2010

California Breast Cancer Research Program Symposium

From Research to Action: Tools for Change

September 24-25, 2010

Oakland Marriott and Convention Center

CALIFORNIA
Breast Cancer
Research Program

From Research to Action: Tools for Change

From Research to Action: Tools for Change
California Breast Cancer Research Program
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OFFICE OF THE VICE PRESIDENT – RESEARCH AND GRADUATE STUDIES

OFFICE OF THE PRESIDENT
1111 Franklin Street, 11th Floor
Oakland, California 94607-5200

August 25, 2010

Dear Conference Attendees:

On behalf of the University of California, we would like to welcome you to the CBCRP's "From Research to Action: Tools for Change" Symposium. We hope you enjoy the symposium sessions, as well as the opportunity to meet with colleagues, friends, and advocates.

The California Breast Cancer Research Program awarded over eight million dollars in research funds this past year, including grants to foster career development and training of breast cancer researchers, translational projects to move scientific discoveries from bench to bedside and into the community, collaborative projects between community-based organizations and researchers, as well as innovative research grants.

The CBCRP staff and the Breast Cancer Research Council have worked hard to bring you this exciting symposium. We want to thank them for their passion and dedication to eradicating breast cancer.

Enjoy the Symposium!

Best Regards,

Mary Croughan

Mary Croughan, Ph.D.
Executive Director
Research Grants Program Office
University of California

Steven Beckwith

Steven V.W. Beckwith, Ph.D.
Vice President-Research and Graduate Studies
University of California

DIRECTOR'S WELCOME

I am tremendously excited by this symposium. It's been three years since our last meeting, and the Program has undergone several significant changes. We have many exciting developments to share with you.

The California Breast Cancer Research Program has always been envisioned to be dynamic, responsive, and highly active in making an impact against breast cancer. We were born from the urgency and dreams of breast cancer advocates frustrated by the slow progress of research, and in the 16 years since our inception, we have helped influence both the pace and the direction of breast cancer research.

"From Research to Action" is the name of our breast cancer research symposium, which arose from our values of accountability and transparency, our responsibility not only to demonstrate our progress towards eliminating the suffering from breast cancer, but also to facilitate the rapid translation of research results into practical use. This year's event will focus on "Tools for Change"—the new methods, tools, and approaches that we are using to change the research paradigm and drive greater progress against the disease. During Friday's plenary session, "Tools for Expanding the Research Paradigm," Susan Love, Laura Esserman, Elly Cohen, and Anna H. Wu will discuss innovative research strategies that are breaking down barriers that have stymied advances for decades.

The research projects initiated under our Special Research Initiatives are underway, and some are beginning to bear results. Saturday's plenary session, "Making Chemical Testing Relevant to Breast Cancer," will include a report from the California Breast Cancer and Chemicals Policy Project. This multidisciplinary team of experts developed an approach for identifying and prioritizing chemicals testing in order to inform California's Green Chemistry Initiative and to include breast cancer risk as a factor in evaluating toxicity for commonly used chemicals in consumer products.

The California Breast Cancer Research Program's founders intended that the strong voices of advocates be heard throughout all aspects of the Program. Our keynote speaker, Angela Padilla, is one of those voices. Co-founder of Bay Area Young Survivors, Angela also led our Breast Cancer Research Council for two years. She will discuss how advocacy can drive the breast cancer research agenda.

I invite you to roam our exhibits, where you'll find valuable resources offered by nonprofit organizations, displays of research results presented by some of our funded researchers, and an art exhibition, wherein you will discover powerful expressions of the impact of breast cancer—the human stories that motivate our research.

We welcome your input, not only about the progress and research directions of the California Breast Cancer Research Program, but also about the ways in which breast cancer has affected your life. I welcome you to visit our booth, where we will be collecting your stories on video. We will share those stories at the end of the symposium.

On behalf of the California Breast Cancer Research Program staff and council, and the University of California, I welcome you to the CBCRP breast cancer research symposium—From Research to Action: Tools for Change. I look forward to your participation.

Mhel Kavanaugh-Lynch

Mhel Kavanaugh-Lynch
Director, California Breast Cancer Research Program

Continuing Medical Education Credits

University of California
San Francisco

Accreditation Statement:

The University of California, San Francisco School of Medicine (UCSF) is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

Designation Statement:

UCSF designates this educational activity for a maximum of 15.50 AMA PRA Category 1 Credits™. Physicians should only claim credit commensurate with the extent of their participation in the activity

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

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 programs. This document and the 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. Other federal and state laws not reviewed below also may govern the manner in which physicians and health-care providers render services for disabled, hearing impaired or other protected categories

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 ("Recipients") to take reasonable steps to ensure that LEP persons have meaningful access to federally funded programs and services. Failure to provide LEP individuals with access to federally funded programs and services may constitute national origin discrimination, which may be remedied by federal agency enforcement action. Recipients may include physicians, hospitals, universities and academic medical centers who receive grants, training, equipment, surplus property and other assistance from the federal government.

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 entitled "Guidance for Federal Financial Assistance Recipients Regarding Title VI and the Prohibition Against National Origin Discrimination Affecting Limited English Proficient Persons – Summary" is available at HHS's website at: http://www.hhs.gov/ocr/civilrights/resources/specialtopics/lep/policyguidancedocument.html.

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 or likely to be encountered 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 to its beneficiaries; 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 depending on the emergent or non-emergent needs of the LEP individual, 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. HHS's guidance provides detailed examples of the mix of services that a Recipient should consider and implement. HHS's guidance also establishes a "safe harbor" that Recipients may elect to follow when determining whether vital documents must be translated into other languages. Compliance with the safe harbor will be strong evidence that the Recipient has satisfied its written translation obligations.

In addition to reviewing HHS guidance documents, Recipients may contact HHS's Office for Civil Rights for technical assistance in establishing a reasonable LEP plan.

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. California Government Code section 7291 recites this legislative intent as follows:

> "The Legislature hereby finds and declares that the effective maintenance and development of a free and democratic society depends on the right and ability of its citizens and residents to communicate with their government and the right and ability of the government to communicate with them.
>
> The Legislature further finds and declares that substantial numbers of persons who live, work and pay taxes in this state are unable, either because they do not speak or write English at all, or because their primary language is other than English, effectively to communicate with their government. The Legislature further finds and declares that state and local agency employees frequently are unable to communicate with persons requiring their services because of this language barrier. As a consequence, substantial numbers of persons presently are being denied rights and benefits to which they would otherwise be entitled.
>
> It is the intention of the Legislature in enacting this chapter to provide for effective communication between all levels of government in this state and the people of this state who are precluded from utilizing public services because of language barriers."

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. You may access a copy of this law at the following url: http://www.spb.ca.gov/bilingual/dymallyact.htm.

Financial Disclosures

The following faculty speakers have disclosed a financial interest/arrangement or affiliation with a commercial company who has provided products or services relating to their presentation(s) or commercial support for this continuing medical education activity. All conflicts of interest have been resolved in accordance with the ACCME Standards for Commercial Support:

David Mankoff, University of Michigan
Merck – Research Funding
Pfizer – Research Funding
Genzyme – Honoraria

This UCSF CME educational activity was planned and developed to: uphold academic standards to ensure balance, independence, objectivity, and scientific rigor; adhere to requirements to protect health information under the Health Insurance Portability and Accountability Act of 1996 (HIPAA); and, include a mechanism to inform learners when unapproved or unlabeled uses of therapeutic products or agents are discussed or referenced.

This activity has been reviewed and approved by members of the UCSF CME Governing Board in accordance with UCSF CME accreditation policies. Office of CME staff, planners, reviewers, and all others in control of content have disclosed no relevant financial relationships.

Shelley Adler	University of California, San Francisco
Lisa Barcellos	University of California, Berkeley
Roxanna Bauitista	Asian & Pacific Islander American Health Forum
Heidi Booth	Greater Los Angeles Council on Deafness, Inc.
Barbara Brenner	Breast Cancer Action
Terri Burgess	Amgen, Inc.
Howard Chang	Stanford University
Moon Chen	University of California, Davis
Elly Cohen	University of California, San Francisco
Barbara Cohn	Public Health Institute
Shanaz Dairkee	University of California, San Francisco
Kathie Dalessandri	University of California, San Francisco
Laura Esserman	University of California, San Francisco
Brunie Felding-Habermann	Scripps Research Institute
Laura Fenster	University of California, Berkeley
Suzanne Fenton	National Institute of Environmental Health and Science
Susan Ferrier	The Sierra Fund
Jim Ford	Stanford University
Karren Ganstwig	Los Angeles Breast Cancer Alliance
Scarlett Gomez	Cancer Prevention Institute of California
Robert Hiatt	University of California, San Francisco
Marc Hurlbert	Avon Foundation for Women
Susan Hurley	Cancer Prevention Institute of California
Shelley Hwang	University of California, San Francisco
Sarah Janssen	University of California, San Francisco
Angela Jo	University of California, Los Angeles
Dale Johnson	Emilem, Inc.
Marjorie Kagawa-Singer	University of California, Los Angeles
Celia Kaplan	University of California, San Francisco
Mhel Kavanaugh-Lynch	California Breast Cancer Research Program
Cheryl Koopman	Stanford University
Hasan Korkaya	University of Michigan
Mary Anne Kreshka	The Sierra Fund

Financial Disclosures

Allison Kurian	Stanford University
Eunjung Lee	University of Southern California
Susan Love	Dr. Susan Love Research Foundation
M. Ellen Mahoney	Breast Cancer Connections
Katherine McKenzie	California Breast Cancer Research Program
Holly Mitchell	Crystal Stairs, Inc.
Kristine Monroe	University of Southern California
Brian Montano	Breast Cancer Early Detection Program
Rachel Morello-Frosch	University of California, Berkeley
Anna Napoles	University of California, San Francisco
David Nelson	Cancer Prevention Institute of California
Trent Northen	Ernest O. Lawrence Berkeley National Laboratory
Tu-Yen Nguyen	Cal State Fullerton
Carmen Ortiz	Circulo de Vida
Debbie Oto-Kent	Health Education Council
Angela Padilla	Bay Area Young Survivors
Rebecca Parsons	Sierra Nevada Memorial Hospital Cancer Center
Richard Pietras	University of California, Los Angeles
Marj Plumb	Plumbline Consultants, Inc.
Klaus Porzig	Stanford University
Michael Press	University of California, Los Angeles
Thu Quach	Cancer Prevention Institute of California
Catherine Quinn	Office of Women'
Michele Rakoff	Breast Cancer Care and Research Fund
Peggy Reynolds	Cancer Prevention Institute of California
Jeanne Rizzo	The Breast Cancer Fund
Eric Roberts	Public Health Institute
Megan Schwarzman	University of California, Berkeley
Gaurav Sharma	The Sandford/Burnham Medical Research Institute
Gina Solomon	Natural Resources Defense Council
Kendra Stone	Charlotte Maxwell Complementary Clinic
Daniel Stram	University of Southern California
Melinda Telli	Stanford University
Catherine Thomsen	California Breast Cancer Research Program
Diana Tisnado	University of California, Los Angeles
Thea Tlsty	University of California, San Francisco
Marlene von Friederichs-Fitzwater	University of California, Davis
Sandy Walsh	California Breast Cancer Organizations
Robert West	Stanford University
Anna Wu	University of Southern California
Mary Alice Yund	University of California, Berkeley Extension
Lauren Zeise	Office of Environmental Health Hazard Assessment
Xiao-kun Zhang	The Burnham Institute for Biological Research
Elad Ziv	University of California, San Francisco

The CBCRP is working to 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
- Encouraging a fragrance free symposium
- Providing symposium materials on a voluntary rather than automatic basis. You want one, you take one

What the Oakland Marriott is Doing:

- Recycling Program—the hotel recycles grease and cardboard
- Paperless hotel check-ins
- Linen reuse program
- Not replacing consumable amenities daily unless they are gone
- No Styrofoam (polystyrene) 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 class on Friday and Saturday morning
- Take full advantage of recycling receptacles
- Remember to recycle your name badge
- Consider attending meetings “fragrance-free”
- If you’re staying at the Oakland Marriott, conserve water and energy by not having your sheets and towels serviced every day

Symposium at a Glance

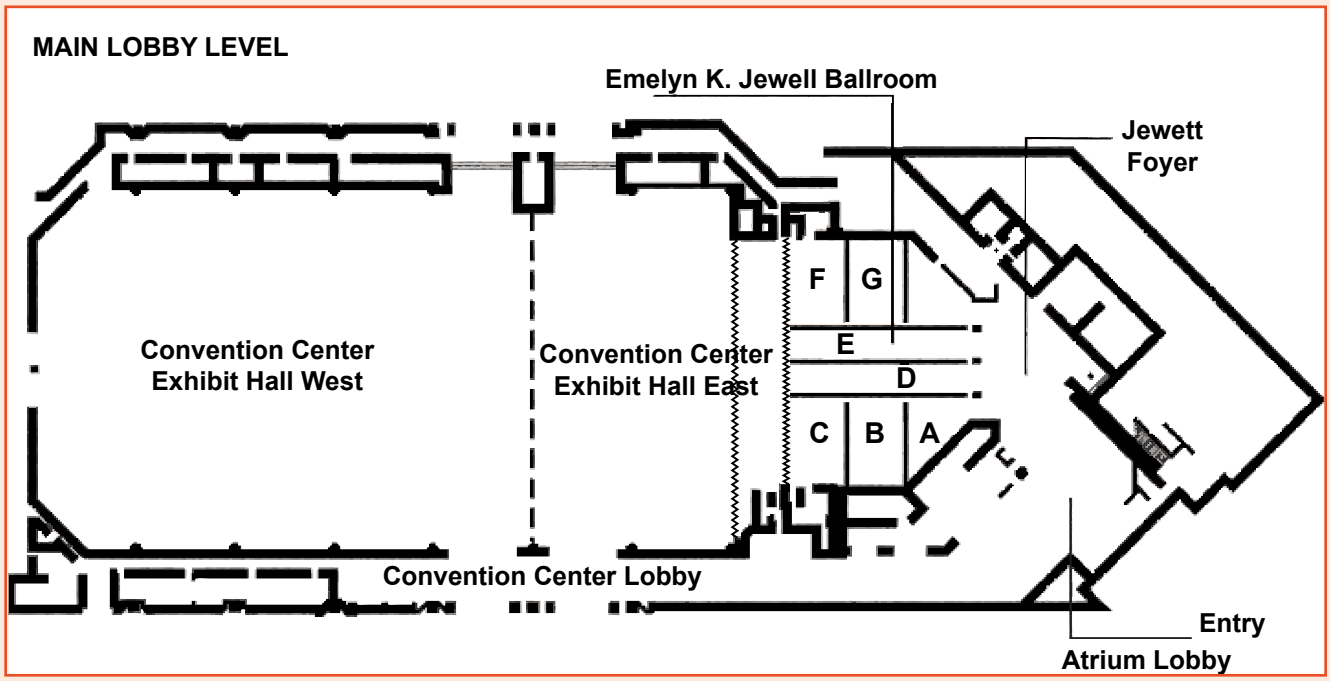
Friday, September 24, 2010

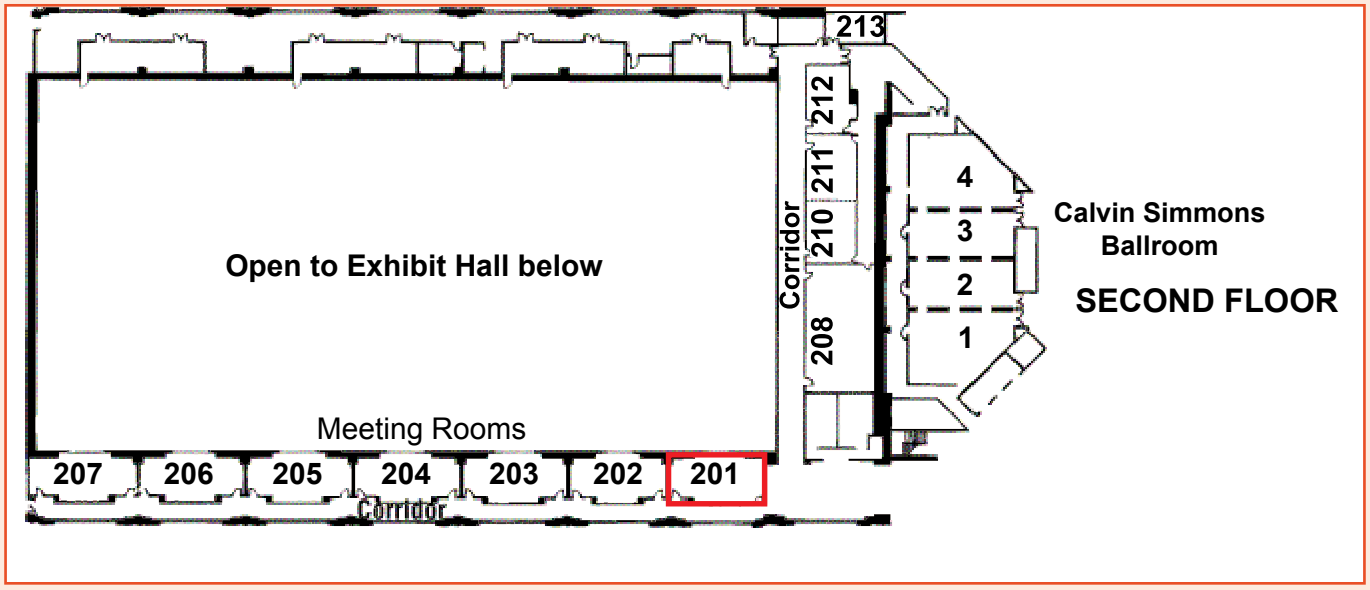
Time	Event	Location
6:00am – 6:45am	AM Yoga Work-Out	OCC 201
7:00am – 9:00am	Poster Set-up	West Hall
7:00am – 6:00pm	Registration	Foyer
7:00am – 9:00am	Continental Breakfast	West Hall
8:00am – 9:00pm	Breast Art Exhibition	West Hall
8:00am – 6:00pm	Exhibitor Showcase	Foyer
8:00am – 8:00pm	Poster Viewing	West Hall
8:00am – 8:15am	**Welcome**	East Hall
8:15am – 10:00am	**Tools for Expanding the Research Paradigm**	East Hall
10:00am – 10:30am	Break	West Hall
10:30am – 12:30pm	**Molecular Pathology – Reshaping How We Look at Breast Cancer**	Jewett A-D
10:30am – 12:30pm	**Breast Cancer 101 Workshop**	East Hall
10:30am – 12:30pm	**Statistical Models Workgroup**	Jewett E-H
12:30pm – 2:00pm	No Host Lunch	
12:30pm – 2:00pm	**Exhibits and Poster Viewing (unattended)**	West Hall
2:00pm – 3:30pm	**Plenary Poster Discussions**	Jewett A-D
2:00pm – 3:30pm	**Community Research Collaboration Workshop**	Jewett E-H
3:30pm – 4:00pm	Break	West Hall
4:00pm – 5:30pm	**New Tools for Researching Disparities and Breast Cancer Risk**	Jewett A-D
4:00pm – 5:30pm	**Translational Projects: Creating Impact through Research**	Jewett E-H
5:30pm – 6:00pm	Break	West Hall
6:00pm – 7:00pm	**CBCRP Listens**	Jewett A-D
7:00pm – 9:00pm	**Networking Reception**	West Hall

Saturday, September 25, 2010

6:00am – 6:45am	AM Yoga Work-Out	OCC 201
7:00am – 12:00 noon	Registration	Foyer
7:00am – 9:00am	Breakfast	West Hall
8:00am – 9:00pm	Breast Art Exhibition	West Hall
8:00am – 4:00pm	Exhibitor Showcase	Foyer
7:00am – 8:15am	**Advocate/Scientist Collaboration Breakfast**	West Hall
8:15am – 8:30am	**Welcome**	East Hall
8:30am – 10:30am	**Making Chemical Testing Relevant to Breast Cancer: The California Breast Cancer and Chemicals Policy Project**	East Hall
10:30pm –11:00am	Break	West Hall
11:00am – 12:30pm	**Improving Breast Cancer Treatment and Delivery**	Jewett A-D
11:00am – 12:30pm	**Exploring Factors Contributing to Breast Cancer**	Jewett E-H
12:30pm – 2:00pm	**Lunch (Keynote Address and Poster Awards)**	East/West Hall
2:00pm – 3:30pm	**Foundations in Breast Cell Biology**	Jewett A-D
2:00pm – 3:30pm	**Health Services in Underserved Communities**	Jewett E-H
3:30pm – 4:30pm	**Poster Presentation**	West Hall
4:30pm – 5:00pm	**Closing Ceremonies**	West Hall

Oakland Marriott Floor Plan





NEED TO STRETCH?

AM Yoga Wellness Work-Out

6:00am – 6:45am | Room OCC 201 (Second Floor)

Friday and Saturday

Yoga is an exercise for the mind, body, and spirit and can be practiced by anyone at any age or fitness level. This session will embrace yoga sequences to reduce overall stress from daily life. Learn how to modify basic poses to suit specific needs. It includes postures and movement.

WELCOME and PLENARY SESSION

Welcome (8:00am – 8:15am) | East Hall

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

Jim Ford, M.D.
Stanford University and
Retiring Chair, CBCRP Breast Cancer Research Council

Plenary Session - Tools for Expanding the Research Paradigm

8:15am – 10:00am | East Hall

Making major advances in breast cancer prevention, detection, and treatments requires not only innovative research, but also new tools for conducting the research. This panel will present projects that are forging new ways of conducting research.

Moderators:

Marc Hurlbert, Ph.D., Avon Foundation for Women

Catherine Quinn, M.P.A., California Office of Women's Health – Women's Health Council

Speakers:

Data Pooling Project to Study Race & Ethnicity in Stage-specific Breast Cancer Survival

Anna Wu, Ph.D. University of Southern California

ATHENA Breast Health Network

Laura Esserman, M.D. University of California San Francisco

"BreastCancerTrials.org"

Elly Cohen, Ph.D. University of California, San Francisco

Dr. Susan Love Research Foundation Avon/Love Army of Women

Susan Love, M.D., M.B.A , Dr. Susan Love Research Foundation

PLENARY SESSION SPEAKERS

Marc Hurlbert, Ph.D.

Dr. Marc Hurlbert is a national leader and recognized change-agent in philanthropic grant making. He currently serves as Executive Director of the Avon Foundation for Women and in a few short years has made substantial impact in breast cancer, fostering collaboration and collegiality among groups working in the field. In his role at Avon, Dr. Hurlbert oversees the global Avon Breast Cancer Crusade, and the Foundation's $35+ million annual grant-making budget, develops overall strategy, sets funding guidelines, manages review committees, and monitors the progress of grant recipients. The Avon Foundation and Avon Products has raised and awarded more than $725 million to support women's causes since 1955.

Dr. Hurlbert was elected by his peers to serve as the Chair (2010, 2011) of the Health Research Alliance, an alliance of 47 member nonprofit organization's who collectively award $1.6-billion in annual health research grants to 5,500 research investigators. He also serves as Chair of Columbia University-New York Presbyterian Hospital Health Sciences Advisory Council Cancer Committee and is a member of the Working Group of the NIEHS/NCI Breast Cancer and the Environment Research Centers. Dr. Hurlbert received his undergraduate degree in biochemistry from the University of Kansas and received his Ph.D. in pharmacology from the University of Colorado Health Sciences Center. He completed his training with a postdoctoral fellowship at New York University Medical Center, Skirball Institute of Biomolecular Medicine. After completing his training, Dr. Hurlbert transitioned to the nonprofit grant-making sector first at the Juvenile Diabetes Research Foundation (JDRF) and then joined Avon in 2004.

Catherine Quinn, M.P.A.

Catherine Quinn, M.P.A., has provided steadfast leadership to community health efforts in the Central Valley and throughout the state for over 20 years. In her years as Executive Director of the California Health Collaborative, Ms. Quinn worked to launch several regional breast cancer screening programs, the statewide California Breast Cancer Treatment Fund, and the Care Coordination and Navigation Program. She continues her passionate commitment to reducing disparities in health access.

PLENARY SESSION SPEAKERS

Laura Esserman, M.D., M.B.A.

Dr. Laura Esserman, M.D., M.B.A., is a Professor of Surgery and Radiology at the University of California, San Francisco, and is the Director of the Carol Franc Buck Breast Care Center, an interdisciplinary clinical program where clinical research and quality improvement is integral to care. She is the clinical leader of the Breast Oncology Program of the NCI designate Comprehensive Cancer Center. She is founder and faculty leader of the program in Translational Informatics spanning the disciplines of bioinformatics, medical and clinical informatics, systems integration, and clinical care delivery. In 1996, she started the Center of Excellence for Breast Cancer Care to integrate clinical care and research, automate tools for the capture of patient and clinical data, and develop systems to tailor care to biology, patient preference, and performance.

Dr. Esserman is nationally and internationally known as a leader in breast cancer and has published over 150 articles. She is the Principal Investigator of the I-SPY Trial program, a multi-site neoadjuvant clinical trial that has evolved into a model for translational research and innovation in clinical trial design. Dr. Esserman is currently developing a University of California-wide breast cancer initiative called the ATHENA Project. It is designed to follow 400,000 women from screening through treatment and outcomes, and incorporate the latest in molecular testing and web-based tools into the course of care.

Susan Love, M.D., M.B.A.

Susan M. Love, M.D., M.B.A., has dedicated her professional life to the eradication of breast cancer. As President of the Dr. Susan Love Research Foundation, she oversees an active $4 million dollar research program centered on breast cancer cause and prevention. She is also a Clinical Professor of Surgery at UCLA's David Geffen School of Medicine.

Dr. Love is best known as a trusted guide to women worldwide through her books and the Foundation website. The completely revised fourth edition of *Dr. Susan Love's Breast Book*, termed "the bible for women with breast cancer" by The New York Times, was released October 2005, and the 5th edition will be coming out in 2010.

A true visionary, Susan Love's most recent project, the Love/Avon Army of Women, is a creative Internet solution to partner women and scientists in order to accelerate basic translational research.

PLENARY SESSION SPEAKERS

Dr. Love received her medical degree from SUNY Downstate Medical Center in New York, and did her surgical training at Boston's Beth Israel Hospital. She founded the Faulkner Breast Center in Boston and the Revlon UCLA Breast Center in Los Angeles. She has a business degree from the Executive MBA program at UCLA's Anderson School.

Elly Cohen , Ph.D.

Elly Cohen has been associated with BreastCancerTrials.org almost from its beginning, guiding it from "idea" to regional Bay Area pilot, and most recently to nationwide service. She is currently Program Director of BreastCancerTrials.org and Senior Analyst with the University of California San Francisco (UCSF) Center of Excellence for Breast Cancer Care. Dr. Cohen participates in workshops designed to increase patient awareness about clinical trials and national efforts to create standards for clinical trial eligibility criteria.

Dr. Cohen earned a bachelor's degree in Biology from Brooklyn College and a Ph.D. in Pathology from Cornell University. Earlier in her career, she was a research neurobiologist and Adjunct Assistant Professor of Anatomy at UCSF. She has published papers in developmental neurobiology and the neurobiology of pain. Dr. Cohen is a breast cancer survivor.

Anna H. Wu, Ph.D.

Dr. Wu's research focuses on the epidemiology of cancer with emphasis on understanding the causes of breast and ovarian cancers. A second area of research interest relates to the study of tobacco-related cancers (e.g., lung, stomach/esophagus, colon) and genes that may be important in the metabolism of tobacco constituents.

PROGRAM

Molecular Pathology – Reshaping How We Look at Breast Cancer
10:30am – 12:30pm | Jewett A-D

Diagnosis and prognosis of breast cancer has been undergoing radical changes in the past decade due to the introduction of array technology and consideration of the contribution of non-epithelial cell types to the aggressiveness and disease progression of breast cancer. This session will examine changes to the paradigm and explore paths for adaptation into clinical practice.

Moderators:

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

Michele Rakoff, Breast Cancer Care and Research Fund

Speakers:

Melinda Telli, M.D., Stanford University

Robert West, M.D., Ph.D., Stanford University

David Mankoff, M.D., Ph.D., University of Washington

Hasan Korkaya, Ph.D., University of Michigan

Breast Cancer 101 Workshop
10:30am – 12:30pm / East Hall

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.

