed that procyanidin B dimers, the major phytochemicals in the seeds and skins of grapes, are the chemicals responsible for the anti-aromatase activity. Lastly, we performed feeding experiments with grape seed extract and demonstrated inhibition of aromatase-mediated mammary tumor growth in mice.

Based on this preclinical data, we hypothesize that post-menopausal women could reduce their breast cancer risk with a grape seed extract dietary supplement through suppression of estrogen. A Phase I chemoprevention trial to evaluate the anti-aromatase activity of grape seed in post-menopausal women is underway to test this hypothesis. The design of this clinical trial will be presented.

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Grape Seed Extract is an Aromatase Inhibitor and a Suppressor of Aromatase Expression

Principal Investigator:
Shiuan Chen

Beckman Research Institute of the City of Hope

Abstract #: B-10
Aromatase is the enzyme that converts androgen to estrogen. It is expressed at higher levels in breast cancer tissues than normal breast tissues. Grape seed extract (GSE) contains high levels of procyanidin dimers that have been shown in our laboratory to be potent inhibitors of aromatase. In this study, GSE was found to inhibit aromatase activity in a dose-dependent manner and reduce androgen-dependent tumor growth in an aromatase-transfected MCF-7 (MCF-7aro) breast cancer xenograft model, agreeing with our previous findings.

We have also examined the effect of GSE on aromatase expression. RT-PCR experiments showed that treatment with 60 µg/ml of GSE suppressed the levels of exons I.3-, PII-, and I.6-containing aromatase mRNA in MCF-7 and SK-BR-3 cells. The levels of exon I.1- containing mRNA, however, did not change with GSE treatment. Transient transfection experiments with luciferase-aromatase promoter I.3/II or I.4 reporter vectors showed the suppression of the promoter activity in a dose-dependent manner. The GSE treatment also led to the down-regulation of two transcription factors, cAMP-responsive element binding protein-1 (CREB-1) and glucocorticoid receptor

(GR). CREB-1 and GR are known to up-regulate aromatase gene expression through promoters I.3/II and I.4, respectively. We believe that these results are exciting in that they demonstrate GSE to be potentially useful in the prevention/ treatment of hormone-dependent breast cancer through the inhibition of aromatase activity as well as its expression.

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Grapefruit Intake and Risk of Breast Cancer in Postmenopausal Women

Principal Investigator:
Malcolm C. Pike

University of Southern California

Poster Presenter:
Kristine Monroe

Abstract #: B-11

New findings stemming from our previously funded CBCRP research suggests that grapefruit intake may be associated with an increased risk of breast cancer among postmenopausal women.

The inhibitory effect of grapefruit juice on the intestinal cytochrome P450 3A4 enzyme system was discovered accidentally in 1989 during a study designed to test the effect of ethanol on a calcium-channel blocker. Grapefruit juice was given to subjects to mask the taste of the ethanol. Subsequent investigations have found that grapefruit interacts with more than 60% of orally administered drugs leading to elevation of serum concentrations. An effect is seen with the whole fruit as well as the juice and chronic consumption may enhance the magnitude of the effect.

Since 1989, the list of drug interactions with grapefruit juice has expanded to include oral estradiol and progesterone. U.S. Food and Drug Administration (FDA) mandated labeling for estrogen and estrogen-progestin products for postmenopausal women now contains warnings that grapefruit juice may increase plasma concentrations of estrogens. Since endogenous estrogens are metabolized in the same manner as exogenous estrogens, we conducted a study to determine whether endogenous levels were significantly affected by grapefruit consumption. We found a statistically significant positive association between whole grapefruit intake (we had no information on grapefruit juice intake) and endogenous serum estrogen level among 242 naturally postmenopausal Latina women not taking menopausal hormone therapy.

Since it is well established that serum estrogen concentration is associated with postmenopausal breast cancer risk, it is plausible that regular intake of grapefruit would increase a woman's risk of breast cancer. Therefore, we recently investigated whole grapefruit intake in association with breast cancer risk among postmenopausal women in the Hawaii-Los Angeles Multiethnic Cohort Study, a prospective cohort that includes over 50,000 postmenopausal women from five racial/ethnic groups. A total of 1,657 incident breast cancer cases were available for analysis.

Grapefruit intake was significantly associated with an increased risk of breast cancer (relative risk (RR)=1.30, 95% confidence interval (CI) 1.06-1.58) for subjects in the highest category of intake, i.e., one-quarter grapefruit or more per day, compared to non-consumers (ptrend = 0.015). The relative risk of breast cancer associated with consumption of ¼ grapefruit or more per day compared to non-consumers was 44% higher among women who had never used hormone therapy; 36% higher in current estrogen therapy users, and 27% higher among current estrogen+progestin therapy users. The risk of breast cancer associated with consumption of grapefruit was 32% higher among lean/ normal weight women and 26% higher among overweight/obese women. Taken together, these results suggest that the risk of breast cancer associated with grapefruit intake is stronger for subgroups of women with lower circulating estrogen levels.

To our knowledge, this was the first report of a commonly consumed food that may increase the risk of breast cancer. If confirmed, these new findings have important public health implications.

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Hereditary Breast Cancer and Novel Hispanic BRCA Mutations: A Recurring BRCA1 Genomic Rearrangement in High-risk Hispanic Families

Principal Investigator:
Jeffrey Weitzel

Beckman Research Institute of the City of Hope

Abstract #: B-12

Goal of the research project: Breast cancer is the most commonly diagnosed cancer in Hispanic women, and is the leading cancer cause of death in this population. Mutations in the BRCA genes are associated with 5-10% of breast cancer cases. The lifetime risk of developing breast cancer in individuals with a BRCA mutation may be as high as 85%. Large rearrangements, dele-

tions or duplications of a portion of a gene that are not detectable by the standard sequencing test, account for up to 15% of deleterious BRCA mutations. There is little information on BRCA mutations in Hispanics. The purpose of this study was to identify rearrangements in the BRCA genes in a cohort of high-risk Hispanic patients. Work performed to date: DNA from 106 Hispanic patients without an identifiable BRCA mutation by standard commercially available techniques was analyzed by a multiplexed quantitative differential PCR (MQDP), a new method to identify large rearrangements. Long range PCR was used to confirm deletion events and to clone and sequence genomic breakpoints, and splicing patterns were derived by sequencing cDNA from the RNA of affected individuals. The extent of shared chromosome markers (e.g. haplotype analysis) was conducted to confirm ancestral links among unrelated families with the same mutation.

Results to date: The same deletion of BRCA1 exons 9 through 12 was identified in five unrelated families. Long range PCR and sequencing indicated a deletion event of 14.7 kb. A 3-primer PCR assay was designed based on the deletion breakpoints, identified within repetitive sequence elements that are prone to rearrangements (AluSp in intron 8 and AluSx in intron 12). Haplotype analysis confirmed common ancestry. Analysis of cDNA demonstrated direct splicing of exon 8 to exon 13 resulting in a frameshift mutation and premature truncation of the BRCA1 protein, typical of deleterious mutations.

Potential impact of work on breast cancer research and patients: We identified and characterized a novel large BRCA1 deletion in five unrelated families–four of Mexican ancestry and one of African and Native American ancestry, suggesting common ancestry. This BRCA1 rearrangement was detected in 3.8% (4/106) of BRCA sequence negative Hispanic families and may account for a substantial proportion of high-risk Hispanic families. An assay for this mutation should be considered for BRCA sequence negative high-risk Hispanic patients. Additional studies are ongoing to determine the prevalence of this rearrangement among similar cohorts. Although the incidence of breast cancer in Hispanic women is less than that for non-Hispanic white women, the results of this study and of our previous work suggest that BRCA mutations may account for a higher proportion of the breast cancers in young Hispanic women.

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Leptin-receptor Gene Polymorphisms and Body Composition among African American, Caucasian, and Hispanic Women

Principal Investigator:
Catherine Carpenter

David Geffen School of Medicine at University of California, Los Angeles

Abstract #: B-13

Introduction: Obesity increases the risk of developing breast cancer after menopause, but before menopause, obesity is protective. Genes the increase the likelihood of obesity may also be related to breast cancer.

Objective: We studied the leptin-receptor gene (LEP-R) in relationship to body composition because the leptin-receptor may share functional pathways with breast cancer.

Methods: We conducted a candidate gene study of LEP-R among two study populations: a clinical sample of 36 healthy, overweight to obese postmenopausal women of Caucasian and African American ancestry (age 45 to 72 y); and, a population-based sample of 729 pre- and postmenopausal healthy women (age 35 to 79 y) who were Caucasian, African American and Hispanic. Both studies measured waist and hip circumferences, height and weight. The clinical study assessed total body fat using DEXA (dual-energy X-ray absorptiometry). For the clinical study, we genotyped LEP-R variants, K109R, Q223R with restriction endonuclease digestion; and K656N using direct sequencing. We genotyped the population sample using Taqman. We adjusted statistical association models for age (clinical sample), or, for age and menopausal status (population-based sample).

Results: In the clinical sample, we observed an association between percent body fat and the K109R variant (age-adjusted p=0.01), that appeared to be limited to African American women. In the population sample, we observed associations of K109R with waist-to-hip ratio (WHR) among Caucasians (p = 0.03) and with waist circumference among African Americans (p = 0.03). We stratified the population sample by body-mass index (BMI) greater than or equal to 30.0, the clinical cut-point for obesity. Among Caucasian obese women (BMI > 30.0), both WHR (p=0.006) and hip circumference (p=0.05) were associated with K109R, while waist (p = 0.009) and hip (p=0.06) were associated among African American obese women. The other LEP-R variants Q223R and K656N were not associated in either

study sample. No associations were observed for Hispanic women.

Conclusion: The findings suggest that the LEP-R variant, K109R, may be associated with body fat and body fat distribution among overweight to obese women.

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BRCA1, Oral Contraceptives, Reproductive Factors and Breast Cancer

Principal Investigator:
Giske Ursin

University of Southern California

Abstract #: B-14

Background: Women with genetic changes (mutations) in the breast cancer susceptibility genes (BRCA1/2) are at a high risk of developing breast or ovarian cancer. We investigated the association between hormonal factors such as nulliparity, late age at first full-term pregnancy, lack of breastfeeding, and use of oral contraceptives and breast cancer risk in women with BRCA1/2 mutations. Methods: Case patients were 1,469 female breast cancer patients from Los Angeles County aged 20-49 years at time of diagnosis with breast cancer. We also recruited 444 control subjects without breast cancer who were of the same race and age and from the same neighborhoods as the case patients. We identified mutations in the BRCA1/2 genes among the case patients. We compared case patients with a BRCA1/2 mutation as well as those without a mutation with the control women with respect to the hormonal factors.

Results: An increasing number of full-term pregnancies were associated with a decreased breast cancer risk regardless of BRCA1/2 mutation status. However, such protection appeared to be limited to women who had their first full-term pregnancy before age 25. Longer breastfeeding duration was statistically significantly protective in the BRCA1/2 non-carriers, but this protective effect was not observed in the BRCA1/2 carriers. Oral contraceptive use overall was not associated with risk of breast cancer in any subgroup, and the use of newer formulations of oral contraceptives was associated with a decreased risk of breast cancer in the BRCA1 carriers as well as the BRCA1/2 non-carriers, but this effect was not evident among the BRCA2 carriers. Conclusions: The protective effect of parity was similar in BRCA1/2 mutation carriers as in non-carriers, while the effect of breastfeeding was not. Use of current formulation of oral contraceptives was not associated with increased breast cancer risk in women regardless of BRCA1/2 mutation status. Further confirmation of this latter association will be important from a public health perspective given the high prevalence of oral contraceptive use in the US.

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Tamoxifen, Soy, and Lifestyle Factors in Asian American Women With Breast Cancer

Principal Investigator:
Anna H. Wu

University of Southern California

Co-Investigators:
Anna H. Wu, Malcolm C. Pike, Lee D Williams, Darcy Spicer, Chiu-Chen Tseng, Mona I. Churchwell, Daniel R. Doerge

Abstract #: B-16

Affiliations of authors: A.H.Wu, M.C. Pike, C.C. Tseng, Department of Preventive Medicine, University of Southern California Keck School of Medicine, Los Angeles, California 90089. D. Spicer, Department of Medicine, University of Southern California Keck School of Medicine, Los Angeles, California 90089. L.D. Williams, M.I. Churchwell, D.R. Doerge, National Center for Toxicological Research, U.S. Food and Drug Administration, Jefferson, AR 72079.

Background: Soyfoods have been a staple in Asia for centuries but the consumption of this food in the west is recent. Intake of soy among women at high risk for or with breast cancer has become a public health concern because genistein, a major component of soy, has weak estrogenic effects on breast epithelium, and has been found to negate the benefit of tamoxifen in some animal and in vitro studies.

Methods: We conducted a cross-sectional study in Asian Americans with breast cancer who were tamoxifen users (n=380) to investigate the association between soy intake and circulating levels of tamoxifen and its metabolites (N-desmethyl tamoxifen (N-DMT), 4-hydroxytamoxifen (4-OHT), and 4-hydroxy-N-desmethyl-tamoxifen (endoxifen).

