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Women’s Health Research at Yale generates research findings that transform the scientific community’s understanding of women’s health, answer important questions, and advance knowledge to improve well-being for all.

To learn more please visit our website at:
  - www.yalewhr.org
  - WHResearch@yale.edu

Gifts Boost Women’s Health Research at Yale

- New Fund Established at Yale-New Haven Hospital
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2011 Grants Target Breast Cancer, Obesity

This year our Pilot Project Program grants focus on two fundamentally important areas of women’s health: breast cancer, the second leading cause of cancer mortality among women; and obesity, which in women, in particular, leads to higher rates of serious secondary health problems including diabetes and heart disease.

“As with all of the studies we have funded, the investigations by this year’s awardees focus on some of the most relevant health concerns that women face. Just as importantly, these investigations will continue our Program’s longstanding practice of generating new scientific information with the aim of providing practical benefits to improve the well-being of women,” said Carolyn M. Mazure, Ph.D., Director of Women’s Health Research at Yale.

Our pilot grants allow Yale investigators to generate previously unavailable data on areas of women’s health. These new findings are needed for researchers to apply for and obtain larger external grants to continue investigating these areas of women’s health. Thus far, our Program has awarded more than $4.2 million in these “seed” grants and the results of our pilot studies have generated nearly $47 million in new external grants – an enormous “return on investment.”


2011 Grants continued on page 4
JOIN THE SOCIETY OF FRIENDS
Consider a donation to Women’s Health Research at Yale in celebration of the birth of a child, a birthday, or to honor that special someone in your life.
Our Society of Friends ensures the future of Women’s Health Research at Yale. Gifts are welcome at all levels. To make an online gift visit www.yalewhr.org or mail your gift to Women’s Health Research at Yale P.O. Box 208091 New Haven, CT 06520-8091

Gifts were made to Women’s Health Research at Yale on behalf of the following people:

In honor of...
Ellen Friedenberg
Julie Ann Sosa, M.D.  Sanziana Roman, M.D.
Dinny Seton Wakerley

In memory of...
Mary M. Lennon

Educational and outreach activities are made possible through the generous support of:

The Community Foundation for Greater New Haven
The Grace J. Fippinger Foundation
Maximilian E. & Marion O. Hoffman Foundation, Inc.
Seymour L. Lustman Memorial Fund
Anonymous Donors

Women’s Health Research at Yale was founded in 1998 with initial funding from The Patrick and Catherine Weldon Donaghue Medical Research Foundation.
Yale-New Haven Hospital Fund to Support WHRY

A new fund has been established by anonymous donors at Yale-New Haven Hospital to support Women’s Health Research at Yale. This important Yale-New Haven Hospital Fund will help sustain the ongoing work of our interdisciplinary research program and advance the shared goal of integrating research findings into the clinical setting.

“We are grateful for this new support and want to sincerely thank the donors who recognize that the hospital and our Program share the goal of translating new research findings on women’s health into practical improvements in clinical care,” said Carolyn M. Mazure, Ph.D.

Focusing on gender differences in health and disease, our Program initiates scientific studies on the most relevant health concerns of women today.

Yale-New Haven Hospital provides comprehensive care in more than 100 medical specialties, including important areas of women’s health that are targets of investigation by our Program. In July, Yale-New Haven was the only Connecticut hospital to place in the top 10 nationally in any category in annual rankings by U.S. News & World Report.

Werth Family Foundation Continues Partnership

The Werth Family Foundation has renewed its support for Women’s Health Research at Yale, enhancing a partnership that began five years ago.

“We very much appreciate this renewed commitment by the Werth Family Foundation,” said Carolyn M. Mazure, Ph.D. “These generous contributions allow us to continue to conduct vital, interdisciplinary research on women’s health and generate new findings on gender differences that enhance the lives of women in the community.”

The renewed giving by the foundation includes funds to support our Pilot Project Program and our Research Cores.

Our pilot grants allow Yale investigators to conduct much needed feasibility studies to generate findings that can be used to apply for and obtain larger external grants. Our Research Cores facilitate interactions between individual scientists and institutions to collaborate on exploring emerging questions on women’s health and gender-specific aspects of health.