Leader: *M. Ellen Mahoney, M.D., F.A.C.S.,* Breast Cancer Connections

PROGRAM

Statistical Models Workgroup
10:30am – 12:30pm / Jewett E-H

This workshop brings together CBCRP funded researchers to exchange and gather new ideas for their ongoing work. It will be informative for community members interested in breast cancer clusters or unequal exposures to pollution and for researchers looking for new approaches to examining multiple risk factors or curious about the new genome wide association study in African American women.

Workgroup Topics:

Model-building with Complex, High-dimensional Exposures

David Nelson, Ph.D., Cancer Prevention Institute of California

Cancer Mapping: Making Spatial Models Work for Communities

Eric Roberts, M.D., Ph.D., Public Health Institute

New Methods for Genomic Studies in African American Women

Daniel Stram, Ph.D., University of Southern California

Plenary Poster Discussions
2:00pm – 3:30pm / Jewett A-D

Selected CBCRP investigators will give oral presentations of their posters.

Moderators:

Mary Alice Yund, Ph.D., University of California, Berkeley

Laura Fenster, Ph.D., California Department of Health Services

Presenters:

B-04 - High Frequency of Aldosterone Synthase (CYP11B2) C/C Genotype in the Marin County Adolescent Risk Factor Buccal Cell DNA Study

Kathie Dalessandri, M.D., F.A.C.S., University of California, San Francisco

B-06 - Variations in Hormone Pathway Genes and Breast Cancer RIsk in the California Teachers Study

Eunjung Lee, University of Southern California

B-02 - Adipose Levels of PBDEs and Risk of Breast Cancer

Susan Hurley, M.P.H., Cancer Prevention Institute of California

C-06 - Nanotherapy for Breast Cancer: Targeting Tumor Associated Macrophages

Gaurav Sharma, Ph.D., The Burnham Institute for Medical Research

D-05 - Extranuclear Estrogen Receptors in Breast Cancer Prognosis and Clinical Management

Richard Pietras, M.D, Ph.D., University of California, Los Angeles

A-04 - Latina Breast Cancer Survivors: Our Experience

Diana Tisnado, M.P.A., Ph.D., University of California, Los Angeles and *Brian Montano, M.P.H.,* Breast Cancer Early Detection Program

Community Research Collaboration Workshop
2:00pm – 3:30pm / Jewett E-H

This workshop will discuss strategies for applying for and conducting community-based participatory research. It will be useful for Community Research Collaboration (CRC) Award recipients, past and present, as well as those interested in applying for a CRC award.

Leader: *Marj Plumb, Ph.D.,* Plumbline Coaching and Consulting, Inc.

New Tools for Researching Disparities and Breast Cancer Risk
4:00pm – 5:30pm / Jewett A-D

This session will present the new tools that the CBCRP is developing through SRI funding. They include a new way to conduct demographics research, a new model for describing breast cancer causation and prevention, and cancer mapping for communities. This session will include interactive demonstrations of how these new tools can be used.

Moderators:

Rachel Morello-Frosch, Ph.D., M.P.H., University of California, Berkeley

Debra Oto-Kent, M.P.H., Health Education Council

Speakers:

Scarlett Gomez, Ph.D., Cancer Prevention Institute of California

Robert Hiatt, M.D, Ph.D., University of California, San Francisco

Eric Roberts, M.D., Ph.D., Public Health Institute

PROGRAM

Translational Projects: Creating Impact through Research
4:00pm – 5:30pm / Jewett E-H

CBCRP investigators who received Translational Research Awards will describe how their research will result in tangible benefits and how they intend to bridge the gap between research and implementation.

Moderators:

Jim Ford, M.D., Stanford University

Karren Ganstwig, Los Angeles Breast Cancer Alliance

Speakers:

Intraductal Therapy of DCIS: A Presurgery Study

Susan Love, M.D., M.B.A., Dr. Susan Love Research Foundation

Stratifying DCIS Biopsies for Risk of Future Tumor Formation

Thea Tlsty, Ph.D., University of California, San Francisco

Genetics of Tamoxifen Response

Elad Ziv, M.D., University of California, San Francisco

Soy Treatment for High-risk Women and DCIS Patients

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

CBCRP Listens
6:00pm – 7:00pm / Jewett A-D

Learn about the new funding direction that the CBCRP is taking and share your thoughts with members of the CBCRP council. Participants are invited to get to know the people who are charting the future of the CBCRP.

Networking Reception
7:00pm – 9:00pm West Hall

This networking reception is an opportunity to meet and connect with other attendees, and to meet and share your views with CBCRP council and staff in a one-on-one, informal atmosphere, while enjoying the food and the musical stylings of William Mininfield.

"A classically trained musician with soulful roots".

E-mail willmin@att.net

EXHIBITOR SHOWCASE

8:00am – 6:00pm | Foyer

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

Alta Bates Summit Medical Center
"We enhance the health and well being of people in the communities we serve through compassion and excellence."

Alta Bates Summit Medical Center offers comprehensive services designed to meet the health care needs of the diverse communities of the greater East Bay Area.

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

Asian & Pacific Islander American Health Forum
The Asian & Pacific Islander American Health Forum (APIAHF) influences policy, mobilizes communities, and strengthens programs and organizations to improve the health of Asian Americans, Native Hawaiians, and Pacific Islanders.

Bay Area Breast Cancer and the Environment Research Center - Zero Breast Cancer
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.

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.

Bay Area Young Survivors (BAYS)
BAYS is a support and action group for women age 45 and under who are living with breast cancer. We are a diverse group united by our passion to survive this disease and to end the epidemic, especially as it affects young women.

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.

Breast Health Access for Women with Disabilities (BHAWD)
Alta Bates Summit Medical Center

To increase the access of women with disabilities to breast health information, screenings and early breast cancer detection

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.

EXHIBITOR SHOWCASE

8:00am – 6:00pm | Foyer

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

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.

Cancer Prevention Institute of California
The mission of the Cancer Prevention Institute of California (CPIC) is to prevent cancer and to reduce its burden where it cannot yet be prevented.

Dr. Susan Love Research Foundation
The Dr. Susan Love Research Foundation works to eradicate breast cancer and improve the quality of women's health through innovative research, education, and advocacy.

Greywater Action
We are a collaborative group of educators, designers, builders, and artists who educate and empower people to build sustainable water culture and infrastructure.

Korean Community Health Services
Korean Community Health Services is a nonprofit organization dedicated to providing healthcare services to the Korean immigrant population throughout northern California. Our mission is to increase quality health care access to the largely uninsured Korean immigrant community in order to encourage and maintain a healthy community.

Mother's Wisdom Breast Health Program
Mother's Wisdom uses a cultural framework design to increase knowledge about breast health and to eliminate psychocultural barriers to mammogram screening, resulting in increased mammography screening among American Indian/Alaska Native (AI/AN) women in California.

Young Survival Coalition
Young Survival Coalition (YSC) is the premier international organization dedicated to the critical issues unique to young women and breast cancer. YSC works with survivors, caregivers and the medical, research, advocacy and legislative communities to increase the quality and quantity of life for women diagnosed with breast cancer ages 40 and under.

BREAST ART EXHIBITION

8:00am – 9:00pm | West Hall

Curatorial Statement

This year's exhibition weaves together the diverse experiences of individuals impacted by breast cancer and it reflects the far reaching impact of the disease. 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

Sarah Barsness

Sarah Barsness was born and raised in the American West. She currently lives, teaches, and makes art in San Francisco. Barsness is currently an Affiliate Artist at the Headlands Center for the Arts in Marin County. She is a former Artist in Residence at Recology – the San Francisco "dump". Recent past exhibits include *Materiality* at Yorkarts, in York, PA; *Cardiovascular*, at UNAM, Cuernavaca, Mexico; a collaborative exhibition with Veronica Sahagun, *I Know How You Feel,* at the Santa Fe Contemporary Art Center, Santa Fe, NM; Gen Art's *Emerge!* in San Francisco; *Cream from the Top,* in Benicia, CA; and *Close Calls* at The Headlands Center for the Arts.

"In *Medusozoa*, jellyfish are stand-ins for the cancer cells that form breast cancer tumors; they also serve as metaphors for breasts removed during mastectomies. Jellyfish are strange creatures: Despite the fact that they actually have no brain, they are able to move through the sea, nourish themselves, and reproduce. They are soulless, often dangerous, but also elegant, ethereal."

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?" Finding the answers was not her goal, but exploring the issues in all of their complexity became her focus. 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. Joanne is the recipient of numerous honors, including a grant from the James Irvine Foundation.

"My life's creative work has been focused on portraying the human form to explain the human experience. This study is a spiritual endeavor—an act of trust between model and artist. What the artist learns is not simply the anatomical structure of that specific human body, but more importantly, what it is to *be* human—to be weary, to feel anger, or to yearn for one another. By such study, we know with the greatest of intensity what it is to be human and we possess the ability to tell our own story and to share aspects of the universal human story."

BREAST ART EXHIBITION

8:00am – 9:00pm | West Hall

Nancy Bellen

Black Rock Desert - Nancy Bellen

Nancy Bellen is from Santa Rosa, California. She worked as a television producer and editor for ten years prior to her diagnosis of breast cancer at the age of 32. A twelve-year survivor, she now works as a film maker and photographer, and as an advocate for women with cancer. Her passion for the past eleven years has been to provide access to quality breast care services for women in her community.

Nancy has also been an advocate with The Breast Cancer Fund and climbed Mt. Fuji as part of the *Mt. Fuji Climb Against the Odds* team. She is one of the artists whose work appears in *Art.Rage.Us; Art and Writing by Women with Breast Cancer,* which has exhibited internationally.

"When people see my work, I want something in them to open. An opening that feels elemental and familiar. Perhaps in a place that has been long forgotten. A place before thought — maybe in the chest. My companion in this dialogue is Rebecca Wilson. Our lives were irrevocably changed by breast cancer; I was diagnosed when I was 32 and Rebecca lost her mother when she was 17. Through photography, I seek to express fear, loss, surrender and grace. Through landscape we explore coming to wholeness after loss and the resiliency of being human."

Dear Talula - Lori Benson

Lori Benson

Fourteen months after giving birth to her daughter Talula, Lori Benson received life-altering news when her doctor called (after a routine mammogram) to tell her she had breast cancer.

Dear Talula began with a suggestion to start filming from Lori's husband, a documentary filmmaker, who recognized the compelling subject matter. Within days of her diagnosis, Lori's friends began videotaping her and the camera soon became an invisible yet pervasive presence in her life. The major moments and tiny details of her experience as a woman, a daughter, a friend, and a new mother going through breast cancer, were all recorded. Mixing verité footage with home movies and family photographs, this 34-minute film is an intimate portrait of a young woman who met the challenges of her breast cancer diagnosis with captivating courage and candor.

The Art of Healing Breast Cancer: A Union of Science and Design, courtesy of CBCRP

An emotionally complex illness like breast cancer requires more than science to bring the deeply-felt understanding that is needed for a sustained effort to reduce or eliminate the devastating impact of this disease. Art helps us understand the experiences of others. In this way, art is the link between science and empathic action. The artists whose works are in this exhibit accepted an invitation to make sculptures in the form of breast

prostheses. Some of the artists are women who have experienced breast cancer; others have been touched by the disease in other ways. No matter who they were, the artists took an interest and used the very thing that conceals the effects of breast cancer and its treatments to reveal things that can guide our collective response to this complex disease.

Art and design pick up where science leaves off and delivers knowledge directly to our hearts. *The Art of Healing Breast Cancer: A Union of Science and Design* shows us what a mastectomy can be like when the veils of shame and fear are pulled aside. We are shown how to look at breasts and their absence with a new kind of interest, without fear or pity. We are given an opportunity to look at the devastation of breast cancer and mastectomy straight on and we are offered the inspiring knowledge that a woman who has lost a breast to breast cancer is likely to feel that she is more of a woman afterwards, not less.

Denise Dalton co-curated the first exhibition of the Breast Art collection in 1997 in order to offer routes of expression for women who have had mastectomies. “After fifteen years of wearing a prosthesis, I realized I wanted to wear something that would be more expressive of the many ways I feel and that would convey this message: It‘s okay to look; this is not shaming; this is me and I am more than a body. I am spirit and this art celebrates my spirit. It is as unique as I am unique. Art is my catalyst for change—a reminder that I have choices and that my ‘completeness‘ comes in many forms.”

Renata Cuellar

Renata Cuellar‘s mother, Ana Pena, was diagnosed with breast cancer. An avid art student, she created this painting as a tribute to her mother as well as to all of those touched by the disease. “I made this painting to emphasize the importance of breast cancer awareness. My intention was to combine visual and verbal communication forms that harmoniously work together to express one message. The two circles represent a Venn diagram unified by a pink, multicolored breast cancer awareness ribbon. The black and white circles represent a life: lost, born, or living. The mission of finding light within darkness has been my objective. Searching for hope presents possibilities, those seen and unseen. I hope this encourages women to be checked regularly for breast cancer. Moreover, this painting was created to support those individuals who have been impacted by breast cancer. You are not alone. A difficult situation can be approached with optimism, life, hope and unity.”

Jeanne Giles

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?”

BREAST ART EXHIBITION

8:00am – 9:00pm | West Hall

Torrie Groening

Torrie Groening has exhibited her work in group and solo shows in Canada and the US. Her work is in several public gallery and museum collections. She has served in a variety of roles as a teacher, master printer, collector, and gallery owner.

"This Elixir, It Won't Fix Her began to take shape as I started to notice—and then created a game of—finding the most offensive or ridiculous pink-ribboned object on offer. At first it was kind of funny, then I just wanted it to end.

This is a personal response to becoming another target of the huge, relentless marketing campaign that is breast cancer. Instead of being comforted or inspired, I felt constantly bombarded and taunted with reminders of cancer in the form of pink ribbons. For me, the pink ribbons were like tumors that showed up on my family's food products and domestic basics.

There is a point in which the pink ribbon industry targets women, and men, on a fundamental level: fear and guilt. Could these pink blessed objects, from sparkly key chains to cars, be purchased for insurance against cancer or to ease the 'survivor guilt' of friends and family who are, so far, the lucky ones?

This Elixir, It Won't Fix Her
- Torrie Groening

In this contemporary, vanitas still life, the frailty of life is seen not by the erosion of the natural objects or by including traditional symbols of death; life (and contemplation of death) is made fleeting by a casual consumer response to one's predicament. Instead of crying in the frozen food section when my son's favorite fruit pops were pink-ribboned, I tried to keep a sense of humor. You would have laughed too at the Castro grocery when I heard someone ask if the nipple clips (pink ribbon Chip-Clips) came in any other color… Nope! They only come in tumor-pink!"

Eleanor Hughes

"I made this collage, *I am Strong* sometime after my surgery for breast cancer in 2003. I needed to make a bold visual statement for myself. I needed to counteract the apprehension I had been feeling since my diagnosis. I visualized my white blood cells as ravenous white dogs gobbling up cancer cells that might be anywhere in my body. 'I am healthy, I am strong, I am well' became a mantra for me during that time. I was learning to practice meditation, changing my diet and some other aspects of my life as well. I also wanted to call on all the positive forces in the universe to speed up my recovery with healing energy and light. I feel that making this collage, living with it, seeing it every day did make me stronger."

Katherine Klein

"My mother was diagnosed with breast cancer in 1978, and was treated for three more cancers before she passed away from lung cancer in 1994. During that time she told me that she never thought about dying from cancer and in the end, she said she was just too tired for another treatment. My paintings are a tribute to her memory. *Cold Morning Creek* was painted during the time of my mother's treatment. *The Walk We Took After the Funeral* was a gathering of my family to a place that my mother loved. It was bitter cold as we wandered down the creek, thinking of her and each other. The images of this walk stayed with me and a few years later I began the paintings. I painted all of us walking in the winter landscape, but couldn't find the right way to put in my mother. This painting remained unfinished until, on a trip to Europe, I visited Notre Dame in Paris. Over the doorway of the cathedral was a relief that depicted the death of an important person, with people crowded around in a small room. This was how I finished the painting."

BREAST ART EXHIBITION

8:00am – 9:00pm | West Hall

Breach and Polypolis Installation photo - Liesa Lietzke

Liesa Lietzke

Liesa Lietzke earned her MFA in sculpture at California College of the Arts in 2009. In her sculptural practice, she creates troubled fetishes, complicating bodily perceptions and flirting with appeal and aversion. As a performer, she creates sculptural costumes and inhabits them in offstage settings. The performances play in the space between preciousness and disturbance; they also struggle with a longing for union and a grieving of irrevocable divisions.

"While one installation is site-specific to this symposium, *Polypolis* and *Stuffagus* and *Pillow* were made in the year before my breast cancer diagnosis. The latter were not explicitly about breast cancer at the time they were made, but instead revealed a prescience operating through my art practice. My sculptural work invades the installation space as bulbous, many-limbed and multi-textured forms, from tiny to larger-than-life, made from discarded/second-hand clothing as well as fabricated materials. They burst through walls; they hang in mid-air. They playfully invite a viewer's touch while simultaneously threatening to overwhelm. Pink and sweetly soft forms contain rotted areas of simulated flesh: these 'skin' areas are made of poured pinkish latex embedded with hair and with small red candies which melt and drip as the latex dries.

The way my themes are translated into impact on the viewer is the driving force behind my formal choices. The work seeks to complicate the self-sense (or proprioceptive awareness) of the viewer's own body. It exposes the tensions and fragilities of the boundaries that separate the self and other, the clean and foul, the interior and exterior. It engages with the sweetened artifice and compulsively cleaned- up cultural overlays that wrap the rebellious and sometimes grotesque flesh. The flesh resists, becoming biomorphic part-objects that grow, multiply, and creep back through the crevices of the clean and precious."

Laura McHugh

"*On the Table* represents my emotional response to a series of treatments for breast cancer: needle biopsy, tissue biopsy, a full mastectomy of my left breast, four intense chemotherapy treatments and radiation. This all transpired within five months of my initial mammogram and diagnosis at the age of 37. I was recently separated from my husband after 14 years of marriage and had just weaned the youngest of my four children from breast feeding. The radiation treatments were so easy compared to everything else I'd been through, but also very hard emotionally. I would start to cry every morning in the middle of the short treatment. I was cold and all alone on the table in the dark room under the loud whirling and clicking machine. I was grateful to be healing, but also terrified to be nearing the end of treatments with nothing more to distract me from having to confront my disease.

The five "tattooed' eyes are where the india ink marks were placed on my chest by the technician in an attempt to reduce radiation exposure to my heart and lungs. The circles and squares represent the light and alignment marks I could see above me on the machine. The tear represents my acceptance, finally, which led to my mental and physical recovery that is now a durable 14 year remission."

BREAST ART EXHIBITION

8:00am – 9:00pm | West Hall

Hratch Nargizian

Hratch Nargizian is a fifth generation metal-smith, born in Armenia. He initially learned the craft from his family and continued his education at Art and Craft school of Yerevan. He apprenticed with Master Garobet and Valodia and committed years of practice to honing his skills. Today he works out of his studio in downtown San Francisco. His work has been exhibited nationally and internationally.

***Vespertine* -** Hratch Nargizian

“Plants can heal; plants can kill. They feed and clothe us, enable us think in new ways, let us forget... Many medications we use today come from their extracts or derivatives. One such drug,Taxol—a cytotoxin—was originally extracted from the bark and needles of the Yew tree. Taxanes are used today in combination with other chemotherapies to treat breast cancer.

Nothing could have prepared me for sister‘s breast cancer diagnosis. Witnessing her willingness to undergo chemotherapy treatments, including Taxane—essentially poisoning her entire body in an effort to kill cancer cells—made me think of the metamorphosis she was undergoing. I began working on *Vespertine* as a gift to honor her and her journey. I envisioned a beautiful spirit emerging from a pod full of thorns and claws. Vespertine is a flower that blooms and releases its fragrance at night; despite the darkness, its delicate blossom unfolds, transforming the night air around it. The spiked pod is from the Datura plant, a genus of the species Vespertine. The pod was cast in silver. The dancing spirit is made of the petals and stamen of a lemon bud, which are cast in gold.”

Leila Noorani

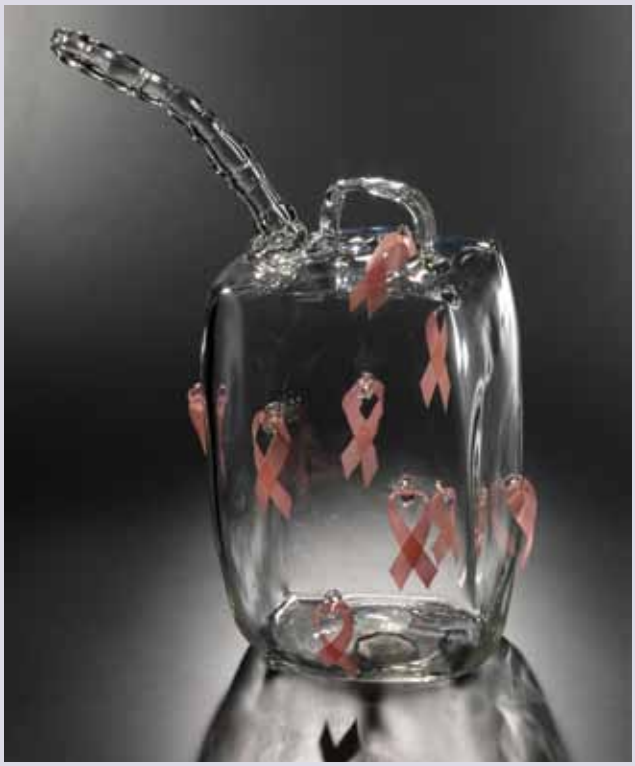
“Printmaking has traditionally been used as a method of creating multiple copies of one image using a single plate. In this series, I use a copper plate to create a sequence of one-of-a-kind prints, each evolution informing the next. In *Quandry*, I drew upon the parallels of this technique and the journey one undergoes during breast cancer treatment. A scarring of the plate begins the story, traditionally called ‘dry-point’, where I draw onto the plate using using a sharp tool. In this case, the countours of a woman‘s head emerged, body exposed, eyes shut. By erasing some of the lines and reworking others, I continue to work into the plate until I am satisfied and ready to pull the second print—which contains traces of the first and new marks unique to the second. In the third and final cell, a complete transformation occurs—where shoulders once were, a sitting figure, adorned with antlers emerges. A warrior or medicine woman has taken her place, bestowed with wisdom delivered through trial.”

BREAST ART EXHIBITION

8:00am – 9:00pm | West Hall

Nancy Otto

"*Pink Gas* was created for the *Think Before You Pink* exhibition benefiting Breast Cancer Action (BCA). BCA's Think Before You Pink Campaign was launched in 2002 in response to the growing concern about the overwhelming number of pink ribbon products and promotions on the market sold to advance the breast cancer cause. The campaign calls for more transparency and accountability by companies that take part in breast cancer fundraising, and encourages consumers to ask critical questions about pink ribbon promotions. The list of pink ribbon products grows every year. From candy to clothing to automobiles, thousands of companies are pinning pink ribbons on their products in an attempt to boost their image and their profits by connecting themselves to a good cause."



***Pink Gas* -** Nancy Otto

Nancy Otto is a sculptor working primarily in glass. She has exhibited nationally in New York at The Judson Church and E3 Galleries, Chicago at Woman Made Gallery, Pittsburgh at Morgan Contemporary Glass Gallery, and at the San Francisco International Airport Museum and Micaela Gallery. Nancy studied at Pilchuck Glass School with Karen Willenbrink, The Studio at Corning with Martin Rosol and Jiri Harcuba, and Haystack Mountain School of Crafts with Nancy Callan and Katherine Gray. Her work has been featured in *Curve Magazine*, the *Best of America Glass Artists and Artisans*, and the *San Francisco Chronicle Magazine*.

Ana Milena Pena

"The first question that arose after being diagnosed with breast cancer was: 'how much time do I have to live?' I underwent treatment, including a radical mastectomy and chemotherapy. Losing my breast and my hair was very difficult and I struggled with definitions of womanhood and femininity.

I used painting as a means to come to terms with the mastectomy. During this process a geisha subconsciously found her way into my work. Losing my breast made me feel as if I was void of any sexual appeal, even to my husband at the time. After noticing the first Geisha in my painting, I noticed another one. The second Geisha seemed to be walking towards my face, gracefully bending her right knee in approval. Geishas are immortal; life goes on and every human form is beautiful."

BREAST ART EXHIBITION

8:00am – 9:00pm | West Hall

Joyce Radtke

"My work as an artist is ever-evolving and often addresses issues of transformation as well as the blending of the spirit and physical worlds. After I was diagnosed with breast cancer, I became fascinated by the story of Persephone, the Greek goddess of eternal spring, of innocence. Abducted into the Underworld, Persephone ate the seeds of the pomegranate, the symbol of fruition and creativity. Eventually she was released, innocent no longer.

I imagine that she felt she had a new chance to find her life again, to embrace the light. Like Persephone, I journeyed into the dark realms and used the seeds of creativity to find my way home. By imagining myself as the goddess of eternal spring, I was able to escape from the pain, the grieving, the dark and barren landscape that the doctors painted for me. Again, after this third time, I will return to the light, to living moments as they come. Diving into healing art and writing, I envision a voice of hopefulness in the face of fear and embrace life in the face of it being taken away."

Persephone's Return - Joyce Radtke

The Woman Inside Project - Melissa Rankin

Melissa Rankin

"*The Woman Inside Project* was born when, in my work as an OB/GYN physician, I had to tell a woman who was pregnant that her biopsy was positive for breast cancer. Inspired to help her memorialize a moment in time—before she gave birth, lost her breasts and everything changed—I offered to cast her torso in plaster. The seed of an idea gestated, and five years and multiple plaster casts later, this exhibition emerged as a way to honor the beauty within each woman, particularly those with breast cancer.

After completing the cast, I hold up the sculpture and say, 'So this is what world sees. Now tell me about the rest of you.' I then listen for as long as it takes for her to unveil the breathtaking woman inside. I transcribe her story into a first person narrative of the beauty that I see within her.

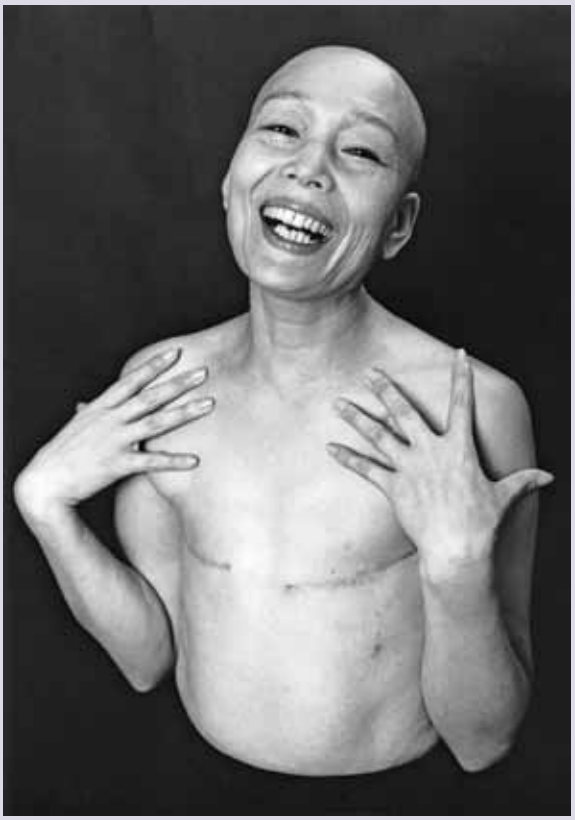
Some of the women I sculpted describe the process as a spiritual healing of sorts, during which I touch their bodies, place bandages over their wounds, then remove the bandages, leaving them feeling whole. For others, the process is traumatic, dredging up painful memories of surgical bandages and scars. Either way, the experiences are authentic and I feel blessed to have been there, holding hands, holding space.

BREAST ART EXHIBITION

8:00am – 9:00pm | West Hall

While traumas such as breast cancer crack us open and force us to grow, we all experience painful wounds that threaten to unravel us. It's how we respond to our wounds that tests us and gives us the opportunity to blossom. The women who participated in this project have created a garden for which I can claim no credit. It has been an honor to be their witness."

Dr. Rankin is practicing gynecologist, a nationally-represented artist, teacher, mother and author of the forthcoming book, What's Up Down There? Questions You'd Only Ask Your Gynecologist If She Was Your Best Friend. She is also the creator of the successful health and wellness blog OwningPink.com and the founder of the Owning Pink Center, an integrative medicine center in Mill Valley aimed at helping women achieve vital wellness.