Results: Serum levels of tamoxifen or its metabolites were unrelated to self reported intake of soy or serum levels of isoflavones. Blood levels of tamoxifen were 81% higher in postmenopausal women aged 65 or older compared to premenopaual women aged 45 or younger (P=0.005); similar patterns of results were observed for the tamoxifen metabolites. Levels of N-DMT were

27% (P=0.03) lower among women in the highest tertile of body mass index (BMI) (kg/m2) (>24.4) compared to those in the lowest category (BMI <=21.5). Women who used hypertensive medications had higher levels of tamoxifen (P=0.02) and of N-DMT (P=0.04) compared to non-users.

Conclusion: We found no evidence that soy intake adversely affected levels of tamoxifen or its metabolites. However, age, menopausal status, BMI and use of hypertensive medications significantly influenced circulating levels of tamoxifen and its metabolites in this population.

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Uncovering Novel Post-translational Modifications in Human Breast Cancer Estrogen Receptor

Principal Investigator:
Christopher Benz

Buck Institute for Age Research

Poster Presenter:
David Britton

Co-Investigators:
D. Britton, C. Atsriku, G. Scott, B. Richter, M. Baldwin, B Schilling, B. Gibson, C. Benz.

Abstract #: B-18

There is more than 30 years of accumulated evidence supporting the critical role of activated estrogen receptor alpha (ERa) in driving development of most human breast cancers and serving as the prime molecular target for lifesaving endocrine therapeutics such as anti-estrogens and aromatase inhibitors. While crystallographic and nuclear magnetic resonance structure analyses have provided critical understanding of how estrogenic and anti-estrogenic ligands modify the secondary structure of the C-terminal ligand-binding domain of ERa, lack of structural information about the N-terminal region of ERa and limited availability of sufficiently powerful analytical tools to catalog ERa post-translational modifications (PTMs) have hampered our understanding of ligand-dependent and ligand-independent ERa activation.

Nearly 40 residues across the 595 amino acids (67 kDa) of human ERa are suspected of undergoing PTMs in vivo, including 8 putative phosphorylation sites which are thought to regulate many ERa functions, particularly gene transactivation. The highly disordered N-terminal 184 amino acids of ERa encompass its critical ligand-independent activation function domain, AF1 (aa 38 to 149), and 14 serine residues of which only five are known to be phosphorylated (S102, S104, S106, S118, S167) in response to activators of receptor tyrosine kinases (e.g. EGF/IGF) and other growth factors that directly activate such intracellular serine phosphorylating kinases as Erk1/2, Akt, PKA and PKC. Modern biochemical and immunochemical methods capable of detecting phospho-amino acids have severe limitations, including presupposed knowledge of the modified amino acid of interest and availability/quality of site- and modification-specific antibodies.

To address these limitations we have extended modern mass spectrometry (MS) and proteomic approaches, including use of ESI-MS/MS (Q-STAR/4000 Q-TRAP) and vMALDI-MSn (vMALDI-LTQ), to interrogate potential phosphorylation sites within the N-terminal domain of ERa extracted and purified from human breast cancer cells (MCF7) and to compare the effects of ligand-dependent (estradiol, E2) and ligand-independent growth factor (EGF) stimulation. These mass spectrometry approaches allowed us to achieve >90% coverage of full-length ERa and analysis (MS and MSn) of all N-terminal serines. Immunoblotting and MS analyses allowed semi-quantitative detection of S104/S106, S118 and S167 phosphorylation changes in ERa after MCF7 exposure to E2 or EGF.

Remarkably, we identified by MS and MSn a novel serine site (S154) showing approximately 5 fold increase in phosphorylation in response to E2 as well as an Erk-activating dose of the vitamin K quinone, menadione (K3); we also confirmed the absence of phosphorylation on other candidate N-terminal serine sites. An antibody specific to phospho-S154, now under development, will facilitate clinical evaluation of this PTM as found in ER-positive human breast cancers. In sum, this novel finding illustrates the analytical power and potential clinical impact of applying comprehensive proteomic and MS strategies to interrogate ERa PTM from human breast cancer cells; hopefully these findings will shed light on the types of environmental and endogenous stimuli involved in human breast cancer development.

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Session B: Cause and Prevention

Elucidating the Mechanism by which the Dietary Indole I3C Can Inhibit Breast Cancer by Regulation of Estrogen Receptor-Alpha

Principal Investigator:
Crystal Marconett

University of California, Berkeley

Abstract #: B-19
The vast majority of breast cancers are classified as estrogen-sensitive, with the ability to respond and grow in the presence of estrogen. The two estrogen receptor (ER) subtypes, ERalpha and ERbeta, are expressed in these cancers, are able to bind to their estrogen ligand, dimerize, and act as transcription factors within the nucleus. ER-alpha can serve as an activating transcription factor for classical target genes, such as Progesterone Receptor (PR), and more recently as an activator of genes such as Insulin-like Growth Factor Receptor 1 (IGF1R) or Insulin Receptor Substrate-1 (IRS-1), which are involved in tumor metastasis.

The ability of breast cancer cells to respond to estrogen is critical to their proliferative capacity. Gulcobrassicin is a naturally occurring compound in vegetables of the Brassica genus, a plant group, which includes broccoli and brussels sprouts. Indole-3-Carbinol (I3C) is a dietary indole, which is released from the compound glucobrassicin during ingestion.

Our lab has previously shown that I3C transcriptionally downregulates ER-alpha expression in the estrogen responsive breast cancer cell line MCF7, having an effect on both the proliferation and growth of hormone sensitive breast cancers.

We are currently isolating the transcription factor(s) responsible for the downregulation of ERalpha in order to elucidate the mechanism by which I3C can inhibit hormone sensitive breast cancer.

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Activity Probes for Monitoring Cytochrome P450 Induction and Drug Interactions in Vivo

Principal Investigator:
Benjamin Cravatt

The Scripps Research Institute

Poster Presenter:
Aaron Wright

Abstract #: C-01
The cytochrome P450 superfamily of enzymes oxidizes several exogenous and endogenous compounds including drugs, carcinogens, fatty acids, and steroids. Additionally, mutations in many P450 genes cause inborn errors of metabolism and contribute to increased risk of cancer. Variations in expression level and activity of several P450 enzymes between individuals can also lead to differences in metabolism and carcinogen formation.

We have created derivatives of 2-ethynylnaphthalene and phenylisothiocyanate as “click chemistry”-compatible activity-based probes for monitoring NADPH-dependent P450 activity in liver microsomal proteomes. These probes were found to label numerous P450s in an activity-based manner both in vitro and in living animals, where the impact of chemical inducers of P450 expression in liver could be detected. Furthermore, in experiments synonymous with drug-drug interactions, the impact on P450 activity due to multiple xenobiotics could be monitored by alterations in probe labeling.

Further work to develop an in vivo chemical probe for monitoring P450 activity may facilitate the determination of those P450 enzymes responsible for carcinogen formation or drug metabolism which in turn could be used for developing more efficacious therapeutics. An activity-based chemical probe approach may help facilitate the determination of those compounds being metabolized by P450 enzymes to carcinogenic compounds that are known inducers of breast cancer pathology, as well as the P450 enzymes responsible for metabolism of breast cancer therapeutics.

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Alteration of Topoisomerase II-alpha Gene in Human Breast Cancer and Its Association with Responsiveness to Anthracycline-based Chemotherapy

Principal Investigator:
Michael F. Press

University of Southern California

Abstract #: C-02

Background: Topoisomerase II-alpha (TOP2A) gene amplification, and not HER2 amplification, may be the predictive marker for responsiveness to anthracycline chemotherapy (AC).

Methods: To address this issue we performed a test set-validation set series of analyses. Amplification of TOP2A and HER2 was evaluated by fluorescence in situ hybridization (FISH) in patients with metastatic breast cancer who participated in a randomized trial (H0648g, n = 469) of anthracycline-based chemotherapy with or without trastuzumab (trade name Herceptin). This group represented the test set. To validate our observations in the H0648g test set we analyzed breast cancers from two other, large, randomized clinical studies of anthracycline-based chemotherapy; one with HER-2 amplification and trastuzumab-based therapy (BCIRG006, n = 3,222) and one without HER-2 amplification and combination-based chemotherapy (BCIRG005, n = 3,298), comparing TOP2A status with clinical outcome. Both of the latter trials were adjuvant trials.

Results: In the H0648g "test set" patients whose breast cancers had TOP2A gene co-amplification and who were treated with doxorubicin (trade name Adriamycin), cyclophosphamide (AC) and trastuzumab had a longer progression-free survival compared to those who were treated with AC alone ($p = 0.03$). Patients treated solely with AC, whose breast cancers had TOP2A gene co-amplification had a statistically significant improvement in duration of survival compared to those without TOP2A gene amplification ($p = 0.004$). Among all women entered in the HER2-positive BCIRG 006 clinical trial, as well as among women who were treated with anthracycline-containing chemotherapy alone, women whose breast cancers showed TOP2A gene co-amplification had a significantly longer disease-free ($p < 0.001$), recurrence-free ($p < 0.001$) and overall survival ($p = 0.01$) compared to women whose breast cancers lacked TOP2A amplification. Unexpectedly, the added beneficial effect of trastuzumab was not seen among TOP2A co-amplified breast cancer patients in the larger BCIRG006 trial.

Conclusions: In patients treated with chemotherapy alone the findings demonstrate that TOP2A gene co-amplification is a useful predictive marker of responsiveness to anthracycline-containing chemotherapy.

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BreastCancerTrials.org: Evaluation of a Pilot Clinical Trial Matching Service

Principal Investigator:
John Park

University of California, San Francisco

Poster Presenter:
Ellyn Cohen

Abstract #: C-03

Background: Difficulties accruing patients to clinical trials is a major impediment to the timely approval of new treatments for breast cancer. As an alternative to current recruitment strategies, we have developed BreastCancerTrials.org (BCT), a web-based service that allows patients to find trials that are customized to their medical histories. BCT is a nonprofit, patient-centered, tool that was developed in collaboration with the National Cancer Institute (as part of caMATCH), UCSF Comprehensive Cancer Center, Center of Excellence for Breast Cancer Care and patients advocates. It was launched in June 2005 as a pilot project listing trials in the San Francisco Bay Area and Sacramento.

Materials and Methods: Patients registering with BCT complete a detailed Personal Health Record (PHR) that is matched to trial criteria. Matches are displayed in a secure Message Center with trial summaries and contact information. Patients can contact research staff directly or invite them to view their PHR online. BCT provides online HELP, phone/email support, and alerts patients to newly registered trials. Nine research consortia in the Greater San Francisco Bay Area participated in the pilot. Measures were acceptance, usability, satisfaction, and quality of patient self-reported data. Most data were collected from web statistics and an online survey of those who completed a PHR. We are currently investigating quality of BCT patient data in an ongoing trial at UCSF by comparing a BCT user's self-reported record and clinic chart.

Results: At 14 months post-launch, 733 patients registered with BCT, 614 (84%) provided consent/started a PHR, and, among these, 428 (70%) completed a PHR. Online HELP was clicked 1687 times. Patients learned of BCT via Internet links (65%) or word of mouth (35%); 25%

had not completed college and 37% were over 55 years of age (8% over 65). Of the patients who completed a PHR, 95% received at least one match and (17%) invited researchers to view their PHR; additional patients may have contacted sites directly. At one year, 20% of patients responded to our survey, 80% found it easy to complete their PHR and only 3% had concerns about privacy. Among survey respondents, 37% contacted a site and 74% were satisfied with site responsiveness. Among the respondents who contacted a research site, 52% were eligible for a trial and among these, 42% enrolled. We will report on the quality of patient self-reported data when the study concludes.

Discussion: This pilot demonstrates that an Internet trial matching service is feasible and has the potential to impact clinical trial accrual. Based upon our experience with the BCT Pilot, we are revising our user interface and data collection methods in anticipation of expanding BCT to a nationwide service. In concert with this effort, we will develop outreach to underserved populations.

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Development of Small Molecule for Hsp70

Principal Investigator:
Chung-Wai Shiau

Burnham Institute for Medical Research

Co-Investigators:
Chung-Wai Shiau, John C. Reed

Abstract #: C-04

It is a critical problem that chemotherapy drugs are often ineffective for treatment of advanced breast cancer. Endogenous cell protection mechanisms in breast cancer cells prevent effective chemotherapy treatment. Heat shock protein 70 (Hsp70) represents one of critical cell protection proteins in breast cancer. Normal cells contain few Hsp70 molecules. However, the amount of Hsp70 molecules in breast cancer is increased hundreds of times. Therefore, breast cancer cells can escape toxicity of chemotherapy drugs, in part, because they contain too much protective Hsp70. The purpose of this research is to generate chemical inhibitors of Hsp70 that might eventually be used as new drugs for treating breast cancer.

Our central hypothesis is that Hsp70 when neutralized will suppress breast cancer growth and make it easier to kill breast cancer cells using conventional anti-cancer drugs. To identify chemicals that inhibit Hsp70, we used robotic instrumentation to screen a large library of chemicals, which each have a different shape (structure) to bind to surface features of the Hsp70 protein. We found 10 compounds could bind to the pocket of Hsp70 where its cofactor ATP binds, displacing ATP. These compounds also show an ability to inhibit activity of Hsp70 in protein re-folding assays. Further, the active chemicals were combined with fragment chemical library to adjust their shape so they fit perfectly on the surface of Hsp70, thus increasing the strength of their binding and hence their potency. This optimization of the shapes of our chemicals is assisted by modern techniques of structure-based drug discovery, especially using high-field nuclear magnetic resonance (NMR) and computer modeling to view the 3-dimensional structure of Hsp70 with our chemical inhibitors bound to it. We are using organic synthesis methods to connect the active compounds with fragment chemicals to confirm the NMR and computer modeling data. Finally, the chemical inhibitors of Hsp70 will be tested for their ability to kill breast cancer cells in the test tube, when used alone or in combination with currently used anti-cancer drugs, such as Taxotere and Adriamycin. If all goes well, then we will be poised beyond the requested funding period to advance the best of our Hsp70 inhibitors into animal models of breast cancer, to more definitively test their anti-tumor activity while also assessing their safety in animals. If those animal studies produce acceptable results, then we will be ready to advance the Hsp70 inhibitors into human clinical trials.

