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WOMEN'S HEART CENTER



IN HER
heart

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Women's Heart Center

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JENNIFER E. VAN EYK, PhD
Barbra Streisand Women's Heart Center
Director, Basic Science Research
Erika J. Glazer Chair in Women's Heart Health

LEADERSHIP UPDATE

I am pleased to announce a bold new era for the Barbra Streisand Women's Heart Center, as we enhance our powerhouse presence in basic and translational science with the recruitment of scientists Jennifer E. Van Eyk, PhD, and Roberta A. Gottlieb, MD.



A pioneer in the emerging science of clinical proteomics, Dr. Jennifer Van Eyk is the Erika J. Glazer Chair in Women's Heart Health, director of Basic Science Research at our center, and director of Cedars-Sinai's new Advanced Clinical Biosystems Research Institute. She examines the proteins produced by our genes and their role in a wide range of conditions, including cardiovascular disease.

Meanwhile, Dr. Roberta Gottlieb — director of Translational Research in the Barbra Streisand Women's Heart Center, the Dorothy and E. Phillip Lyon Chair in Molecular Cardiology in honor of Clarence M. Agress, MD, and director of Molecular Cardiobiology — brings top-level expertise in longevity, cell recycling, cell signaling, and myocardial stem cells, areas with great promise for cardio-protection breakthroughs in the leading healthcare threat to women.

These stellar recruitments are part of our three-pronged strategy to create a full breadth of critical research capabilities in three overarching areas: basic and translational science, clinical science, and population health science. Now the focus turns to seeking a population/social scientist who can integrate scientific findings about women's heart disease with the holistic study of human behavior and nuanced population statistics. This hire will enable us to conduct broadscale epidemiological studies that support large clinical trials and better understanding of the spread and shifting realities of women's heart disease.

Over the long term, this three-part approach will lead to new and better biomarkers to help diagnose heart disease and develop more personalized treatments.

Scientists of the caliber of Dr. Van Eyk and Dr. Gottlieb are crucial to advancing our mission at the vanguard of women's cardiovascular care. But as medical innovation depends on visionary philanthropists nearly as much as trailblazing physician-scientists, we owe a debt of gratitude to such generous donors as Erika J. Glazer and Dorothy and Phillip Lyon. Creative scientists need a supportive environment, the freedom to explore, and state-of-the-art facilities in which to conduct their work. Our philanthropic partners make that possible, so that we can strive to achieve what others would now call the impossible.

Thank you for your interest in and support of our efforts. And stay tuned for more exciting developments in the months ahead!



C. Noel Bairey Merz, MD, FACC, FAHA

Director, Barbra Streisand Women's Heart Center at the Cedars-Sinai Heart Institute
Director, Preventive and Rehabilitative Cardiac Center
Director, Linda Joy Pollin Women's Heart Health Program
Professor of Medicine, Cedars-Sinai Heart Institute
Women's Guild Chair in Women's Health

RESEARCH UPDATE

Roberta Gottlieb, MD, Explores How the Heart Protects Itself From Injury

Poetry often speaks of the resilience of the human heart, and now researchers know there is biological truth to that notion as well. The heart protects itself in many ways, including a system of cellular recycling called “autophagy” at which women’s hearts appear to excel.

In autophagy, eco-conscious cells transport and recycle unwanted debris and return it to the metabolism. Autophagy is important for removing damaged mitochondria, the organelles responsible for energy production, particularly in the heart. Damaged mitochondria spew out free radicals that contribute to aging, and autophagy — which removes these mitochondria and facilitates their replacement — is a key factor in longevity.

“It seems that as long as estrogen is on board, the level of autophagy is increased,” says Roberta A. Gottlieb, MD, director of Translational Research in the Barbra Streisand Women’s Heart Center. “Based on initial observations in animal studies, female mice appear to do more recycling and, as a result, may have more cardio-protective factors than males.”