Our three current Cores focus on three vital women’s health concerns: cardiovascular disease, addictive behaviors, and trauma.

Thanks to Our Friends, We Have Met Our Match!

When the Community Fund for Women & Girls awarded its single-largest and first-ever multi-year grant to Women’s Health Research at Yale earlier this year, the support required our program to match the grant. Leaders of our program and the Fund hoped the matching component would prompt increased philanthropic efforts by women who wished to play a role in advancing women’s health and gender-specific medicine.

We are thrilled to announce that we exceeded our match, and support from women was critical in making this happen. To our many friends, thank you for your help in strengthening our ties to the community and moving scientific research forward to improve the well-being of women.
Innovations in Women’s Health | Summer 2011

2011 Pilot Project Program Awards
(continued from cover)

The 2011 grants and recipients are:

**Targeting the Spread of Breast Cancer**

Anthony J. Koleske, Ph.D., Professor of Molecular Biophysics and Biochemistry

Titus J. Boggon, Ph.D., Assistant Professor of Pharmacology

Metastasis, or spread, of a primary tumor is the greatest cause of mortality from breast cancer. Chemotherapy is used after surgery and radiation in cases of invasive and metastatic breast cancer, with the goal of eradicating cancer cells that have escaped the primary tumor.

To become metastatic, breast cancer cells must penetrate their own outer membrane. To do so, these breast cancer cells form protrusions that degrade the membrane from within, allowing cells to escape. Ultimately, this process can lead to the spread of cancer cells from a primary tumor to the bloodstream and the lungs.

Drs. Koleske and Boggon have identified three proteins which form a control “switch” in breast cancer cells which, when turned on, enables breast cancer cells to invade surrounding tissues and form secondary tumors. Now, in this interdisciplinary study, co-funded by Yale Cancer Center, the two scientists plan to identify the small molecule compounds that disrupt the interaction of these three proteins, thus, preventing this switch from turning on.

By identifying compounds that disrupt the formation of this switch, Koleske and Boggon will take a first step toward generating a new class of drugs to limit the spread of breast cancer cells. The two scientists envision developing these drugs for use alongside chemotherapy and radiation after surgical removal of primary tumors, with the aim of improving long-term survival outcomes of breast cancer patients.

**Controlling Diet-Induced Obesity in Women**

Matthew S. Rodeheffer, Ph.D., Assistant Professor of Comparative Medicine, and of Molecular, Cellular and Developmental Biology

Many studies show that the excessive accumulation of abdominal fat around vital organs is associated with increased risk of developing health problems. However, these conclusions were based on data obtained almost exclusively from studies in men or male animal models.

The prevailing view had been that women primarily accumulate fat under the skin throughout the body instead of mainly in the belly, and therefore obese women were less likely to develop secondary health problems like diabetes. However, recent epidemiological studies indicated that obese women are up to three times more likely than obese men to develop diabetes.

This suggests that either obese women accumulate more abdominal fat than is currently appreciated or...
that excessive accumulation of subcutaneous fat in women also increases the risk of developing secondary health problems. Thus, according to Dr. Rodeheffer, understanding the cellular mechanisms that underlie the gender differences related to the accumulation of white adipose tissue will provide knowledge to formulate improved risk-assessment strategies and interventions in women.

His hypothesis is that accumulation of all white adipose tissue – abdominal fat and subcutaneous fat – in women may contribute to the development of obesity-related health problems. Whereas most previous studies of how fat deposits are regulated at the cellular level have used male animal models and inferred results for females, this new study will use female animal models.

This study is designed to gain an understanding of the functions and actions of cells that control white adipose tissue mass in women at the onset of diet-induced obesity. Determining these cellular mechanisms is highly relevant to everyone’s health, but particularly important to women because women suffer greater obesity-related health consequences.

Fast Facts:
Why these pilot projects are critical

Breast Cancer:

➤ After lung cancer, breast cancer is the leading cause of cancer mortality among women.

➤ Based on current incidence rates, 1 in 8 women will be diagnosed with breast cancer in their lifetimes.