To date, potent Hsp70 inhibitors have never been produced or tested as cancer therapies. However, recently it was shown that chemicals that inhibit a molecule with similar functions, called Hsp90, have anti-tumor activity and an acceptable safety profile. Hsp90 inhibitors are now in Phase II clinical trials for refractory cancers. Our project is innovative for tackling Hsp70 as a new possible cancer target. Our project is also innovative because it uses advanced methods of drug discovery and optimization that normally exist only at pharmaceutical companies. Most companies are risk adverse, and will not pursue targets such as Hsp70 because they are insufficiently validated. Our goal will determine whether Hsp70 and related proteins are valid drug discovery targets for breast cancer, and our project will produce chemical inhibitors to understand more about the role of Hsp70 in breast cancer biology and the underlying mechanisms of chemoresistance and radioresistance.

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Session C: Detection, Prognosis and Treatment

Factors Influencing Mammography Screening Among Thai Immigrant Women

Principal Investigator:
Mary Jo Clark and Bulaporn Natipagon-Shah

University of San Diego and Thai Health and Information Services, Inc.

Abstract #: C-05

Introduction: Asian women have lower rates of breast cancer but higher mortality rates than other racial/ethnic groups due to late diagnosis. Little information has been obtained regarding breast cancer screening in subsets of Asian women such as Thai immigrant women.

Aim of the study: To identify factors that influence mammography screening among Thai immigrant women in Southern California.

Methodology: Focus groups were conducted with Thai immigrant women in Los Angeles and San Diego counties to identify factors that influence participation in mammography screening. Focus group findings were then used to construct a telephone survey questionnaire to determine the extent to which identified factors were present in the Thai population.

Innovative elements and community involvement: Members of the Thai community helped to identify factors influencing mammography use by Thai women. They also validated the researchers' interpretation of the focus group findings and used those findings to construct a telephone survey questionnaire to examine the extent of identified factors in the population. The women also served as a source of contacts for obtaining telephone survey interview participants. Findings of both portions of the study will be used by community members to design subsequent interventions to promote mammography screening in this ethnic population.

Findings: Factors in each of six dimensions of health were found to influence mammography screening in this cultural population. For example, age (a biophysical factor) was found to influence women's beliefs about their chances of developing breast cancer. Similarly, cultural beliefs in karma and family and work responsibilities, both sociocultural factors, limited participation in screening activities.

Potential impact: Knowledge of the extent of the identified factors in the Thai population will help us design programs to improve mammography screening and early diagnosis of breast cancer screening in this population and subsequently to reduce breast cancer mortality rates.

Identifying Metastatic Breast Cells from Peripheral Blood

Principal Investigator:
Kristen Kulp

Lawrence Livermore National Laboratory

Co-Investigators:
Kristen S. Kulp, Susan L. Fortson, Mark G. Knize, Kuang Jen Wu, Elena S.F. Berman, Ligang Wu, and James S. Felton, LLNL

Abstract #: C-06

The survival rate of women diagnosed with breast cancer is highly dependent on the timely diagnosis and treatment of metastases. Since breast tumors have been shown to shed cells from the primary tumor into the circulatory system, it is possible that detecting and characterizing these circulating tumor cells in peripheral blood will reveal whether there is a potential risk for future tumor development. However, detection methods must be improved in order to correlate the presence of circulating tumor cells in the blood with metastasis. The goal of our project is to combine epithelial cell isolation techniques with Time-of-flight Secondary Ion Mass Spectrometry (ToF-SIMS) to analyze and identify circulating breast cells that have the potential cause metastasis.

ToF-SIMS is an imaging mass spectrometry technique that can create chemical images of individual cells. These images contain substantial molecular information, which can be used to predict the cells' metastatic potential. To fully utilize all of the chemical information that is present in the individual cell images, we use multivariate statistical methods, such as principal component analysis (PCA), to reduce large spectral data sets to a small number of manageable variables and graphically represent the similarities and differences among cells.

Using commercially available methods of cell isolation, such as magnetic bead technology and density gradient centrifugation, we are able to separate epithelial cells from peripheral human blood. The CELLection Kit™ is a reliable method that allows us to retrieve tumor cells from whole blood by binding the cells to magnetic beads with antibodies that are specific to epithelial cells. Once bound to the beads, a magnetic chamber is used to isolate the tumor cells from the blood. The second isolation method combines the commercially available OncoQuick™ method with flow cytometric techniques. This method separates cells based on size and uses cell sorting to further separate the epithelial cells from the background blood cells. The isolate epithelia cells are attached to silicon substrates, washed and dried using a

specifically derived sample preparation protocol, and then individual cells are analyzed using ToF-SIMS. Isolation results show that the CELLection™ method gives us the highest recovery of epithelial cells, but both recovery methods seem to be consistent and reliable techniques. Neither isolation process affects the chemical signature of the cell as determined by ToF-SIMS analysis.

Developing a combined ToF-SIMS and multivariate statistical analysis approach will allow us to classify the isolated cells based on their metastatic potential. This research gives us the necessary tools to develop a method of sensitive and specific metastatic cell detection, which is the foundation for developing a cheaper, less invasive test for breast cancer metastases.

This work was performed under the auspices of the U.S. DOE by LLNL under contract no. W-7405-Eng-48 and supported by NCI grant CA55861, CA BCRP 10IB-0077 and LLNL-LDRD funding 04-ERD-104.

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Identifying Targeted Treatments for Wound-like Breast Cancers

Principal Investigator:
Howard Chang

Stanford University

Abstract #: C-07

The main goal of this research is to discover treatment strategies for breast cancers that exhibit behaviors like a wound. Each time a person cuts her finger, a remarkable choreography of genes and cells unfolds. Cells that are normally dormant are now invigorated to divide rapidly, remodel the surrounding matrix, migrate across tissue planes, and send forth chemical signals to recruit new blood vessels-all in an effort to close up the wound. These dramatic processes in wound healing may also constitute the ideal genetic tools for cancer metastasis.

We discovered that some breast cancers exhibit wound-like features and can be distinguished by a gene expression signature—a specific pattern of 512 genes. In a survey of 295 early stage breast cancers, approximately 40% of tumors exhibited the wound signature, and these patients have a three-fold increased risk of death. The wound signature identified these high risk tumors independently of known risk factors for poor outcome. Therefore, therapies that specifically target cells exhibiting the wound signature are needed for patients with wound-like breast tumors. Recently, we discovered that mutations in a novel combination of two cancer promoting genes, MYC and CSN5, are responsible for wound signature activation in breast tumors. The collaboration between MYC and CSN5 depended on abnormal protein turnover, a process that may be blocked by the FDA-approved drug bortezomib.

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Increasing Mammography Screening for Latinas with Diabetes

Principal Investigator:
Stergios Roussos and Christine Noguera

CBEACH/San Diego State University Research Foundation and Golden Valley Health Centers

Co-Investigators:
C. Noguera ([1]), S. Roussos ([2]), H. Guzman ([1]), M. Bunyard ([3]), H. Roehlk ([3]), M. Sigarroa ([3])

[1]Golden Valley Health Centers; [2]Center for Behavioral Epidemiology and Community Health; [3]Women of Courage

Abstract #: C-08

Latinas experience health disparities in both breast cancer and diabetes. Latinas have a lower survival rate than non-Latina white women, due predominantly to later diagnosis. Latino mortality rates of Type 2 diabetes are 1.5 times higher than non-Latino groups. Breast cancer and diabetes are linked in two ways that may be used to reduce disparities for both illnesses for Latinas. First, obesity/overweight and inactivity—both preventable – are leading risk factors for both breast cancer and diabetes for Latinas. Second, women with diabetes are less likely to receive age-appropriate mammography despite more health visits (where the complexity of caring for chronic illness is predicted to interfere with mammography).

This Collaborative Pilot Award project will advance an existing community health center and researcher partnership to improve cultural and linguistically appropriate services (CLAS) in the Central Valley, home to one of the highest concentrations of Latinos in the USA. The Pilot Award project will develop and test an intervention that adds breast cancer prevention to an evidence-based, culturally-tailored Diabetes Program serving Latinas in order to improve mammography.

The Specific Aims of this Pilot Award are:

1. Develop an intervention that incorporates breast cancer prevention into an evidence-based diabetes program in a manner that is consistent with the program's cultural tailoring to Latinos.

2. Assess differential change in mammography

compliance for Latinas age 40 and over in the diabetes program alone with those participating in the diabetes + mammography program.

3. Identify and prepare the programmatic/intervention components, research components, and infrastructure of the community-research partnership necessary to apply and successfully implement a Full Award.

A Collaborative Team will consist of members from Golden Valley Health Centers, CBEACH, and the Community Advisory Group (CAG) representing community members with a stake in breast cancer, diabetes, and health disparities. The Team will modify the diabetes registry to track and prompt for age-appropriate mammography, modify monthly mailers so that culturally tailored education and reminders include breast cancer prevention (while avoiding stigma and fear related to mammography), and train the diabetes program team to comply and support mammography screening guidelines. Once developed, the intervention will be tested by comparing changes in age-appropriate mammography among participants in the diabetes program versus the diabetes-mammography program. Diabetes program participation rates and self-management variables (e.g., HbA1C levels) will be tracked to assess influences related to the intervention. The Pilot project will provide information on intervention appropriateness and feasibility, ideal recruitment and retention strategies, estimated effect size, and protocols that would support planning and implementation of a Full Award to assess the efficacy of the intervention.

Screening and cancer disparities for Latinas are correlated with cultural and linguistic factors. Given that over 25% of Latinas have diabetes, adaptation of diabetes care to take advantage of more frequent visits and opportunities to strengthen patient-provider relationship may allow for a quick and non-threatening way to improve mammography for Latinas.

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MR Imaging of Benign, Pre-malignant and Pre-invasive Breast Lesions: Can They Be Differentiated?

Principal Investigator:
Min-Ying Lydia Su

University of California, Irvine

Poster Presenter:
Chung-Ho Chen

Co-Investigators:
Jeon-Hor Chen, M.D., Garima Agrawal, M.D., Orhan Nalcioglu, PhD, Min-Ying Lydia Su, PhD

Abstract #: C-09
Purpose: The currently favored working hypothesis of human breast cancer evolution suggests sequential stages from normal, hyperplasia, hyperplasia with atypia, in-situ cancer, and ultimately, invasive carcinoma. Fibrocystic change (FCC) is a commonly encountered benign diagnosis. The hyperplasic lesions, especially those with atypia, are associated with a higher risk of developing cancer, and hence are termed as pre-malignant lesions. Ductal carcinoma in situ (DCIS) is a pre-invasive cancer. This study compared MRI features of benign lesions (FCC), pre-malignant hyperplasic lesions, and pre-invasive (DCIS) lesions.

Material and Methods: A retrospective analysis of all breast MRI performed at 1.5T from 2002 to 2005 identified 44 pathological-proven FCC, 16 pre-malignant cases (Hyperplasia, ADH, ALH, LCIS) and 34 DCIS. Their MR morphological features and enhancement kinetics were compared. Feature descriptor was analyzed based on BI-RADS MRI Lexicon. The morphologic criteria included mass type lesion (focus/foci: < 5mm, mass: > 5 mm), and non-mass type lesion (focal area, linear, ductal, segmental, regional, multiple regions, diffuse enhancement). The internal enhancement patterns included punctuate, clumped, dendritic, heterogeneous, and homogeneous. The evaluation of enhancement kinetic curve was based on the initial phase (within the first 2 minutes or when the curve starts to change) as fast, medium, and slow; and late phase (after 2 minutes or after the change) as persistent, plateau, and washout. When the kinetic curve showed initial fast/medium up-slope followed by washout or plateau, it was considered as suspicious of malignancy.

Results: While the pre-malignant and pre-invasive groups had a similar percentage presenting as mass type lesion (50% vs. 41%), FCC is less likely, only 29%. Non-mass type lesion appeared in similar frequency, 50%, 56% and 57% for pre-

malignant, pre-invasive lesions, and FCC, respectively. One DCIS (3%) and 6 FCC (14%) were not enhanced. The subtypes of non-mass lesions (diffuse, linear, segmental) between these 3 groups were not significantly different. The analysis of internal enhancement patterns showed that DCIS was more likely to present clumped pattern (10/19, 53%) and less likely punctate pattern, (2/19, 11%); while pre-malignant lesions showed equal frequency presenting these two patterns (37.5%). FCC was more likely to present the heterogeneous enhancement (11/25, 44%). The malignant type enhancement kinetics was only seen in 46% FCC and 46% pre-malignant lesions, whereas it was seen more frequently in 75% DCIS.