Dr. Gottlieb, who also is director of Molecular Cardiobiology at the Heart Institute and the Dorothy and E. Phillip Lyon Chair in Molecular Cardiology in honor of Clarence M. Agress, MD, joined Cedars-Sinai in September 2013 after seven years at San Diego State University, where she was director of the Shiley BioScience Center, and 15 years in the Department of Molecular and Experimental Medicine at Scripps Research Institute. She has authored several book chapters and published 140 papers in peer-reviewed journals.

Her lab in the Heart Institute employs cell biology, biochemistry, and molecular biology to reveal and understand the molecular and cellular processes that determine whether cardiac cells will survive and repair themselves — or die from external damage or cellular suicide.

In addition to her groundbreaking work on autophagy, Dr. Gottlieb was the first scientist to report the presence of programmed cell death in the heart after ischemia (inadequate blood supply) and reperfusion (the restoration of blood flow).



To move findings from the lab to clinical practice as quickly as possible, she is inventing new tools when none exist. “We’re working on developing a blood test to determine how well autophagy is working in the peripheral blood,” says Dr. Gottlieb, who has a patent filed on the technology.

The breakdown and removal of debris help ensure cellular survival. Unfortunately, this recycling process diminishes with age, as the mechanisms intended to clean up debris begin to break down. The rate of autophagy also decreases when confronted with such conditions as diabetes, obesity, and metabolic syndromes.

What can we do to preserve and promote this invaluable recycling system? Her studies in animal models show that exercise and regular fasting can help.

Fasting gives the system a chance to take a break. “You get rid of things that otherwise will build up in the cell,” she explains. The heart is particularly vulnerable to this cellular buildup. “Heart failure patients have a higher accumulation of this debris.”

The possibilities are exciting. “If we can induce autophagy to clear the cellular debris and damaged mitochondria, can we avert heart failure? That’s one thing we’d very much like to know,” she says.

PROTEINS AND HEART RHYTHM Cedars-Sinai Heart Institute researchers have found that six proteins — five more than previously thought — are responsible for the cell-to-cell communication that regulates the heart and helps limit the impact of heart attacks and strokes. “When there is less cell communication, which occurs in failing hearts, chances are greater of disturbances in heart rhythm that can result in disability or death,” said Robin Shaw, MD, PhD, staff physician in Cardiology, lead author on the study, which was reported in *Science Daily* and other media.





THE CLUES IN OUR PROTEINS

Jennifer E. Van Eyk, PhD, sees life as a series of complex patterns and sequences — an astonishing molecular landscape whose imagery she'd like to hang on the walls of her new office at Cedars-Sinai. The display would be more than mere decoration: Once decoded, these patterns may reveal the mysteries of women's heart disease.

For this renowned scientist, the clues lie in our proteins. These crucial cellular building blocks can also serve as biomarkers, or physiological indicators of disease, in addition to providing guideposts toward targeted therapies. Dr. Van Eyk's focus is on clinical proteomics, the large-scale study of proteins to inform personalized treatments and improve patient outcomes. "Everywhere there's a clinical decision," she says, "we should be able to provide a biomarker to support it."

Dr. Van Eyk recently joined Cedars-Sinai from Johns Hopkins, drawn by the opportunity to head basic science in the Barbra Streisand Women's Heart Center and run the new Advanced Clinical Biosystems Research Institute. Equipped with two high-tech laboratories, this research enterprise is so forward-thinking, she says, "it isn't just cutting-edge, it's *making* the cutting edge."

As director of Basic Science Research in the Barbra Streisand Women's Heart Center and the Erika J. Glazer Chair in Women's Heart Health, Dr. Van Eyk is ramping up studies looking into the molecular basis of sex and gender differences in heart disease.

She already has developed a number of tests to determine the presence of certain proteins in the blood, which could denote heart attack or heart disease. One of these proteins is troponin, the subject of her PhD dissertation. It regulates muscle contractions in the heart, turning them on and off like a light switch.