➤ It is estimated that more than 230,000 women will be diagnosed with breast cancer this year.

➤ Metastasis, the spread of cancer, is the primary cause of mortality from breast cancer.

Obesity:

➤ A little more than one-third of U.S. adult women are obese.

➤ Serious health consequences are associated with being obese, including increased risk of diabetes, high blood pressure, stroke, heart disease, and osteoarthritis.

➤ In recent years, rates of obesity among U.S. women aged 20-34 years old have been increasing more rapidly than in any other age group of women or men.

➤ The best way to safely lose weight is to use more calories than consumed, through healthy food choices and physical activity. Before starting a weight-loss plan, talk to your health care provider.

Sources: National Cancer Institute, U.S. Department of Health and Human Services Office on Women’s Health

Support the Pilot Project Program
by visiting www.yalewhr.org or
maint your gift to:

Women’s Health Research at Yale
c/o Ramona E. Gregg
P.O. Box 208091
New Haven, CT 06520-8091

Women’s Health Research at Yale is a program within Yale University School of Medicine. Yale University is a 501(c)(3) non-profit organization.
The Increasingly Recognized Association of Depression and Heart Disease: Are there Gender-Specific Risks?

Approximately 20 percent of patients with various forms of cardiovascular illness also suffer from diagnosed depression.

Moreover, cardiovascular disease and depression not only can accompany one another, but scientists investigating the interplay between psychological factors and physical conditions have known for some time that depression is a risk factor for cardiovascular disease for both women and men. Furthermore, both in community studies and among clinical samples of those with cardiovascular disease, depression is a much more potent risk factor for mortality from heart disease than other psychosocial factors.

In terms of gender difference, emerging evidence indicates that the percent of women with depression post-heart attack is higher than it is for men, and that the risk for cardiac disease conferred by an existing depression is particularly high for young women, compared either to older women or men who suffer from this clinical syndrome, according to Dr. Viola Vaccarino.

Vaccarino, one of Women’s Health Research at Yale’s earliest investigators and now Professor and Chair of Epidemiology at Emory University’s Rollins School of Public Health, returned to Yale in May to give a grand rounds lecture on the relationship between depression and cardiovascular disease, and the gender-specific risks that are beginning to be revealed.

Each year, in collaboration with our Program, the Department of Psychiatry’s Women’s Behavioral Health Division invites a researcher to lecture on a topic of mutual interest. This year, we invited Vaccarino because of her contributions to the understanding of how women differ from men in experiencing cardiovascular disease. Through research supported by Women’s Health Research at Yale, she was one of the first investigators to show that significantly fewer women than men had chest pain as the chief symptom of heart attack, and to establish that women, particularly young women, fared worse than men after cardiac bypass surgery.

More recently, Vaccarino’s evolving research has focused on the association between two highly prevalent health conditions - depression and cardiovascular disease - with an emphasis on underlying factors linked to both conditions.

Vaccarino studies the effects of several kinds of factors that may explain the association between depression and cardiovascular disease. These include unhealthy lifestyle (smoking, poor diet and lack of exercise), inherited genetic traits and/or family history, and, perhaps a critically important, particularly in women, yet less explored factor – the effects of severe stress early in life, such as maltreatment during childhood and adolescence.

Vaccarino said she believes that all these factors are contributory, yet the effects of stress have garnered less attention until relatively recently. She maintains that various types of early severe stress, especially abuse in childhood, have a lasting psychological and biological effect, and alongside current lifestyle vulnerabilities and genetic susceptibilities, play an important role in the heightened risk of cardiovascular disease.

“The hypothesis is that women experience more of these early severe stressful events, and that this kind of exposure, even if it goes away, remains as a
psychological scar that also affects biology,” Vaccarino said in a recent interview. “As a consequence, the body’s hormonal stress-response systems, which are known to affect cardiac function, do not develop the way they should, and there can be enduring effects on the cardiovascular system.”