Conclusion: There are no MRI features that can clearly distinguish between the benign FCC, hyperplasic lesions and DCIS. Malignant type enhancement kinetics was a good indicator for DCIS, but nearly half of FCC and hyperplasic lesions also showed this kinetic feature. FCC was more likely to show heterogeneous pattern, DCIS was more likely to present clumped pattern; and the pre-malignant lesions were more likely to show punctuate pattern. Correct diagnosis of FCC may avoid unnecessary biopsy; early diagnosis of DCIS will improve patient's prognosis; also accurate diagnosis of hyperplasia with or without atypia will help determine whether the patient should receive additional excision biopsy. Understanding the differences in their MRI features will aid in a better diagnosis to distinguish between them, and to impact on their management.

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Multi-modality Imaging for Breast Cancer

Principal Investigator:
Gultekin Gulsen

University of California, Irvine

Abstract #: C-10

Motivation: Although mammography is very sensitive in detecting early breast cancer, it does not work well in women who have dense breast tissues, breast implants, or scar tissues due to previous treatment. It has been proven that dynamic contrast enhanced (DCE)-MRI detects malignant cancers which are occult on mammogram and ultrasound, and as such it has becoming the most popular imaging modality for screening young women. DCE-MRI is also considered as the most sensitive detection modality in women who have breast implants, or scar tissues. However, despite its high sensitivity, DCE-MRI also detects many benign lesions. The low specificity may lead to great anxiety to patients, and unnecessary biopsy or over-treatment. There is a great need to develop another imaging modality that can provide supplemental information to improve the specificity of DCE-MRI, particularly for young women.

Methods: We are developing a novel breast-imaging platform to provide co-registered tri-modality imaging capability: Optical Imaging (OI), DCE-MRI and MR spectroscopy (MRS). As an adjunct to another imaging modality, the OI systems can provide valuable complementary information, particularly in patients whom the conventional imaging is less optimal, such as young women with dense breasts. Moreover, MRS can provide the choline levels in the lesions, which is elevated in malignant lesions compared to benign lesions. The combination of OI and MRS with DCE-MRI will allow a better characterization of breast lesions, thus an improved specificity, due to enhanced information gathered by this multi-modality system.

Progress: We have already developed the prototype optical breast cancer imager and integrated with the 4T MRI system. The performance of the optical imaging system was tested inside the MRI using phantoms that simulated the breast tissue. Furthermore, the combined system was tested using a couple of volunteers. Although the measurements were successful, the optical interface integrated into the MRI breast coil was found to be uncomfortable by the volunteers. Besides, the thickness of the interface did not enable us to reach close to the chest wall. Consequently, a new, more comfortable, and thinner interface was designed. Once the construction of the new interface is completed and tested, the performance of DCE-MRI, DCE-MRI & MRS and the tri-modality system in distinguishing benign and malignant breast cancer tumors will be assessed with a small clinical study.

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Session C: Detection, Prognosis and Treatment

Brominated Flame Retardants (PBDEs) in Breast Adipose of Women with and without Breast Cancer

Principal Investigator:
Mytro Petreas

California Department of Toxic Substances Control

Co-Investigators:
Petreas, M.*, Hurley S†, Brown FR.*, Goldberg D†, Reynolds P†

*California Department of Toxic Substances Control, Berkeley, CA; †Northern California Cancer Center, Berkeley, CA

Abstract # C-11

Background: Investigations on possible links between environmental exposures to chemicals and breast cancer have resulted in contradictory results, partly because the decreasing body burdens of the studied chemicals (dioxins, DDT, PCBs) limit statistical power. Not all environmental exposures to chemical contaminants are decreasing, however. Concentrations of the polybrominated diphenyl ethers (PBDEs) are increasing exponentially, and we recently reported on the extremely high body burdens in California women. PBDEs are used as flame retardants and are known endocrine disrupters and developmental toxicants. No links to breast cancer have been investigated, but the ubiquity of PBDEs fuels the public's anxiety.

Objective: The purpose of this study was to analyze breast adipose specimens for PBDEs, analyze questionnaire data, and conduct a case-control analysis to determine whether (after adjusting for other risk factors) PBDEs contribute to breast cancer. As a secondary objective we plan to investigate the determinants of PBDE exposures in our population.

Methods: In the late 1990s, we collected breast adipose samples in the course of our earlier case-control study that investigated the presence of organochlorine contaminants and breast cancer (Petreas et al. 2004; Reynolds et al. 2005). We have extensive questionnaires from these women on their health histories, occupation, demographics, diet, hobbies and activities. We analyzed the specimens for PBDEs and explored statistical associations between the measured levels of PBDEs and information from the questionnaires to see: a) whether women with breast cancer have higher levels of PBDEs than women without breast cancer, and b) what variables are linked to increased body burdens of PBDEs.

Results: Preliminary results from 155 participants confirm our earlier findings that California women have the highest levels of PBDEs, almost a hundred times higher than those reported from Europe and Japan. The concentrations of the five major PBDE congeners are shown along with major PCB congeners. PBDE congeners were highly correlated with each other (correlation coefficients varied from 0.70 to 0.98, $p<0.01$), suggesting similar sources of exposure. Results from a case-control analysis and a multiple linear regression to identify determinants of body burdens will be presented.

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Breast Tumor Responses to Novel TGF-beta Inhibitors

Principal Investigator:
Kelly Harradine

University of California, San Francisco

Co-Investigators:
Kelly Harradine and Rosemary Akhurst

Abstract #: C-12

Transforming growth factor-beta (TGFβ) is a secreted protein that is generated in abundance from tumors cells; and, there is a strong correlation between high levels of tumor-derived TGFβ and poor prognosis. In cell culture and animal models, TGFβ has been shown to promote processes that stimulate metastasis. Moreover, animal models have shown that inhibition of TGFβ signaling can be effective and safe in reducing breast tumor metastasis. As a result of these successes in animals, various anti-TGFβ therapeutics are currently entering clinical trials for oncology applications. Despite the potent anti-metastatic action of TGFβ inhibitors for certain tumors, it has been known for a decade that TGFβ can have tumor promoting actions depending on the tumor context. Thus, the inherent complexity of TGFβ action in cancers calls for a tailored application based on the biological profile of the individual tumor, which may be defined by molecular analysis. In general, relatively benign tumors are growth inhibited by TGFβ, whilst more aggressive tumors are stimulated to invade and metastasize. The dichotomous actions of TGFβ necessitate the selection of those tumor subtypes that will have positive therapeutic response.

The purpose of this project is to design a molecular screen for clinicians that will predict the breast tumor's response to novel small molecule inhibitors of TGFβ signaling (positive or negative), ultimately facilitating patient selection for treatment. A second aim will be to determine at the molecu-

lar level how the drugs work, which will lead to identification of new therapeutic targets. To this end, our first aim is to profile the gene expression patterns of breast tumors to study gene signatures associated with TGFβ clinical outcome. We will use a panel of fifty-one breast carcinoma cell lines that have been extensively characterized with respect to gene profiles, and these cell lines will be treated with two distinct and novel TGFβ inhibitors. They will be measured for responses in terms of proliferation, cell viability, apoptosis, invasion, and migration. Then, biocomputational analysis will be used to define the predictive genetic signatures of the various tumor response subtypes. Finally, the gene expression responses of the breast carcinoma subtypes will be analyzed further in an effort to identify the actual targets of the biological response to TGFβ inhibitors.

The information generated from this study will help predict which patients are most likely to benefit from anti-TGFβ therapy, and spare patients who will not respond well to treatment. Ultimately these could lead to breakthrough clinical trials, so that these promising and relatively non-toxic inhibitors can be used effectively.

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Cannabidiol as a Novel Inhibitor of Id-1 Gene Expression in Aggressive Breast Cancer Cells

Principal Investigator:
Sean McAllister

California Pacific Medical Center

Abstract #: C-13

The spread (metastasis) of aggressive breast cancer cells to other parts of the body is the final and fatal step during cancer progression. Clinically, there are still limited therapeutic interventions for aggressive breast cancers available. Clearly, effective and non-toxic therapies are urgently required. The Id-1 gene, a helix-loop-helix type transcription factor, has recently been shown to be a key regulator of the metastatic potential of breast and additional cancers. We previously determined that aggressive breast cancer cells became significantly less invasive in vitro (in culture) and less metastatic in vivo (in mice) when Id-1 expression was reduced using a technique called gene antisense therapy. It is not possible at this point, however, to use this technology to reduce Id-1 expression in patients with metastatic breast cancer.

In our search for a non-toxic drug that could inhibit Id-1 expression, a potential candidate agent was discovered. Here we report that cannabidiol (CBD), a compound extracted from cannabis and with a low toxicity profile, can down-regulate Id-1 expression in aggressive human breast cancer cells. The CBD concentrations effective at inhibiting Id-1 expression correlated with those used to inhibit the proliferative and invasive characteristics of aggressive breast cancer cells. CBD was able to inhibit Id-1 expression at the mRNA and protein level in a concentration-dependent fashion. Most importantly, constitutive expression of Id-1 in breast cancer cells abolished the effects of CBD on cell invasiveness. This suggests that Id-1 is indeed a key factor whose expression needs to be down-regulated in order to observe the effects of CBD on the reduction of breast cancer cell aggressiveness. In conclusion, CBD represents the first non-toxic drug that can significantly decrease Id-1 expression in metastatic breast cancer cells leading to reduction of tumor aggressiveness.

CBD and additional analogs based off its structure could be used as inhibitors of Id-1 and might be of benefit for patients with breast cancers. Cannabinoids are already being used in clinical trials for purposes unrelated to their anticancer activity and these compounds have been reported to be well tolerated. We expect that using CBD as a template will lead to the discovery of more potent and efficacious drugs. This research could lead to a new area of investigation in the treatment of aggressive forms of breast cancer with novel cannabinoid compounds.

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Differential Optical Mammography

Principal Investigators:
Gregory Faris and Christopher Comstock

SRI International

Abstract #: C-14

We are developing a new imaging method for detection and diagnosis of breast cancer based on differential optical mammography. This imaging method relies on inhalation of mixtures of oxygen and carbon dioxide gases to elicit a response from the angiogenic vasculature of tumors though either changes in hemoglobin oxygenation or vasoactivity. Near infrared light is especially well suited for this imaging method since hemoglobin is a strong absorber in this spectral region. This imaging modality also promises to be safe because the radiation is non-ionizing and there is no significant risk associated with its use. Since contrast is provided via inhalation of oxygen rich gases there is no delay between inhalation and image acquisition. We have observed a dramatic increase in contrast between cancerous and nor-

mal tissue on tumor bearing mouse models.

We have completed imaging experiments using a syngeneic mammary adenocarcinoma animal model. Currently we are performing image analysis to understand variability in the vasoactive response. We have also finished developing the imaging system to be used in clinical trials. Preliminary imaging with this system provided detailed images of female breast tissue. So far only healthy volunteers have been imaged. The next steps are determination of the optical transmission response of healthy breast tissue to inhalation of carbogen followed by preliminary clinical studies on women scheduled for biopsies. This will be the most important part of our study. It will help determine how successful the technique is in selective detection of cancerous tissue in the patients.

If this optical technique is successful, it promises to be a complementary imaging modality to x-ray mammography since the cost associated with optical imaging is very small compared with other modalities like MRI and PET.

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Determinants of Response to Microtubule Stabilizing Drugs

Principal Investigator:
Tatana Spicakova

Stanford University

Abstract #: C-15

The taxane compounds paclitaxel (Taxol) and docetaxel (Taxotere) have been important components of chemotherapy regimens to treat breast cancer, however, patients' intrinsic or acquired resistance to these drugs have largely deterred their clinical utility. Taxanes specifically target the cellular microtubules and ultimately cause cell death. The best studied mechanism of resistance to taxanes is the upregulation of a protein called P-glycoprotein (P-gp) which pumps these drugs out of cells; however, there is evidence that the majority of taxane resistant breast tumors do not function via the P-gp mechanism and other resistance mechanisms exist. Elucidating these additional resistance mechanisms remains an important question in breast cancer biology and is the focus of our research. We hypothesize that altered levels and/or aberrant modification of microtubule associated protein MAP-Tau confers resistance to taxanes as a result of altering the properties of the drugs' target, the microtubules.

MAP-Tau gene spans multiple exons that are spliced to produce at least seven isoforms, each containing a projection domain (PD) at the amino terminus and microtubule-binding domain (MBD) near the carboxyl terminus. The isoforms vary in the number of microtubule binding repeats (MTRs) in the MBD, the size of projection domain and the presence/absence of other alternatively spliced exons throughout the mRNA body. The number of microtubule-binding repeats (MTRs) can regulate affinity for microtubules and the MAP-Tau isoforms have been reported to contain either 3 or 4 repeats (designated 3R or 4R respectively). Not surprisingly, splice variants with 4 MTRs have demonstrated increased affinity for binding microtubules in comparison to 3 MTRs. Whether taxane resistant breast cancers show altered 4R/3R ratio has not been yet determined nor has it been investigated whether the length of the projection domain or presence/absence of alternatively spliced exons throughout the mRNA body affects the outcome of taxane treatment.