For decades, doctors have used a single level of troponin as the reliable sign of a heart attack in men and women. New evidence suggests the threshold is a moving target, and women with heart attacks have been shown to register lower troponin levels at the time of attack than do men. An initial study suggests that the current troponin threshold misses 20 percent of heart attacks in women.

“We’re at the very beginning of understanding that men and women experience different symptoms and causes of heart disease.

Those differences begin at the molecular level, so that is where Dr. Van Eyk will lead us.”

—DR. C. NOEL BAIREY MERZ

“We miss properly diagnosing heart attacks in at least one out of every five women, because doctors are trained to look for high troponin levels,” says C. Noel Bairey Merz, MD, director of the Barbra Streisand Women’s Heart Center and Women’s Guild Chair in Women’s Health. Identifying the troponin level is one of many diagnostic tools commonly used on women but based on medical research done on men. It illustrates the egregious knowledge gap that still exists when it comes to screening and diagnosis for heart disease in women.

Pearl Grumet experienced the problems caused by that gap first-hand: She suffered four heart attacks and visited five hospitals that failed to accurately diagnose her heart disease before she found the Barbra Streisand Women’s Heart Center.

In April 2008, Pearl was traveling with her husband, Mark, from their San Dimas, Calif., home to the Imperial Valley. On the way, her left arm suddenly went numb and she felt nauseous. At a nearby hospital, doctors told Pearl she’d had a heart attack and would need a heart valve replacement. Slender and fit, she was surprised — even more so when specialists in La Jolla, Calif., told her that her angiogram showed no blockage. “I was petrified,” says Pearl. “And confused.”

She began keeping a three-ring binder of test results and hospital reports, a sad record of conflicting messages and “brush-offs,” as she continued to have attacks but no chest pain. One doctor admitted: “We don’t know what’s wrong. When you find out, please tell us.” Finally, another sent her to Cedars-Sinai, where she found Dr. Bairey Merz.

Dr. Van Eyk, Dr. Bairey Merz, and Pearl co-exist on a vibrant continuum — basic scientist, physician-scientist, and patient — in which each plays a critical part in moving discoveries forward.

Though Pearl’s angiogram again registered as normal, Dr. Bairey Merz knew what was wrong — coronary microvascular dysfunction (CMD), which is more common in women and doesn’t show up on standard angiograms. Other specialized tests showed that Pearl’s heart muscle hadn’t been damaged, despite the series of onslaughts.

Now on medication for her CMD, Pearl says she is feeling well. She has become an advocate for women’s heart health and a participant in a long-running clinical trial headed by Dr. Bairey Merz investigating the effectiveness of noninvasive approaches for the detection and assessment of heart disease in women.

“More information needs to get out there for women and for physicians,” says Pearl. “If people aren’t willing to be part of research studies, how will doctors make the next discoveries?”

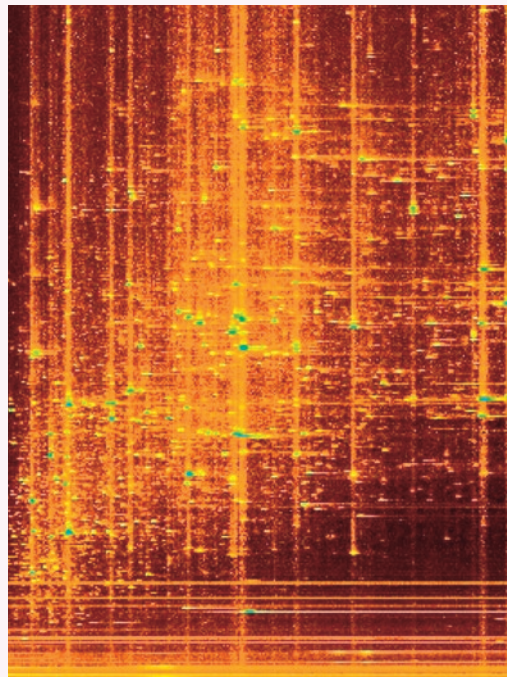
“We’re at the very beginning of understanding that men and women experience different symptoms and causes of heart disease,” explains Dr. Bairey Merz. “Those differences begin at the molecular level, so that is where Dr. Van Eyk will lead us.”