Feeling Naked. Feeling Reborn - Trix Rosen

Trix Rosen

"In 1998, Takami Yao had undergone a double mastectomy. She told me that she had been scared when diagnosed with breast cancer, assuming that she would die. Following the chemotherapy, when her hair was falling out, she made a decision to shave her head. When she looked in the mirror, she realized that she was more beautiful than she had ever been. She saw herself reborn, and knew at that moment that she was going to live.

As a photographer, I saw both Takami's scars and her beauty. I dared to look deeper because she wasn't afraid to show me. How optimistic and courageous to look inward, to face loss, and become stronger through the experience. The landscape of our body is forever changing. Like a topographic map, the lines and shadings reflect our physical and psychological journey through life – through adolescence, childbirth, illness, menopause, and old age. My photographs show that it is possible to face these transfiguring changes, however painful and frightening, and yet still create new beginnings.

Takami's photographs depict a woman who bravely explores the physical and emotional contours of her new form. These portraits can be viewed as a narrative about her life and also as a defining moment of change. Bald, breast-less and scarred, she is as she appears to be–fearless and beautiful, essentially and eternally female."

Anne Spooner

"Years ago, one of my older brothers found a nest of abandoned baby birds and brought them home. Our mother tended to the orphaned birds on our screened-in porch that summer. When September came around and the birds were old enough to make it on their own, my mom decided to let them go. Not too long after she set them free, she was in the backyard and one of the birds flew down from a tree and landed on her shoulder. It was as if the bird was saying, 'I remember you'.

I had been working with bird forms in my art for several years before I was diagnosed with breast cancer late in 2007. The birds took on a much deeper meaning. *A True Story* touches on the baby bird story of long ago, portraying a message that birds symbolize hope, protection, compassion and healing. Even though a cancer diagnosis lands you in a dark place, there is light ahead. Just like those resilient little birds, I know my spirit is strong, too."

BREAST ART EXHIBITION

8:00am – 9:00pm | West Hall

The Art for Recovery Breast Cancer Quilts Project & UCSF Helen Diller Family Comprehensive Cancer Center

The Breast Cancer Quilts Project gives voice to women coping with breast cancer by inviting them, their families and friends to create quilt squares using images that express their personal experience with illness. These women come from across the United States and from underserved communities throughout the Bay Area, including women coping with breast cancer who are incarcerated.

The squares are assembled into full-sized quilts that tell a collective story of the inner realities of the illness experience. There are now almost 70 quilts in the collection; they travel around the country for exhibition and hang in rotating displays in the public areas of various locations on the UCSF Medical Center Campus.

If you are interested in making a quilt square, please visit the Art for Recovery website at http://cancer.ucsf.edu/afr for instructions.

Zero Breast Cancer & The Plexus Art Group

"I was only 47 when I first found a tumor. Two weeks after surgery and one day before chemotherapy, I married my soul mate, Bill Mentzer. In 1996, I helped to form the group that is now Zero Breast Cancer. Eleven years after my breast cancer diagnosis the tumor returned and required a second round of surgery, chemotherapy, and radiation. That gave me six more years of a wonderful life. Now I am living today with another recurrence—metastatic breast disease. When my dear friends and fellow artists in the Plexus Art Group asked me, 'what can we do to support you?' my answer was quick: 'I'm going to lose my hair again when the chemotherapy starts. Let's create comfortable hats (not wigs) that are works of art. Let's show the world beauty!'

Flapper Chic - Diana Shore

The Plexus Art Group responded with enthusiasm, generosity, and their usual creativity, and I was gifted with several lovingly made hats to wear when I lost my hair to chemotherapy. This helped enormously to improve my sense of strength, femininity and confidence. Beyond that, and in keeping with our Plexus mission, we decided to create and exhibit one-of-a-kind hats that we could use to raise money for Zero Breast Cancer" –Roni Peskin Mentzer

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

Visit us at the CBCRP booth!

- Share your story
- Tell us what you think about the research directions that the CBCRP should take
- Meet the CBCRP staff
- Learn about the new research opportunities the CBCRP has to offer

ADVOCATE/SCIENTIST COLLABORATION BREAKFAST

7:00am – 8:15am | West Hall

Attendees will be able to join informal small group discussions led by advocates on critical topics and important gaps in breast cancer research.

Discussion Topics:

Advantages to Including Advocates in Basic Science Research

Sandra Walsh, California Breast Cancer Organizations

Sandy Walsh was diagnosed with breast cancer in 1984. She was a founder of the Y-ME Affiliate (now Network of Strength) in Northern California. Currently she is president of California Breast Cancer Organizations (CABCO) and represents them on the National Breast Cancer Coalition's (NBCC) Board of Directors. Sandy has reviewed grants for the Department of Defense Breast Cancer Research Program; serves on the Scientific Advisory Task Force for the California Teachers Study, a prospective cohort of 133,000 teachers; and is on the Scientific Advisory Committee for the Avon/Love Army of Women. Sandy serves as field director for Northern California for the NBCC, and has served on the council for the California Breast Cancer Research Program.

Conducting Research that Drives Environmental Health Policy

Jeanne Rizzo, The Breast Cancer Fund

Jeanne Rizzo's vision guided the Breast Cancer Fund to adopt its bold breast cancer prevention mission to identify and advocate for the elimination of the environmental and other preventable causes of the disease. Under her leadership, the organization has become a national leader in translating the growing body of scientific evidence linking breast cancer and environmental exposures into strategic policy initiatives.

The scientific evidence is presented in landmark science reports, *State of the Evidence: The Connection between Breast Cancer and the Environment*, and *The Falling Age of Puberty in U.S. Girls: What We Know, What We Need to Know*, by Sandra Steingraber, Ph.D.

Ms. Rizzo guides current strategic policy initiatives to reduce our exposure to bisphenol A, to address the safety of personal care products, and to reform the broken Toxic Substances Control Act. Recent victories include the passage of federal legislation banning toxic chemicals linked to breast cancer from children's toys and California laws that created the first statewide biomonitoring program, advanced the safety of cosmetic products, and initiated a groundbreaking "green chemistry" initiative in the state.

She serves on the Council of the California Breast Cancer Research Program and as an appointed member of the National Institute of Health Interagency Breast Cancer and Environment Research Coordinating Committee.

Cultural Considerations when Researching Access to Care

Debra Oto-Kent, Health Education Council

Debra Oto-Kent is executive director of the Health Education Council, which is dedicated to promoting healthy communities and preventing disease among at-risk populations. Ms. Oto-Kent founded the Council in 1991 after working for more than 13 years in the nonprofit health sector. She received her undergraduate degree in health science and safety studies from San Diego State University and her master's degree in health education and behavioral science from UCLA's School of Public Health. Ms. Oto-Kent's primary area of interest and expertise is health education — with an emphasis on traditionally underserved populations, such as the socio-economically disadvantaged and diverse ethnic populations — about which she has written and spoken extensively. She has served on boards and committees of numerous local and statewide health promotion organizations including her current service as a founding board member of the Capitol Community Health Network and board

member for CANFiT. Ms. Oto-Kent received the Outstanding Women of Achievement in Healthcare Award from the Downtown Capitol Chapter of Business and Professional Women and the Sacramento Women's Council's Leadership Award; 2010 Service and Advocacy Award from the Martin Luther King, Jr. Celebration Committee Greater Sacramento area and other recognitions. She is a past chair of the California Breast Cancer Research Program council and an 11 year breast cancer survivor.

Developing Community Research Collaborations

Carlina Hansen, San Francisco Women's Community Clinic

Carlina Hansen has been the Executive Director of San Francisco's Women's Community Clinic since 2002. She started at the Clinic as a Health Education Volunteer while working as a Senior Project Coordinator at the Tides Center, a local nonprofit incubator and fiscal sponsor. Carlina has worked in the nonprofit sector in San Francisco for 13 years. She volunteers at San Francisco General Hospital as a health educator in the Women's Clinic. She has also volunteered for Maitri (a local AIDS hospice), Healing Waters (which provides outdoor adventure opportunities for people with HIV and AIDS) and is on the Advisory Board of Garden for the Environment, where she recently completed a Master Gardener and Composter Training Program. She has served on the Executive Committee of the Women's Health Advisory Committee of the Department of Public Health and currently serves on the Executive Committee of the Women's Working Group on Universal Health Care. She is a graduate of the Women's Foundation of California's Women's Policy Institute and of CompassPoint's Executive Leadership Circles. She was recently voted 2007 Young Executive Director of the Year by Young Non Profit Professionals Network (YNPN).

Making Your Research Relevant – the Importance of Advocates

Michele Rakoff, Breast Cancer Care and Research Fund

A patient advocate for more than 20 years, Michele Rakoff is a breast cancer survivor and the Executive Director of the Breast Cancer Care & Research Fund. She is a founding Board member of the Los Angeles Breast Cancer Alliance (LABCA), Vice President of the California Breast Cancer Organizations (CABCO) and Board member of the National Breast Cancer Coalition (NBCC). She took an advocate seat on the California Breast Cancer Research Program's (CBCRP) Breast Cancer Research Council and was the recipient of a community research collaborative (CRC) grant after she served her term. She also participated as a peer-reviewer for the Department of Defense Breast Cancer Research Program (DoD BCRP) and is a NBCC Project Lead graduate. Currently, Ms. Rakoff holds an advocate seat on the California Teachers Study Scientific Task Force; is a member of the Love/Avon Army of Women Scientific Advisory Committee; and a Data Safety Monitoring Board member of a CBCRP research study. Presently, she is collaborating with the Beilinson Hospital, Rabin Medical Center in Israel as they develop their comprehensive breast center. Ms. Rakoff believes that the advocate voice is important and that well educated, trained advocates must be included in every aspect of research, clinical decision-making, and public policy issues.

ADVOCATE/SCIENTIST COLLABORATION BREAKFAST

7:00am – 8:15am | West Hall

Socially Responsible Drug Development

Barbara Brenner, Breast Cancer Action

Barbara A. Brenner is a tireless activist who believes that everyone can — and is needed to — make a difference in ending the breast cancer epidemic. Her passion is contagious, and her effectiveness as a leader of the breast cancer movement is demonstrated in the growth and achievements of Breast Cancer Action since she took the helm as executive director in September 1995. Ms. Brenner joined the board of Breast Cancer Action (BCA) in September 1994, one year after she was diagnosed with breast cancer. In 1996, she had a local recurrence of breast cancer, which resulted in a mastectomy.

Ms. Brenner is highly sought after by the national media, and has appeared in the New York Times, USA Today, the Washington Post, ABC News, and CBS Evening News. She is co-author of the chapter, “Cancers,” in *Our Bodies, Ourselves: Menopause* (The Boston Women’s Health Book Collective, 2006). She is also the author of the chapter, “Sister Support: Women Create a Breast Cancer Movement,” in *Breast Cancer: Society Shapes an Epidemic* (Palgrave, 2000).

She holds a bachelor’s degree in government from Smith College and a law degree from Boalt Hall School of Law at the University of California, Berkeley.

Ms. Brenner is an inspirational speaker about breast cancer and the movement and how people can get involved to steer the tide of the disease.

Funding Opportunities in 2010-2011

Investigator-Initiated

We are offering investigator initiated grant funding for:

- Innovative Developmental and Exploratory Awards (IDEA)
- Translational Research Awards
- Community Research Collaboration Awards
- Conference Awards

► The IDEA, Translational Research Award, and IDEA–competitive renewal applications require a "letter of intent" (LOI) that must be approved prior to submitting a full application.

► The Community Research Collaboration Award applications have an optional pre-application research plan review

► ***Submission Deadlines***

October 14, 2010	All Letters of Intent and pre-application review plans
December 1, 2010	Conference Awards
February 24, 2011	All other applications

Special Research Initiatives

We have two special RFPs in 2010 for:

Understanding Behavioral, Social, and Physical Environment Factors and Breast Cancer among Immigrants.
An estimated $1,200,000 will be available to fund transdisciplinary pilot studies. RFP released in September 2010.

► ***Submission Deadline***
December 14, 2010

Making Chemicals Testing Relevant to Breast Cancer.
An estimated $3,600,000 to fund development and validation of new toxicity testing methods. RFP expected in November 2010.

► ***Submission Deadline***
Application Deadline: Early 2011

Go to www.cabreastcancer.org/apply/ for more information about all of these funding opportunities.

PROGRAM

Welcome (8:15am – 8:30am) | East Hall

Mistress of Ceremonies:

Holly J. Mitchell, CEO, Crystal Stairs, Inc.

Speakers

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

Jeanne Rizzo, R.N., Executive Director of Breast Cancer Fund and
Incoming Chair, CBCRP Breast Cancer Research Council

Holly Mitchell
Mistress of Ceremonies

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

She has received statewide honors and recognition including the LA County Commission for Women 2nd District Woman of the Year Award, the National Women's Political Caucus, LA African American Women's Public Policy Institute (LAAAWPPI), LAAAWPAC, and the Black Women for Political Action (BWOPA). Holly J. Mitchell was recognized and selected by L.A. County Supervisor Mark Ridley-Thomas as his 2009 Woman of the Year.

Holly has a career-long history of public policy development and advocacy, as a former advocate with the Western Center on Law and Poverty, the California Black Women's Health Project and as a former consultant to the Senate Health and Human Services Committee.

She serves on various governing boards, including Liberty Hill Foundation and Verbum Dei High School.

In June, Holly successfully won her primary bid for the 47th State Assembly District and will be on the general election ballot in November.

She is a native Angeleno and the proud mother of Ryan!

PROGRAM

PLENARY SESSION – Making Chemical Testing Relevant to Breast Cancer: The California Breast Cancer and Chemicals Policy Project

8:30am – 10:30am | East Hall

The CBCRP funded an expert panel to gather and synthesize scientific evidence for better addressing breast cancer in the state laws and regulations governing the production and use of chemicals. The panel identified key biological processes associated with breast cancer and then determined the toxicity tests currently available to evaluate a chemical's ability to affect those processes. The panel members will describe their findings and their recommendations for prioritizing chemicals and developing new tests relevant to breast cancer development and progression. The panel will also discuss the impact of this work in their fields, future research, and California policies.

Moderator:

Gina Solomon, M.D., M.P.H., Natural Resources Defense Council (NRDC)

Speakers:

Megan Schwarzman, M.D., M.P.H., University of California, Berkeley

Sarah Janssen, M.D., Ph.D., M.P.H., Natural Resources Defense Council (NRDC)

Dale Johnson, Pharm.D., Ph.D., Emiliem, Inc.

Shanaz Dairkee, Ph.D., California Pacific Medical Center

Lauren Zeise, Ph.D., Office of Environmental Health Hazard Assessment, California Environmental Protection Agency

PLENARY SESSION SPEAKERS

Gina Solomon, M.D., M.P.H.

Gina Solomon is a Senior Scientist at the Natural Resources Defense Council (NRDC) and an Associate Clinical Professor of Medicine at the University of California at San Francisco (UCSF) where she is also the Director of the Occupational and Environmental Medicine Residency Program and the Associate Director of the UCSF Pediatric Environmental Health Specialty Unit. Her work has included over 40 scientific papers, book chapters, and reports on air pollution, pesticides, global warming, and other environmental and occupational threats to health. Dr. Solomon serves on the US EPA Science Advisory Board Drinking Water Committee, the National Toxicology Program Board of Scientific Counselors, and the California Scientific Guidance Panel for biomonitoring. Dr. Solomon attended medical school at Yale and did her postgraduate training in internal medicine, public health, and occupational and environmental medicine at Harvard.

Megan Schwarzman, M.D., M.P.H.

Dr. Schwarzman's work focuses on endocrine disrupting substances, reproductive environmental health, U.S. and European chemicals policy, and the implications for human health and the environment of the production, use and disposal of chemicals and products. She is a research scientist at the Center for Occupational and Environmental Health (COEH), in UC Berkeley's School of Public Health, and Associate Director of Health and Environment for the interdisciplinary Berkeley Center for Green Chemistry. She earned her medical degree from the University of Massachusetts, completed her specialty training in Family Medicine at the University of California, San Francisco, and earned a master's of public health from the University of California, Berkeley. Dr. Schwarzman also practices medicine part time at San Francisco General Hospital.

PLENARY SESSION SPEAKERS

Sarah Janssen, M.D., Ph.D., M.P.H.

Dr. Sarah Janssen is a Senior Scientist in the Health and Environment Program of the Natural Resources Defense Council (NRDC). In her capacity as a scientist with NRDC, Dr. Janssen provides scientific expertise for policy and regulatory decisions on a number of toxic chemicals, including hormone-disrupting substances which interfere with fertility and reproduction. Her work has included research on flame retardants, cosmetics, plastics and plasticizers, breast cancer and threats to adult reproductive health and child development. She is board-certified in Preventive Medicine with a subspecialty in Occupational and Environmental Medicine. Dr. Janssen is also an Assistant Clinical Professor at the University of California, San Francisco in the Division of Occupational and Environmental Medicine and works part time at Kaiser Permanente of Northern California. She is also a member of the Executive Committee of the San Francisco Bay Area chapter of Physicians for Social Responsibility. Dr. Janssen completed her M.D. and Ph.D. in Molecular and Integrative Physiology at the University of Illinois, Urbana-Champaign in 2001. She did her residency training at the University of California, San Francisco, which included a M.P.H. in Environmental Health Sciences from the University of California, Berkeley. Dr. Janssen is the author of numerous peer-reviewed publications and book chapters.

Dale E. Johnson, Pharm.D., Ph.D.

Dale Johnson is an Adjunct Professor in Molecular Toxicology at University of California, Berkeley where he teaches Computational Toxicology and is on the affiliated faculty of the Berkeley Center for Green Chemistry. Dr. Johnson is also a member of the Green Ribbon Science Panel for the State of California green chemistry initiatives and the expert panel for the California Breast Cancer and Chemicals Policy Project. He is also President & CEO of Emiliem, Inc. a biotechnology company focused on molecular targeted therapies and diagnostics. He has over 30 years experience in biopharmaceutical research and development activities where he has led and managed small units in start-up companies to multi-national groups in large corporations. Prior to Emiliem, he served as VP, Drug Assessment & Development at Chiron Corporation and previously VP, Preclinical Development. Prior R&D and executive positions include: Eos Biotechnology, Lederle (American Cyanamid), International Research and Development Corp. (a preclinical CRO), and Hoechst-Roussel Pharmaceuticals Inc. He received BS, PharM.D., and Ph.D. (Toxicology) degrees from the University of Michigan where he was an AFPE Fellow.

He is a Diplomate of the American Board of Toxicology and co-editor of the journal *The Chemistry of Metabolic and Toxicological Processes, Current Opinion in Drug Discovery & Development.*

Shanaz H. Dairkee, Ph.D.

Dr. Shanaz H. Dairkee is a senior scientist at the California Pacific Medical Center Research Institute where she leads a translationally focused research program in breast cancer. Her laboratory is committed to the application of clinically derived model systems for studying Cellular and Molecular Changes in Breast Cancer, and has published groundbreaking work in this field. This research aims to improve tumor targeting and prevention through a better understanding of basic tumor biology. Dr. Dairkee received her doctorate in Human Genetics and Development from Columbia University in the City of New York. She did postdoctoral research at the University of California, Berkeley and remained on the research faculty of the Department of Molecular Biology to pursue the development of high throughput methodologies for the detection of cancer associated cellular changes. She continued research in this area at the Lawrence Berkeley National Laboratory. Dr. Dairkee has received grant awards from the National Cancer Institute, US Environmental Protection Agency, California Breast Cancer Research Program, the biotech industry, and private foundations.

She currently serves in the NIH scientific review process for extramural funding in the area of tumor progression and metastasis. Ongoing research in her group includes the application of cells from high-risk individuals to investigate the functional interaction between genes and environmental chemical exposure in cancer development and progression. Among many others, a unique resource developed by her laboratory includes a vast repository of live, interactive cells from clinical samples to foster multi-disciplinary work involving direct experimentation with malignant human tissue.

PLENARY SESSION SPEAKERS

Lauren Zeise

Dr. Lauren Zeise is chief of the Reproductive and Cancer Hazard Assessment Branch of the California Environmental Protection Agency. She oversees or is otherwise involved in a variety of California's risk assessment activities, including cancer and reproductive toxicant assessments; development of frameworks and methodologies for assessing cumulative impact, nanotechnology, green chemistry/safer alternatives, and susceptible populations; the California Environmental Contaminant Biomonitoring Program; and health risk characterizations for environmental media, food, fuels and consumer products. Dr. Zeise's research focuses on human interindividual variability, dose response, uncertainty and risk. She was the 2008 recipient of the Society of Risk Analysis's Outstanding Practitioners Award and is a National Associate of the National Academy of Science's National Research Council (NRC). She has served on various advisory boards and committees of the Environmental Protection Agency, Office of Technology Assessment, World Health Organization, and National Institute of Environmental Health Sciences. She has also served on a numerous NRC and Institute of Medicine committees and boards, including the committees that produced Toxicity Testing in the 21st Century: A Vision and Strategy, Science and Decisions: Advancing Risk Assessment, and Understanding Risk: Informing Decisions in a Democratic Society. Dr. Zeise received her Ph.D. from Harvard University.

PROGRAM

Improving Breast Cancer Treatment and Delivery
11:00am – 12:30pm | Jewett A-D

The treatments for breast cancer and the methods for delivering services are evolving rapidly. The speakers in this session will describe some of the ways that care providers are evaluating when to treat women, ways to treat advanced disease, and how to get these services to women more effectively.

Moderators:

Jim Ford, M.D., Stanford University

Barbara Brenner, J.D., Breast Cancer Action

Speakers:

Comparing Risk-reduction Strategies for Breast Cancer

Allison Kurian, M.D., Stanford University

New Approaches for Treating Brain Metastases

Brunie Felding-Habermann, Ph.D., The Scripps Research Institute

Providing Breast Cancer Services to Rural Women

Marlene von Friederichs-Fitzwater, Ph.D., M.P.H., University of California, Davis, and *Rebecca Parsons*, The Sierra Fund

PROGRAM

Exploring Factors Contributing to Breast Cancer
11:00am – 12:30pm | Jewett E-H

Understanding the risks for developing breast cancer may direct us toward effective preventive strategies. The presentations in this session will explore how external factors such as diet and exposure to chemicals early in life and in the workplace may contribute to the disease.

Moderators:

Peggy Reynolds, Ph.D., Cancer Prevention Institute of California

Jeanne Rizzo, R.N., The Breast Cancer Fund

Speakers:

Early Exposure to Chemicals and Breast Cancer Risk

Barbara Cohn, Ph.D., M.P.H., M.C.P., Public Health Institute

Grapefruit, Hormones, and Postmenopausal Breast Cancer Risk

Kristine Monroe, Ph.D., University of Southern California

Breast Cancer Risks in California Nail Salon Workers

Thu Quach, Ph.D., M.P.H., Cancer Prevention Institute of California

KEYNOTE LUNCHEON
12:30pm – 2:00pm | West Hall

Mistress of Ceremonies:

Holly J. Mitchell, CEO, Crystal Stairs, Inc.

Cornelius L. Hopper Poster Award Presentations

Cornelius Hopper, M.D., Vice President for Health Affairs, Emeritus, University of California System-wide

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

Keynote Address:

Angela Padilla, J.D., co-founder, BAYS (Bay Area Young Survivors); board president, Circulo De Vida; and former chair, CBCRP Breast Cancer Research Council

PROGRAM

Foundations in Breast Cell Biology
2:00pm – 3:30pm | Jewett A-D

The breast is populated by a variety of different types of cells, each with its own job. By investigating how these cells are functioning and interacting with each other as cancer develops, we should be able to devise ways to intervene in the process. The researchers in this session will describe how their insights into how breast cells work is helping them open new avenues for treating the disease.

Moderators:

Terri Burgess, Ph.D., Amgen, Inc.

Sandy Walsh, California Breast Cancer Organizations

Speakers:

Characterization of Wound-like Breast Cancer

Howard Chang, M.D., Ph.D., Stanford University

Nur-77, Defining New Target for Cancer Treatment

Xiao-Kun Zhang, Ph.D., The Burnham Institute

Identifying Drug Resistant Breast Cancer Using Nanotechnology

Trent Northen, Ph.D., Lawrence Berkeley National Laboratory

PROGRAM

Angela Padilla, J.D.

Angela is the founder and leader of Bay Area Young Survivors, the first support and activist group for women under forty-five affected by breast cancer in the Bay Area. When she was diagnosed with breast cancer in 2002, Angela decided to share her experience very publicly by working with photographer Stefanie Atkinson to document her experience in a photography show that they exhibited at our 2003 Symposium. Angela is a recipient of Lifetime Television's Breast Cancer Hero award. She is a lawyer by profession.

Health Services in Underserved Communities
2:00pm – 3:30pm | Jewett E-H

Breast cancer is a disease that touches every Californian, but the availability of treatment and services varies widely. The presentations in this session will show how collaborative partnerships are identifying ways to provide breast health services to segments of our population who have barriers to receiving them.

Moderators:

Marjorie Kagawa-Singer, R.N., Ph.D., University of California, Los Angeles

Tu-Uyen N. Nguyen, Ph.D., M.P.H., California State University, Fullerton and Orange County Asian & Pacific Islander Community Alliance

Speakers:

Underserved Women with Breast Cancer at End of Life

S*helley Adler, Ph.D.,* University of California, San Francisco and *Kendra Stone*, Charlotte Maxwell Complementary Clinic

Breast Cancer Control for Deaf and Hard-of-Hearing Women
Heidi Booth, Greater Los Angeles Council on Deafness, Inc. and *Angela Jo, M.D. M.S.H.S.,* University of California, Los Angeles

Psychosocial Health Promotion for Latinas

Anna Napoles, Ph.D., M.P.H., University of California, San Francisco and *Carmen Ortiz, Ph.D.,* Circulo de Vida

PROGRAM

Poster Presentations

3:30pm – 4:30pm

West 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 3:30 pm – 4:30 pm.