Our laboratory has developed several taxane resistant variants from four breast cancer cell lines (MCF-7, MDA-MB-231, BT-549 and T-47D) by continuous exposure to docetaxel and the P-gp inhibitor PSC. RT-PCR assays confirmed that these variants are negative for P-gp transcripts, and therefore became resistant to taxanes via unknown alternative mechanisms. We are using these cell lines to test our hypothesis that aberrant expression levels of MAP-Tau isoforms are associated with altered response to taxane treatment. We have been analyzing the expression levels of each MAP-Tau isoform by Western blotting, semi-quantitative PCR and real time RT-PCR analysis using isoform specific primers. Our preliminary results show that T47D taxane resistant cell lines express substantially higher levels of MAP-Tau compared to the parental cell line, making these particular variants the best cellular model for further characterization. Elucidating the molecular mechanisms that determine response to taxanes will allow us to predict which patients are not likely to respond to taxane therapy prior to treatment as well as make a tremendous impact on designing strategies to enhance currently available treatments and improve breast cancer patients' prognosis.

Augmenting immune responses against breast cancer with IL-15 cytokine complexes.

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Session C: Detection, Prognosis and Treatment

Augmenting Immune Responses against Breast Cancer with IL-15 Cytokine Complexes

Principal Investigator:
Ananda Goldrath

University of California, San Diego

Poster Presenter:
Mark Rubenstein

Abstract #: C-16
The goal of our research is to establish methods for using the immune system to treat breast cancer. The need for improved therapies is well established. Individuals with this disease must not only cope with the threat of a shortened life, but also with the prospect of undergoing conventional therapies, which are painful and offer only moderate chances of success in many cases. An alternative to conventional treatment is immunotherapy. Immunotherapy involves harnessing the body's natural defenses against disease, the immune system, to directly attack cancer cells. Select cancers, such as metastatic melanoma, have proved surprisingly amenable to this type of treatment when compared with conventional therapies. The advantages of immunotherapy are not only in the durability of the anti-cancer response, but also in the lack of severe side effects, as the immune system can selectively destroy cancerous cells and leave normal cells untouched. Unfortunately, in the majority of cancers, including breast cancer, immunotherapy has proved ineffective. It is unclear why some cancers respond to immunotherapy while most do not. Two possibilities are that certain cancers either suppress the ability of the immune system to respond or fail to fully activate the immune system. We propose a new approach to overcome such limitations using a novel drug, which is a synthetic version of a natural immune-enhancing substance found in the body. This drug, which is up to 50-fold more active than an earlier version, has proved effective in dramatically enhancing the activity of a number of immune cells that are known to mediate anti-cancer responses. We believe that evaluation of this drug in the context of a mouse model of breast cancer is the critical first step in determining the drug's feasibility in the treatment of human breast cancer.

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Early Breast Cancer Detection Using 3-D Ultrasound Tomography

Principal Investigator:
Thomas Nelson

University of California, Davis

Co-Investigators:
Nebeker J, Comstock CE, Wallace AM, Boone JM

Abstract #: C-17
The goal of this IDEA project is to improve early detection of breast cancer by building an ultrasound scanner that can image the entire breast thus standardizing ultrasound breast imaging to provide high quality images improving detection of nonpalpable breast cancers that cannot be seen with mammography in women at high risk of breast cancer, especially in women with dense breasts.

Specifically, our goal was to design, construct and begin testing a dedicated volume breast ultrasound (VBUS) scanner for the entire breast. To date we have successfully designed the scanner, a scanning table for the pendant breast and the necessary imaging and computer systems to obtain volume breast images. The scanner uses no compression, is fully automated and makes a complete scan in less than 30 seconds under operator control. We have performed a series of measurements to characterize scanner performance with satisfactory results. We also have obtained images from normal volunteers as part of validating performance and determining that the scanner is ready for clinical evaluation. We are preparing to expand our clinical imaging to a broader clinical trial.

The volume breast ultrasound (VBUS) scanner described in this proposal utilizes a novel imaging technology to improve breast cancer detection and diagnosis. First, the scanner obtains a volume data set for the entire breast improving visualization of breast tissue and providing more precise localization of suspicious breast lesions. Second, the scanner provides a standardized scanning environment reducing much of the variability present in current ultrasound scans leading to more accurate diagnosis and a better prognosis. Third, the scanner uses volume imaging and spatial compounding to reduce speckle and improve lesion conspicuity.

The significantly improved image quality and tissue contrast permits detection of breast lesions smaller than the current median size of 11 mm with mammography. Additionally, since ultrasound does not use radiation VBUS scanner offers a lower risk alternative to mammography. VBUS may offer a lower cost alternative to full-field-digital-mammography and magnetic resonance

imaging. VBUS volume data also provides improved localization of breast lesions that could be used to guide biopsy devices with improved precision. Development of a VBUS scanner is expected to assist in identifying and diagnosing breast cancer earlier thereby reducing mortality risk and improving the quality of life for the patient.

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Lymphangiogenesis Preconditions Normal Lymph Nodes to Attract and Support New Metastatic Lesions

Principal Investigator:
Barbara Garmy-Susini

University of California, San Diego

Abstract #: C-18

Lymph nodes are the initial sites of metastasis for most solid tumors, including breast carcinoma and melanoma1-2. We show here that primary tumors can precondition lymph nodes for tumor metastasis by inducing lymphangiogenesis in draining and distal lymph nodes, thereby facilitating the appearance of metastatic lesions. Lymphangiogenesis in lymph nodes is required for tumor metastasis to lymph nodes and this depends on the ligation of two receptors expressed by lymph node lymphatic endothelium, integrin α4β1 and VEGFR3, a lymphatic endothelial cell receptor for VEGF-C3. Moreover, VEGF-C can account for this activity since localized stimulation of lymphangiogenesis in lymph nodes by intradermal injections of VEGF-C accelerates tumor metastasis selectively to the stimulated lymph node. VEGF-C stimulation of lymph node lymphangiogenesis facilitates long range tumor homing to the lymph node even after injection of tumor cells into footpads of non-tumor bearing mice. Significantly, inhibition of local lymph node lymphangiogenesis with antagonists of VEGF-R3 or integrin α4β1 prevented metastasis to lymph nodes without affecting primary tumor lymphangiogenesis or tumor growth while systemic administration of these antagonists suppressed lymphangiogenesis and metastasis to local and distant lymph nodes. These studies demonstrate that lymph node lymphangiogenesis is both necessary and sufficient to promote lymph node metastases and that integrin α4β1, VEGF-R3 and VEGF-C play fundamental roles in tumor invasion through the lymphatics.

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Real-Time 3D Ultrasound Image-Guidance for Breast Surgery

Principal Investigator:
Michael Bax

Stanford University

Abstract #: C-19

The primary goal of breast cancer surgery is to remove all of a cancerous tumor together with a sufficient margin of surrounding healthy tissue to ensure that no cancerous cells remain. The likelihood of recurrence if a sufficient margin is not removed is significantly higher; this may result in additional surgeries and often removal of the whole breast.

Surgeons generally operate without any image feedback during breast cancer surgery. The goal of this research is to provide these surgeons with an ultrasound-based 3D visualization and surgical navigation tool for use before, during, and after surgery to ensure success. Such an advanced imaging system will improve the likelihood of success by assisting in the surgeon's primary tasks: (1) locating the tumor before to the operation; (2) planning and executing an operation using a minimally-invasive route; (3) removal of the tumor; and (4) evaluation after surgery to verify that no cancerous tissue was left behind.

This project will begin with system development. We have a prototype freehand 3D ultrasound system using a commercially-available 2D ultrasound system to acquire images, an optical tracking system to track the ultrasound probe and surgical instruments, and a computer workstation to reconstruct and visualize the 3D image in real time. First the system will be further developed for operating room use, then preliminary 3D data will obtained before, during, and after a series of routine cancer removal surgeries. The system must be straightforward and easy-to-use to be useful during surgery. A substantial element of this research will be the development of a useful, intuitive approach to displaying 3D imagery of the tumor and its surroundings to the surgeon during the operation, while giving the surgeon a simple interface for interacting with the system. The preliminary data will be used to develop the image presentation and interaction components. The complete system will then be validated the operating room.

The development of an innovative 3D visualization and navigation tool for use before, during, and after a procedure will give surgeons a new tool to provide additional insight into the physical configuration of the surgical site and the require-

ments of the procedure, in turn enabling more effective surgery with fewer negative side effects.

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Vaccine for Cancer and Infectious Diseases

Principal Investigator:
Albert Deisseroth

Sidney Kimmel Cancer Center

Co-Investigators:
YC Tang, H Akbulut, J Maynard, and L Pedersen

Abstract #: C-20
Recent analyses of influenza vaccination clinical data shows that there is no survival advantage above the age of 55 and a 4 fold lower antibody response to the multivalent inactivated particle influenza vaccination in individuals over the age of 55. This poor response to vaccines may be due to decreased numbers of antigen naïve CD8 and CD4 T cells, and the acquisition of functional defects in CD4 helper cells, like decreased expression of the CD40L in activated CD4 cells. In order to develop a method to overcome these defects in the immune response in older individuals, we have designed an adenoviral vector (Ad-sig-TAA/ecdCD40L) for the in vivo activation and tumor antigen loading of dendritic cells (DCs). This adenoviral vector encodes a fusion protein composed of an aminoterminal tumor associated antigen (TAA) fragment fused to the extracellular domain (ecd) of the CD40 ligand (CD40L) at the carboxyl terminal end. Two sc injections of this vector have broken tolerance to breast cancer specific tumor associated antigens in two separate TAA.Tg transgenic mouse models (mice transgenic for rat Her-2-Neu (rH2N) and human MUC-1 (hMUC-1)). Her-2-Neu and MUC-1 are tumor associated antigens which are overexpressed in poor prognosis breast cancer as well as in adenocarcinomas of the prostate, ovary, colon and lung. Overexpression of the MUC-1 is an predictor or poor prognosis which is independent of grade and stage. MUC-1 is expressed on the tumor stem cell or tumor initiating population in breast cancer. The immunoprotection induced by this vaccine extends for over a year and is independent of CD4 cells. We showed that the sc injection of the hMUC-1/ecdCD40L protein following the sc injection of the Ad-sig-TAA/ecdCD40L vector (this vector prime-protein boost is called VPP) increases the levels of both the cellular and humoral immune response over that achievable with just the vector injections alone in the hMUC-1.Tg mice. The antibodies from hMUC-1 VPP vaccinated mice bind to biopsy specimens of human cancers of the breast and prostate. Importantly, the VPP vaccination can induce an immune response even in 18 month old mice which completely suppresses tumor growth in old (18 month old) mice. The Ad-sig-rH2N/ecdCD40L vaccination suppresses the evolution of spontaneous breast cancer in the rH2N.Tg mouse model. The Ad-sig-TAA/ecdCD40L/ecdCD40L vector prime-TAA/ecdCD40L protein boost vaccine can also be used to induce a humoral and cellular immune response against antigens (Annexin A1) which are specific for the luminal membrane of tumor vascular endothelial cells. The Ad-sig-TAA/ecdCD40L vector prime-TAA/ecdCD40L protein boost strategy may be of value in the prevention and treatment of breast cancer as well as other epithelial neoplasms and infectious diseases.

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A Mass Spectrometric Approach to BRCA1 Function

Principal Investigator:
Peter Kaiser

University of California, Irvine

Poster Presenter:
David Meierhofer

Abstract #: D-01
BRCA1 is a gene that is important to prevent development of breast and ovarian cancers. The importance of BRCA1 in protection from these cancers is underlined by the fact that in 50-90% of hereditary breast and ovarian cancers BRCA1 is inactivated due to mutations. Despite intense research, our molecular understanding of BRCA1's function in breast cancer prevention is very limited.

Recently, several research groups found that BRCA1 mediates the attachment of a small protein, called ubiquitin, to other proteins. Attachment of this small protein ubiquitin has long been known to regulate the function of the proteins it is attached to. Thus, identification of the proteins to which BRCA1 attaches ubiquitin is crucial to understand how BRCA1 protects from breast and ovarian cancers.

There are a large number of proteins to which ubiquitin gets attached with the help of various different cellular factors. BRCA1 is most likely only involved in attaching ubiquitin to a few proteins. The goal of our research is to develop strategies to identify these direct targets of BRCA1. To this end, we compare the sets of proteins that have ubiquitin attached in normal cells and in cells from patients carrying a defec-

tive BRCA1 gene. Proteins that do not get ubiquitin attached in cells with defective BRCA1 are likely to be direct BRCA1 targets. In addition, the function of BRCA1 to attach ubiquitin to other proteins has been shown to be stimulated after induction of DNA damage. We are therefore also detecting proteins that are modified with ubiquitin specifically in response to DNA damage. Lastly, we apply a new strategy to identify transient binding partners of BRCA1 as well as BARD1 with the aim to link BRCA1 with new cellular pathways and identify direct targets for BRCA1.

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Analysis of MicroRNA Expression in Breast Cancer Stem Cells

Principal Investigator:
Yohei Shimono

Stanford University

Abstract #: D-02

Breast cancer stem cells are a minority population of cancer cells that have higher tumorigenic capacity than other cancer cells. It is proposed that breast cancer stem cells maintain whole cancer mass and a tumor can easily regenerate if enough cancer stem cells remain after treatment. MicroRNAs (miRNAs) are genomically encoded short RNA species that can control expression of many target genes simultaneously. miRNAs are expressed in a tissue specific manner and recent accumulating evidence propose variety of roles including cell proliferation, apoptosis, differentiation, and stem cell maintenance. In addition, abnormal expression of miRNAs in human cancer is associated with cancer progression and patients' prognosis.