“The question we want to answer is, ‘Why is the troponin threshold different?’” says Dr. Van Eyk. “Now we have the opportunity to find out.” Patterns are emerging in the laboratories of the Advanced Clinical Biosystems Research Institute, as investigators hunt down other proteins that may provide a more sensitive reading of a heart attack before troponin kicks in. “The important role of other biomarkers may be one thing that’s different for women and heart disease,” says Dr. Van Eyk.

In the Discovery Lab, a team of researchers search proteins for novel markers of disease and wellness. “In the Translation Lab, we work to validate these biomarkers or test innovative technologies and be the first to offer them in a real, patient-centered environment,” says Dr. Van Eyk.

That environment is the Advanced Health Sciences Pavilion where Heart Institute researchers, physicians, and nurses share the same floor, interacting freely in close proximity to clinics. The Pavilion provides a physical space where basic science can inform and improve patient care — and where observations made in the clinic can flow back to inspire new questions in the lab.

With a dedicated team of researchers, cutting-edge equipment, and an ideal setting for collaboration, Dr. Van Eyk is excited about what’s ahead. “We are at a magical point in time,” she says, “when we can make significant leaps in our knowledge.”



PROTEIN SHAKE

Proteins are often called the workhorse molecules of life, taking part in every cellular function, from cell division and metabolism to the transfer of genetic information. They also act as powerful biomarkers — physiological indicators of how a disease is likely to progress and how someone might respond to treatment.

Within the labs of the Advanced Clinical Biosystems Research Institute, under the direction of Jennifer Van Eyk, PhD, the patterns of these busy macromolecules are revealing new opportunities to target heart disease and other conditions.

The fast-emerging field of clinical proteomics — Dr. Van Eyk’s expertise — uses sophisticated robotics and powerful data processing to identify and quantify vast numbers of proteins at a rate and precision previously unimaginable. The results are essential to predicting how a specific patient will respond to different treatments — just like gene mapping can help predict a person’s likeliness to develop a disease.

The research of Dr. Van Eyk and her peers points to a day when, for every single clinical decision, there will be a known protein to aid with a quantitative measure, and treatments can be precisely tailored to each patient or patient group.

Above: A projection of the data acquired from the proteomic analysis of a fraction of a single drop of blood.

EDUCATION and COMMUNITY OUTREACH



THE LINDA JOY POLLIN WOMEN'S HEART HEALTH PROGRAM

at the Barbra Streisand Women's Heart Center works tirelessly to improve female cardiovascular wellness by promoting increased awareness of gender-specific risks — and better education about how to reduce them.

The Linda Joy Pollin Women's Heart Health Program was launched in April 2013 and established through a founding gift from Irene Pollin (pictured above, with Dr. C. Noel Bairey Merz), founder of Sister to Sister: The Women's Heart Health Foundation, the nation's first organization dedicated to women's heart disease detection, education, and prevention. The name of the Linda Joy Pollin Women's Heart Health Program honors Irene's daughter, who died from congenital heart disease at age 16.

Following are a few highlights of the recent education and community outreach efforts by the Linda Joy Pollin Program:

VISITING CLINICIANS PROGRAM

The Barbra Streisand Women's Heart Center recently hosted visiting cardiologists Avital Porter, MD, Rabin Medical Center, Israel, and Suzette Elias-Smale, MD, MSc, Radboud University Medical Center, Netherlands. In addition, two cardiac rehabilitation specialists from Thailand — Sumeta Jeracotechueantaveechai and Thanitta Thanaklaptinya — met with faculty and observed best practices at the center.