Poster Session A

Survivorship

3:30pm – 4:30pm

West Hall

A-01
Breast Health Behaviors in Immigrant Afghan Women in Northern California
Aida Shirazi, Rona Popal, and Joan Bloom

A-02
Creating Sustainable Community-Campus Partnerships to Develop New Scientists
Natasha Riley, Georgia Sadler, and Vanessa Malcarne

A-03
Health Anxiety, Pre-sleep Cognitive Activity, Sleep Effort, and Insomnia Symptoms in Breast Cancer Patients before Chemotherapy
Michelle Rissling

A-04
Latina Breast Cancer Survivors: Our Experience
Brian Montaño and Diana Tisnado

A-05
Mindful Movement Program for Breast Cancer Survivors
Holly Kiger and Rebecca Crane-Okada

A-06
Post-treatment Regret among Young Breast Cancer Survivors
Sara Fernandes-Taylor

A-07
Rushing for Life—Follow Up, Follow Through—Breast Cancer Measurement Outcomes Study
Tracy Hardy-Mosbey and Kimlin Ashing-Giwa

A-08
Increasing the Voice of African Americans in Breast Cancer Research
Carolyn Tapp and Kimlin Ashing-Giwa

A-09
Sister Survivor: African American Breast Cancer Coalition
Gloria Harmon and Kimlin Ashing-Giwa

A-10
Video Conference Breast Cancer Support Groups: A Viable Option for Rural Women?
Mary Anne Kreshka, Jim Perkins, Susan Ferrier, and Cheryl Koopman

Presenter: Marlene von Friederichs-Fitzwater

A-11
A Study of Breast Cancer-related Lymphedema Knowledge, Awareness, and Care among Kaiser Permanente Northern California Patients and Clinicians

Presenters: Marilyn Kwan, Ling Shen, Julie Munneke, Emily Tam, and Paula Partee

A-12
Talking about Empowerment with a Peer Counselor Predicts Increased Marital Satisfaction in Women with Breast Cancer
Caroline Bliss-Isberg and David Spiegel

Presenter: Lynne Wittenberg

A-13
Process of Discussions with Peer Counselors Predicts Change in Trauma Symptoms in Newly Diagnosed Women with Breast Cancer
Caroline Bliss-Isberg and David Spiegel

Presenter: Lynne Wittenberg

A-14
Reducing Mammography Disparities for Latinas through Community Health Centers: Lessons on Community-Academic Design and Implementation of Intervention Research
Stergios Roussos and Christine Noguera

Presenter: Felicia Batts

Poster Session B

Etiology and Prevention

3:30pm – 4:30pm

West Hall

B-01
A Strategy for More Efficient BRCA Analysis in an Underserved Latina Population
Jeffrey N. Weitzel

Presenter: Raquel Ogaz

B-02
Adipose Levels of PBDEs and Risk of Breast Cancer
Myrto Petreas

Presenter: Susan Hurley

B-03
Enhancing the Power of Genetic Association Studies in African American Women
Daniel Stram

B-04
High Frequency of Aldosterone Synthase (CYP11B2) c/c Genotype in the Marin County Adolescent Risk Factor Buccal Cell DNA Study
Georgianna Farren and Margaret Wrensch

Presenter: Kathie Dalessandri

B-05
Neighborhood Environment Obesity in Pre-adolescent Girls
Irene Yen

B-06
Variations in Hormone Pathway Genes and Breast Cancer Risk in the California Teachers Study
Eunjung Lee

B-07
Leptin-receptor Gene and Body Composition among African American, Caucasian, and Hispanic Women
Leslie Bernstein

Presenter: Catherine Carpenter

B-08
Model-building with Complex, High-dimensional Exposures
David Nelson

PROGRAM

Poster Session C

Treatments

3:30pm – 4:30pm

West Hall

C-01
ABC: Antidepressant Medication Use and Breast Cancer Mortality
Reina Haque

C-02
Antibody-based Targeting of Breast Cancer Stem Cells
Claudia Gottstein

Presenter: Iskender Teber

C-03
Cell-free Production of Water Soluble ErbB Proteins
Paul Henderson

C-04
Compounds Blocking Assembly of LRH-1 in Breast Cancer
Cindy Benod

C-05
Intraductal Therapy of DCIS: A Presurgical Study
Susan Love

C-06
Nanotherapy for Breast Cancer: Targeting Tumor Associated Macrophages
Gaurav Sharma

C-07
Oral Contraceptives Use and Survival Among Patients with Invasive Breast Cancer
Yani Lu

C-08
Treating Breast Cancer Brain Metastases with Cytotoxic Lymphocytes
Barbara Mueller

C-09
Combating Breast Cancer with the Wellderly Immune Repertoire
Brunhilde Felding-Habermann

C-10
Reducing Surgical Morbidity of Breast Cancer Staging
Steven Chen

PROGRAM

Poster Session D

Detection and Prognosis

3:30pm – 4:30pm

West Hall

D-01
Blood Oxygen Level Dependent (BOLD) Contrast in the Breast
Rebecca Rakow-Penner

D-02
Detection of Cathepsin-B Activity in the Lymph Nodes Using Dendritic Fluorescent Probes
Ella Jones

Presenter: David Pham

D-03
Development of a Computer Aided Diagnosis (CAD) System for Breast MRI
Ke Nie

D-04
Differential Optical Mammography
Gregory Faris and Christopher Comstock

D-05
Extranuclear Estrogen Receptors in Breast Cancer Prognosis and Clinical Management
Richard Pietras

D-06
Factors Influencing Mammography Screening among Thai American Women
Mary Jo Clark and Bulaporn Natipagon-Shah

D-07
Nanostructure-Initiator Mass Spectrometry Based Tissue Imaging to Identify Metabolic Biomarkers of Breast Cancer Subtypes
Trent Northen

D-08
Precision Image-guided Biopsy of Tumors in Dense Breasts
Thomas R. Nelson

D-09
Sound Speed Tomography for Early Breast Cancer Detection
Jakob Nebeker

D-10
Accuracy of Diagnostic Mammography at Facilities Serving Vulnerable Women
Lauren Elizabeth Goldman

D-11
Novel Small Proteins for PET Imaging of HER2
Zhen Cheng

D-12
The Roles of SATB1 in Breast Tumorigenesis
Laurie Friesenhahn

PROGRAM

Poster Session E

Pathogenesis

3:30pm – 4:30pm

West Hall

E-02
A Genetic System for Identification of Mammary Stem Cells
Dannielle Engle

E-03
Chemokine Receptor (CXCR4 and CXCR7) Function in Breast Cancer
Morgan O'Hayre

E-04
From the Normal Biology of Phosphorylated Prolactin to a Novel Therapeutic for Breast Cancer
Ameae Walker

E-05
Human Breast Cancer Lymphovascular Tumoral Emboli Recapitulate an in vitro Mammosphere Stem Cell Phenotype
Sanford H. Barsky

E-06
Identifying GATA3-regulated miRNAs Involved in Breast Cancer Metastasis
Jonathan Chou

E-07
Molecular Strategy to Inhibit Breast Cancer Metastasis
Frances Brodsky

Presenter: Chih-Ying Chen

E-08
Proteome-wide Analysis of Protein Ubiquitination in Breast Cancer
Stefan Grotegut

E-09
Role of AGR2 in Mammary Glad Development and Cancer
Mikhail Geyfman

E-10
Role of RNA Helicase p68 in Breast Cancer
Daojing Wang

E-11
Tissue Factor Signaling in Breast Tumor Progression
Florence Schaffner

E-12
Twist Target Genes Modulate Tumor Angiogenesis
Janine Low-Marchelli

E-13
Proline Metabolism in Metastatic Breast Cancer
Adam Richardson

E-14
Pygo2 Opens Chromatin and Expands Mammary Progenitor Cells
Bingnan Gu

E-15
Control of BRCA2-mediated Homologous Recombination
Damon Meyer

E-16
Investigating the Role of Estrogen Receptor in Breast Cancer Endocrine Resistance using Solexa ChIP-Sequencing
Hei Chan

PROGRAM

Closing Ceremonies

4:30pm-5:00pm | West Hall

Raffle

(Must be present to win)

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About the CBCRP

About the California Breast Cancer Research Program:

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

Created by the State Legislature in 1993, the California Breast Cancer Research Program (CBCRP) is the largest state-funded breast cancer research program in the nation and is administered by the University of California, Office of the President. To date, the CBCRP has awarded 894 grants to 101 scientific institutions and community entities, totaling more than $213 million for research in California to prevent, treat, and cure breast cancer. Awards include traditional investigator-initiated projects, community-based collaborative research projects, and program-directed special research initiatives. Grants from the CBCRP fill gaps not traditionally funded by other research programs to jump-start new areas of investigation that push the boundaries of research and foster new collaborations. The CBCRP is funded through the voluntary tax check-off program on personal income tax form 540, a portion of the state tobacco tax, and individual contributions. For more information, call 888 313-2277 888 313-2277, or visit www.cabreastcancer.org.

Breast Cancer Research Council Members

To continue to fund innovative research, the California Breast Cancer Research Program (CBCRP) must rely on an expert committee of volunteers. The committee, the Breast Cancer Research 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.

2009-2010 Breast Cancer Research Council

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Barbara Brenner (7/1/08-8/31/11)
Executive Director, Breast Cancer Action

Karren Ganstwig (09/1/07-08/31/10)
Los Angeles Breast Cancer Alliance

Jeanne Rizzo (7/1/08-8/31/11)
President/CEO, Breast Cancer Fund

Donna Sanderson (9/1/09-8/31/12)
Executive Director, Susan G. Komen for the Cure

Nonprofit Health Organization Representatives

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Chronic Diseases Program Director, Asian & Pacific Islander American Health Forum

Carlina Hansen (9/1/09-8/31/12)
Executive Director, Women's Community Clinic

Medical Specialist

Klaus Porzig, M.D. (9/1/06-8/31/10)
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Industry

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Senior Group Director, Genentech, Inc.

Teresa Burgess, Ph.D. (7/1/08-8/31/11)
Director of Oncology Research, Amgen, Inc.

Scientist/Clinician

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Principal Investigator, Asian American Network for Cancer Awareness Research and Training (AANCART)
Associate Director, Population Research, UC Davis Cancer Center

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Genetic Epidemiology and Genomics Lab, School of Public Health

Laura Fenster, Ph.D. (9/1/07-8/31/10)
California Department of Public Health, Environmental and Occupational Disease Control

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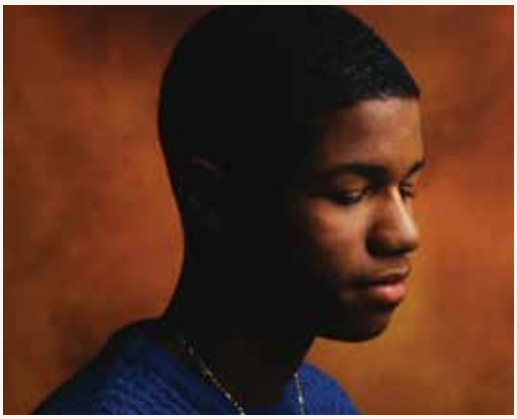

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Abstracts Section

Note: Abstracts Index appears in the Supplement

Session A: Survivorship

Breast Health Behaviors in Immigrant Afghan Women in Northern California

Principal Investigators:
Aida Shirazi, Rona Popal, and Joan Bloom, Ph.D.

Afghan Coalition and University of California, Berkeley

Abstract #: A-01
The purpose of this community-based participatory research (CBPR) qualitative pilot study was to provide a preliminary understanding of how Afghan women in Northern California view their breast health. The specific aims were: (1) To identify what the Afghan women believe to be their greatest concerns and barriers to breast health care; and 2) To identify Afghan women's knowledge and attitudes toward breast health care.

The results were based on both demographic characteristics and in-depth semi-structured interviews conducted with 53 non-English speaking first generation immigrant Muslim Afghan women 40 years and older with no history of breast cancer living in Northern California.

ATLAS.tL, a qualitative software program, was used for the management and evaluation of qualitative data. Codes and categories were systematically sorted, compared and contrasted until they were "saturated". Themes and concepts were used to compare within and across transcripts in the data set and across cases.

Among the participants 28.3% had a clinical breast examination (CBE) less than 2 years ago, 30.2% more than two years ago, and 41% reported never having a CBE. Among the 65.9% who reported having had a mammogram, more than half reported having had one more than the two years ago and almost 34% reported never having had a mammogram.

Qualitative analysis of the findings generated a number of themes. The key themes were: (a) Understanding and meaning of health and concept of prevention; (b) Gender roles and family structure; (c) Religious and spiritual beliefs related to health; (d) Female modesty practices; (e) Low level of knowledge about breast cancer, lack of awareness of breast cancer symptoms, risk factors, screening procedures and guidelines; (f) Access barriers; (g) Health care provider needs; (h) Preferred sources of breast health information and education.

In summary, the findings showed very low levels of knowledge and awareness about breast cancer and low utilization of screening and early detection examinations for breast cancer among Afghan immigrant women. The findings also suggest a significant need for a community based breast health education program that recognizes the unique social, cultural and religious dynamics of the Muslim Afghan community.

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Creating Sustainable Community-Campus Partnerships to Develop New Scientists

Principal Investigators:
Natasha Riley, M.A.; Georgia Sadler, Ph.D.; and Vanessa Malcarne, Ph.D.

Vista Community Clinic; University of California, San Diego; and San Diego State University Research Foundation

Poster Presenter: Natasha Riley, M.A.

Abstract#: A-02
Goal of the Research Project: The goal of this research project is to help resolve the under- representation of African American and Hispanic American women in breast cancer research studies. The project aims to utilize a Community-Campus Partnership to test an educational intervention about clinical trials that is hypothesized to significantly increase African American and Hispanic American women's clinical trials knowledge, positive attitudes toward clinical trials participation, research study participation, and clinical trials advocacy, compared to a control group. This study involves the recruitment of 420 African American and Hispanic American women to participate in a randomized controlled educational trial.

Strategies utilized in this research project were developed during a three phase pilot project that included: (1) The validation of an array of standardized psychosocial survey instruments for use with Hispanic women; (2) The development of a Breast Cancer Clinical Trials Education Program (BCCT), utilizing a sister hood theme, and developed in conjunction with African American and Hispanic American women through a series of focus groups and; (3) a RCT to test the newly developed BCCT education program.

Description of the work performed to date: The partnership continues to report back to the community describing research progress and success through community presentations. Regular meetings are also held with community members in order to receive valuable input into the current study and recruitment process.

The partnership has also given students at the partnering institutions permission to use the research data. These undergraduate and graduate students are new scientific researchers, interested in breast cancer and health disparities research. Many of them are from underrepresented communities, and have will join the pool of future researchers. Students, as well as the community partner have received ongoing mentoring and assistance from the academic partners in the research development, implementation and communication process. As a result, multiple abstracts have been developed and submitted for consideration for presentations at national scientific conferences, with many of them being published. In addition, a manual script describing the focus group process conducted during the second phase of the pilot project is in press at the Journal of Cancer Education.

In addition to presentations and publications, the partnership's PIs also received numerous awards including, but not limited to, the 2008 Faith Fancher Award, the Margaret Hay Edwards Award, and the Community Health Champion Award.

Potential Impact of Your Work on Our Approach to Breast Cancer and Breast Cancer Patients: The work of this partnership represents the essence of CBCRP's approach to Breast Cancer Research through one of the major aims of *"bringing community members and experienced researchers together to study meaningful breast cancer related issues."* This project brought together experienced researchers from the Moores UCSD Cancer Center and San Diego State University to work with Vista Community Clinic to develop a research program that will both add to the body of knowledge about African American and Hispanic American women's participation in breast cancer clinical trials, and increase the number of experienced scientists available to conduct future research.

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Health Anxiety, Pre-sleep Cognitive Activity, Sleep Effort and Insomnia Symptoms in Breast Cancer Patients before Chemotherapy

Principal Investigator:
Michelle Rissling, M.S.

University of California San Diego

Poster Authors: Michelle Rissling,[1] Loki Natarajan,[3] Sue Lawton,[2] Monique Cornejo,[2] Sonia Ancoli-Israel[1,2]

[1] SDSU/UCSD Joint Doctoral Program in Clinical Psychology
[2] Department of Psychiatry, University of California, San Diego
[3] Department of Family and Preventive Medicine

Abstract #: A-03

Chronic insomnia is prevalent in breast cancer patients both during and following chemotherapy. Psychophysiological models of insomnia suggest that pre-sleep cognitive arousal due to sleep effort and cognitive activity may be both a precipitating and perpetuating factor. Furthermore, psychophysiological arousal resulting from health-related anxiety may also precipitate both pre-sleep cognitive arousal and insomnia. This study examined this theory in recently-diagnosed breast cancer patients. We present preliminary analyses on data collected after diagnosis but before the start of chemotherapy.

Twelve women (mean age=50.5 yrs, SD=9.5, range: 36-63) diagnosed with stage I–III breast cancer and 11 yoked, age- and education matched healthy controls (mean age=52.7 yrs, SD=10.9, range: 38-77) were studied both before (BL) and after 4 cycles of chemotherapy (C4). The Short Health Anxiety Inventory (SHAI), Glasgow Sleep Effort Scale (GSES), the Glasgow Content of Thoughts Inventory (GCTI) and the Insomnia Severity Index (ISI) were administered at both time points. We present preliminary analyses using independent t-tests (α= 0.05) conducted on BL data.

At BL, patients reported significantly higher health anxiety (SHAI; mean= 12.47, SEM=1.58) and insomnia symptoms (ISI; mean=13.11, SEM=2.04) as compared to healthy women (SHAI: mean=8.76, SEM=0.83; ISI: mean=8.08, SEM=1.22) (SHAI: t=-2.19, df=19, P=0.04, d=0.69; ISI: t=-2.23, df=19, P=0.04, d=0.96). Although not statistically

significant, patients also reported higher sleep effort (GSES; mean=5.60, SEM=1.1) than controls (mean=3.73, SEM=0.76) and higher pre-sleep cognitive activity (GCTI) at BL (mean=55.10, SEM=5.28) than controls (mean=45.33, SEM=3.06) at BL.

Preliminary results of this small sample suggest that breast cancer patients may experience more health anxiety and insomnia symptoms compared to healthy women. In addition they may also experience increased sleep effort and pre-sleep cognitive activity prior to the start of chemotherapy, but larger sample sizes are needed to confirm these findings. These results suggest that breast cancer patients may have increased vulnerability to health-related anxiety, sleep-interfering cognitions and insomnia symptoms during this period.

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Latina Breast Cancer Survivors: Our Experience

Principal Investigators:
Brian Montaño, M.P.H and Diana Tisnado, M.P.A., Ph.D.

Partnered for Progress and University of California, Los Angeles

Poster Presenter: Diana Tisnado, M.P.A., Ph.D.

Poster Authors: Diana Tisnado, M.P.A., Ph.D.*, Brian Montaño, M.P.H.**, Jenifer Metz, M.P.H.,** and Carolyn Mendez-Luck***

* University of California, Los Angeles Division of General Internal Medicine and Health Services Research
**Partnered for Progress
***University of California, Los Angeles Department of Community Health Sciences

Abstract #: A-04
Introduction: A breast cancer diagnosis and its treatment is a major life challenge, with an impact on the woman herself and everyone who cares for her. Research is urgently needed to understand the patterns of survivorship care and to identify areas in need of intervention, particularly for populations known to be at risk of disparities in cancer treatment and outcomes such as ethnic minorities. Partnered for Progress Latina Task Force and staff have partnered with academic researchers to conduct the study. The aims of this study are to examine experiences of access to and quality of care in Latinas with breast cancer entering the survivorship phase of care; barriers and facilitators of receiving high quality survivorship care; and to learn how Latinas conceptualize and experience being a breast cancer survivor.

Methods: This work is using a qualitative approach with semi-structured focus group discussions with Latinas between 6 months and 10 years post-breast cancer diagnosis. Participants were recruited through health events, *Promotoras*, the PFP newsletter, flyers at hospitals, and support groups. To date we have reached our goal of 12 focus groups. Over 70 Latina survivors participated, 56% in Spanish and the rest in English. Participant ages ranged from 30-75 years, and breast cancer stage varied from Stage I to Stage IV.

Results: Qualitative analyses are in progress and include input from all study partners. Recurring issues emerging in preliminary analyses include: confusion over survivorship care plans and concerns over quality of care; issues of health insurance coverage such as being uninsured or underinsured, loss of coverage due to inability to work, and limited choices within many health plans; sources of support including family, faith/spirituality, cancer support groups, and activation for self-care; and challenges such as anxiety, fatigue, depression, cognitive after-effects of treatment, and perceived stresses on children, marriage, and extended family.

Conclusion: The results of this pilot study will provide invaluable information regarding needs in the community, which will be used to design and assess the acceptability of one or more interventions to help Latinas and other women with breast cancer. We expect this work to result in identification of factors that will inform intervention development, peer reviewed manuscripts and community reports addressing descriptions of Latinas' experiences with care, and future grant proposals for research evaluating culturally and linguistically appropriate interventions.

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Mindful Movement Program for Breast Cancer Survivors

Principal Investigators:
Holly Kiger, M.N., R.N., and Rebecca Crane- Okada, Ph.D., R.N., C.N.S., A.O.C.N.

WISE & Healthy Aging and City of Hope

Abstract #: A-05
Goal of the Research Project: The goal of this community-based pilot study was to test the effects of a 12-week mindful movement program (MMP) on older female breast cancer survivors. MMP is unique in that there is no formal sitting meditation or prescribed body movements or postures. Movement is self-directed and mindful. With verbal cues from the class leader, often with music, participants are encouraged to move their bodies in ways that are comfortable, fun, creative, and natural to them. Participants become aware of their thoughts, feelings, and sensations in the 'present moment' and express them nonjudgmently in self-directed movement. We specifically looked at feasibility of the program, acceptability to participants, and how the program affected their everyday lives with respect to mindfulness and quality of life, including fear of recurrence, anxiety, and upper body symptoms.

Description of the Work: A total of 105 breast cancer survivors contacted the research team and 95 were screened as eligible for the study. Of these, 49 enrolled (51%), 30 assigned to participate in the MMP and 19 to a control group who answered the same questionnaires at the same time points. Participants ranged in age from 50-90 years (average 65.6) and were 9.8 years since diagnosis (range 1-32 years). The majority was White, unpartnered, and retired. At entry into the study, 67% reported prior experience with support groups.

At the end of the 12 weeks of classes, MMP participants showed significantly decreased fear of recurrence (p=.02) and improved mindfulness (p=.026). Control group participants reported significantly fewer upper body symptoms at the same 12 week time point (p=.042). At 18 weeks no significant differences were noted, suggesting that the significant effects seen for those in MMP at 12 weeks were retained.

Overall, participants' comments about MMP from three focus groups conducted with 17 of 29 experimental group participants were very favorable and affirming of the significance of mindful movement, as distinct from other forms of exercise, movement, or meditation. They talked about how the program had helped them in rediscovery "of parts of myself through movement that I thought I had lost," or reconnecting with "the joy of moving," and feelings of more freedom and enjoyment of the present moment in everyday life. Two of the focus groups voiced appreciation that breast cancer was not a major focus of the sessions describing it instead as a 'subtext' for this group 'of sisters.'

Feasibility: We were able to conduct the MMP intervention as proposed. Three 12-week sessions were held. We were able to enroll 21% ethnic minority breast cancer survivors, but did not reach our anticipated total enrollment of 75 breast cancer survivors.

Impact of the Work: While the results of the pilot study are promising a larger study will be needed to determine more specifically what effects, if any, can be realized for breast cancer survivors. Preliminary data does support a decreased fear of recurrence and increased mindfulness.

Funding: California Breast Cancer Research Program of the University of California, Grant Number 14AB-1200.

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Post-treatment Regret among Young Breast Cancer Survivors

Principal Investigator:
Sara Fernandes-Taylor, B.A.

University of California, Berkeley

Poster Authors: Sara Fernandes-Taylor, B.A., and Joan R. Bloom, Ph.D. (mentor)

Abstract #: A-06
The study addresses: (1) what women regret about their breast cancer treatment 5 years later, and (2) what characteristics of disease and treatment predict post-treatment regret.

Interviews were conducted with breast cancer survivors in the San Francisco Bay Area. Participants were interviewed following diagnosis. Five years later, women were asked whether they had any regrets about their cancer treatment (N =449). Qualitative analysis was used to identify regret content, and logistic regression was used to determine what characteristics of treatment predicted regret.

Forty two point five percent women in the sample regretted some aspect of treatment. The most common regrets were primary surgery (24.1%), chemotherapy and/or radiation (21.5%), reconstruction (17.8%), and problems with providers (13.1%). In addition, women regretted inactions (59.2%) (actions that they did not take) more than actions that they did take (30.4%). This represents a novel finding in the study of post-treatment regret, which has largely focused on regrets over actions. Quantitative analysis revealed that women who were anxious about the future (OR=1.32; $p<0.03$) or had problems communicating with physicians (OR =1.26; $p <0.02$) during treatment were more likely to express regret 5 years later. In addition, women with new or recurrent cancers 5 years later were significantly more likely to regret some aspect of their treatment (OR = 5.81; $p<0.001$).

This research supports addressing the psychosocial aspects of cancer care and improving physician-patient communication. Evidence is also provided for addressing the unique emotional needs of women with recurrent cancers, who may experience an undue burden of regret.

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Rushing For Life—Follow Up, Follow Through—Breast Cancer Measurement Outcomes Study

Principal Investigator:
Tracy Hardy-Mosbey and Kimlin Ashing-Giwa, Ph.D.

Rushing for Life and City of Hope

Poster Presenter: Tracy Hardy-Mosbey

Poster Authors: Tracy Hardy, Fred Mosbey

Abstract #: A-07

Rushing for Life's purpose is to bridge the gap of inequalities between breast cancer patient's care treatment and the healthcare system by identifying the disproportions in our society and finding adequate solutions to resolve them appropriately. This particular study conducted by Rushing For Life is called "Follow Up and Follow Through". We will facilitate the study utilizing our Measurement Outcome Studies Research System and Methodologies that will result in a Matrix which consist of pertinent data studies we will use to populate. (Basically, a template with a documented plan of action). This system will provide adequate accountability that allows the Medical staff to track and update pertinent information on the patient as well as follow up on their progress. They can also perform friendly extraction queries as needed to provide them with crucial data about the patient.

The first phase will start by tracking and identifying these patients with Breast Cancer and/or they might be high risk, have family history etc. We use resources by way of government, medical facilities, communities, cancer agencies, etc., starting by State and region.

The Matrix will have close to real time accessibility and can be used for identifying purposes and very versatile queries which will allow medical professionals to review and follow up with thier patients based on the storing of critical information, thus Follow up - Follow through is administered. As mentioned earlier, there will be a period of criteria gathering and studies from Patients, in coordination with Medical, Government, Cancer Agencies and other resources available which will identify these high risk patients in various ways. All permissible parties will have access to data for quality assurance purposes and other general purposes.

The goal is promoting a positive interaction between Patient and Doctor starting with a healthy communication between the parties. It also introduces patients to understanding how important it is that they take their health serious and feel comfortable consulting doctors as necessary. It also promotes best practices with Doctors and their at risk patients and leaves a trail of the interactions. This system helps reduce disparity gaps as it pertains to breast cancer patients by promoting early detection and prevention, as well as helping to restore integrity into the medical profession.

The first phase study begins in California since it is in the top five with breast cancer rates. Upon success we'll branch into rural areas and areas that have high risk populations. We have already started data collection and research for several. The matrix "Follow up Follow Through" can be utilized widespread in other territories and can be a template for other major diseases.

The fact is when it comes to cancer deaths, breast cancer is the second cause of cancer deaths among black women with lung cancer being first. Even though black women have a lower rate of cancer compared to whites, they seem to have a much higher incidence rate - (at risk for death more) and we haven't taken into consideration other minority

populations besides black women. Early detection can help save lives, but lives are still being needlessly lost and so it is not enough. Communication is one of the keys to prevention.

The future is bright and this big gap of people with health disparities can be reduced using "follow up - follow through" which will work well with the new healthcare reform. California gaps could be reduced within the next two years with this system in place if studies are continued throughout 2010/11 and the action plan is implemented. California will also serve as the catalyst for other states with similar issues.

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Increasing the Voice of African Americans in Breast Cancer Research

Principal Investigators:
Carolyn Tapp and Kimlin Ashing-Gwia, Ph.D.

Women of Color and City of Hope

Poster Presenter: Carolyn Tapp

Poster Authors: Kimlin Ashing-Giwa, City of Hope; Carolyn Tapp, Women of Color Breast Cancer Survivors Support Project; Gloria Harmon, Women of Essence; Monica Rosales, City of Hope; Koko McDowell, Kommah Seray Inflammatory Breast Cancer Foundation; Virginia Martin and Jewell Williams, Sisters Breast Cancer Survivors Network; Rhonda Holbert-Santifer, Celebrate Life Cancer Ministry; Vickie Race, Faith, Hope, and Charity; Mark Race, Faith, Hope, and Charity, Phyllis Clark, Healthy Heritage Movement; Angela Agbasi, Women of Color Breast Cancer Survivors Support Project; Joy Steward, The Wellness Community; Leah Lewis, ACS; Eudora Mitchell, Southern California Witness Project

Abstract #: A-08
Introduction: African American representation and participation in cancer research in California is declining. Using community-based participatory research (CBPR) to address disparities in the engagement of ethnic minorities in research and inequities in health outcomes is held as a promising approach. Engaging underrepresented communities can take various forms, one approach is to employ the conference format as a multi-foci strategy to connect, co-educate, train and stimulate community scientific partnerships.

Approach and Purpose: A Joining Forces conference was designed to bring together broad stakeholders including advocates and researchers to share ideas about advancing the breast cancer research agenda of African Americans. The conference, "Increasing the Voice of African Americans in Breast Cancer Research - A Dialogue between Advocates" was held by the Center of Community Alliance for Research and Education (CCARE) at the City of Hope National Medical Center (COH).

The objectives of the conference were to: (1) Bring together breast cancer survivor advocate organizations and researchers to dialogue and exchange ideas to generate CBPR proposals; (2) Conduct educational and preliminary training presentations on the purpose and elements of CBPR; (3) Provide appropriate resources including funding to facilitate collaborative research projects.

Methods: The planning committee for the conference included advocacy organizations, breast cancer survivors, researchers and policy makers. The conference leadership included African American breast cancer survivor-advocacy organizations representing Los Angeles, Riverside, and San Bernardino Counties. The 1-day conference agenda included: (1) An overview of the State of Breast Cancer within the African American community focusing on epidemiology, prevention via lifestyle practices, treatment, and survivorship; (2) survivorship and advocacy presentations by breast cancer survivors, (3) discussion about funding opportunities, (4) presentations about facilitators and barriers to community-research partnerships; (5) breakout sessions were researchers met with advocates, (6) culturally appropriate affirmations (e.g., singing, poetry), and (7) call to actions and future directions.