In this project, we are exploring whether miRNAs are important regulators of breast cancer stem cell function. Single cell suspensions derived from human or mouse breast cancers were sorted by flow cytometry (FACS) to collect breast cancer stem cell population and other less-tumorigenic cancer cell population. Then we compared the expression of 460 miRNAs between cancer stem cells and non-tumorigenic cancer cells by using seven sets of human breast cancers, three sets of mouse breast cancers, and human normal breast tissue samples. miRNA expression profiling revealed that 30 out of 460 miRNAs were specifically expressed in breast cancer stem cell population compared to the non-tumorigenic cancer cells.

Currently, we are identifying the target genes of the breast cancer stem cell miRNAs by computational analysis to determine the underlying molecular and signaling pathways. We speculate that miRNAs and target genes identified in this project are involved in maintenance and/or differentiation of human breast cancer stem cells. This research may clarify the difference between breast cancer stem cells and other less-tumorigenic breast cancer cells. Inhibitors of miRNAs could be new class of therapeutic agents that target breast cancer stem cells to eliminate "the origin of breast cancer."

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Angiogenesis in the Progression of Premalignant Breast Ductal Proliferations

Principal Investigator:
Min-Ying Lydia Su

University of California, Irvine

Poster Presenter:
Philip Carpenter

Co-Investigators:
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Abstract #: D-03

Breast cancer arising from milk ducts is thought to progress through stages from normal ducts to increased but non-malignant growth (ductal hyperplasia, atypical ductal hyperplasia [ADH]), increasing grades of tumor confined to the ducts (ductal carcinoma in situ [DCIS]), and finally to invasive cancer. The mechanisms responsible for this progression are incompletely understood. Angiogenesis, the proliferation of new blood vessels in a growing tumor, is necessary for the mass to obtain oxygenation and nutrients as it grows. The point at which angiogenesis begins in tumor progression is known as the "angiogenic switch." Angiogenesis in invasive breast cancer is well documented, but little is known of the role of angiogenesis in pre-malignant ductal disease, or when the angiogenic switch occurs during the evolution of breast malignancy. It is important to study angiogenesis because anti-cancer drugs that target angiogenesis are available, and because the presence of angiogenesis allows the visualization of lesions by magnetic resonance imaging (MRI). The goal of this study was to

document angiogenesis during the progression of ductal diseases by special staining and microscopic evaluation of the markers of new blood vessel formation, CD31 and CD105.

A gene often mutated in breast cancer, p53, may be involved in the process of angiogenesis and was measured in breast duct cells. Other angiogenesis related proteins, thromospondin 1 (TSP1) and vascular endothelial growth factor (VEGF), were also measured. The number of new blood vessels in breast samples from 81 patients was determined, and the staining intensity of 0 to 3+ was evaluated for the other proteins. The vessel counts for CD31 revealed 0.8 +/- 2.2 vessels around normal ducts, and a significant increase in density to 18.1 +/- 5.6 vessels for the progression to increased but non malignant growth ($p < 0.0001$). The mean vessel density progressively increased to 22.4 +/- 9.0 for ADH, 25.4 +/- 18.1 for low grade DCIS, 27.0 +/- 11.6 for intermediate grade DCIS and 28.9 +/1 8.9 for high grade DCIS. This progressive increase in mean density was significant by the Jonckheere-Terpstra test for ordered alternatives ($p=0.0001$). A similar increase in vessel density was noted in tissues stained with CD105. The proteins involved in the regulation of angiogenesis, including p53, TSP1 and VEGF showed greater staining of hyperplasia than normal ducts, but only slight increases of these markers as the lesions progressed. These data provide evidence that new blood vessel growth occurs early in the sequence of breast cancer progression, and may be related to the increase in angiogenic regulatory proteins also observed during this progression. This work is important because it offers insights into the role of angiogenesis in breast cancer progression, and it provides an explanation for why these lesions are sometimes detected by MRI.

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Breast Cancer Studies in a 3-D Cell Culture System

Principal Investigator:
Kristiina Vuori

Burnham Institute for Medical Research

Poster Presenter:
Amy Howes

Abstract #: D-04

How a particular breast cancer will respond to a given therapy is influenced by a number of factors. One such important factor is the tumor microenvironment. Breast tumors exist in a complex environment where cells are growing, dividing, and invading other tissues. As a result of these changes, the cancer cells are subjected to stresses, such as limiting amounts of oxygen and nutrients. These so-called metabolic stresses affect how the cells communicate with each other and how they respond to signals from the environment.

The growth of human cancer cells as spheroids better recapitulate the metabolic stresses seen in living tissues than traditional cell culture in a 2-D monolayer. One of our goals was to establish a 3-D system using human breast cancer cells. We have grown the human breast cancer cell line, T47D, as multicellular spheroids and used this as a model system to address how breast cancer cells, exhibiting cell-cell interactions and under metabolic stress, respond to radio- and chemotherapies.

We have examined how T47D spheroids respond to a combination therapy of low-dose radiation and rapamycin treatment (currently in clinical trials for several cancer types). The combination of rapamycin and radiation caused a 15-day delay in spheroid growth following the cessation of treatment, compared to 0 days or 3 days following sole radiation or rapamycin treatment, respectively. This suggested that the combination treatment caused significantly more cell death than either treatment alone. Our subsequent experiments address the mechanism by which the cells die, and whether this cell death occurs in the nutrient and oxygen-stressed cells in the center of the spheroids. The outcome of this research provides further insight into how cells within a tumor respond to radio- or chemo-therapy, which may lead to better predictions of clinical response.

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Classification of BRCA1 and BRCA2 Variants

Principal Investigator:
Giske Ursin

University of Southern California

Poster Presenter:
Eunjung Lee

Abstract #: D-05

BRCA1 and BRCA2 are the two well-established breast cancer susceptibility genes. Screening women for the presence of deleterious genetic changes (mutations) in these genes can identify women who are at high risk of developing breast cancer. However, a substantial proportion of the identified genetic changes are not clearly deleterious or neutral. How to interpret the presence of changes of unknown significance is problematic.

Various approaches to classifying these many unclassified variants (UVs) into deleterious versus not deleterious or neutral variants have been proposed, but few studies have tried to evaluate these classification schemes. In this study, we applied several criteria to classify the significance of UVs identified among 1469 early onset breast cancer patients in Los Angeles. We used four criteria: (i) how common the changes are (rare changes are likely to be deleterious), (ii) physicochemical severity of the changes on the resulting protein, (iii) whether the site of change is evolutionarily conserved across species (highly conserved are more likely to be deleterious), and (iv) a web-based algorithm called Polyphen, which evaluates the structural and chemical nature of the changes. We expected that a method that correctly classifies deleterious UVs would identify a subgroup of women that would have characteristics similar to those with known deleterious mutation of BRCA1/2 such as family history of breast cancer. We found that BRCA1 UV carriers who were classified as a high risk group by all classification methods were more likely to have a mother or sister with a family history than those without any deleterious or unclassified changes in BRCA1. Specifically, women classified by the Polyphen method as having a deleterious variant were 3.5 times as likely to have a positive first degree family history as those without any deleterious or unclassified changes in BRCA1. Application of these methods, especially Polyphen, may help to evaluate significance of BRCA1 UVs when consulting patients in clinical settings.

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Comparative Metabolic Profiling of Breast Cancer

Principal Investigator:
Chen Yang

The Burnham Institute for Medical Research

Abstract #: D-06

Comparative metabolic profiling of cancerous and normal cells improves our understanding of the fundamental mechanisms of tumorigenesis and opens new opportunities in target and drug discovery. We are developing a novel methodology of comparative metabolome analysis that integrates the information about both metabolite pools and fluxes associated with a large number of key metabolic pathways in model cancer and normal cell lines. The data were acquired using [U-13C]glucose labeling followed by two-dimensional NMR and GC-MS techniques and analyzed using isotopomer (i.e., an isomer that differs in the position of its isotopic substitution positions) modeling approach. Significant differences revealed between breast cancer and normal human mammary epithelial cell lines are consistent with previously reported phenomena, such as upregulation of fatty acid synthesis. Additional changes established for the first time in this study expand a remarkable picture of global metabolic rewiring associated with tumorigenesis and point to new potential diagnostic and therapeutic targets.

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Discovery and Characterization of Novel Mutation Pathways in Eukaryotes

Principal Investigator:
Ewa Lis

The Scripps Research Institute

Poster Presenter:
Floyd Romesberg

Abstract #: D-07

Breast cancer is a genetic disease that begins with the mutation of DNA. Traditionally mutation, and therefore cancer, has been attributed to failure of the DNA replication and repair systems. More recently, researchers have come to appreciate that the cell must play an active role with the potential to induce mutations in response to stress. The capacity of cells to mutate themselves presents a novel approach to cancer prevention/treatment namely through the inhibition of proteins required for mutation. Our approach is to study mutation processes in yeast, then translate these finding to human breast cancer. Yeast has proven to be an excellent model organism to dissect out evolutionarily conserved cellular pathways, such as cell cycle and DNA repair pathways.

Mutation in response to most types of DNA damage is thought to be mediated by the error-prone sub-branch of post-replication repair and the associated translesion synthesis polymerases. To further understand the mutagenic response to DNA damage, we screened 4,847 yeast deletion strains to identify genes involved in damage induced mutation of the CAN1 gene. We identified each of the known components of error-prone post-replication repair as well as two additional genes, FYV6 and RNR4. Genetic characterization of FYV6 and RNR4 demonstrate that they act in the same DNA repair pathway, and that this pathway is distinct from that of the conventional translesion polymerases. This novel pathway appears to be mediated by an increase in dNTP (nucleotide) levels that facilitates lesion bypass by the replicative polymerase, called PolD, and is as important as error-prone post-replication

repair in the case of UV- and MMS-induced mutation, but solely responsible for EMS-induced mutation. We propose that Rnr4/Pold and mutagenic post-replication repair constitute the two dominant pathways by which yeast induce mutation in response to DNA damage. Finally, we show that Rnr4/PolD-induced mutation is efficiently inhibited by a small molecule inhibitor of ribonucleotide reductase, suggesting that if similar pathways exist in human cells, intervention in some forms of mutation may be possible.

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Essential Role of CSN5 in Breast Cancer Progression

Principal Investigator:
Adam Adler

Stanford University School of Medicine

Abstract #: D-08

Normal wound healing and cancer growth share many features, such as rapid cell proliferation, cell migration, and new blood vessel growth. Thus, it has been proposed that cancers are "wounds that do not heal". Activation of two genes, CSN5 and MYC, can induce a set of genes involved in wound healing and predict the risk of human breast cancer progression. While the role of MYC in many types of cancer has been extensively studied, the role of CSN5, a multi-functional signaling protein, in cancer development remains poorly understood. Here we show that CSN5 is required for the tumorigenic properties of primary human breast cancer cells. The tumorigenic effects of CSN5 required components of its signaling complex, and the enzymatic activity of CSN5 was also essential. Inhibition of the enzymatic activity of CSN5 in a mouse model of breast cancer blocked breast cancer progression. These results pinpoint CSN5 enzymatic activity as a promising therapeutic target in breast cancer progression.

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High Resolution Imaging of the Dynamic Tumor Cell-vascular Interface in Transparent Zebrafish

Principal Investigator:
Konstantin Stoletov

University of California, San Diego

Abstract #: D-09

Understanding the in vivo mechanisms of tumor cell invasion and metastasis has been severely limited by the inability to image this dynamic process in live animals in high resolution. Progress has also been limited by the inability to visualize the early stages of tumor formation and vascular remodeling. Consequently, little is known about how human cancer cells invade through complex tissues and interact with the newly remodeling vasculature to initiate tumor formation and metastasis.

To address these limitations, we have developed a new xenograft model that combines the optical clarity and powerful genetics of zebrafish with high resolution confocal microscopy and GFP technology (fluorescence cell imaging). Using this unique system, we studied the role of human metastatic gene RhoC in promoting breast cancer metastasis. RhoC is overexpressed in highly aggressive inflammatory breast cancer however the exact mechanisms by which it enhances tumor cell metastasis are unknown. We made the important discovery that RhoC facilitates a primitive amoeboid-like migration pattern leading to increased breast cancer cell intravasation.

High resolution imaging at the vascular-tumor cell interface revealed that this process is mediated by the protrusion of large membranes processes that penetrate deep into the vessel lumen. This process requires the secretion of the vascular permeability factor VEGF, which disrupts the vessel wall allowing membrane penetration and cell intravasation. Our results provide novel insight into mechanisms of cancer cell invasion and intravasation and provide important new information on how RhoC and VEGF cooperate to facilitate cell metastasis in living tissues. Development of this model also provides a simple and cost effective vertebrate system to investigate the action of anti-cancer and anti-angiogenic agents on cancer progression.

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Session D: Normal and Tumor Biology

Inflammation Alters Transcription by the Estrogen Receptor in Breast Cancer

Principal Investigator:
Eliot Bourk

University of California, San Diego

Abstract #: D-10

Estrogen acts through the estrogen receptor (ER), a powerful regulator of cell behavior that can switch specific genes either "on" or "off." While most of the known genes regulated by ER are activated in response to estrogen, we have recently discovered a mechanism by which estrogen can act through ER to specifically decrease the expression of other genes as well. These genes, which are normally repressed by estrogen, can be reactivated if the breast cells are subsequently exposed to inflammation. The overall questions addressed by this research are:

- Which genes are directly shut off by ER in response to estrogen?
- How are these genes reactivated by inflammation?