COMMUNITY EDUCATION

A Women's Heart Health Panel, featuring C. Noel Bairey Merz, MD, FACC, FAHA, director of the Barbra Streisand Women's Heart Center, and Lori Kupetz, Cedars-Sinai patient advocate, as part of the Hadassah National Convention at the Venetian/Palazzo Hotel, Las Vegas, will be held in July 2014.

"Women and Heart Disease: What You Should Know" was the keynote speech by Dr. Bairey Merz at the Hadassah Southern California Women's Wellness Day in Los Angeles.

"Women and Heart Disease: What Every Woman Should Know," was presented by Puja K. Mehta, MD, FACC, director of the Non-invasive Vascular Function Research Laboratory and co-director of the Cardio-Oncology Program, to the National Charity League at Westlake Village.

Chrisandra Shufelt, MD, MS, NCMP, associate director of the Barbra Streisand Women's Heart Center, and director, the Women's Hormone and Menopause Program, spoke to the National Council of Jewish Women/Los Angeles.

RESEARCH

Experts in women's heart disease and cancer are pursuing an active research agenda in the Cardio-Oncology Program at Cedars-Sinai, launched in 2012 by the Barbra Streisand Women's Heart Center and the Saul and Joyce Brandman Breast Center — A Project of Women's Guild. The growing complement of studies aims at developing preventive strategies for women survivors of breast cancer, who are at increased risk of premature heart disease.

WEAR RED DAY

Some 350 Cedars-Sinai employees helped raise awareness of women's heart disease by turning out Feb. 7 for Wear Red Day for Women. C. Noel Bairey Merz, MD, director of the Barbra Streisand Women's Heart Center at the Cedars-Sinai Heart Institute, spoke at the event about progress and challenges regarding women and heart disease. She discussed the ways the disease treats women and men differently. Heart disease kills more women than men, yet women receive fewer interventions to prevent and treat the disease, she said. Wear Red Day, part of a national event begun by the National Heart, Lung and Blood Institute in 2003, was sponsored by the Linda Joy Pollin Women's Heart Health Program at Cedars-Sinai.

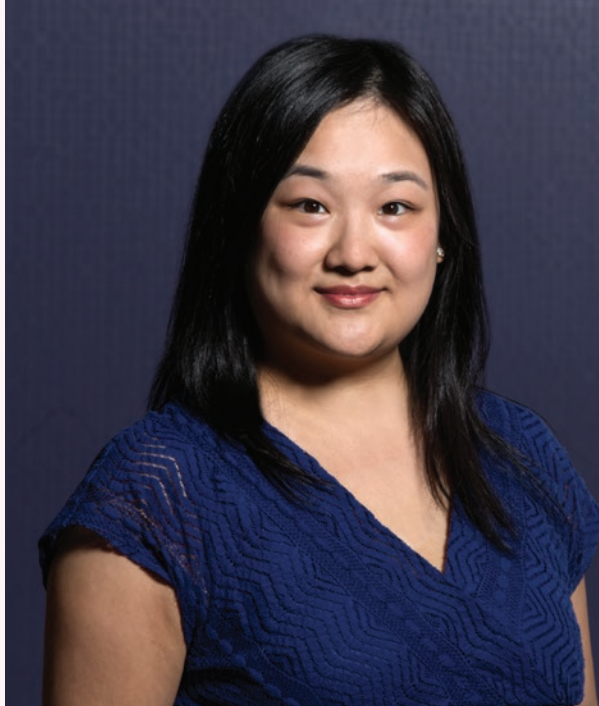
PUBLICATIONS

"Screenings, not statins, best hope for women's heart health," an op-ed authored by Dr. Bairey Merz and Irene Pollin, recently appeared in newspapers nationwide. The article drew attention to the need for women to get screened for heart disease risk and to follow that critical preventive measure with lifestyle changes, medication, and/or referrals to cardiologists.

PROGRAM DEVELOPMENT

"Every Beat That Counts: Hadassah's Heart Health Program" — Education and outreach specialists at the Barbra Streisand Women's Heart Center are exploring ways to collaborate with and disseminate this U.S. initiative by Hadassah to educate, engage, and empower women to live healthier lives.