Results: In total, 77 individuals attended the conference. The conference participants consisted of researchers (25%), advocates (40%), and survivors (35%). The types of cancer-related services that participants were involved in consisted of education, information, resources (38%), support (36%), and access to care/navigation (20%). Conference benefits reported by participants included an increased capacity for utilizing research in advocacy (94%), increased urgency for research on African Americans (89%), and increased knowledge about community-participatory research (86%). In addition, 71% reported they planned to work on a community-research partnership to develop a research proposal in the next year. The follow-up data documents that 6 agencies reported significant

increases in participating in breast cancer programs and funding (10-100% increases). These benefits were attributed in part due to the conference and partnering with a scientific investigator.

Conclusion: Conference outcomes indicate that the African American survivor-advocate community is ready and available to collaborate with researchers to engage in the research process. In addition, there is a need for further training within both the advocacy and scientific communities to better prepare these constituents to collaborate. However, this conference helped to initiate collaborations among researchers and community organizations to generate the next set of CBPR proposals with direct benefit for California underserved communities

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Sister Survivor: African American Breast Cancer Coalition

Principal Investigators:
Gloria Harmon, B.A., and Kimlin Ashing-Giwa, Ph.D.

Women of Essence and City of Hope

Poster Presenter: Kimlin Ashing-Giwa, Ph.D.

Poster Authors: Kimlin Ashing-Giwa, City of Hope; Carolyn Tapp, Women of Color Breast Cancer Survivors Support Project; Gloria Harmon, Women of Essence Monica Rosales, City of Hope; Koko McDowell, Kommah Seray Inflammatory Breast Cancer Foundation; Virginia Martin and Jewell Williams, Sisters Breast Cancer Survivors Network; Rhonda Holbert-Santifer, Celebrate Life Cancer Ministry; Vickie Race, Faith, Hope, and Charity; Mark Race, Faith, Hope, and Charity, Phyllis Clark, Healthy Heritage Movement; Angela Agbasi, Women of Color Breast Cancer Survivors Support Project; Joy Steward, The Wellness Community; Leah Lewis, ACS; Eudora Mitchell, Southern California Witness Project

Abstract #: A-09
Introduction: Support groups play a positive role in improving breast cancer and quality of life outcomes. However, there is limited research on the role of support groups among African American breast cancer survivors (AABCS). AABCS have expressed preference for support groups that are culturally sensitive.

Purpose: Eleven advocacy grassroots organizations and Dr. Ashing-Giwa (COH) formed the African American Breast Cancer Coalition (AABCC). The coalition implemented this study using the CBPR framework and qualitative methodology with the following objectives: (1) identify the elements of structure and process for African American support groups and (2) the most culturally-appropriate paradigm for developing AABCS support groups.

Methods: AABCS were interviewed in focus groups (5 with support group members, 4 with non-support group members) to get a clear idea of the structure and process of the groups. A preliminary guide on 'how to' develop AABCS support groups was developed. The coalition was involved in all study activities including study planning, instrumentation, study implementation and dissemination of findings.

Results: 75 AABCS participated. The qualitative analysis unveiled 3 themes: (1) Emotional Impact of Breast Cancer, (2) Emotional Distress, and (3) Emotional Boosters. Support group provide culturally and linguistically competent informational, navigational, supportive and spiritual care. The findings suggest the groups are critically important to the survivors' family functioning and emotional well-being. Specifically, groups are critically important to the survivor's family functioning (67%) and emotional well-being (84%). Further, the support groups had a positive impact on outlook on life (83%), spirituality or religious faith practices (83%), and their ability to talk about cancer (80%). The importance of support groups becomes more evident in the post-treatment/survivorship phase when emotional and social support from family, friends and medical providers dwindles. The themes of acceptance, belonging, and validation were woven throughout the interviews.

Conclusion: These support groups function as an extension of a culturally prescribed way of life waving a fictive kin network with a spiritual base through the lens of the breast cancer experience. Our findings and overall Coalition outcomes demonstrate the potential of community-research partnerships to address health disparities through coalition building, prioritizing direct community benefit, training/capacity building among community members and infusing cultural and socio-ecological dimensions into the process.

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Session A: Survivorship

Video Conference Breast Cancer Support Groups: A Viable Option for Rural Women?

Principal Investigators:
Mary Anne Kreshka , M.A.; Jim Perkins, DrP.H.; Susan Ferrier, R.N., and Cheryl Koopman, Ph.D.

Northern Sierra Rural Health Network, Stanford University

Poster Presenter: Marlene von Friederichs-Fitzwater, Ph.D.; University of California, Davis Cancer Center

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Abstract #: A-10
In 2004, the Institute of Medicine identified the support group as the most common and useful intervention for women with breast cancer. Breast cancer support groups are described as meetings of patients/survivors led by a professionally trained facilitator, often a counselor or social worker, where there is an exchange of information and learning among the participants. Unfortunately, women in rural areas often do not have access to such support groups. This community-based participatory study reports on the quantitative and qualitative outcomes of a video conference breast cancer support group led by a professional support group facilitator using a workbook-journal entitled *One in Eight: Women Speaking to Women*, created for women who live in rural areas and have been diagnosed with breast cancer. *One in Eight* was developed to educate women about other women's experiences and alternative approaches for coping with breast cancer and to provide women with a sense of emotional support through a printed medium. It draws from supportive-expressive group therapy, which encourages expression of distressing emotions, improving social support and encouraging active coping when feasible. Over the course of this study, participants were assigned to eight groups conducted via videoconferencing, with each group comprised of eight weekly 90-minute sessions. The group facilitator was based in Grass Valley, CA, and women participated from the rural counties of northern California at four videoconferencing sites. For the qualitative arm of the study, the tapes were transcribed for coding and analyses; two independent coders developed a coding manual, coded the tapes, tested for inter-coder reliability and analyzed the results. A random selection of participants was also surveyed in telephone interviews. Common themes and patterns were then identified and included categories of Diagnosis, Fears, Doctor/Patient Communication, Coping, Survivorship, and Benefits of the Support Group. In addition to increasing our knowledge about the breast cancer experiences of women who are more isolated, the women reported the benefits they gained from participating in the video conference support group ranging from "reduced anxiety and fear," and "ease of use and comfort level with the process of videoconferencing," to "learning from each other what our doctors did not tell us."The findings will be shared with the participating communities and used to inform services and resources for rural women diagnosed with breast cancer.

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A Study of Breast Cancer-related Lymphedema Knowledge, Awareness, and Care among Kaiser Permanente Northern California Patients and Clinicians

Principal Investigator:
Marilyn Kwan, Ph.D.

Kaiser Permanente

Poster Presenters: Ling Shen, Julie Munneke, Emily Tam, and Paula Partee

Poster Authors: Marilyn L. Kwan (PI)[1], Julie R. Munneke[1], Paula N. Partee[1], Claudia Samayoa[1], Ling Shen[1], Emily K. Tam[1], Lynn M. Ackerson[1], Carol P. Somkin[1], Saskia R.J. Thiadens[2]

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Abstract #: A-11

Background: Breast cancer survivors have reported dissatisfaction regarding their education on breast cancer-related lymphedema (BCRL) risk from clinicians. In addition, misconceptions about the development and treatment of BCRL exist among clinicians. Within the Kaiser Permanente (KP) Northern California Medical Care Program, we will evaluate BCRL management by (1) determining BCRL knowledge and referral patterns among breast cancer patients who may have been diagnosed with BCRL and (2) assessing BCRL knowledge and patient referral among primary care clinicians, oncologists, and surgeons.

Methods: Patient information on BCRL diagnosis, care and management, education and support services, and doctor-patient relations is collected from a 20-minute telephone interview that began in February 2010. Clinician information on BCRL knowledge, referral patterns, and education is collected from a 10-minute internet survey that began in May 2010.

Results: To date, 122 patients have participated in the telephone interview. During breast cancer diagnosis and treatment, 60 women (49%) reported receiving information about BCRL risk reduction practices and were aware of practices except for avoidance of temperature extremes (only 60%) and repetitive movements (only 48%). Patients were supportive of improving BCRL education delivered by one-on-one clinician counseling (95%), health education workshops (86%), and brochures (86%). Interestingly, support for newsletters and educational emails were generally positive yet lower at 68% and 62%, respectively. The patients also felt that the surgeon (25%) and oncologist (34%) should be mainly responsible for providing BCRL information. Of 69 patients with a confirmed BCRL diagnosis, about half (48%) were diagnosed by physical therapists, and the remainder were diagnosed primarily by oncologists (28%) or surgeons (13%). A total of 61 (88%) were referred to physical therapy, of which 77% were fitted for a compression garment, 46% had manual lymphatic drainage, and 54% received education in self-care.

To date, 398 clinicians have completed the internet survey, of which 89% were physicians and 10% were nurse practitioners. A total of 56 surgeons (14%), 25 oncologists (6%), 198 primary care physicians (50%), and 85 obstetricians/gynecologists (21%) responded. Over 65% of the clinicians had been working for KP for at least five years. Preliminary results will be available during the CBCRP conference in September.

Conclusions: The BC LINK Study is a first step in improving BCRL knowledge and education within an HMO setting. Results will be used to guide future educational interventions on BCRL.

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Talking about Empowerment with a Peer Counselor Predicts Increased Marital Satisfaction in Women with Breast Cancer

Principal Investigators:
Caroline Bliss-Isberg, Ph.D., and David Spiegel, M.D.

WomenCARE and Stanford University School of Medicine

Poster Presenter: Lynne Wittenberg, M.P.H.

Poster Authors: Lynne Wittenberg, M.P.H.,[1] Maya Yutsis, Ph.D.,[1] Janine Giese-Davis, Ph.D.,[1,2,3] Caroline Bliss-Isberg, Ph.D.,[4] Path Star, J.D.,[1] Debra Houston, LMFT,[4] David Spiegel, M.D.[1]

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Abstract #: A-12

Background: The goal of the Peer Navigator study was to examine whether matching women newly diagnosed with breast cancer ("sojourners") with a trained peer counselor improves quality of life over the first year post-diagnosis. Of the 104 newly diagnosed women randomized to the study, 52 were randomly assigned to be matched with a peer counselor ("navigator") (N=30), who is also a breast cancer survivor. Matched pairs had weekly contact for 3-6 months following the sojourner's diagnosis.

Prior research indicates that increased distress in both women newly diagnosed with breast cancer

and their spouses often predicts decreases in marital satisfaction. Peer support may alleviate some of the family-related distress. In this randomized trial of peer navigation, we found that women who were matched with a navigator significantly increased their marital satisfaction over 12 months compared with a control group who decreased.

Methods: Matched pairs completed contact rating forms during their match, as well as a marital satisfaction questionnaire at baseline, 3, 6 and 12 months. We hypothesized that certain topics (empowerment, expressing feelings) or positive affect ratings (e.g., understood, helped) reported in contact evaluations would predict this increase in marital satisfaction. We averaged ratings across all contact sheets (by woman) each sojourner and her navigator completed. We ran a stepwise forward regression using contact sheet data from 32 married sojourners to predict change over time in marital satisfaction. Independent variables included: total time spent in contacts, positive and negative affect ratings, and frequency of discussion topics.

Results: We found that sojourners reporting more frequent discussions of empowerment reported greater increases in marital satisfaction over 12 months in a linear all-in regression (p=.01). In contrast, we also found that sojourners' mean negative affect ratings (e.g., frustrated, depressed), were associated with decreased marital satisfaction (p=.04). These were the only sojourner variables associated significantly with relationship satisfaction change. Next we conducted a second regression entering sojourner's rating of empowerment discussions on the first step and navigator ratings of each of the contact sheet variables in the second step (stepwise forward for the latter). Significant additional variance was explained by navigators' ratings of less frequent cancer resources discussions, which were associated with greater increases in marital satisfaction for sojourners (p=.002).

Conclusions: Peer discussions about empowerment and less time conveying information about cancer resources resulted in greater marital satisfaction for sojourners. By providing one-to-one peer support, navigators may have buffered rather than taxed sojourners' marital relationships, thus contributing to improved marital adjustment. As navigators modeled ways to cope with and survive breast cancer, sojourners may have conceptualized this as "empowerment" when rating topics discussed during contacts. The peer navigator intervention may have improved sojourners' coping behaviors and reduced anxiety and distress, which may also have improved their partners' coping skills, resulting in greater relationship satisfaction. Our results demonstrate that peer counseling programs for women with breast cancer may improve spousal/partner relationships by relieving some of the emotional burden that partners often experience after a cancer diagnosis.

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Process of Discussions with Peer Counselors Predicts Change in Trauma Symptoms in Newly Diagnosed Women with Breast Cancer

Principal Investigators:
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WomenCARE and Stanford University School of Medicine

Poster Presenter: Lynne Wittenberg, M.P.H.

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Abstract #: A-13
Background: The Peer Navigator Clinical Trial evaluated the effectiveness of a one-to-one peer counseling program designed to improve quality of life and reduce distress in women with newly diagnosed breast cancer ("Sojourners"). Of the 104 newly diagnosed women randomized to the study, half (N=52) were randomly assigned to be matched with a trained and supervised peer counselor ("Navigator") (N=30), who is also a breast cancer survivor. Matched pairs had weekly contact for 3-6 months following the Sojourner's diagnosis.

Methods: Sojourners completed a contact evaluation form after each contact, as well as a trauma

symptom questionnaire checklist (PCLC), among other measures, at baseline, 3, 6 and 12 months. We tested whether Sojourners' report of positive and negative feelings and topics discussed during contacts with their Navigators was associated with a change in trauma symptoms using the PCLC.

Results: Sojourners who reported higher average positive feelings (e.g., helped, relieved) during contacts increased in total trauma symptoms over 12 months (β=.59, *p*=.01). In contrast, we observed a non-significant decrease in trauma symptoms (β = -.41, *p*=.059) among sojourners who reported higher average negative feelings (e.g., frustrated, afraid). Sojourners who reported more frequent expression of feelings
(β = -.*p*=.04) and discussions of sexuality
(r = -.34, *p*=.02) decreased (improved) in total trauma symptoms, while those who reported more frequent discussions of social issues decreased in arousal symptoms (a subset of trauma symptoms in the PCLC) (r = -.30, *p*=.04). In addition to these variables, the linear regression model included negative affect ratings, total time spent in contacts, and active coping discussions, which accounted for only 8% of the variance in change in PCLC.

Conclusions: Although we hypothesized that higher average positive affect ratings during contacts would predict a decrease trauma symptoms, the reverse was true, suggesting that Sojourners focusing on positive more than on difficult feelings during contacts with their Navigator may be hindered from confronting their cancer-related trauma. Medical professionals, family, and friends often assume that avoidant coping strategies and "being positive" will help women cope with their cancer. However, our results suggest that openly talking about negative feelings with a peer counselor may enable newly diagnosed women to process trauma associated with a recent cancer diagnosis. Our findings indicate that peer navigation programs that foster emotional expression of negative feelings often associated with diagnosis and treatment may lead to a reduction in trauma symptoms in women with breast cancer.

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Reducing Mammography Disparities for Latinas through Community Health Centers: Lessons on Community-Academic Design and Implementation of Intervention Research

Principal Investigators:
Stergios Roussos, Ph.D., M.P.H., and Christine Noguera, M.S.

San Diego State University Research Foundation and Golden Valley Health Centers

Poster Authors: S. Roussos (1, 2), C. Noguera (2), F. Batts (1), M. Bunyard (3), H. Roehlk (3), M. Sigarroa (3), M. Hovell (1)

1-Center for Behavioral Epidemiology and Community Health; 2 – Alliance for Community Research and Development; 2-Golden Valley Health Centers; 3-Women of Courage

Abstract #: A-14

Community-Based Participatory Research (CBPR) contributes to the prevention and control of breast cancer through the individual and synergistic strengths of community-academic teams. Project Perlas is a CBCPR project addressing disparities in mammography screening among Latina patients in community health centers within the Central Valley of California. Latinas with diabetes are less likely to receive age-appropriate mammography despite more health visits, as the complexity of caring for chronic illness can interfere with preventive services. Perlas is an innovative intervention that takes advantage of a highly prevalent chronic illness among Latinas (diabetes) to prompt for mammography screening, a periodic preventive service.

The development of the Perlas intervention and research design to understand its effects were created through close collaboration by the community-academic team. The community partners include administrative and clinical staff from a network of 25 community health centers and breast cancer survivors with and without diabetes. Community Latino members, breast cancer survivors and clinical members were also represented on the team. The academic team was composed of behavioral epidemiologists and community health researchers specializing in health disparities.

This presentation describes the intervention components and research design elements of this ongoing study. The decisions and negotiations during the design process are presented while illustrating how the team worked to ensure valid research methods, relevance and utility to clinical and community partners, and cultural competency. The final intervention includes patient and provider education and clinical prompts tailored to Latino culture and to the organizational culture of community health centers. The research design includes pre-post intervention repeated measures for mammography and diabetes with process evaluation of project implementation. The adoption of electronic medical records (EMR) during the study allows for an exploration of how EMR may be support intervention and measurement activities.

The summary of lessons learned during the collaborative design and development process will help community-academic teams understand how to balance research goals (e.g., internal validity, theory-driven methods) with organizational goals of caring for undeserved, vulnerable patients given limited resources. Insights are shared about how community and academic partners serve as teachers and students in the process of community-based participatory research. Recommendations are provided for community-academic collaboration in research design and intervention development to address disparities in breast cancer prevention.

A Strategy for More Efficient BRCA Analysis in an Underserved Latina Population

Principal Investigator:
Jeffrey N. Weitzel, M.D

City of Hope

Poster Presenter: Raquel Ogaz

Poster Authors: Raquel M. Ogaz, B.A.,[1] Kathleen R. Blazer, M.S.,[1] Josef Herzog, B.S.,[1] Christopher Haiman, Ph.D.,[2] Rohit Varma, M.D.,[2] Guillermo Rivas,[1] Garry Larson, Ph.D.,[1] Jeffrey N. Weitzel, M.D.[1]

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Abstract #: B-01

Breast cancer is the most common cancer and the leading cause of cancer death in Latina women. Mutations in BRCA genes are associated with 5% of all BC and a larger proportion of young women with BC. Large rearrangements, not detectable by standard sequencing, account for up to 15% of deleterious BRCA mutations. The lifetime risk of developing BC associated with a BRCA mutation may be as high as 85%. We previously reported on the prevalence of deleterious BRCA mutations (31% of 110 families) in a Latina high-risk clinic in Los Angeles, and also identified a unique recurrent large BRCA1 rearrangement (deletion of BRCA1 exons 9-12). BRCA1 185delAG was detected in independent Latina families, and through haplotyping we established that they shared a common ancestral origin with Jewish carrier families. We hypothesized that a panel of recurrent Latina BRCA mutations to prescreen high risk patient samples will demonstrate clinical utility and reduce genotyping cost.

Using a new high-throughput Sequenom® platform, we developed a prototype multiplex panel to test for recurrent BRCA mutations, including 185delAG, and a 3-primer assay to test for the BRCA1 rearrangement mutation. We screened two population-based cohorts (combined n=2,702), the Multiethnic Cohort (MEC) and the La Puente Latino Eye Study (LALES) cohort. BRCA1 del (ex 9-12) was detected in the LALES cohort and BRCA2 3492insT, a known founder mutation of Spanish origin, was detected in both cohorts. We created a clinical protocol and procedure that enabled sample collection, DNA extraction, amplification and mutation panel analysis on the Sequenom platform within a 72 hour time frame. We piloted this 18 mutation panel in the clinical genetic cancer risk assessment setting. Positive assays were confirmed in a CLIA-approved laboratory by sequencing of the specific segment, and comprehensive BRCA sequencing was performed on all samples with negative results. We applied the panel prospectively in a pilot study of 23 consecutive Latina breast cancer patients referred to the City of Hope Cancer Screening & Prevention Program Network for genetic cancer risk assessment.

A substantial proportion (4/7, 57%) of deleterious BRCA mutations were detected by the panel in this proof of principle pilot study in our high risk clinic, suggesting strong translational potential. All 4 mutations were confirmed by commercial sequencing. The majority of these patients were from an underserved/uninsured clinic, and the pre-screening procedure (with an estimated panel assay cost of $5/sample, and $250 for re-confirmation of detected mutations by the CLIA-certified commercial laboratory) saved an estimated $6,600 over the alternative of complete sequencing (representing a 15% savings on the budget for genotyping all 23 patients).

Our data suggest that the development of and testing for a panel of recurrent BRCA mutations in high risk Latina populations will reduce testing cost and enable more women to benefit from limited resources. Knowledge about the genetic etiology of breast cancer in Latinas will facilitate screening and cancer prevention. Acknowledgements: CBCRP Grant #12IB-0050; NCI 1R03 CA139588

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Adipose Levels of PBDEs and Risk of Breast Cancer

Principal Investigator:
Myrto Petreas, Ph.D., M.P.H.

Cancer Prevention Institute of California

Poster Presenter: Susan Hurley, M.P.H.

Poster Authors: S. Hurley, D. Goldberg, P. Reynolds, D. Nelson (Cancer Prevention Insitute of California), M. Petreas (California Department of Toxic Substances Control).

Abstract #: B-02

Background: Polybrominated diphenyl ethers (PBDEs) are a class of over 200 organohalogenated

compounds widely used as flame retardants in consumer products and building materials. Because they readily leach out of the products in which they are embedded, PBDEs have become pervasive environmental contaminants and human exposures are widespread.

Objective: The objective of this study was to evaluate the risk of breast cancer associated with measurements of PBDEs in the breast fat of women.

Methods: We conducted a hospital-based case control study among 78 women diagnosed with invasive breast cancer and 56 controls diagnosed with benign breast conditions who underwent surgical breast biopsy at two hospitals in the San Francisco Bay Area, CA.

Breast adipose tissue samples were collected at the time of biopsy and analyzed for five congeners of PBDEs (BDE-47, BDE-99, BDE-100, BDE-153, and BDE-154). Statistical models were used to estimate the risk of breast cancer, after taking into account age and race. Results: Average PBDE levels were high, consistent with previous reports of elevated levels among the California population. No statistically significant elevated risks of breast cancer were found for any of the congeners, or for the total PBDEs measured.

Conclusions: Our results provide no evidence of an association between PBDE adipose concentrations measured at the time of diagnosis and breast cancer risk. However, given the strong biologic rationale for the carcinogenic potential of PBDEs, coupled with widespread exposures, further study is warranted. Future studies would benefit from a larger sample size, a more representative control series, and/or a prospective design.

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Enhancing the Power of Genetic Association Studies in African American Women

Principal Investigator:
Daniel Stram, Ph.D.

University of Southern California

Abstract #: B-03

A great deal of research has focused on how genetics affect disease susceptibility, including breast cancer. Many studies collect genetic data to compare people with a disease (cases) and those free of that disease (controls). After such a study is completed, a great deal of data has been generated which raises the question: can we reuse genetic data from participants genotyped as controls from other studies, or does each new study needs its own controls?

Given the huge investments made recently in large scale genotyping of cases and controls for various diseases, the ability to leverage existing data would represent an enormous savings of money and time. We are studying whether studies where cases and controls are sampled differently will give correct answers and are as powerful statistically as when new control data is also genotyped. This question is especially important in understanding the genetic causes of disease in as yet relatively understudied population groups, such as African Americans, in order to speed up progress as much as possible.

We give theoretical results about the power of studies that reuse existing control genotypes based on statistical considerations. We also provide analysis of real data from a major study of the genetic causes of breast cancer in African American women in order to shed practical light upon this issue.

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High Frequency of Aldosterone Synthase (CYP11B2) C/C Genotype in the Marin County Adolescent Risk Factor Buccal Cell DNA Study

Principal Investigator:
Georgianna Farren, M.D., and Margaret Wrensch, M.P.H., Ph.D.

Zero Breast Cancer and University of California, San Francisco

Poster Presenter: Kathie Dalessandri, M.D.; F.A.C.S.

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Abstract #: B-04
DNA from buccal cell samples from 174 controls and 164 age-matched Caucasian women from Marin County diagnosed with breast cancer from 1997-1999 were analyzed for their aldosterone synthase (cytochrome P450 XIB2-*CYP11B2*) genotypes as part of a study using the OncoVue risk estimation model (InterGenetics Incorporated). DNAs were genotyped for a T to C polymorphism in the *CYP11B2* gene promotor (rs 1799998). In agreement with previously reported studies fromother Caucasian population studies, the Marin County study found an overall genotype frequency for the C/C genotype of 20% with no significant difference between cases and controls. When we stratified the study participants by OncoVue risk score, we found that the elevated risk individuals (greater or equal to 1.5x SEER average for the investigated age range), had a significant 2.4-fold enrichment in the frequency of the *CYP11B2* C/C genotype from 20% to 48%. This is of interest because previous studies have shown that the genetic influence of the C/C genotype on breast cancer risk acts in an age dependent manner. At younger ages (below age 50), it is associated with decreased risk of breast cancer but at older ages it contributes to increased risk. Recent cardiovascular studies have shown that increases in C reactive protein with age is also associated with the *CYP11B2* C/C genotype. This may be associated with increased inflammation. Breast cancer may also be associated with increased inflammation as a person ages. We theorize that at the time of menopause, ovarian hormone-dependent estrogen and progesterone levels fall and ovarian hormone-independent stimulation by aldosterone and cortisol (stress hormones) predominate and may lead to an increase in alveolar type breast cancer and also an increase in breast density. In a study in mammary organ cultures in an animal model, when incubation in a medium of insulin and prolactin plus aldosterone and hydrocortisone was done for 10 days, mammary alveolar lesions predominated. Vitamin D supplementation prevented the alveolar lesions from forming. There is a known increase in lobular cancer (alveolar lesions) seen in Marin County. We postulate that this is because of an increased stimulation by an ovarian hormone-independent mechanism by aldosterone and cortisol after menopause that may lead to inflammation. The increased frequency of *CYP11B2* C/C genotype found in elevated risk women and the previously published associations of this genotype with inflammation and increased breast cancer risk with aging needs further exploration. These observations are hypothesis generating for future studies.

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Neighborhood Environment Obesity in Pre-adolescent Girls

Principal Investigator:
Irene Yen, Ph.D.

University of California, San Francisco

Poster Authors: Irene H Yen (PI), CW Leung, N Adler, BA Laraia, RA Hiatt, D Nickleach, LH Kushi

University of California, San Francisco and Kaiser Permanente Division of Research

Abstract #: B-05
Neighborhood socioeconomic status, resources and built environment characteristics could contribute to children's overweight or obesity. Few studies have addressed this question with longitudinal data or direct observations of neighborhood features. We conducted street observations during the baseline year in a study of 6- and 7-year-old girls (Cohort Study of Young Girls' Nutrition, Environment, and Transitions, n=215). Neighborhood data were collected using a modified St. Louis Audit Tool. Exploratory factor analysis of 40 of the items yielded five scales: mixed residential and commercial; food and retail; recreation; walkability and; physical disorder. Other predictors included a neighborhood deprivation measure (a combination of eight census variables) and household income. We analyzed three years of BMI z- scores from follow-up data, calculated from age-specific BMI percentiles based on Centers for Disease Control standards, adjusting for age and race/ethnicity.

Neighborhood deprivation was associated with change in BMI z-scores over three years depending on the girls' household income (p for interaction=0.01). With higher levels of neighborhood deprivation, BMI z-scores stayed the same among girls from lower income households (beta=0.027, p=0.21) but, surprisingly decreased among girls from higher income households (beta=-0.054, p=0.04). The effect of the "mixed residential and commercial" scale on change in BMI z-scores also differed by household income (p=0.03). Although specific neighborhood stores and services were not associated with girls' change in BMI, neighborhood economic characteristics did predict a change in BMI.

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Session B: Etiology and Prevention

Variations in Hormone Pathway Genes and Breast Cancer Risk in the California Teachers Study

Principal Investigator:
Eunjung Lee

University of Southern California

Abstract #: B-06

It is well established that the female hormones, estrogen and progesterone, are important for the development of breast cancer. It therefore seems plausible that normal variation in genes involved in production (synthesis) and breakdown (metabolism) of these hormones may affect breast cancer risk. We investigated whether variation in genes in the estrogen and progesterone synthesis and metabolism pathways were associated with breast cancer risk. We analyzed data from a breast cancer case-control study nested in the California Teachers Study.