The body's immune system is ideally adapted to fighting off pathogenic microorganisms like bacteria and viruses. However, inflammation in the wrong context can harm us by driving the progression of diseases including breast cancer. Inflammation has been demonstrated by many breast cancer studies to correlate with increased aggressive tumor behavior, including angiogenesis and metastasis. Tumor-associated macrophages produce pro-inflammatory cytokines such as IL-1beta that influence the behavior of breast cancer cells. In previous work in my mentor's (Dr. Michael Rosenfeld) lab we identified a specific macrophage/cancer cell interaction that causes de-repression of ER target genes.

This project is based on preliminary data obtained using an exclusive technology developed in our laboratory (ChIP-DSL) that enabled us to rapidly scan the genome for genes regulated by the estrogen receptor. Our pilot experiments have enabled us to narrow down the list of potential negative ER target genes from ~20,000 down to 18 high probability targets. This selection process allows us to focus on the ER-mediated gene repression machinery within breast cancer cells and determine how certain genes are reactivated under the influence of localized inflammatory conditions.

Our experiments involve techniques for investigating gene expression, using the polymerase chain reaction (PCR) method to measure the expression levels of the ER target genes, the chromatin immunoprecipitation (ChIP) method to reveal the machinery that regulates these genes, and RNA interference (RNAi) to block the expression of specific proteins that may regulate these genes.

Our goal is to identify a new class of estrogen regulated genes that are subject to control by inflammation, and will provide insight into how breast cancer cells can reactivate these pathogenic genes.

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LMO4 Can Interact with Smad Proteins and Modulate Transforming Growth Factor-beta Signaling in Epithelial Cells

Principal Investigator:
Xiaoman Xu

University of California, Irvine

Abstract #: D-11

The LIM-only protein 4 (LMO4) transcription factor plays critical roles in mammalian development, and has been proposed to play roles in epithelial oncogenesis, including breast cancer. As LMO4 is highly expressed in the epithelial compartments at locations of active mesenchymal-epithelial interactions, we reasoned that LMO4 might act by modulating pathways involved in mesenchymal-epithelial signaling. One candidate is the transforming growth factor-beta (TGFβ) cytokine pathway, which plays important roles both in development and cancer. Our results show that the transcriptional response to TGFβ in epithelial cells is sensitive to LMO4 levels; both up- and down-regulation of LMO4 can enhance TGFβ signaling as assessed by a TGFβ-responsive reporter gene. Furthermore, LMO4 can interact with the MH1 and linker domains of receptor-mediated Smad proteins, and associate with the endogenous TGFβ-responsive Plasminogen Activator Inhibitor-1 gene promoter in a TGFβ-dependent manner, suggesting that such interactions may mediate the effects of LMO4 on TGFβ signaling. When introduced into mammary epithelial cells, LMO4 potentiated the growth-inhibitory effects of TGFβ. These results define a new function for LMO4 as a co-activator in TGFβ signaling, and provide a potential novel mechanism for LMO4-mediated regulation in development and oncogenesis.

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Session D: Normal and Tumor Biology

LMO4 Controls Cell Proliferation and Apoptosis of Mammary Epithelial Cells by Regulating Expression of the BMP7 Gene

Principal Investigator:
Zhengquan Yu

University of California, Irvine

Abstract #: D-12

The nuclear LIM-only protein LMO4 is a transcriptional regulator that becomes upregulated in breast cancer, especially estrogen receptor negative tumors, and its overexpression in mice leads to hyperplasia and tumor formation. Here, we show that deletion of LMO4 in the mammary glands of mice leads to impaired lobuloalveolar development due to decreased epithelial cell proliferation. With the goal of discovering potential LMO4-target genes, we also developed a conditional expression system in MCF-7 cells for both LMO4 and a dominant negative (DN) form of its co-regulator, Co-factor of LIM domains (Clim/Ldb/Nli). We then used DNA microarrays to identify genes responsive to LMO4 and DN-Clim upregulation. One of the genes common to both datasets was BMP7, whose expression is also significantly correlated with LMO4 transcript levels in a large dataset of human breast cancers, suggesting that BMP7 is a bona fide target gene of LMO4 in breast cancer. Inhibition of BMP7 partially blocks the effects of LMO4 on apoptosis, indicating that BMP7 mediates at least some functions of LMO4. Gene transfer studies show that LMO4 regulates the BMP7 promoter, and chromatin immunoprecipitation studies show that LMO4 and its co-factor Clim2 are recruited to the BMP7 promoter. Furthermore, we demonstrate that HDAC (histone deacetylase)-2 recruitment to the BMP7 promoter is inhibited by upregulation of LMO4 and that HDAC2 knockdown upregulates the promoter. These studies suggest a novel mechanism of action for LMO4: LMO4, Clim2 and HDAC2 are part of a transcriptional complex, and increased LMO4 levels can disrupt the complex, leading to decreased HDAC2 recruitment and increased promoter activity.

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Mammary Invasion and Remodeling Occurs via a Novel Activated Epithelial State

Principal Investigator:
Andrew Ewald

University of California, San Francisco

Abstract #: D-13

The mammary gland is built during embryonic and adult development, but is then subject to repeated, hormonally driven cycles of invasion and regression during the normal hormonal cycle, pregnancy, lactation, and involution. We sought to determine the underlying cellular mechanisms driving these normal mammary epithelial invasion events as a means of understanding pathological mammary epithelial invasion during breast cancer. We determined the cellular mechanisms underlying epithelial invasion using organotypic cultures of normal mammary tissue. We found that epithelial invasion involves a transition from an "inactive", bilayered, polarized state to an "active" partially polarized, multilayered state, which exhibits vigorous, continual cell rearrangements. This transition from a bilayer to a multilayer is reversible, involves coordinate changes in multiple cell adhesion pathways (adherens junctions, tight junctions, and desmosomes), and depends on proliferation and signaling through matrixmetalloproteinases (MMPs) and Rho kinase (ROCK).

Importantly, we observed that normal mammary epithelial invasion in vivo involves cyclical entry and exit from this same "active" epithelial state. Invading normal ducts were in the "active" epithelial state, while adjacent, non-invasive ducts were in the "inactive" state. We also saw cyclical "activation" of this epithelial state during normal estrus-associated remodeling of the mammary epithelium in mice. We then used this characteristic signature of the "activated" epithelial state to test if common mechanisms were utilized during pathologic invasion in a clinically validated mouse model of breast cancer (MMTV-PymT). Importantly, hyperplasias, adenomas, and carcinomas displayed features of the "active" epithelial state. Early aspects of breast cancer progression may therefore arise from inappropriate persistence of a fundamentally normal "active" epithelial state.

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Session D: Normal and Tumor Biology

Oxidative Stress Pathways Highlighted in Tumor Cell Immortalization

Principal Investigator:
Shanaz H. Dairkee

California Pacific Medical Center

Poster Presenter:
Aejaz Sayeed

Abstract #: D-14
Objective: An improved understanding of cell immortalization and its manifestation in clinical tumors could facilitate novel therapeutic approaches. The goals of this study were (1) to expand the representation of clinical breast cancer in basic research by isolating and immortalizing tumor cells derived from a wide spectrum of pathological specimens (2) to compare gene expression profiles before and after immortalization of such tumor cell populations, with those of currently used breast cancer cell lines, and (3) to evaluate the significance of immortalization associated changes identified here in determining tumor aggressiveness and patient outcome.

Description of work: Expression profiling analyses of primary breast tumor cultures before and after induction with the immortalizing gene, hTERT, as well as widely used spontaneously immortalized breast cancer cell lines, identified a common signature characteristic of tumor cell immortalization. An important and unique feature of this "Immortalization Signature" (ImmSig) was the significant upregulation of oxidoreductase genes. Silencing the hTERT gene by RNA interference reversed ImmSig expression, increased cellular reactive oxygen species (ROS) levels, altered mitochondrial membrane potential, and induced apoptotic and proliferation changes in immortalized cells. In clinical breast cancer samples, ImmSig expression was inversely correlated with patient survival (P=0), and was particularly relevant to the outcome of ER positive tumors.

Clinical relevance: Our data support the notion that ImmSig expression assists in surmounting normal barriers related to oxidative and replicative stress response in tumor cells. Targeting a subset of aggressive breast cancers by reversing ImmSig components could be a practical therapeutic strategy.

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Structural Characterization of Aromatase

Principal Investigator:
Yanyan Hong

Beckman Research Institute of the City of Hope

Abstract #: D-15
The third-generation aromatase inhibitors (AIs), including anastrozole, letrozole, and exemestane, are widely used as the first-line drugs in the endocrine treatment of estrogen-dependent breast cancer in postmenopausal women. Although these AIs are potent and specific, resistance to them does occur. Therefore, new AIs could provide alternative treatments for breast cancer patients who are not responsive to current AIs. However, the structural basis of drug binding to aromatase is not well understood because the three-dimensional (3-D) structure of aromatase is unknown.

In our laboratory, a structurally stable and functionally active human aromatase has been expressed in E. coli and has been successfully purified. Using this purified aromatase, molecular features of the interaction of different substrates and inhibitors with aromatase were studied by UV-visible spectral analysis. Proteomic studies of this purified aromatase combined with MOLDI-TOF MS revealed a 3-D fold of human aromatase, and indicated that helices B and C and the B-C loop of aromatase might undergo dramatic conformational changes when the enzyme binds to steroidal substrate or inhibitor. Moreover, efforts to crystallize aromatase have generated needle cluster crystals.

Based on site-directed mutagenesis, proteomic analysis, and computer modeling, we proposed a clamping mechanism of androstenedione and exemestane binding to the active site of aromatase. We also investigated the mechanism basis for the aromatization reaction and exemestane-mediated irreversible inhibition of human aromatase. To examine the accuracy of the predicted active site pocket of aromatase and the hypothetical clamping mechanism of steroid binding to aromatase, we recently investigated the interaction of aromatase with four different classes of substrates and inhibitors, each having its own unique structural features. We also compared the interaction of aromatase with two synthetic A-ring modified steroids. This study demonstrates the importance of the A ring of steroidal inhibitors for their binding to aromatase, and provides useful information in the development of new AIs for the treatment of hormone-dependent breast cancer.

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Session D: Normal and Tumor Biology

Targeting Up-regulated Notch Signaling in Inflammatory Breast Cancer

Principal Investigator:
Sanford Barsky

The Ohio State University College of Medicine

Abstract #: D-16

Inflammatory breast cancer (IBC) is a type of human breast cancer with high metastasis due to the presence of florid lymphovascular tumor emboli. We have recapitulated this phenotype in a human xenograft mouse model of IBC (MARY-X). In this xenograft, the tumor emboli are mediated by an overexpressed E-cadherin / alpha and beta-catenin axis and grow in vitro as spheroids. These spheroids are very similar to the embryonal blastocyst which also overexpresses E-cadherin. When the spheroids were disrupted with anti-E-cadherin, the disadhered cells underwent apoptosis. When undisrupted, these spheroids and corresponding emboli resist the apoptosis-inducing effects of chemotherapy / radiotherapy. Because of the resemblance of these spheroids to the embryonal blastocyst, the source of embryonal stem (ES) cells, we reasoned that the spheroids might not only contain stem cells but express stem cell-associated signaling which might be exploited therapeutically. We indeed found known stem cell markers (Stellar, H19, Rex-1, Nestin) to be highly expressed within the MARY-X spheroids. In addition, RT-PCR analyses of MARY-X revealed the expression of OCT4, SOX2, and Nanog, transcriptional determinants essential for the pluripotency and self-renewal of stem cells. Most importantly, CD133, a surface marker for human leukemic / gliomic stem cells, was also strongly expressed by 60% of the cells of the MARY-X spheroids and the lymphovascular emboli of human IBC. Only this CD133+ subpopulation expressed both the stem cell transcriptional determinants mentioned previously as well as the capacity for self-renewal and tumorigenicity. Tumorigenicity capacity could be observed within spheroids with as few as 50 cells or within single cells if grown in and co-injected with Matrigel. These stem cells also exhibited stem cell-associated signaling. Both increased expression of notch receptors and increased notch signaling via notch cleavage and downstream increased expression of target genes, HES-1, HES-5, were detected. In addition, gamma-secretase inhibitors, inhibitors which effectively blocked notch cleavage and downstream signaling of target genes, caused marked apoptosis of the CD133+ IBC cells in vitro, even when they were cytoprotected within their embolic niche. This effect was also observed in vivo with marked shrinkage of the size of tumor xenograft nodules with gamma-secretase inhibitor treatment. This anti-tumor effect was independent of the E-cadherin / alpha and beta-catenin axis which remained intact. Our results suggest that activation of notch signaling pathways are essential for the maintenance of viable tumor emboli and CD133+ "stem cells", in particular, and that inhibiting these notch pathways with gamma-secretase inhibitors may achieve selective targeting of stem cells within the lymphovascular emboli and ultimately a novel and effective therapy for IBC.