Q & A

Janet Wei, MD

*2013–2014 Constance Austin Women's Heart Fellow,
Barbra Streisand Women's Heart Center*

Q: *What interested you in pursuing a fellowship in women's heart disease at Cedars-Sinai?*

A: Cardiac imaging can help provide a personalized assessment of an individual's cardiovascular risk and improve the diagnosis and treatment of women with heart disease. After I completed my residency in internal medicine and a general cardiology fellowship at Cedars-Sinai, I knew that a fellowship in women's heart disease would offer a tremendous opportunity for growth. I find Connie Austin's spirit inspiring, and I'm grateful to be the recipient of her generosity.

Q: *How important is mentorship in developing a career as a young cardiologist?*

A: It's critical. Dr. Noel Bairey Merz has been a true champion for young women cardiologists and has encouraged and supported me in my academic career development. I am truly fortunate to receive her guidance. Other Cedars-Sinai faculty members have been wonderful mentors and role models to me as well, and they show me the possibilities that the future may hold.

Q: *How is the fellowship helping to improve your research skills?*

A: During my prior clinical training, I had limited time to hone my research skills. Here I enjoy access to biostatisticians and grant coordinators, interact with fellow team members in weekly research meetings, and collaborate with local and national investigators to analyze and present our data. The fellowship provides me with dedicated research time, apart from my clinical duties.

Q: *What is your research focus?*

A: My research focus is the detection of coronary microvascular dysfunction (CMD), a problem with the small arteries of the heart that often does not show up on traditional diagnostic exams. I had previously assessed the safety of coronary reactivity testing (CRT) in diagnosing CMD, as part of the Women's Ischemia Syndrome Evaluation (WISE) investigation led by Dr. Bairey Merz. We found that CRT is relatively safe, but it is an invasive test, so we're looking at other options.

Currently, I am collaborating with Louise Thomson, MBChB, director of Clinical Cardiac MRI in the Cedars-Sinai Heart Institute, to assess the use of noninvasive magnetic resonance imaging in diagnosing CMD. In addition, I am applying for National Institutes of Health funding to develop a global atherosclerosis measure using MRI, so we can potentially use this tool in the future. No one has done this before.

Dr. Janet Wei is a recipient of the Sports Spectacular Endowed Fellowship Award and the American Heart Association Women in Cardiology Excellence in Training Award. She is enrolled in the Heart Institute National Institutes of Health-sponsored T32 Training Program in Advanced Heart Disease Research and the Cedars-Sinai Clinical Scholars Program, an innovative initiative providing funding, career guidance, education, and skill acquisition to residents, fellows, and young faculty who aspire to become clinical scientists.

GIFTS FROM THE HEART

A Passion for Science and Justice

Growing up in Los Angeles, Erika Glazer used to spend every weekend at the beach, swimming or surfing — a typical outdoorsy, active teenager. Then came an eight-month internship at age 16, during which she sat for long hours inside a cardiology lab at Cedars of Lebanon. Although it might have cut down on her time in the sun, the experience proved transformative for the self-described science-and-math geek. “I remember one of our projects involved a pediatric incubator for babies born with heart defects. It was so exciting to be there,” she recalls. “I was in my element.”

Today, despite the demands of being one of LA’s most dedicated philanthropists, a highly successful real estate and equities investor, and co-owner of the NBA’s Golden State Warriors, Glazer still geeks out on math and science. She becomes visibly energized when asked to talk about the highly complex field of proteomics and the research of Jennifer E. Van Eyk, PhD. “I guess I’m a frustrated physician!” Glazer says.

A prominent cardiac scientist, Dr. Van Eyk is widely regarded as a leader in clinical proteomics, the study of proteins for clinical applications (see cover story). She was recently recruited to Cedars-Sinai as director of Basic Science Research at the Barbra Streisand Women’s Heart Center, where her lab will focus on determining the molecular origins of gender differences in heart disease.