We genotyped 450 single nucleotide polymorphisms (SNPs) in 32 genes for 1351 non-Hispanic Caucasian women with breast cancer and 1395 women without breast cancer. The most significant associations with breast cancer risk were observed for several SNPs in *SLCO1B1*, a gene involved in the transport of estrogen metabolites from the blood into liver cells. Among the 38 *SLCO1B* SNPs, nine were associated with breast cancer risk in postmenopausal women. In addition, some of these SNPs appeared to be associated with a higher risk in women who were using estrogen-progestin combined hormone therapy. Although none of the *SLCO1B1* associations were statistically significant after correcting for multiple testing, the role of *SLCO1B1* in breast cancer etiology in postmenopausal women warrants further investigation. Polymorphisms in the other hormone pathway genes we analyzed were not associated with breast cancer risk in pre- or postmenopausal women.

Our results should be confirmed, but suggest that variation in hormone pathway genes may predict which subgroup of women are at particularly high risk of breast cancer if they use hormone therapy.

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

Principal Investigator:
Leslie Bernstein, Ph.D.

UCLA School of Medicine

Poster Presenter: Catherine Carpenter, M.P.H., Ph.D.

Abstract #: B-07

Elevated levels of body fat have been shown in epidemiologic studies to increase postmenopausal breast cancer risk. We conducted a candidate gene study of the leptin-receptor (*LEPR*) and body composition because functional *LEPR* variants may promote greater amounts of body fat, and may therefore be related to risk of breast cancer.

LEPR was studied clinically at the University of Southern California among 36 healthy, overweight postmenopausal Caucasian and African American women (age 45 to 72 y); and, in a population sample of 729 healthy pre- and postmenopausal Caucasian, African American and Hispanic women (age 35 to 80 y) from a multi-ethnic case control study conducted by Dr. Esther John of the Cancer Prevention Institute of California. Both studies measured height, weight, waist and hip circumferences. The clinical study measured body fat with DEXA (dual-energy X-ray absorptiometry) conducted by Dr. Victoria Jaque. Dr. Sue Ingles' laboratory at the of conducted the genotyping. We genotyped variants *Lys109Arg, Gln223Arg* with restriction-endonuclease digestion and *Lys656Asn* using direct sequencing. The population sample was genotyped with Taqman. We statistically adjusted for age in the clinical sample, and, age and menopause in the population sample.

The percent body fat - *Lys109Arg* clinical association (age-adjusted p=0.01), was limited to African Americans. In the population sample, *Lys109Arg* was associated with waist-to-hip ratio (WHR) among Caucasians (p = 0.04), and marginally with waist circumference (p = 0.09) and WHR (p = 0.09) among African Americans (population). Lys109Arg was associated with WHR (p = 0.006) among obese Caucasians (BMI > 30.0), and, waist (p = 0.010) and hip circumferences (p=0.06) among obese African Americans. *Gln223Arg* and *Lys656Asn* were not associated.

Lys109Arg may lead to increased body composition among obese women.

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ABC: Antidepressant Medication Use and Breast Cancer Mortality

Principal Investigator:
Reina Haque, Ph.D.

Kaiser Permanente

Poster Authors: Reina Haque (PI), Chantal Avila, Jiaxiao Shi, Joanie Chung, Craig Cheetham, Virginia P. Quinn

Kaiser Permanente Southern California

Abstract #: C-01
Overview of the research topic and relevance to breast cancer: Thousands of women diagnosed with breast cancer (BCa) are taking tamoxifen to improve their chances of survival. Despite its success in reducing the risk of future BCa, tamoxifen's side effects include stroke and blood clots, hot flashes, and night sweats. Increasingly, antidepressants have been used to relieve some of these symptoms. Of concern, a few recent laboratory-based studies suggest that certain common antidepressants called selective serotonin re-uptake inhibitors (SSRIs) interfere with tamoxifen's effectiveness. Recent reports even caution physicians not to prescribe these antidepressant medications with tamoxifen. Very few studies have attempted to assess the effect of the interaction between antidepressants with tamoxifen on long-term outcomes.

The research question: The overarching goal of the study is to determine whether women are at an elevated risk for overall death or BCa death when they use antidepressants while receiving tamoxifen therapy.

General methods: We assembled a large group of socioeconomically diverse women from the membership of the Kaiser Permanente Southern California health plan who were diagnosed with their first BCa in 1996-2006 and followed through 12/31/07 to determine how many of these patients died. We then compared the mortality rates among mutually exclusive groups of antidepressant users: (1) paroxetine, (2) fluoxetine, (3) other SSRIs (sertaline & citalopram), (4) tricyclics, (5) other types, (6) multiple types, and (7) a comparison group of non-users of antidepressants (i.e., only tamoxifen).

Preliminary results: We identified 12,835 ER+ early stage (0-II) BCa survivors from the SEER-affiliated tumor registry. After excluding ineligibles (not continuously enrolled (n=1343) or no exposure to tamoxifen (n=3944)), we had 7,548 women. Cause of death through 12/31/07 included BCa (n=394, 5.2%); cardiovascular disease (n=183, 2.4%); other causes (n=408, 5.4%); and unknown causes (n=268, 3.6%); leaving 6,295 (83.4%) women alive by end of follow-up. We examined crude and adjusted rates of Bca and overall mortality using Cox proportional hazards modeling. We adjusted for age at diagnosis, year, race/ethnicity, income, medical utilization, comorbidity, stage, primary and adjuvant cancer therapy, and other tumor characteristics (histology, grade, lymph nodes, PR). We did not observe a significant association between paroxetine use and mortality (HR=1.29, 95% CI: 0.91-1.82). However, we did find significant associations between fluoxetine (HR=1.47, 95% CI: 1.15-1.89) and other SSRIs (HR=2.36, 95% CI: 1.39-4.01) with overall mortality. Among women with good adherence to tamoxifen (80% medication possession ratio), the association between fluoxetine and other SSRIs with all cause mortality became stronger. Of note, these estimates were based on small numbers of deaths and need to be interpreted with caution.

Impact and next steps: Our results suggest that concomitant use of tamixofen and some antidepressants may affect survival. Although we were able to adjust for a numerous potential confounders, these preliminary data need to be evaluated in larger samples of BCa survivors.

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Antibody-based Targeting of Breast Cancer Stem Cells

Principal Investigator:
Claudia Gottstein, M.D.

University of California Santa Barbara

Poster Presenter: Iskender Teber

Poster Authors: Iskender Teber,[1,2] Anne Wallace,[3] Lincoln Johnson,[2] and Claudia Gottstein[1,2]

[1] California NanoSystems Institute, University of

California Santa Barbara
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Abstract #: C-02
Introduction: A recently postulated hypothesis states that a subpopulation of cells in a tumor with stem cell-like properties, termed "tumor initiating cells" or "cancer stem cells" are the major drivers for tumor progression, metastasis and recurrence. These cells are not easily eliminated with conventional therapies, and therefore may be enriched after conventional therapy. If the hypothesis is true, treatment strategies would have to be reconsidered, and relapses of tumors after many years could be explained and potentially specifically treated. A cell surface protein marker, called CD44, has been used as a marker for breast cancer stem cells. While CD44 is not an ideal therapeutic target due to its wide expression on many cell types, it can be used to guide identification of other biomarkers co-expressed on CD44 positive breast cancer cells. The isolation of antibodies that recognize such co-expressed markers from breast cancer patients' blood leukocytes is the focus of this research. Such antibodies would be invaluable tools to test the tumor stem cell hypothesis and specifically target breast cancer stem cells.

Methods: To derive recombinant antibody pools, blood was obtained from breast cancer patients and antibody producing blood cells were separated by density gradient centrifugation. Ribonucleic acid (RNA) from these cells was isolated and analyzed by microfluidic electrophoresis. The genes encoding for antibodies were amplified from the RNA. In pilot experiments for the selection of such antibodies on breast cancer tissues, control antibodies were cloned and expressed on the surface of a bacteriophage. Sections of human breast cancer tumors grown in mice were incubated with recombinant phage and labeled with fluorescent nanoparticles. Recombinant phage were recovered from the tissue via laser capture microdissection and the recovered antibody genes amplified via PCR. Human primary breast cancer tissues were stained for CD44 with fluorescent nanoparticles to visualize target cells for the selection.

Results: We have obtained high quality RNA (RNA integrity number >8) from human blood lymphocytes and have successfully amplified the DNA coding for antibody variable regions. In pilot experiments on sections of tumors grown in mice, we were able to visualize single tissue binding phage, recover the phage via laser capture microdissection and reamplify the DNA of the antibody coding region. This serves as a proof-of-principle for the proposed methodology. Immunofluorescence staining of primary human breast cancer material revealed positive epithelial staining for CD44 in 8/11 invasive ductal breast carcinomas. These clinical specimens will serve as target for the antibody selections.

Conclusions: We completed several proof-of-principle milestones towards delivering tools for the analysis and targeting of breast cancer stem cells. These tools will serve to test whether treatment strategies have to be redesigned to include the specific elimination of breast cancer stem cells, and also may enable specific targeting of these cells for prognostic or therapeutic applications.

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Cell-free Production of Water Soluble ErbB Proteins

Principal Investigator:
Paul Henderson, Ph.D.

University of California, Davis

Abstract #: C-03
Over 30% of proteins are bound to cell membranes, which makes them difficult to isolate in a soluble and active form. We have implemented recently developed nanolipoprotein particles (NLPs) to allow the preparation of membrane-bound proteins in an active form. In particular, we are focused on tyrosine kinase receptors, which mediate the growth and spread of breast cancer and are already targets of several chemotherapeutics. The ability to study these receptors outside the cell environment will enable structural and mechanistic studies for improved understanding of breast carcinogenesis and development of novel drug screening strategies. Given that membrane-associated proteins account for the majority of drug targets, such as the targeting of HER2 (also known as ErbB2) by Herceptin, it is important to develop novel technologies to gain access to this important class of proteins. This proposal is focused on developing a new biotechnology application leading to formation of NLPs capable of solubilizing HER2 and other related membrane-bound proteins. The NLPs present a distinct advantage over currently used model membranes in terms of particle size monodispersity and solubility. This poster summarizes our progress

towards synthesizing homo- and heterodimers of ErbB receptors in NLPs and characterizing them for structure and function.

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Compounds Blocking Assembly of LRH-1 in Breast Cancer

Principal Investigator:
Cindy Benod, Ph.D.

University of California, San Francisco

Poster Authors: Cindy Benod, Ph.D. (PI), Robert Fletterick, Ph.D. (mentor)

Abstract #: C-04
The nuclear receptor LRH-1 (liver receptor homolog-1) is expressed at high levels in breast tumor cells and surrounding adipose tissue. Increased expression and its newly appreciated role in early development suggest that LRH-1 may be a worthy target in breast cancer research. Its roles in carcinogenesis are unknown, but in breast cancer cells uniquely, recent studies showed that LRH-1 powerfully enhances expression of aromatase, the enzyme that converts androgen to estrogen, stimulating tumor progression. Among the hundreds of genes under LRH-1 control are two cyclins regulating the G to S transition in cell cycles. Enhanced expression of these may be important in tumor maintenance. I hypothesize that inhibitors of LRH-1 transcriptional activity would slow or inhibit multiple pathways associated with breast cancer progression. Thus, the goal of this project is to identify small molecules that inhibit LRH-1 transcriptional activity in breast cancer cells.

In collaboration with Dr. Shoichet's lab, sophisticated computational chemistry calculations were carried out to examine the fit of test compounds into the LRH-1 hormone binding site. The experiments were run to favor discovery of compounds which fit the hormone binding site but extended outwards to deny formation of the surface binding site on the receptor for attachment of essential coregulators. We screened 8 million commercially available compounds from the Zinc database. At the end of this computational and careful chemical evaluation, we purchased a small number of potential LRH-1 inhibitors. To assess the binding of these compounds to LRH-1, we employed two innovative biochemical assays: Differential Scanning Fluorimetry and Surface Plasmon Resonance technology. The first assay was coarse, and the second quantitative. Together, these methods identified three compounds that bound to LRH-1 and predicted that the LRH-1 molecule would be destabilized when the compounds bind. The biological activity of these candidates is being investigated using cell-based assays of LRH-1 function. LRH-1 transcriptional activity in the presence of these compounds is being measured for several breast cancer cell lines. Effects on breast cancer cells proliferation will be quantified. For compounds that have desired effects, crystallographic studies will be performed to reveal the mode of binding and conformational changes in the receptor.

The major impact of this study is to provide breast cancer researchers with compounds that could be powerful tools to study the importance of LRH-1 in tumor progression. Furthermore, the discovery of LRH-1 specific inhibitors would provide a new route to block aromatase and possibly lead to pharmaceuticals with new and unexplored mechanisms of action to treat breast cancer. The critical role of LRH-1 in regulating aromatase transcription in malignant breast, but not in normal breast, bone or brain, suggests that these inhibitors may be more selective and might not have the side effects observed for current aromatase inhibitors.

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Intraductal Therapy of DCIS: A Presurgical Study

Principal Investigator:
Susan Love, M.D.

Dr Susan Love Research Foundation

Poster Authors: Susan M. Love, M.D., F.A.C.S.; M. Ellen Mahoney, M.D., F.A.C.S.; Dixie J. Mills, M.D., F.A.C.S

Abstract #: C-05
Background: Previous animal models have demonstrated the effect of intraductal administration of cytotoxic agents in treating and preventing breast cancers originating in the epithelial cells. Two human safety trials have been conducted with women undergoing mastectomies. This study will test the safety and feasibility of this approach neoadjuvantly in women with ductal carcinoma-in-situ.

Methods: Thirty women with (DCIS) diagnosed by minimally invasive biopsy techniques are be-

ing recruited for an IRB approved study testing the effects of neoadjuvant pegylated liposomal doxorubicin (Doxil) delivered through the affected duct on histology and imaging. The affected duct is cannulated and a ductogram performed to document both absence of perforation and presence of dye in the diseased duct. 20 mg (10 cc) of Doxil is then instilled into the duct. Six weeks later, just prior to the planned surgery, the MRI is repeated. Biomarkers are being examined in the cores and surgical tissue, pre and post injection.

Results: To date fourteen women have consented to the study. The first was not treated because of technical difficulties with the ductogram. Of the remaining thirteen women, three sustained perforated ducts and were not treated, in two women we were unable to cannulate the duct; five received the full dose of drug into the correct duct and one had a smaller dose into an adjacent duct, the seventh woman had a placebo dose of saline injected. The treatment has been very well-tolerated by all 7 subjects, with only some pain and local erythema noted. Pathology results have shown some decrease in mitotic activity, squamous metaplasia, fat necrosis and inflammation. Biomarker changes are being analyzed.

Challenges: The rural setting of this study has on the one hand limited recruitment while serving as a source of pride to the community as a whole with substantial support from local clinicians and the work maintains high visibility. The fact that this study has been successful in a community setting is evidence of the translatability of the concept. The approach is acceptable to women and appears to be well tolerated.

Summary: This research is feasible in a community setting. We are testing the concept of using the ductal system itself as a drug delivery system to affect the natural history of a disease confined to the duct. We are testing our ability to correctly identify the orifice of the affected duct by inspection of the mammogram. The treatment appears to be well-tolerated by the patients.

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Nanotherapy for Breast Cancer: Targeting Tumor Associated Macrophages

Principal Investigator:
Gaurav Sharma, Ph.D.

Sanford-Burnham Medical Research Institute

Poster Authors: Gaurav Sharma (PI), Priya Karmali, Michael Ramirez, Hui Xie, Erkki Ruoslahti, Jeffrey Smith (mentor)

Abstract #: C-06

Macrophages are versatile, plastic cells that are a key component of the body's immune system. They have a variety of biological roles which include initiating an immune response, scavenging debris, tissue remodeling and killing target cells such as bacteria etc. Macrophages are often prominent in tumor tissues, comprising up to 80% of the cell mass in breast carcinoma. Evidence currently available suggests that these tumor associated macrophages (TAMs) are reprogrammed by cancer cells and have little cytotoxicity for tumor cells. In fact, TAMs actually promote tumor cell proliferation and metastasis by secreting a wide range of chemicals. The pivotal role played by TAMs in tumor growth and metastasis combined with the limitations of conventional cancer therapies highlight the importance of investigating TAMs as a validated therapeutic target for cancer therapy.

The goal of my research project is to work at the interface of nanotechnology and medicine to develop "smart" nanoparticles that will selectively target and kill TAMs but not normal tissue or breast epithelial cells, thereby suppressing tumor progression and metastasis while limiting any side-effects of the anti-cancer therapy. Towards this end, we have developed a novel anti-macrophage agent that can be selectively targeted to TAMs. This agent consists of a FDA approved drug (clodronate) encapsulated in nanoparticles made from PLGA, a FDA-approved biodegradable and biocompatible copolymer. Clodronate belongs to a class of bisphosphonate (BP) compounds that are used in the clinic to prevent or inhibit osteoporosis. Once delivered inside the cell cytoplasm, BPs reacts with nonhydrolyzable analogue of ATP resulting in apoptosis. Encapsulation of clodronate in a nano-particulate system therefore allows for an efficient delivery of the drug to macrophages as they rapidly internalize particles.

We have fabricated clodronate-loaded particles (clodNPs) in the size range 200 – 300 nm and with high drug encapsulation efficiency of 40 – 60%.

We next showed that treatment with clodNPs killed mouse macrophages in a concentration dependent manner while there was no effect on cell viability on cells treated with empty NPs and drug only. Non-macrophage cells used as control were not affected upon incubation with clodNPs. To test if these particles can be targeted to TAMs we functionalized them with LyP-1, a newly identified tumor targeting peptide. In particular the LyP-1 peptide recognizes a subpopulation of activated macrophages in tumors that express the receptor for this peptide. Our *in-vivo* results using BALB/c mice bearing 4T1 breast tumors show a preferential accumulation of LyP-1-functionalized NPs in tumors compared to control particles. Our preliminary tumor therapy experiments show a 40% reduction in tumor volume of mice treated with LyP-1-functionalized clodNPs compared to vehicles.

The potential impact of this study is extremely high; my studies will not only provide the proof-of-concept for targeting TAMs but can also lead to a new therapeutic candidate for treating tumors with minimal side-effects. My studies will also provide the framework for a highly promising approach for targeting macrophages in other diseases, where they play an important role, such as atherosclerosis, AIDS, and infectious diseases like leishmania.

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Oral Contraceptives Use and Survival among Patients with Invasive Breast Cancer

Principal Investigator:
Yani Lu, M.D.

City of Hope

Poster Authors: Yani Lu (PI), Huiyan Ma, Jane Sullivan-Halley, Sophia S Wang, Katherine D. Henderson, James V Lacey Jr., Leslie Bernstein (mentor)

Abstract #: C-07

Objective: To examine if prediagnostic oral contraceptive (OC) use influences survival among women with invasive breast cancer.

Methods: 4564 women ages 35 to 64 years with newly diagnosed invasive breast cancer participated in the Women's Contraceptive and Reproductive Experiences (CARE), a study of risk factors for breast cancer, between 1994 and 1998. Since then (median follow-up=8.6 years), 1055 of these women died, 828 from breast cancer. Multivariable adjusted relative risks and 95% confidence intervals were estimated for risk of all-cause mortality and breast cancer-specific mortality using Cox proportional hazards models. Models included race, study site, tumor stage, estrogen receptor status and tumor grade to account for their effects on survival.

Results: Women who used OC for over 10 years had a 21% decrease in risk for death from any cause and a 12% decrease in risk for death from breast cancer when compared to women who never used oral contraceptives. These effects were stronger among women who reported a family history of breast cancer and women who used oral contraceptives within ten years of their breast cancer diagnosis.

Conclusions: Our results suggest that oral contraceptive use may have a favorable influence on survival for breast cancer patients; although the underlying characteristics of oral contraceptive users or unmeasured factors influencing oral contraceptive use might also contribute to the associations we observed in this study and thus require further investigation.

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Treating Breast Cancer Brain Metastases with Cytotoxic Lymphocytes

Principal Investigator:
Barbara Mueller, Ph.D.

Torrey Pines Institute for Molecular Science

Poster Authors: Barbara M. Mueller (PI), Michelle J. Hickey, Judy Rabano, Kate L. Erickson, Colin C. Malone and Carol A. Kruse

Torrey Pines Institute for Molecular Studies, San Diego CA (BMM, JR); Sanford/Burnham Medical Research Institute, La Jolla, CA (MJH, KLE, CCM, CAK)

Abstract #: C-08

Women living longer with breast cancer now frequently present with brain metastases. Current treatments for brain metastases are ineffective and there is a need for new therapeutic strategies. We propose that allo-reactive cytotoxic lymphocytes (alloCTL) may be effective as a therapy for brain metastases. alloCTL are lymphocytes from an unrelated blood donor that are trained to recognize

cancer cells as "foreign" and kill them, not unlike what happens in the rejection of an organ transplant from an unrelated individual. The goals of this research project are to evaluate the functionalities and characteristics of human alloCTL generated against human breast cancer cells in cell culture and to determine the therapeutic efficacy of alloCTL delivered to breast tumors growing in the brains of mice.

With funding from the CBCRP we have established a robust protocol to generate alloCTL from unrelated blood donors directed against human breast cancer cells. We have characterized the resulting alloCTL for their immunological markers and have demonstrated their ability to specifically kill breast cancer cells including those with high propensity to metastasize to the brain. We have established a mouse model in which the brain metastatic human breast cancer cell line MDA-MB-231BR grows intracranial tumors in immune deficient mice. In this model, treatment with alloCTL suppresses tumor growth. Intratumoral injection of alloCTL also prolongs the survival of mice with established intracranial breast tumors compared to untreated controls and to controls treated with unstimulated lymphocytes. We are currently evaluating the migratory ability that allows alloCTL to move through the brain and seek out breast cancer targets.

alloCTL are showing great promise clinically in patients with primary brain tumors. They may also be an effective and non-toxic therapy for brain metastases. The objective of our study is to establish proof-of-principle that alloCTL can effectively treat breast cancer in the brain. This may lead to a new treatment modality for women with breast cancer metastases to the brain.

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Combating Breast Cancer with the Wellderly Immune Repertoire

Principal Investigator:
Brunhilde Felding-Habermann, Ph.D.

The Scripps Research Institute

Abstract #: C-09

Breast cancer diagnosis and treatment have much improved, but some tumor types stubbornly resist therapy. Our goal is to identify novel markers of hard-to-treat breast cancer for the development of novel effective therapies. This is achieved through a combination of two major approaches using our novel model of triple-negative inflammatory and metaplastic breast cancer, the most aggressive type of this disease. In the first approach, we are tapping into the immune repertoire of healthy long-lived people (the wellderly) to identify antibodies that can block breast cancer growth. We hypothesize that many 'wellderly' individuals may have encountered developing breast cancer cells in their bodies over the years, but remained clinically disease free over decades - in many cases despite non-favorable genetic disposition and accumulating risk factors encountered over a lifetime. In the second approach, we are comparing the gene expression profiles of variants of our breast cancer cell model that represent increasingly aggressive and treatment resistant stages of the disease.

Our work during the first year of this project has focused on:

- constructing an Fab antibody library of the "Wellderly"
- generation of monoclonal antibodies directed against the progressive stages of our novel cell model using hybridoma technology
- initial characterization of the obtained antibodies
- comparative gene profiling and pathway analysis to identify changes from the primary tumor to local treatment-resistant recurrence and to end-stage pleural effusion
- along with validation studies and functional analyses of disease driving genes in our model

Our results identified genes associated with epithelial to mesenchymal transition (EMT) as a predominant set of changes during progression of this triple negative inflammatory and metaplastic breast cancer. Analyses of the adhesive, migratory and invasive properties of these cells indicated that EMT is a major driver of malignant progression in this model. Consistent with this notion, the tumor recurrence and pleural effusion derived tumor cells are strikingly more tumorigenic in SCID mice the cells from the primary breast cancer. Other major changes were seen in cytoskeletal genes, chemokines and their receptors, drug transporter proteins, metalloproteinases and matrix proteins.

Our developments and findings support our origi-

nal research plan and contribute important new information on mechanisms that drive progression of hard-to-treat triple negative breast cancer. Our analyses have lead to the identification of an array of novel potentially clinically and functionally important markers in this breast cancer type. Our functional validation studies have revealed new leads for possible inhibition of triple-negative breast cancer progression and opened focused avenues for the upcoming, intensive studies on functional molecular pathways that are critical for aggressive breast cancer development.

Finding antibodies that can curb breast cancer growth and identifying their targets, combined with knowledge on the genetic changes that occur during disease progression of hard-to-treat and ultimately unresponsive breast cancer will help understand the nature of aggressive breast cancer, define specific new ways for inhibition, and provide tools for clinical therapy.

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Reducing Surgical Morbidity of Breast Cancer Staging

Principal Investigator:
Steven Chen, M.D.

University of California, Davis

Abstract #: C-10

Background: Axillary Lymph Node Dissection is a standard component of therapy in node positive breast cancer. Lymphedema continues to be one of the most feared complications of this operation. We hypothesized that lymphedema may be related to the resection of lymphatic channels from the upper extremity and that a novel technique, axillary reverse mapping, would be able to identify these lymphatics.

Methods: We identified patients planning to undergo an axillary lymph node dissection for breast cancer who had not had prior axillary dissections more extensive than sentinel node biopsy. These patients were then mapped intraoperatively using 2.5 mL of Lymphazurin Blue dye injected subcutaneously into the proximal arm prior to the start of their axillary dissection. A standard axillary dissection was then performed. Notation was made of the ability to localize a blue lymphatic channel, the location of any blue lymph nodes, and the status of blue lymph nodes in terms of harboring metastasis. Quality of life surveys, arm measurements, and a standardized lymphedema assessment survey were performed on all patients preoperatively and at regular intervals post-operatively.

Results: To date, we have performed eight reverse mappings. Our patients average age has been 45 years old. Our success rate has be 75% in identifying either a blue lymphatic or a blue lymph node. No resected blue lymph nodes have contained cancer. 1 of 8 patients has developed lymphedema. No patient has developed any adverse sequelae to the blue dye injection.

Discussion: This represents one of the first studies of this technique. Our results demonstrate the feasibility of surgeons who are otherwise experienced in lymphatic mapping to rapidly adopt this novel technique. Further refinement of the technique will be needed, once oncologic safety has been established to further increase its usability in this patient population. A randomized trial to ascertain the effect of saving these blue lymphatics/lymph nodes is warranted.

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Session D: Detection and Prognosis

Blood Oxygen Level Dependent (BOLD) Contrast in the Breast

Principal Investigator:
Rebecca Rakow-Penner, M.S.

Stanford University

Poster Authors: Rebecca Rakow-Penner, M.S., Bruce Daniel, M.D., and Gary H. Glover, Ph.D.

Stanford University School of Medicine, Department of Radiology

Abstract #: D-01
Goal: To detect tumor oxygenation in breast tissue with MRI.

Blood oxygen level dependent (BOLD) contrast MRI has the potential to non-invasively detect breast tumor oxygenation. This information may help characterize tumors, predict susceptibility to treatment, and monitor chemotherapeutic response. We have developed a robust methodology for detecting BOLD contrast on healthy volunteers and evaluated the method on 3 breast cancer patients.

For this study, we focused on optimizing how to acquire BOLD contrast in the breast and began to understand the results. First, a single shot fast spin echo (SSFSE) sequence was compared to a gradient echo (GRE) pulse sequence for data acquisition. In order to induce changes in oxygenation, it was necessary to alter the systemic oxygenation of the patients and volunteers. Thus, we evaluated 3 hyperoxic stimuli on 15 healthy volunteers to determine the stimulus with the strongest response in the breast: air interleaved with carbogen (95% O2, 5% CO2), air interleaved with oxygen, and oxygen interleaved with carbogen. The stimulus which produced the best results across all the volunteers was then used for the patient study.

Our results indicated that an SSFSE pulse sequence produced significant BOLD contrast results in the breast compared to a GRE pulse sequence and that oxygen interleaved with carbogen yielded the best results in healthy volunteers. We also noted that BOLD contrast in healthy glandular breast tissue positively correlates to carbogen and breast cancer negatively correlates to carbogen. Thus, it is possible to detect changes in breast cancer oxygenation with MRI.

In conclusion, we have developed a robust protocol for detecting changes in breast cancer oxygenation with MRI. Future research involves testing the protocol on a larger patient population. Impact: Detecting tumor oxygenation with BOLD MRI may provide a biomarker for evaluating whether a patient will respond to antiangiogenic therapy.

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Detection of Cathepsin-B Activity in the Lymph Nodes Using Dendritic Fluorescent Probes

Principal Investigator:
Ella Jones, Ph.D.