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The Identification and Modification of Rad51 Recombinase Inhibitors and their Applications in Inhibiting Breast Tumor Growth

Principal Investigator:
Jiewen Zhu

University of California, Irvine

Abstract #: D-17

The cytotoxicity of chemotherapy and radiation, two major treatments in advanced cancers, is directly related to an ability to cause DNA damage. The increased ability of cancer cells to recognize this damage and initiate DNA repair would have a negative impact upon therapeutic efficacy and result in resistance to these therapies. Therefore, the use of inhibitors of DNA repair pathways has the potential to enhance the cytotoxicity of genotoxic anticancer agents. Choosing Rad51 recombinase as a candidate is advantageous, because it is constantly overexpressed in cancer cells but not in normal somatic cells. Therefore, inhibition of Rad51-mediated pathways will have a much greater impact on the survival of the tumor cells than that of normal cells and appears to provide an exciting opportunity to selective killing of tumor cells. Previous studies have shown that inhibition of Rad51 function, by overexpressing exogenous BRC peptide, was able to arrest breast cancer cell growth and render cancer cells hypersensitive to ionizing radiation treatment. Therefore, the goal of this research project is to identify and modify small molecular compounds to effectively inhibit Rad51 recombinase. We expect these small molecules will provide a novel therapeutic treatment for breast cancer patients in near future.

Small molecular Rad51 inhibitors (IBR1/2) have been identified by a high-throughput reverse yeast-two-hybrid screening method from a library of 24,000 compounds. In vitro assays suggest that IBR2 binds to Rad51; and this binding interferes with its multimerization, a critical event

for proper functioning of Rad51-mediated homologous recombination repair, as indicated by gel filtration assay. Molecular modeling studies, using DOCK or ICM software, suggest that IBR2 may structurally mimic a BRC motif in binding with Rad51. A series of IBR analogues were then synthesized and tested for their inhibitory effects on breast cancer cell growth; and structure-activity relationship analysis was performed using reverse yeast-two-hybrid assays and cell growth inhibition assays. The results suggested that the presence of a properly substituted phenyl moiety is essential for activity, which supports the current IBR2-Rad51 binding model. In IBR2-treated breast cancer cells, Rad51 became susceptible to degradation via proteosome-mediated pathway, and the growth rates of cancer cells were significantly reduced. IBR2 can also significantly retard xenografted breast tumor growth up to 60-70% at a dosage of 10-50 mg/kg in nude mice, without apparent general toxicity. Combination treatment of IBR2 with ionizing radiation enhanced its cytotoxic effect on tumor cells. These studies demonstrate a therapeutic potential of IBR molecules targeting Rad51 for degradation in breast cancer cells.

This project may provide new therapeutics in breast cancer treatment. First, IBR compounds alone can be used in inhibiting breast tumor growth. Second, since these compounds can enhance the sensitivity of breast cancer cells to irradiation, a combinatory therapy with lowered dosages can then be developed.

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The Identification of an Enzyme that Regulates Ether Lipid Signaling Pathways in Cancer

Principal Investigator:
Benjamin Cravatt

The Scripps Research Institute

Poster Presenter:
Sherry Niessen

Abstract #: D-18

Many metabolic enzymes, including lipases, oxidoreductases, and glutathione S-transferases, are believed to make key contributions to primary tumor progression, invasion, and metastasis. As such, there is an urgent need for elucidating the precise roles that metabolic enzymes play in cancer biology, so as to uncover new potential therapeutic targets and biomarkers. Using activity based protein profiling (ABPP), an advanced proteomic technology that assesses the activity of many enzymes in parallel within native proteomes, we have identified the serine hydrolase KIAA1363 as being highly elevated in numerous pathogenic human cancer cell lines. These included cell lines from several tumorigenic origins including the breast, ovary, and skin. Moreover, this enzyme was found to be raised in a number of primary human tumors compared to their corresponding normal tissues. Together, these data suggest an important role for KIAA1363 in human tumorigenesis.

Using retroviral gene transfer in combination with either RNAi or overexpression technology we have demonstrated that KIAA1363 is not only necessary but also sufficient to support several of the in vitro and in vivo pathogenic properties of both breast and ovarian human cancer cell lines. The overexpression of KIAA1363 leads to an augmentation of the in vitro proliferation and migration potential and the in vivo tumor growth of cancer cells. Moreover, a reduction of KIAA1363 activity decreased both the migration potential and the in vivo tumor growth of cancer cells. Importantly, KIAA1363's ability to regulate these properties was entirely dependent upon its catalytic activity. The molecular mechanism by which KIAA1363 regulates the pathogenic properties of human cancer cell lines was addressed using a global metabolite profiling strategy in combination with metabolic labeling studies to determine that KIAA1363 serves as a central node in an ether lipid signaling pathway that bridges the platelet-activating factor (PAF) and lysophosphatidic acid (LPA). Biochemical studies revealed that KIAA1363 regulates this network by hydrolyzing the metabolic intermediate 2-acetyl monoalkylglycerol to monoalkylglycerol (MAGE). Perturbation of KIAA1363 levels or catalytic activity in human cancer cell lines directly correlates with changes in the concentration of these metabolites.

The significance of ether lipids, such as LPA, in cancer biology is demonstrated by the fact that LPA is an established biomarker of ovarian cancer being elevated nearly 10 fold in ascites fluid and LPA has been shown to regulate many of the pathogenic properities of cancer cell lines. Significantly, we have found that KIAA1363-regulated cellular migration is dependent on the bioactive lipid LPA, as the addition of as little as 10 nm alkyl-LPA rescued the migratory defect induced by an inhibition of KIAA1363 activity. These findings indicate that KIAA1363 is an important molecule in human cancer biology.

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Session D: Normal and Tumor Biology

The Importance of the MAPK Pathway During Mammary Gland Development

Principal Investigator:
Jimmie Fata

California Pacific Research Institute

Abstract #: D-19

The goal of this research was to model normal development of the breast and subsequently evaluate the importance of the mitogen activated kinase (MAPK) signaling pathway, which is often deregulated in breast cancer.

Transforming growth factor-alpha (TGF-alpha) and fibroblast growth factor-7 (FGF7) exhibit distinct expression patterns in the mammary gland. Both factors signal through MAPK; however, their unique and/or combined contributions to mammary morphogenesis has not been examined. In ex vivo mammary explants, we show that a sustained activation of MAPK for 1 hour, induced by TGF-alpha, was necessary and sufficient to initiate branching morphogenesis, whereas a transient activation (15 minutes) of MAPK, induced by FGF7, led to growth without branching. Unlike TGF-alpha, FGF7 promoted sustained proliferation as well as ectopic localization of, and increase in, keratin-6 expressing cells. Simultaneous stimulation by FGF7 and TGF-alpha indicated that the FGF7-induced MAPK signaling and associated phenotypes were dominant: FGF7 may prevent branching by suppression of two necessary TGF-alpha-induced morphogenetic effectors, matrix metalloproteinase-3 (MMP-3/stromelysin-1) and fibronectin. Our findings indicate that expression of morphogenetic effectors, proliferation, and cell-type decisions during mammary morphogenesis are intimately dependent on MAPK activation.

Our results indicate that the MAPK pathway, which is deregulated in the majority of breast cancers, is absolutely needed in the normal development of the breast.

JEF and AJE were supported by the California Breast Cancer Research Program (6FB-0131 and 11FB-0015).

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The Role of Slit Family Guidance Cues in Breast: Adhesive Factors and Tumor Suppressors

Principal Investigator:
Lindsay Hinck

University of California, Santa Cruz

Abstract #: D-20

Development of many organs, including the mammary gland, involves dramatic changes in shape and form as tissues are molded into three-dimensional structures. The mammary gland is a tree-like structure composed of bi-layered ducts, comprising an outer layer of cap/myoepithelial cells and an inner layer of luminal epithelial cells surrounding a central lumen. During development, the enlarged termini of ducts, termed end buds, establish the primary ductal architecture and drive the prodigious growth of the gland that establishes the mammary tree.

My laboratory is interested in understanding mechanisms that regulate ductal architecture and we have identified two signaling systems responsible for adhesive interactions between the bi-layered sheets of mammary epithelium. SLITs (Slit), like NETRINs (Ntn), were originally characterized as guidance cues that direct neurons and their axons to targets during neural development. In mammary gland, SLIT2 and NTN1 are broadly distributed throughout the epithelial compartment, whereas their receptors, ROBO1 (Robo1) and NEOGENIN1(Neo1), are restricted to the outer myoepithelial cell layer. Loss-of-function mutations in any one of these genes results in adhesive defects that are confined to the end bud structure. Ductal defects, in which the luminal epithelial cell layer peels away from the myoepithelial cell layer, are only revealed when both Slit2 and Ntn1 are deleted. These and other studies have led us to propose a model in which the two cues act in parallel through their respective receptors to mediate adhesive interactions between distinct epithelial cell types. We suggest that this type of short-range adhesion maintains tissue structure, while allowing cell movement and re-organization during periods of rapid tissue growth and remodeling.

Our studies on normal mammary development have also revealed a potential role for SLITs as tumor suppressors. We found that loss of both Slit2 and Slit3 in the mammary epithelium leads to increased proliferation and ductal lesions. To investigate, we identified candidates whose misexpression may contribute to the invasive phenotype. We discovered a dramatic upregulation of the chemokine receptor CXCR4 in Slit2-/-;Slit3-/- epithelium, and a concomitant upregulation of its

ligand SDF1 (CXCL12) in the surrounding stroma. The SDF1/CXCR4 signaling pathway is emerging as a key player in human breast cancer with roles in both regulating the growth of primary tumors and in directing the migration of metastasizing cells. With our on-going studies, we are investigating how loss of Slits and their Robo receptor leads to changes in Sdf1/Cxcr4 expression and the consequences of this in breast cancer progression.

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Twist Activation in Breast Cancer Metastasis

Principal Investigator:
Jing Yang

University of California, San Diego

Abstract #: D-21

In breast cancer patients, almost all deaths are caused by the spreading and growth of breast tumor lesions in distant organs, including lung, liver, bone and brain. The process by which tumor cells spread from a primary site to distant organs and establish secondary tumors is termed "metastasis." During tumor metastasis, tumor cells need to obtain the ability to break away from their neighbor cells and migrate. Our previous studies showed that tumor cells activate a gene named Twist to gain motility, invade and metastasize. Twist can promote a developmental program termed epithelial-mesenchymal transition (EMT), during which cells lose cell-to-cell contact and thus can invade as single cells.

However, the role of EMT in tumor metastasis is still highly debated due to the difficulty in capturing single tumor cells that have turned on the EMT program to metastasize in human breast tumors. We propose a reversible EMT model to describe the dynamic changes that tumor cells experience during tumor metastasis. In this model, breast cancer cells activate Twist and undergo EMT to break away from their neighbors and spread into distant organs. Once reaching those organs, these tumor cells "switch off" Twist and the EMT program, colonize and grow in distant organs. To test this hypothesis, we have established an inducible Twist mouse model. In this model, when the mice develop primary breast tumors, we can switch on/off Twist and the EMT program, and test its contribution to breast cancer metastasis. We are in the process of examining the effect of Twist activation on mammary gland structure and breast cancer progression. We believe that these experiments will demonstrate the in vivo roles of Twist and EMT in breast tumor invasion and metastasis.

In early stage breast cancer patients, studies showed that 70-80% of patients receiving chemotherapy would have survived well without it upon removal of their primary tumors. Unfortunately, due to the lack of reliable means to identify metastasis high-risk patients, all patients face the decision on whether the stressful and costly chemotherapy is necessary for them. Since an EMT is likely an early event to allow carcinoma cell spreading, genes in EMT hold promise to be useful prognostic markers for metastatic breast tumors. The signaling pathways controlling EMT are also excellent candidates for cancer therapeutics.

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At the Interface of Lipid Metabolism and Receptor Signaling: Lipid Rafts and the (De)regulation of ERBB2

Principal Investigator:
Ralf Landgraf

University of California, Los Angeles

Abstract #: D-23

Elevated cellular levels of the ERBB2 (HER2) growth factor receptor are clinically important in 25-30% of breast cancers. As several lines of targeted therapy are aimed at ERBB2 our ability to understand the molecular basis of responsiveness and emergence of drug resistance has increasingly moved to the forefront. As a membrane embedded receptor, the immediate environment of ERBB2 is made up of lipids and other membrane proteins that are either embedded into or attached to the membrane Mutual interactions of lipids and proteins result in a recruitment and assembly of functionally distinct microenvironments. "Lipid rafts" are critical microdomains within the cell membrane that gathers signaling partners of ERBB2, including its dominant co-receptor ERBB3 and downstream targets. However the crosstalk between lipid metabolism, membrane lipid profile and the assembly of receptor-based signaling platforms is currently poorly understood. In the case of ERBB2, extracellular domains of the receptor that are critical in the control of intrinsic catalytic activity have also been implicated in determining the localization of ERBB receptors to rafts, the interaction with complex glycolipids, such as gangliosides, and are the same domains are known to be the target of Herceptin binding. The raft localization of receptors and complex glycolipids is expected to be influenced by the abundance and distribution of saturated long chain fatty acid containing phospholipids that are, together with cholesterol, critical building blocks of lipid rafts. Raft microdo-

mains are, therefore, not only assembly platforms for ERBB2 signaling, they have the potential to play a key role in the integration of growth factor receptor signaling and lipid metabolism. This is further underscored by the enhanced sensitivity of cancer cells to the all-out inhibition of long chain fatty acid synthesis by FAS or ganglioside production, as well as reported correlations between Herceptin resistance and long chain fatty acid profiles, a correlation for which we currently lack a mechanistic explanation. A better understanding of this understudied interplay between ERBB2 and lipid rafts will provide mechanistic insights into the intrinsic control of cell growth, resistance to therapy, and how environmental/dietary factors may influence the course of the disease and success of treatment.

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