Dr. Van Eyk is also the director of Cedars-Sinai’s Advanced Clinical Biosystems Research Institute. And now, thanks to Glazer’s significant support, the scientist boasts another eminent title: the inaugural Erika J. Glazer Chair in Women’s Heart Health.

“What she’s working on is fascinating,” says Glazer of Dr. Van Eyk. “Her research could change the reality for women and heart disease.”

The fact that women have been underrepresented in heart research — and the shortage of information on gender differences — hasn’t escaped Glazer’s notice. “It’s an astonishing injustice,” she says.

A desire to right such wrongs underlies much of her philanthropy — from spearheading initiatives to aid the homeless to establishing college scholarships for underserved students whose immigration status denies them access to loans. Many of these scholars are now starting careers as engineers, chemists, or nurses.

In 2012, Glazer was invited to attend an event hosted by Barbra Streisand to build awareness for women’s heart health and gender inequities. She was immediately motivated to take action.

With the recruitment of Dr. Van Eyk, she has found a perfect counterpart. Glazer affectionately calls her “Jenny” — a testament to the close bond the two women quickly developed based on mutual respect and a shared interest in discovery.

Glazer’s fascination with discovery — fueled in that cardiology research lab when she was a teenager — has never left her. She remains as active as ever, enjoying travel to “weird places.” She even signed up for a space flight to be taken in 2015. “I’m keeping a bucket list,” she admits.

Fortunately for women everywhere, that list includes satisfying the science geek inside with an investment in heart research that could save the lives of countless women worldwide.





IN THE NEWS

Alumni Award

C. Noel Bairey Merz, MD, FACC, FAHA, director of the Barbra Streisand Women's Heart Center, director of the Linda Joy Pollin Women's Heart Health Program, and Women's Guild Chair in Women's Health, will receive a Professional Achievement Award from the University of Chicago Alumni Association on June 7 as part of its 73rd Annual Awards Ceremony. Dr. Bairey Merz is being honored for "making a historic and global impact" on the treatment of women's heart disease. "Through her pioneering research, the differences in preventing, diagnosing, and managing ischemic heart disease between men and women grew drastically," said the Alumni Association Board of Governors in the award announcement.

WoMentoring Leadership Network

Puja K. Mehta, MD, co-director of the Cardio-Oncology Program and director of the Vascular Function Research Laboratory, spoke at the inaugural event of the WoMentoring Leadership Network. Sponsored by the Jewish Vocational Service, the event centered around the theme of "Woman to Woman: Living Your Authentic Life."

Women in Cardiology Trainee Award

Janet Wei, MD, the Constance Austin Women's Heart Fellow at the Barbra Streisand Women's Heart Center, earned a Woman in Cardiology Trainee Award for Excellence from the American Heart Association (see Q&A page 10).

American College of Cardiology Honors

Janet Wei, MD, and Sherwin de La Cruz, MD, won Best Abstract Poster and Best Fellow in Training Abstract Poster at the American College of Cardiology Scientific Sessions on March 30 in Chicago for their work titled "Differences in Adenosine and Regadenoson on Myocardial Perfusion Reserve Index: A Report from the Women's Ischemia Syndrome Evaluation-Coronary Vascular Dysfunction (WISE-CVD) Study, a project of the Linda Joy Pollin Women's Heart Health Program" that was simultaneously published in the *Journal of the American College of Cardiology*.

Cardio-Oncology Program Featured in *Women's Day*

The Barbra Streisand Women's Heart Center's Cardio-Oncology Program was highlighted in a *Women's Day* special feature about the link between cancer and heart disease.

For more information on the Barbra Streisand Women's Heart Center at the Cedars-Sinai Heart Institute, call 310-423-9680 or go to cedars-sinai.edu/womensheart

To make a gift, please contact Allyson Tom at 323-866-6240 or Allyson.Tom@cshs.org, or visit cedars-sinai.edu/whc