University of California, San Francisco

Poster Presenter: David Pham

Abstract #: D-02
Background: Metastatic breast cancer primary route of proliferation is through the lymphatic system. Accurate assessment of lymph nodes is critical for staging the disease progression and determination of therapeutic options for patients. Lymphadenectomy is the current clinical method for lymph nodes assessment, which involves microscopical examination of surgically removed lymph nodes. This painful and invasive procedure causes nodal destruction and swelling and is not always analytically reliable. Molecular imaging affords non-invasive options for visualizing lymph nodes. However, available imaging techniques cannot accurately ascertain the malignancy of the infected lymph nodes, because they show only anatomical structures without revealing the bioactivities associated with disease progression. Cathepsin-B (Cat-B), a lysosomal protease, is an established biomarker for metastatic breast cancer and is implicated in the pathway for invasion of cancerous cells into the lymph nodes through the destruction of the basement membranes.

Method: We have developed an fluorescence imaging probe with the potential to highlight diseased lymph nodes by being selectively turned on in the presence of Cat-B. The developed molecular probe is consisted of three components:

(1) a dendritic polyester platform that allows for tumor homing,
(2) Cat-B specific peptidic substrates at the periphery,
(3) molecular weight modifier mPEG surface groups.

Natively, the probe is in the off state, because the fluorescence quencher moiety is placed adjacent to the fluorescence dye on the peptidic substrate. Fluorescence is activated when Cat-B proteolytically removes the fluorescence quencher moieties from the probe. *In vivo*, this 'light switch' design will highlight the bioactivity of Cat-B, affording a viable method for non-invasive assessment of lymph nodes.

Results: The synthesized peptidic reporter NH2-GK$^{(5\text{-FAM})}$QVSGFRFGC$^{(DACM)}$G-CONH2 have been assayed with Cat-B, and shown to have comparable specificity with known Cat-B substrates (Table 1). We have further demonstrated that the dendritic probe is efficiently activated by breast cancer cell lines, MCF-7 and DU-4475, that overexpressed Cathepsin-Bin *in vitro* studies.

Conclusion: The demonstrated Cat-B specificity of the peptidic reporter warrants further *in vivo* investigations of this probe. The *in vitro* results has highlight the promising utility of this probe in non-invasive assessment of metastatic breast cancer in the lymph nodes.

Table 1:
Proteolysis Data of Cathepsin-B Substrates

Cathepsin B Substrates	Km (mM)	kcat (s^{-1})	kcat / Km ($M^{-1}\bullet s^{-1}$)
Cbz-FR-AMC (@ pH 6.0)	0.6	33.8	54.6
NH2-GK$^{(5\text{-FAM})}$ QVSGFRFGC$^{(DACM)}$G-CONH2 (@ pH 5.5)	1.0	45.5	47.8
NH2-GK$^{(5\text{-FAM})}$ QVSGFRFGC$^{(DACM)}$G-CONH2 (@ pH 7.4)	2.8	40.8	14.6

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Development of a Computer Aided Diagnosis (CAD) System for Breast MRI

Principal Investigator:
Ke Nie, M.S.

University of California, Irvine

Poster Authors: Ke Nie (PI), Jeon-Hor Chen, Muqing Lin, Daniel Chang, Yu Hon, Orhan Nalcioglu, Min-Ying Lydia Su, Ph.D. (mentor)

Abstract #: D-03
In 2007, the American Cancer society has issued a guideline recommending annual breast MRI screening to women with greater than 20-25% lifetime risk for breast cancer. There are well-established indications that will qualify a patient for receiving clinical MRI exams for screening, diagnosis, staging, or therapy evaluation, approved by the insurance company. Many more clinical breast MRI examinations are expected to be performed. However, the low specificity may lead to great anxiety to patients, and many unnecessary biopsy or overtreatment. As the use of breast MRI increases, how to improve the diagnostic accuracy in breast MRI is becoming a more and more important problem. Furthermore, due to the mature clinical indication for breast MRI, there is a pressure for the small community hospitals or imaging centers to perform breast MRI. They may have well qualified mammographers, but not trained in reading breast MRI. On the other hand, the MRI radiologist may not be trained in breast imaging. The experience and training of radiologists in interpreting MRI raises a critical concern. Thus there is a critical need to develop computer-aided diagnosis system for breast MRI diagnosis.

The current available Computer-Aided Diagnosis (CAD) systems developed commercially can extract most important information from a large number of images obtained in a single MR examination to help radiologists' interpretation. But, this approach offers only a display platform, not a true CAD which can provide "an intelligent thinking and final impression". To respond to this great need, we are developing an automated CAD system to aid in detection and diagnosis of breast cancer on MRI.

Our CAD system was built based on 116 cases with both mass type and non-mass enhancement types lesions. The current system could automatically detect and segment suspicious region (possible lesion), then analyze their morphologic and kinetic features. A full panel of all morphology, texture, and enhancement kinetics information could be automatically obtained to allow differentiating between malignant and benign lesions. The selected specific features were trained using both non-linear artificial neural network and linear regression classifiers. A final score between 0-1 will be given to each detected lesion to indicate its malignancy level. Despite of the strong association between breast density and cancer risk, one major problem hampering incorporating of breast density into risk model is the lack of reliable quantitative measurement of density. Compared to mammog-

raphy, MRI provides 3-dimensional coverage of the entire breast with strong contrast between fatty and fibroglandular tissues, thus has a high potential to provide quantitative density information. Thus, we extend the work from analyzing the lesion alone to quantifying the normal tissue. We further developed a dedicated tool to measure the normal tissue density and its relative distribution to fatty tissue, which would allow new investigations between density and cancer risk.

Overall, with the grant support, we already have 7 papers and over 20 conference proceedings published. We believe the research will finally benefit patients who are recommended to undergo MRI, especially those with dense breasts, particularly in young or Asian women.

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Differential Optical Mammography

Principal Investigators:
Gregory Faris, Ph.D. and Christopher Comstock, M.D.

SRI International and University of California, San Diego

Poster Presenter: Greg Faris, Ph.D.

Abstract #: D-04
Early detection of tumors in breast tissue is paramount for appropriate treatment intervention to enable complete patient recovery. While X-ray mammography remains the method of choice for early disease detection, near infrared light based detection modalities are gaining momentum as optical technologies matures and scientists exploit natural chromophores in blood, hemoglobin [Hb] and oxyhemoglobin [HbO_2] as contrast agents to image breast tissue. Since tumor tissue is often characterized by leaky and abnormal vasculature and hypoxia, we postulate that exogenous contrast agents such as inhalation of hyperoxic/hypercapnic gases could provide sufficient signal to distinguish between diseased and healthy tissue in the case of breast cancer. To extract signal from tumorogenic tissue, we employ differential imaging in the data analysis. Analysis of recent clinical results confirm the viability of the technique.

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Extranuclear Estrogen Receptors in Breast Cancer Prognosis and Clinical Management

Principal Investigator:
Richard Pietras, M.D., Ph.D.

University of California, Los Angeles School of Medicine

Poster Authors: RJ Pietras (PI), DC Marquez-Garban, L Goodglick, M Fishbein, D Elashoff, J Klein.

Abstract #: D-05
Estrogens are hormones that are well known to promote breast cancer. These effects are exerted by the binding of estrogens to tumor cell proteins termed estrogen receptors (ER). These receptors were once thought to occur only in the cell nucleus, and detection of ERs in the nucleus is the basis of the "ER assay" used in the clinic to plan patient care. However, it is now known that ERs also occur outside the nucleus, with numerous studies showing that ERs at or near the tumor cell surface membrane (termed mERs) serve important roles in activating signals inside the tumor cell that stimulate gene changes and tumor growth.

The current ER assay that measures only nuclear ER fails to predict responses to endocrine therapy in about half of patients with advanced breast cancers, thus indicating an urgent need to improve ER assays. This may be possible by developing new assays to correlate not only nuclear ER but also mER with patient outcome. As a primary aim of this project, we are studying archival human tumor specimens in order to design innovative assays to measure mER and to combine this clinical data with nuclear ER assays. For these studies, preserved tumor specimens (initially collected at the time of surgery) from 75 patients with primary breast cancer are being obtained, including samples from 10 patients with tissues for comparison from the primary tumor, paired metastases (spread to lymph nodes or distant organs) and nearby normal tissue. Tissue specimens are cut in small sections and mounted on slides to test different methods for optimal detection of mER. For these studies, antibody molecules that specifically bind estrogen receptors are being used. Antibodies are labeled with probes to allow visualization of microscopic deposits that mark the location of mERs under fluorescent and light microscopy. We have achieved detection of mER expression and are beginning to correlate data with nuclear ER assays and with outcome data in

order to assess prognostic benefit and predictive value for patient responses to hormonal therapies. Laboratory studies are also being done in parallel to isolate and characterize molecular properties of tumor cells with high mER levels to understand how the mERs function. Initial findings suggest that breast tumor cells with a high density of membrane-associated ER constitute a small subset of the bulk tumor population and co-express biomarkers commonly detected in tumor progenitor cells.

Since mERs regulate breast cancer gene expression and progression, assays to detect mER may augment current prognostic data based only on nuclear ER and improve patient management decisions and survival. Further understanding of mER activity may also lead to new therapeutic interventions in the clinic.

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Factors Influencing Mammography Screening among Thai American Women

Principal Investigators:
Mary Jo Clark, Ph.D., R.N., and Bulaporn Natipagon-Shah, Ph.D., R.N.

University of San Diego and Thai Health Information Service

Poster Presenter: Mary Jo Clark, Ph.D., R.N.

Abstract #: D-06
In order to validate and further explore factors influencing mammography screening derived from a series of focus groups with Thai women in Southern California, telephone interviews were conducted with Thai women in four Southern California counties. Interviewees completed a survey instrument that focused on knowledge about breast cancer as experienced by Thai women and the need for breast cancer screening. The relative importance of factors motivating and impeding breast cancer screening, and perceived causes of cancer prevalent in the this ethnic population were also explored. Interviews were conducted by Thai-speaking nurses with women over 40 years of age who self-identified as Thai. A convenience sample of women was recruited from agencies serving the Thai community and cluster sampling was used to obtain the target number of participants. Participants were asked to rate the relative importance of factors in promoting or impeding breast cancer screening as well as their intentions to obtain or not obtain a mammogram in the following year. Findings will lay the foundation for interventions to promote mammography screening in this ethnic population.

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Nanostructure-Initiator Mass Spectrometry Based Tissue Imaging to Identify Metabolic Biomarkers of Breast Cancer Subtypes

Principal Investigator:
Trent Northen, Ph.D.

Lawrence Berkeley National Laboratory

Poster Authors: Wolfgang Reindl, Ben P. Bowen, and Trent R. Northen (PI)

Abstract #: D-07
The goal of this project is to use our recently developed tissue imaging technique, Nanostructure-Initiator Mass Spectrometry (NIMS), for the identification of metabolites as biomarkers which can be used to discriminate between different breast cancer subtypes. Functional tissue imaging provides a tremendous opportunity to gain insights into the pathological processes of breast cancer and it allows to distinguish the effects of different tumor tissue microenvironments. Current approaches are focused on genomic and proteomic imaging. However, the importance of the cellular metabolism in cancer pathology coupled with the utility of small molecule biomarkers make it critical to develop complementary metabolite imaging approaches. Unfortunately, technical limitations of existing mass spectrometry approaches have largely limited this possibility. We have developed NIMS as a new surface based mass spectrometry approach that is well suited for metabolite profiling and imaging from frozen tissue sections combining high lateral resolution (10-75 μ m), sensitivity (highest reported including single cancer cells), and lack of matrix. Preliminary imaging results reveal dramatic metabolic differences between normal and tumorous breast tissue. Breast cancer is a very heterogeneous disease for which several subtypes (e.g. basal and luminal) can be distinguished and for which a broad range of drug sensitivities or resistance can be observed, making it difficult to select the most efficient treatment. The availability of metabolic biomarkers for particular drug responses

would be an important resource for the selection of the appropriate medication.

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Precision Image-guided Biopsy of Tumors in Dense Breasts

Principal Investigator:
Thomas R. Nelson, Ph.D.

University of California, San Diego

Poster Authors: TR Nelson, J Nebeker, AM Wallace, H Ojeda-Fournier

Abstract #: D-08
The goal of this project is improve biopsy accuracy and the biopsy experience for patients requiring a breast biopsy. To do this we assessed the performance of dedicated volume breast ultrasound imaging (VBUS) system with compact robotic biopsy device to provide precision image-guided breast lesion biopsy. Improved detection and biopsy of small lesions is essential for improving breast cancer survival. Most cancers arise in dense ductal tissue where ultrasound performs better than mammography. Small lesions (~2-3 mm) are difficult to biopsy using hand held techniques. Minimally invasive robotic devices potentially can assist physicians perform more precise biopsies thereby improving breast diagnosis and management.

Our design has integrated our VBUS system with a compact robotic device having a 6-DOF articulated arm to reach any breast location within ±1.0 mm carrying up to a 3.0 kg load. A load sensor measured force (F_x, F_y, F_z), and torque (T_x, T_y, T_z) providing real-time data regarding biopsy device insertion and penetration forces. System performance was evaluated by scanning a variety of breast test objects having simulated lesions using a pendant patient breast position. We measured targeting error and reproducibility in air using acrylic spheres (3, 6, 9, 12, and 15 mm) and in GelWax based breast test objects with (lesion sizes 2-15 mm). Volume data provided 3-dimensional lesion coordinates. Targeting and guidance algorithms optimized the path for insertion of a Mammotome™ vacuum biopsy device. Physician guidance is used to direct robot motion and device insertion.

Overall the VBUS volume image data were acquired in 20 sec/slice (volume < 20 min.) showing ~1 mm spatial resolution with lesions clearly identified. Lesion targeting and guidance algorithms showed insertion trajectory prior to device motion. Initial positioning located the device adjacent to skin surface; insertion was under physician guidance. Robotic reproducibility was excellent with lesion targeting accuracy to within ±1 mm. Gel test objects provided force feedback data regarding object deformation to improve targeting small lesions.

Volume imaging improved lesion localization and biopsy device placement, especially for small lesions. Robotic devices may provide more precise device placement assisting physicians with biopsy procedures. This work demonstrates the potential to translate the capabilities of two rapidly developing areas of medicine: volumetric imaging and robotic devices into a fully-functional clinical volume image-guided, physician-directed robotic breast biopsy system.

Supported in part by CBCRP Grants: 11IB-0035, 13NB-0176, 15GB-0023

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Sound Speed Tomography for Early Breast Cancer Detection

Principal Investigator:
Jakob Nebeker, B.S.

University of California, San Diego

Poster Authors: Jacob Nebeker and Thomas Nelson

Abstract #: D-09
The goals of this dissertation (JN) and IDEA (TN) projects are to improve early detection of breast cancer by building an ultrasound scanner that can image the entire breast. We also are incorporating capability to measure sound speed and attenuation in addition to reflectivity we can gain additional diagnostic information regarding breast lesions further improving diagnostic accuracy. Because breast tumors have been shown to have a markedly higher sound speed than healthy tissue, sound speed has the potential to be a valuable new indicator of cancer. Standardizing ultrasound breast imaging provides high quality images improving detection of non-palpable 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 acquire approximately 150 B-mode images completely around the breast. Spatially compounding the images creates a high-detail reflection image. We also obtain reflected data to create sound speed and sound attenuation images. Back-projecting the time delays and attenuation along each ray over all angles produces sound speed and attenuation images.

We have performed a series of measurements to characterize scanner performance with satisfactory results. Gel wax test object data that we can distinguish lesions down to approx 1mm in diameter in the reflection images and approx 3mm in size in the sound speed and attenuation images. Reconstructed sound speed contrast resolution has been measured to be approx 0.3% (1500 m/s +-5 m/s) for synthetic phantoms and 1% (1460 m/s +- 15 m/s) for gel wax phantoms). 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 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. Fourth, we simultaneously image sound reflection, speed, and attenuation, and finally the scanner does not use uncomfortable compression and ionizing radiation. We believe this approach has the potential to improve on the state of the art for early breast cancer detection, especially in women with dense breasts.

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Accuracy of Diagnostic Mammography at Facilities Serving Vulnerable Women

Principal Investigator:
Lauren Elizabeth Goldman, M.D.

University of California, San Francisco

Poster Authors: L. Elizabeth Goldman, M.D., M.C.R. (PI),[1] Rod Walker, M.S.,[2] Diana L. Miglioretti, Ph.D.,[2,3] Rebecca Smith-Bindman, M.D.,[4] Karla Kerlikowske, M.D.[1]

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Abstract #: D-10
Background: Breast cancer missed on diagnostic mammography may contribute to delayed diagnoses, while false-positive results may lead to unnecessary invasive procedures. Whether accuracy of diagnostic mammography at facilities serving vulnerable women differs from other facilities is unknown.

Objective: To compare the diagnostic accuracy of diagnostic mammography at facilities serving vulnerable women to those serving non-vulnerable women.

Design: We examined 168,251 diagnostic mammograms performed at Breast Cancer Surveillance Consortium facilities from 1999-2005. We used hierarchical logistic regression to compare sensitivity, false positive rates, and cancer detection rates.

Subjects: Women ages 40-80 years undergoing diagnostic mammography to evaluate an abnormal screening mammogram or breast problem.

Measures: Facilities were characterized according to the populations served based on the proportion of mammograms performed on women with lower educational attainment, racial/ethnic minorities, limited household income, or rural residences.

Results: Sensitivity of diagnostic mammography did not vary significantly across vulnerability groups adjusted for patient-level characteristics, but false-

positive rates among diagnostic mammograms to evaluate a breast problem were higher at facilities serving vulnerable women: lower educational attainment (odds ratio (OR) 1.39; 95% confidence interval (CI) 1.08, 1.79); racial/ethnic minorities (OR 1.32; 95% CI 0.98, 1.76); limited income (OR 1.34; 95% CI 1.08, 1.66), and rural residence (OR 1.55; 95% CI 1.27, 1.88).

Conclusions: Diagnostic mammography to evaluate a breast problem at facilities serving vulnerable women has higher false positive rates than at facilities serving non-vulnerable women. This may reflect concern about incomplete follow-up after abnormal diagnostic mammography and/or high cancer prevalence in vulnerable women.

Implications: Interventions to improve diagnostic mammography accuracy at facilities serving vulnerable women may reduce unnecessary invasive procedures.

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Novel Small Proteins for PET Imaging of HER2

Principal Investigator:
Zhen Cheng, Ph.D.

Stanford University

Poster Authors: G. Ren, [1] Z. Miao, [1] J.M. Webster,[2] R. Zhang,[2] S. S. Gambhir,[1] F. A. Syud,[2] Z. Cheng[1]

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Abstract #: D-11

Affibody molecules are novel scaffold proteins and suitable for rapidly developing molecular probes for a variety of tumor targets. It has been shown that Affibody molecules against human epidermal growth factor type 2 (HER2) can be labeled with different radionuclides and can specifically image HER2 expressions and modulations both in cells and in preclinical animal models. In our research, we have further developed strategies for discovery even smaller Affibody analogs, 2-helix proteins, for *in vivo* HER2 molecular imaging.

Methods: A library of anti-HER2 2-helix Affibody analogs were chemically synthesized using solid phase peptide synthesizer. Helices 1 and 2 that contain the binding domain were preserved while a third helix was truncated. A number of both sequence mutations and synthetic strategies to optimize the affinity of 2-helix proteins were developed. The lead candidate cyclic peptide was then selected and was site specifically radiolabeled with several positron emission tomography (PET) radionuclides including 18F, 68Ga or 64Cu. The resulting molecular probes were then evaluated for microPET imaging of HER2 in SKOV3 tumor mice.

Results: Several constrained 2-helix peptides with high HER2 affinity were successfully identified (for example: MUT-DS, KD = 5 nM). Conjugation with a metal chelator or radiofluorination agent still preserved high binding affinity. Radiolabeled (68Ga, 64Cu or 18F) probes displayed high stability in mouse serum and specificity towards HER2 in cell culture. Biodistribution and microPET imaging studies further revealed that the probes had rapid, high and specific HER2 positive tumor uptakes and excellent tumor imaging ability.

Conclusions: 2-helix small proteins with high affinity to tumor biomarkers can be discovered and used for *in vivo* molecular imaging. PET radionuclides labeled MUT-DS showed promising results for imaging HER2 expression and modulation *in vivo*.

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Abstract #: D-12

The Roles of SATB1 in Breast Tumorigenesis

Principal Investigator:
Laurie Friesenhahn

Poster Authors: Ellen Ordinario, Hye-Jung Han, Laurie B. Friesenhahn, Francis Rodier, Judith Campisi, Debopriya Das, Joe W. Gray, Y oshinori Kohwi and Terumi Kohwi-Shigematsu

Life Sciences Division, Lawrence Berkeley National Laboratory, University of California, Berkeley

SATB1 acts as a genome organizer by tethering a large number of genomic loci onto the SATB1 regulatory network via specialized

DNA sequences called base unpairing regions (BURs). Genes that are bound to SATB1 are assembled with chromatin-remodeling enzymes and transcription factors which SATB1 recruits. We have previously shown that SATB1 has critical roles in promoting both tumor growth and metastasis of breast tumors by reprogramming the chromatin organization and transcription profiles of breast cancer cells. This was determined by examining the effects of SATB1 knockdown or ectopic expression in human breast cancer cell lines (MDA-MB-231, Hs578T, BT549, and SKBR3) in nude mice. We have followed up on our studies by examining the effects of SATB1 expression in non-tumorigenic, immortalized MCF10A cells. We found that at least in one MCF10A cell line, SATB1 expression promoted the epithelial-mesenchymal transition in vitro. These SATB1-expressing MCF10A cells also promoted tumor growth and metastasis in nude mice, indicating an oncogenic activity of SATB1. SATB1 expression does not promote tumorigenesis in all MCF10A cell lines, however. This indicates that the oncogenic activity of SATB1 requires certain conditions to be met in MCF10A cells. Although comparative genomic hybridization array patterns did not show any major changes between these cell lines, we found that, in those MCF10A cells that have a potential to form tumors in mice when SATB1 is expressed, the G2 checkpoint fails. We also show data on the drug resistance of breast cancer cells when SATB1 is expressed. These data are consistent with our previous observation that SATB1 does have an important function in promoting breast cancer progression.

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A Genetic System for Identification of Mammary Stem Cells

Principal Investigator:
Dannielle Engle, B.A.

University of California, San Diego/Salk Institute

Abstract #: E-02

Mammary development and tumorigenesis exhibit potentially important similarities. The growth of the mammary gland and its invasion through the stroma are reminiscent of the steps involved in tumor progression and metastasis. Mammary stem cells play a key role in the development and maintenance of the breast. These cells have the ability to self-renew and generate the different cell types of the breast such that an entire functional mouse mammary gland can be regenerated from a single mammary stem cell. Similarly, it has been shown that some tumors contain a population of cells with disproportionate ability to generate new tumors upon implantation in mice. As these cells can replicate and generate the same cell types present in the primary tumor, they have been operationally termed cancer stem cells. In addition to these two stem like characteristics, cancer stem cells are also thought to be resistant to cancer therapies. Therefore, if even a single cancer stem cell survives after the treatment of a tumor, it could result in cancer relapse. Unfortunately, pure populations of mammary stem cells or breast cancer stem cells have not yet been identified, making it difficult to determine which signals regulate stem cell activity, how cancer stem cells contribute to breast cancer, and whether cancer stem cells can be effectively targeted and eliminated. Using properties important for development of the mouse mammary gland and stem cell function, my research focuses on improving mammary stem cell identification, isolation, and characterization.

It has been proposed that some tissue stem cells exist in a dormant state. I will introduce an artificial gene into mice that permits visualization of cells with different rates of division. In addition, mammary gland development has been shown to rely on Wnt signaling, a pathway that is also critical for stem cell function in several other tissues. For this reason, the artificial gene is designed to also label cells responding to Wnt. Before generating these mice, I confirmed the artificial gene is functional by stimulating Wnt signaling *in vitro*. Once I have finished generating these mice, I will be able to test my hypothesis that mammary stem cells exhibit and rely on these two features to maintain their activity by assessing the ability of Wnt responding cells with different rates of division to re-grow a mammary gland after transplantation. In addition, I setup a culturing system that recapitulates mammary development in order to establish a parallel *in vitro* model for use with this mouse. Using this *in vitro* model, I am optimizing modulation of Wnt signaling to test its effect on mammary stem cell activity. Ultimately, utilizing the genetic system during development to isolate cells based on their functional properties, we will be able to isolate mam-

mary stem cells and determine what signals are essential for stem cell activity during development and tumorigenesis. Understanding the molecular signals that govern normal mammary development and mammary stem cell activity is likely to provide additional markers for early detection, targets for treatment, and inroads to the prevention of breast cancer.

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Chemokine Receptor (CXCR4 and CXCR7) Function in Breast Cancer

Principal Investigator:
Morgan O'Hayre, B.S.

University of California at San Diego

Poster Authors: Morgan O'Hayre (PI), Catherina Salanga, Jing Yang, and Tracy Handel (mentor)

Abstract #: E-03

Chemokines and their receptors play an important role in the immune system by guiding the migration of cells involved in routine immune surveillance and inflammatory responses. However, they can also be exploited by cancer cells to facilitate metastasis and enhance tumor growth. Our work focuses on elucidating the roles of the chemokine, CXCL12, and its receptors, CXCR4 and CXCR7, in breast cancer. Although CXCR4 and CXCR7 are not normally expressed in breast tissue, they are often expressed on breast cancer cells and are known to contribute to metastasis and primary tumor growth, respectively. However, the extent by which CXCR4 and CXCR7 serve redundant verses distinct functions has not been established, nor the underlying mechanisms of how they contribute to disease. Thus, our goal is to explore how these two chemokine receptors function independently and in conjunction in breast cancer progression.

In order to address these questions, we derived sublines from the MDA-MB231 human breast cancer cell line that express low levels of both receptors, high levels of CXCR4, high levels of CXCR7 or high levels of both receptors. Consistent with published observations, our results indicate that cells with high expression of either CXCR4 or CXCR7 resulted in accelerated tumor growth compared to those with low expression. Furthermore, we found that high CXCR4 but not high CXCR7 resulted in increased metastasis, consistent with previous findings from studies of the individual receptors. However, we observed striking differences in the effects of dual receptor expression on tumor growth depending on "dose" of the receptors. When both CXCR4 and CXCR7 are expressed at moderate levels, an increase in tumor growth and metastasis is observed compared to cells with either receptor expressed alone. However, upon high expression of CXCR7 with CXCR4, an inhibitory effect is observed, whereupon tumor growth rate is significantly reduced, even compared to the control cells with very low levels of receptor expression. In order to better understand the molecular mechanisms underlying these contrasting results, we are currently comparing how differential levels of receptor expression influences intracellular signaling events involved in cell survival and proliferation. Additionally, we have demonstrated that a key distinction between these two receptors is that CXCR4 primarily localizes at the surface of MDA-MB231 breast cancer cells, while CXCR7 largely localizes inside the cell. Therefore, receptor localization may be important for understanding the dose-dependent differences of CXCR4 and CXCR7 expression on tumor growth/metastasis.

Results thus far suggest that CXCR4 and CXCR7 do not serve redundant functions although they influence each other's functions both at the cellular level and in breast cancer growth and metastasis. Understanding the mechanisms by which CXCR7 cooperates with CXCR4 when expressed at moderate levels, and how it is inhibitory when expressed at high levels will be an important goal of future studies. These findings could have significant implications in terms of disease aggressiveness and the effectiveness of targeting the receptors and downstream signaling pathways for the treatment of breast cancer.

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From the Normal Biology of Phosphorylated Prolactin to a Novel Therapeutic for Breast Cancer

Principal Investigator:
Ameae Walker, Ph.D.

University of California, Riverside

Abstract #: E-04

We and others have provided evidence that links increased exposure to the hormone prolactin (PRL) to the development of breast cancer. However, PRL comes in two major forms, unmodified (U)

and phosphorylated (P*). The CBCRP project was designed to determine the different functions of U- and P*-PRL in the mammary gland. What we found is that U-PRL increases cell proliferation (both positively and by hampering the effects of proteins that normally inhibit cell proliferation) and that P*-PRL essentially does the opposite. In addition, P*-PRL promotes cell-specific function. In other words, P*-PRL has anti-cancer activities. To take advantage of these activities, we have developed a stable, synthetic version of P*-PRL, called S179D PRL. S179D PRL not only inhibits basal and U-PRL-stimulated growth of breast cancer cells, but also and very importantly it entirely blocks estrogen-stimulated growth. Since a greater proportion of breast cancers have PRL receptors (molecules that would allow them to respond to S179D PRL) than estrogen receptors, the potential therefore exists for S179D PRL to be a more widely useful therapeutic than either estrogen receptor antagonists or aromatase inhibitors.

To increase our understanding of how both types of PRL work in the intact gland, we determined the distribution of PRL receptors, and obtained several unexpected results: First, except during lactation, almost all PRL receptors on duct-lining mammary cells were found on the side facing the duct lumen and not on the side facing the blood. In order for either form of PRL in the blood to interact with these receptors it is therefore necessary for it to pass between the cells to first gain access to the duct. Second, we found two binding proteins in ductal fluids, one that alters the availability of both forms of PRL (type 1) and one that alters the way U-PRL interacts with the PRL receptor (type 2). We have determined that the type 2 binding protein is produced in much lower amounts by breast cancer versus normal tissue from the same patients. Together, these results suggest that ductal content of U-PRL versus P*-PRL and the binding proteins may be more relevant to development of disease than circulating PRL, although it is clear that blood PRL does gain access to the ducts. Third, we have shown that the cells underneath the duct lining cells, known as myoepithelial cells, have lots of PRL receptors, suggesting they are a heretofore unrecognized important target of PRL. These cells proliferate, migrate and invade underlying connective tissue during development of the gland in pregnancy, and are thought to be the source of a particularly aggressive, but less common form of breast cancer. Follow up on this finding will determine whether this form of breast cancer might also be responsive to S179D PRL.

Thus, funding by CBCRP has markedly developed our understanding of the vastly different roles of the two forms of PRL in normal mammary gland biology and the development of breast cancer. Furthermore, the work has identified S179D PRL as a potential novel therapeutic for breast cancer.

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Human Breast Cancer Lymphovascular Tumoral Emboli Recapitulate an *in vitro* Mammosphere Stem Cell Phenotype

Principal Investigator:
Sanford H. Barsky, M.D.

University of California, Los Angeles (now at University of Nevada & Nevada Cancer Institute)

Abstract #: E-05

Background: The existence of stem cells in human cancers has been inferred by clonality experiments and marker studies *in vitro* and clinical observations *in vivo* concerning tumor recurrences and emerging drug resistance. We have studied the existence of stem cells in a human model of inflammatory breast cancer, termed MARY-X, a model which forms spheroids which are similar to normal tissue stem cell-derived mammospheres. Comparing MARY-X with common non-IBC breast carcinoma and normal cell lines, we found specific embryonal stem cell markers within the MARY-X spheroids. RT-PCR analyses of MARY-X also revealed the expression of transcriptional determinants essential for the pluripotency and self-renewal of human embryonal stem cells. Since MARY-X spheroids, when injected into mice, form tumors with florid lymphovascular emboli, we wondered whether tumor emboli from actual human cancers also recapitulated a mammosphere stem cell phenotype.

Design: We carried out laser capture microdissection of tumor emboli in 200 cases of human breast cancer including cases of both infiltrating ductal as well as lobular cancer. These cases included all of the common molecular classes of breast cancer including luminal A, luminal B, luminal C, Her-2/neu positive and triple negative including the basal subtype. The common denominator which was studied in all of these cases was the lymphovascular embolus.

Result: By both RT-PCR and IHC, lymphovascular emboli exhibited five-ten fold higher stem cell

markers including Stellar, H19, Rex-1, Nestin, CD133 and Aldehyde Dehydrogenase 1 (ALDH1) as well as stem cell transcriptional determinants including OCT4, SOX2, and Nanog than the non-embolic tumoral areas. In addition, stem cell signaling pathways specifically involved in self-renewal and pluripotency including Bmi-1, Hedgehog and Notch 3 were activated selectively within the lymphovascular tumor emboli. These observations held true irrespective of the molecular class of breast cancer from which the embolus was derived and irrespective of the adhesion status (presence or absence of E-cadherin) of the embolus.

Conclusion: Our findings indicate that the lymphovascular embolus is not simply a cellular fragment that detaches from the main tumor but rather represents a selection for a stem cell phenotype. This finding may explain the increased resistance of lymphovascular tumor emboli to chemotherapy and the decreased disease-free survival and poorer prognosis exhibited by patients with significant lymphovascular emboli.

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Identifying GATA3-regulated miRNAs Involved in Breast Cancer Metastasis

Principal Investigator:
Jonathan Chou, B.S.

University of California, San Francisco

Abstract #: E-06

Despite recent advances in our understanding of breast cancer, patients who develop metastatic disease often have poor prognoses. Mortality from breast cancer is often due to metastasis, a process by which malignant cells from the primary tumor spread to distant sites such as the lung, brain, and bone. To do so, tumor cells must first enter the circulatory system by recruiting new blood vessels (known as angiogenesis), exit from the circulatory system, and survive at a distant site to form a secondary tumor. Although this emphasizes the key role that angiogenesis plays in promoting metastasis, the molecular basis of this process is largely unknown. Thus, the focus of my project is to investigate the molecular and cellular events that lead to metastasis and identify mechanisms that may suppress this deadly process. We have previously shown that GATA3 is a master regulatory transcription factor that specifies mammary luminal cell fate, and is lost during breast cancer progression. Interestingly, re-expression of GATA3 in tumor cells transplanted orthotopically suppresses metastasis to the lung *in vivo*.

To understand how GATA3 prevents metastasis, we have conducted a screen to identify microRNAs (miRNAs) regulated by GATA3. miRNAs modulate global gene expression post-transcriptionally, and have recently been implicated to be important during tumor development and metastasis. Our results indicate that GATA3 induces the expression of microRNAs, including miR29b, that regulate genes involved in blood vessel recruitment and permeability, including vascular endothelial growth factor (VEGF). When cultured in low oxygen conditions, cells expressing these miRNAs suppress the induction of VEGF. In addition, we found that miR29b is lost during mammary tumor progression, concomitant with the loss of GATA3. Current studies are being conducted to determine if miRNA restoration in breast tumor cells may also prevent metastasis *in vivo*.

These findings suggest a novel mechanism by which miRNAs regulate angiogenesis, and may serve as a basis to develop new anti-angiogenic agents to treat breast cancer.

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Molecular Strategy to Inhibit Breast Cancer Metastasis

Principal Investigator:
Frances Brodsky, D.Phil.

University of California, San Francisco

Poster Presenter: Chih-Ying Chen

Abstract #: E-07

This study examines a novel cellular pathway as a potential target for breast cancer therapeutics. Clathrin is a major coat protein which sorts and transports materials at the cell membrane, the internal Golgi network and other internal cell compartments. Our recent work demonstrated that clathrin through its interaction with a second protein called Hip1 (Huntingtin interaction protein 1) also controls how cells move and spread. We found that cells depleted of clathrin or Hip1 are defective in movement. It is known that the Hip1 is present in excess in many breast cancer cells. Excessive Hip1 in breast cancer cells might be linked to their increased spreading behavior. To validate whether elevated levels of Hip1 expression correlate with

increased metastatic potential, we will perform metastasis assay in mice using breast cancer cell lines expressing different levels of Hip1 and assess the tumorigenic ability. Small molecule inhibitors will be screened for competing with Hip1 and clathrin interaction using recombinant protein expression and peptide binding assays. Identification of effective small molecule inhibitors provides a starting point for further drug discovery.

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Proteome-wide Analysis of Protein Ubiquitination in Breast Cancer

Principal Investigator:
Stefan Grotegut, Ph.D.

Sanford-Burnham Medical Research Institute

Poster Authors: Stefan Grotegut, Sonia del Rincon, Jeff Rogers, Charles H. Spruck

Abstract #: E-08
This project is aimed to identify changes in the breast tumor cell's intrinsic enzymatic activity that facilitate these cells to leave their place of origin and colonize new organs (i.e. metastasize).

During metastasis, breast tumor cells undergo a multi-step process ultimately enabling them to leave their primary site and spread throughout the body to find new niches. In this process, many proteins are being altered ('post-translational modified') and subsequently change their biological function, sub-cellular localization, or stability. One of the well-known post-translational modifications is ubiquitination, in which a highly abundant protein called ubiquitin is covalently attached to specific protein substrates. This 'linkage' plays an important role in the regulation of many cellular functions including division, differentiation, protein trafficking, response to DNA damage, and gene transcription, among others. A wealth of experimental evidence supports the notion that derangement of ubiquitin-mediated proteolysis contributes to various human malignancies including breast cancer.

To date, little is known about how this ubiquitination activity can contribute to breast cancer cells' invasive growth and how the ubiquitination pattern differs in metastatic cells compared to their non-malignant counterparts. Furthermore, there are no adequate experimental tools to identify the ubiquitination of protein substrates on a proteome-wide scale. Importantly, the ubiquitin-proteasome system has been recognized as a valid target for the treatment of some malignancies, thus deciphering the change of breast tumor cells' intrinsic enzymatic activity could warrant for the development of enhanced diagnostic tools and effective treatment of breast cancer patients.

To assess the breast tumor cell's ubiquitination activity, we have developed a novel proteomic approach by combining protein microarrays (where >8,300 human recombinant proteins are spotted onto glass microscope slides) with an ubiquitination reaction of cellular extracts. This innovative technique is capable of identifying substrates of ubiquitination in breast tumors as they progress to a malignant phenotype. Using the 4T1 mouse model of breast cancer, which consists of five isogenic murine mammary carcinoma cells lines at different metastatic levels, more than 100 alterations in specific target protein ubiquitination were detected, indicating a possible regulatory role of protein ubiquitination during the process of breast cancer progression.

The identification of the biological consequences of some of these protein modifications is currently being investigated and will aid in gaining insight into how the cells' intrinsic enzymatic activity has become distorted and how this could drive the metastatic process of breast cancer. It is our hope that this study will greatly impact the early diagnosis and the refinement of breast cancer treatment and prevent breast cancer mortalities, which occur primarily due to metastasis.

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Role of AGR2 in Mammary Gland Development and Cancer

Principal Investigator:
Mikhail Geyfman, B.S.

University of California Irvine

Abstract #: E-09
AGR2 is a protein disulfide isomarase that is expressed significantly higher in breast tumors compared to normal mammary epithelium. The severity of breast cancer prognosis also correlates positively with AGR2 expression. AGR2 is also present selectively in breast tumors that express estrogen receptor.

We analyzed expression of AGR2 in normal mice through post-pubertal mammary gland development. I have generated and validated a trangenic mouse line that overexpresses AGR2 in mammary epithelium after doxycycline administration. These experiments showed that AGR2 is highly expressed during pregnancy and lactation when alveolar development is at its highest. The AGR2 overexpression line was generated and initial results promise to provide valuable information about the role of AGR2 in tumor formation. Overexpression of AGR2 leads to increased ductal branching and alveolar development that can be a pre-cancerous phenotype. Results obtained with this line as well as analysis of normal mice provide important clues about potential biological role of AGR2 in normal mammary gland biology and cancer.

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Role of RNA Helicase p68 in Breast Cancer

Principal Investigator:
Daojing Wang, Ph.D.

Lawrence Berkeley National Laboratory

Abstract #: E-10

Background and purpose. Two major challenges in diagnosis and therapy of breast cancer lie in its heterogeneity and drug resistance. RNA helicase p68 (DDX5) has been shown to be involved in all aspects of RNA metabolism and serves as a transcriptional co-regulator. Strikingly, a recent study demonstrated a new role of p53 in modulating miRNA processing, probably through the p53–Drosha/p68 interactions. As a result, the gene expression regulated by p53-Drosha/p68 is under intensive investigation. Previous work has shown that p68 is one of the potential 6-gene predictors of breast cancer resistance to Lapatinib, a dual ErbB2/EGFR tyrosine kinase inhibitor. Furthermore, we and others have shown that p68 is involved in a complex protein-protein interacting network (e.g., Ca^{2+}/CaM binding). This study is designed to mechanistically define the role of p68 in human breast cancer using an integrative biology approach.

Experimental procedures. We utilized a multifaceted strategy including cellular and molecular biology and various emerging technologies. Specifically, we measured the expression pattern of p68 at both mRNA and protein levels for a panel of ~50 breast cancer cell lines. We performed immunohistochemistry of p68 using human breast tumor microarrays containing a total of 225 cases of normal and malignant (various grades and stages) tissues of the breast. We knocked down p68 in two representative breast cancer cell lines (SKBR3 and MDA-MB-231) and investigated their proliferation and responses to Lapatinib before and after p68 knockdown. Finally, we carried out SILAC-based proteomic profiling of these breast cancer cells after p68 knockdown and identified p68-targeted proteins and networks contributing to the drug responses.

Results. P68 expression pattern is distinct among different subtypes of breast cancers. More aggressive basal A and B subtypes have predominantly high p68 protein expression while low p68 expression is predominantly associated with the luminal subtype. Knockdown of p68 inhibits the proliferation of breast cancer cells and sensitize them to cancer drugs such as Lapatinib. Importantly, we identified cofilin-1, a major actin severing and -depolymerization protein, as a key target of p68 through proteomics studies. Knockdown of p68 increases cofilin expression. Cofilin has been previously implicated in platinum-resistance of ovarian cancer cells, and migration and invasion of breast cancer cells. Therefore, our results suggest that high p68 expression may contribute to drug resistance and metastasis of breast cancer cells through cytoskeletal reorganization by promoting actin polymerization.

Conclusions. RNA helicase p68 may contribute to personalized medicine by serving as a new molecular marker to characterize breast cancer subtypes, as a predictor for drug resistance, and as a target for a combinational therapy to circumvent drug resistance of aggressive tumors.

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Tissue Factor Signaling in Breast Tumor Progression

Principal Investigator:
Florence Schaffner, Ph.D.

The SCRIPPS Research Institute

Poster Authors: Florence Schaffner,[1] Henri Versteeg,[1] Barbara Mueller,[2] and Wolfram Ruf[1]

[1] The SCRIPPS Research Institute
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Abstract #: E-11

Hypercoagulopathy is frequently observed in cancer patients. Coagulation is a cascade of events that starts with the binding of Factor VII to Tissue Factor (TF). The complex formed is the first step of well-regulated events that leads to the formation of a clot. The TF-VIIa complex can activate a G-protein coupled receptor, protease activated receptor 2 (PAR2). In human breast cancer, TF and PAR2 expression were found to be upregulated and phosphorylation of the TF cytoplasmic tail is associated with breast cancer relapse. Despite evidence that TF is implicated in tumor angiogenesis, the biology of TF signaling in breast cancer is unknown.

To assess in greater depth the role of TF and especially the potential signaling transduced by the cytoplasmic tail, we used a murine spontaneous breast cancer model, the PyMT model. We generated PyMT mice that lack the TF cytoplasmic tail. These mice developed palpable tumors later than control mice, resulting in reduced tumor growth. In addition to a delayed angiogenic switch in early tumor development, the analysis of established tumors also showed that the TF cytoplasmic tail regulates vessel size as well as macrophage recruitment in this model. The simultaneous deletion of PAR2 with the TF cytoplasmic domain in this model does not increase tumor latency. Thus, tumor cell PAR2 signaling is linked to functions of the TF cytoplasmic domain.

These results emphasize the role of TF signaling in breast tumor progression by regulating tumor angiogenesis and recruitment of immune cells. These new results are the basis of ongoing studies to better understand the biology of TF in breast cancer beyond its well established role in thrombosis.

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Twist Target Genes Modulate Tumor Angiogenesis

Principal Investigator:
Janine Low-Marchelli, B.S.

University of California, San Diego

Poster Authors: Janine M. Low-Marchelli (PI),[1,2] Veronica C. Ardi,[3] Etienne Danis,[1] Andrew T. Chang,[1,2] James P. Quigley,[2,3] Jing Yang (mentor)[1,2]

University of California, San Diego[1] Biomedical Sciences Program[2]
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Abstract #: E-12
Most breast cancer mortalities arise from aggressive metastases. A gene-regulatory protein called Twist has been shown to promote metastasis in breast cancer and is associated with disease progression. The goals of this research project are to understand the biological and pathological functions of Twist and how breast cancer metastasis may be caused. To do this, we proposed two major goals: first, to identify what genes Twist controls directly, and second, to define what these genes do in the context of cancer.

We first identified genes under the direct control of Twist using a new technology called ChIP-Sequencing. This technology enabled us to successfully identify 14,000 places in the human genome to which Twist was bound. After matching the binding sites to specific genes using a ranking system based on a computer algorithm, we were able to create a list of genes that might be directly controlled by Twist. We compared this list of genes to another list of genes we previously had generated in our lab from a technique called microarray analysis, which tells us whether the gene is either turned "on" or "off" by Twist. Using these two methods we can begin to understand how Twist controls expression of genes in the human genome and how Twist might cause cancer cells to become aggressive.

After identifying direct targets of Twist, we next sought to understand their roles in metastasis. Other groups have identified an association between Twist expression in tumors and increased blood vessel growth, or angiogenesis, an important process that allows the tumor to survive and for metastatic cells to spread. Interestingly, genes that are classically thought to promote tumor angiogenesis such as VEGF or FGF were not found in our list of genes controlled by Twist. However, some of the genes we identified by ChIP-Sequencing and microarray analysis belong to a family of genes that direct nerve fiber growth. This family of genes also has roles in blood vessel branching or giving directional cues to blood vessels during embryonic development. It is possible that the gene pathways participating during blood vessel development may become pathologically re-activated by Twist in breast carcinogenesis. To test whether these nerve fiber genes are necessary for our cells to stimulate angiogenesis, we removed them from the Twist expressing cells and tested the ability of these cells to promote the formation of new blood vessels in an animal model. Removing one of the genes from our Twist cells caused a significant decrease in angiogenesis. In another experiment, removing a

different gene from our Twist cells caused the blood vessels to form improperly, leading to hemorrhage.

These experiments suggest that Twist controls genes that are important for directing blood vessel growth to the tumor. By identifying new targets to disrupt angiogenesis, our research may lead to the development of new breast cancer metastasis therapies.

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Proline Metabolism in Metastatic Breast Cancer

Principal Investigator:
Adam Richardson, Ph.D.

Sanford-Burnham Medical Research Institute

Abstract #: E-13

The goal of this work is to determine the role of proline biosynthesis in breast cancer metastasis and to test if inhibiting proline biosynthesis reduces the ability of breast tumor cells to metastasize. Recently we mapped the central carbon metabolism of several breast carcinoma cell lines using ^{13}C stable isotope labeling. We discovered that *de novo* proline synthesis is greatly increased in breast cancer lines that are able to metastasize. We propose a model in which proline biosynthesis acts as an anti-apoptotic signal and increases metastatic potential. In this model, epithelial cells that have gained the ability to invade the surrounding stroma also experience an increase in proline pool size through collagen degradation. In non-transformed cells, the resulting enlarged proline pool causes a p53-regulated apoptotic response via reactive oxygen species produced by proline dehydrogenase. Tumor cells are able to avoid death due to down-regulation of proline oxidation. As the tumor progresses to the stage of metastasis and cells detach from the extracellular matrix, they must produce their own proline through *de novo* synthesis. Therefore, it is plausible that enzymes of the proline biosynthetic pathway are potential targets for the suppression of metastasis in some human cancers.

Pyrroline-5-carboxylase 1 (PYCR1) is considered the rate-limiting step of proline biosynthesis. Although this gene has historically been identified as the major producer of proline in human systems, we now know that two additional PYCR-encoding genes, PYCR2 and PYCRL, also play a significant role. Here we report the characterization of the three human PYCR genes in both a biochemical and cellular context. We have expressed and purified functional PYCR1, PYCR2 and PYCRL using an *E. coli* system, allowing us to characterize the enzymatic functions of each PYCR. We additionally report on the cellular function of each of the PYCR enzymes, particularly their relative contribution to proline biosynthesis. We have utilized two approaches during this *in situ* characterization. First, we suppressed the expression of the PYCR genes in the metastatic MCF10-CA1a breast tumor cell line (both individually and in combination) using siRNA and measured proline biosynthesis via ^{13}C labeling and mass spectrometry. Second, we introduced each of the PYCR genes into the MCF10-AT1 breast carcinoma cell line (which does not natively express any of the PYCR enzymes) and again performed flux analysis. The results of these characterizing experiments will be presented, as well as the impact of each PYCR on the ability of breast carcinoma cells to survive, proliferate and metastasize. Overall, this study contributes to our knowledge of metabolic changes associated with the metastatic phenotype in breast cancer and to the development of anti-metastatic therapies.

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Pygo2 Opens Chromatin and Expands Mammary Progenitor Cells

Principal Investigator:
Bingnan Gu, Ph.D.

University of California, Irvine

Abstract #: E-14

The recently identified breast cancer stem cells (BCSCs) are a minor pool of transformed stem cells that can escape from available therapeutic agents and initiate new breast tumors. A better understanding of the molecular control of BCSCs and their physiological counterparts may provide new targets for more effective therapies. Wnt signaling pathway plays an important role in regulating breast stem/progenitor cells. Aberrant activation of Wnt signaling results in breast cancers with an expanded stem cell pool. Pygopus 2 (Pygo2) is an evolutionarily conserved activator of the Wnt signaling pathway and is over-expressed in breast cancer. Deletion of Pygo2 from the mouse genome leads to reduced Wnt signaling and compromised proliferation of breast stem/progenitor cells, suggesting that it may serve as a new molecular therapeutic target for interfering with breast stem

cell activities. However, the underlying molecular mechanism by which Pygo2 regulates the activity of these cells is largely unknown.

In this project we are studying the role of Pygo2 in chromatin remodeling of mammary epithelial cells. My current data implicate that Pygo2 is a novel regulator of methylation and acetylation of histones, a group of small proteins that pack the long DNA molecules into repetitive units inside the cell nucleus and regulate gene expression. Specifically, we are investigating how Pygo2 recognizes and binds to a specific type of histone modification (H3K4me3) on target chromatin, and in turn recruits protein complexes that have other histone modifying activities (e.g., acetylation). By making changes to the Pygo2 PHD domain and knocking down Pygo2 protein by RNA interference, we have successfully established the functional requirement of the Pygo2-H3K4me3 interaction in the expansion of mammary progenitor cells. We showed that the binding of Pygo2 PHD domain to H3K4me3 is enhanced by additional binding with BCL9 protein. The ternary complex formation is likely required for the proliferation of mammary progenitor cells in colony formation assays. Furthermore, we have demonstrated that by association with histone H3K4me3, Pygo2 also plays a positive role in facilitating the methylation of H3K4, which promotes the activation of Wnt/β-catenin target gene expression. To further understand the molecular function of Pygo2 in chromatin regulation, we are performing purification and characterization of the Pygo2-containing protein complex using mass spectrometry analysis.

Epigenetic events such as histone modifications and DNA methylation have been linked to breast cancer. It has been proposed that cancer-associated epigenetic changes inactivate tumor suppressor genes. Drugs that may correct these epigenetic changes are being tested in clinical trials for cancer therapy. Before such epigenetic drugs become widely used for breast cancers, it is essential for us to understand how normal epigenetic patterns are established/maintained and how these alterations occur in breast cancer. We anticipate that successful completion of the proposed research will provide key molecular insights of how Wnt signaling controls breast stem/progenitor cell activities and may uncover a novel link between chromatin regulation, transcriptional control, and breast cancer stem cell activation.

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Control of BRCA2-mediated Homologous Recombination

Principal Investigator:
Damon Meyer, Ph.D.

University of California, Davis

Abstract #: E-15

Breast cancer affects about 1 in 8 women during their lifetime and of these about 10% of the individuals with breast cancer is genetically predisposed and about 10-30% of these have a mutation in the BRCA2 gene. BRCA2 has been shown to be involved in DNA repair by associating with the eukaryotic RecA homolog RAD51, which promotes homologous recombination and thereby maintain genome stability. Recently, a truncated BRCA2 protein was shown to stimulate RAD51-mediated strand invasion *in vitro*. Therefore, the examination of proteins that influence BRCA2/RAD51-mediated strand invasion and subsequent events could give insight into the development of breast cancer. BRCA2 is known to interact with a small acidic protein DSS1, which is required for BRCA2 stability and thought to have a significant role in BRCA2-dependent recombinational repair but has not been explicitly tested. In addition, RAD51 interacts with the motor protein RAD54, which is involved in stimulating RAD51-mediated strand invasion but is unknown whether it can stimulate BRCA2/RAD51-mediated strand exchange. Following BRCA2/RAD51-mediated strand invasion is the extension of heteroduplex DNA by a DNA polymerase that facilitates the recombinational repair by stabilizing heteroduplex DNA. Genetic evidence supports the involvement of DNA polymerase lambda in the extension of heteroduplex DNA following strand invasion, but this has not been confirmed in biochemical reactions. Therefore, I propose to examine the role of both DSS1 and RAD54 in BRCA2/RAD51-mediated strand invasion and the extension of the strand invasion intermediate in a reconstituted recombination reaction by DNA polymerase lambda.

Specifically, the role of DSS1 and RAD54 in BRCA2/RAD51-mediated strand invasion will be tested *in vitro* using a linear D-loop assay that measures a labeled ssDNA oligo invading an unlabeled dsDNA oligo to generate a D-loop product. Furthermore, the subsequent extension of D-loops by DNA polymerase lambda will be test using a D-loop extension assay, which measures extension of a labeled ssDNA oligo following D-loop formation. Particular attention will be paid to the requirement of PCNA/RFC in D-loop extension. Controls in both assays

will be used by changing the amount or presence of the protein and/or oligos. The study of factors that influence BRCA2/RAD51-mediated recombination and subsequent extension of strand invasion intermediates will aid in the understanding of the genetic and molecular events leading to breast cancer. Understanding the proteins that interact with and help facilitate the function of BRCA2 may prove to be attractive targets in preventing or treating breast cancer since 80% of individuals possessing a BRCA2 mutation will develop breast cancer in their lifetime.

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Investigating the Role of Estrogen Receptor in Breast Cancer Endocrine Resistance using Solexa ChIP-Sequencing

Principal Investigator:
Hei J. Chan, B.S.

Poster Authors: Hei Jason Chan,[1,2] Haiqing Li,[3] Hanlin Gao,[4] Yate-Ching Yuan,[3] and Shiuan Chen[2]

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Beckman Research Institute of City of Hope, Duarte, CA

Abstract #: E-16

Aromatase inhibitors (AIs) and anti-estrogens are two main therapeutic strategies currently in use for the treatment of estrogen receptor (ER) positive breast cancer. Both strategies are very successful in the treatment of this type of breast cancer, but unfortunately, many patients eventually develop resistance to these agents, and treatment options are limited for these patients who has acquired resistance. To overcome this problem, it is necessary to understand the mechanism underlying the development of acquired resistance to these agents using clearly defined model systems. The ER is a steroid nuclear receptor that plays a key role not only in breast cancer cell proliferation, but also in resistance to endocrine therapy. One of the main actions of ER is the transcriptional activation or repression of genes in response to E2 stimulation. This occurs through the "classical" mechanism of direct binding to Estrogen Response Element (ERE), and through "non-classical" interactions with other DNA-binding complexes. All of these physical interactions of ER with chromatin will be captured by chromatin immunoprecipitation followed by Solexa deep sequencing (ChIP-seq) for detection across the entire genome. Our lab has generated an MCF7 cell line that stably expresses the aromatase gene (MCF7aro) as a model for hormone dependent breast cancer. In order to study endocrine resistance, we derived another cell line called the Long Term Estrogen Deprived (LTEDaro) cell line, which was derived from the MCF7aro cell line by culturing MCF7aro cells without any hormones over a long period. By comparing the genome-wide profiles of ER binding sites in these hormone-responsive and resistant lines, we were able to detect differences in ER binding. Our ChIP-seq results show that LTEDaro cells had enrichment of ER binding sites near transcription start sites (TSS) under both DMSO and E2 treatments, whereas in the MCF7aro cells this is observed only in the E2 treated cells. De novo motif discovery confirmed the presence of the estrogen response element (ERE), and also the consensus sequence for Fox transcription factor binding. Mapping of known motifs in LTEDaro ER binding sites showed an increase in Sp1 and AP1 occurrence. Overlap analysis shows a high degree of similar binding sites between E2 and DMSO treatment for both cell lines. Interestingly, comparison of LTEDaro DMSO with MCF7aro E2 also shows a high number of overlapping sites. Taken together, the distance to nearest TSS and overlap analyses shows clear difference of ER behavior in LTEDaro cells. Coactivators such as Sp1 and AP1, and other proteins such as the Fox family of transcription factors may play an important role in the resistance phenotype. Overall, our data supports the hypothesis that ER in LTEDaro cells actively binds DNA and drives cell proliferation independently of E2.

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From Research to Action: Tools for Change

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