She points to some reports that have begun to suggest such a link:

- A study published in 2007 in the Proceedings of the National Academy of Sciences found an association between maltreatment during childhood and clinically significant indicators of cellular inflammation (an early sign of cardiovascular disease) in adulthood. This study followed a population of more than 1,000 New Zealanders from birth to age 32.

- A 2004 survey of information from more than 17,000 adult members of a health maintenance organization in California, reported in the journal Circulation, found an association between childhood maltreatment and ischemic heart disease, a condition characterized by reduced blood supply in the heart muscle due to coronary artery disease (plaque buildup in the arteries).

Although neither of these studies analyzed the outcomes by gender, another study, which did include an analysis by gender, suggests that this relationship may be localized more powerfully in women. This study, by Mazure and colleagues published in the Journal of Clinical Psychiatry in February 2004, found an association between childhood maltreatment and cardiovascular disorders in a nationally representative sample of more than 5,000 adults, about half women and half men, diagnosed with depression at age 18 or older.

The results of this study showed that a reported history of childhood abuse or neglect was associated with an almost nine-fold increase in cardiovascular disorders in women (but no effect in men), as well as a significant increase in the odds of lifetime depressive disorders for both women and men. Moreover, the study results suggest, childhood maltreatment may also be associated with a younger onset of cardiovascular disease in women.

Many previous studies have demonstrated that women experience depression at twice the rate for men, and that men have higher rates of cardiovascular disease than premenopausal women. However, interestingly, in this nationally representative sample of more than 5,000 women and men, these expected sex difference ratios in depression and cardiovascular disease were found only in those who did not report a history of childhood maltreatment. In those reporting childhood maltreatment, the protection against cardiovascular disease normally experienced by women was reduced as was the lower vulnerability to depression typically experienced by men.

It may turn out, according to Vaccarino, that these types of severe enduring stress result in both cardiovascular disease and depression through common pathways that damage the cardiovascular system, impair the immune system, and alter a key part of the neuroendocrine system called the HPA axis (hypothalamic-pituitary-adrenal axis) which is responsible for regulating reactions to stress as well as mood and emotions.

“To ultimately understand the link between cardiovascular conditions and depression and, importantly, prevent the development of these conditions,” Vaccarino said, “we need to look in detail at how stress affects these systems and we need to focus on sex differences.”
Q & A with Dr. Vaccarino  
Cardiovascular Disease, Depression and Gender-Specific Risk

Q: What is the one critical issue regarding women and cardiovascular disease that we need to understand in order to reduce morbidity and mortality?

A: There are many issues that need to be addressed to fully understand the pathophysiology, risk factors, diagnosis and clinical care of cardiovascular disease in women. My own perspective is that the area of mind-heart connections is a relatively neglected area that may be particularly important for women’s risk, and may become very fruitful in defining women’s cardiovascular risk and developing effective prevention strategies.

Q: You have stated that we need to look at the specific pathways and underlying mechanisms that may explain the link between stress early in life, particularly childhood maltreatment, and cardiovascular disease in women with depression.

A: One is dysregulation of neuroendocrine systems involved in the stress response, which could increase cardiovascular risk through a “wear and tear” mechanism. Another involves immune mechanisms leading to increased cellular inflammation, which is an underlying phenomenon of many chronic conditions. Others include genetic factors and metabolic factors, such as insulin resistance and metabolic syndrome, which are also influenced by stress.

Q: If you could design studies that would substantially help gain an understanding of this apparent gender-specific risk, what would those studies be?

A: A lifespan study is really needed, which has not yet been done with respect to cardiovascular risk and gender differences. Such a study would take a long time to complete and be expensive, but would be the most rigorous way to examine and answer this question.

Dr. Vaccarino’s interest in the interconnections between psychological and biological health, particularly as they relate to heart disease in women, was fostered during her years at Yale. Soon after Women’s Health Research at Yale was established in 1998, Vaccarino was twice awarded pilot funds to study cardiovascular disease. Both studies revealed important gender differences, finding that:

- women fared significantly worse than men following heart bypass surgery - with women suffering more pain, infection, lower physical functioning and twice the likelihood of readmission to the hospital. These findings laid the groundwork for studying why these differences exist, and demonstrated the importance of developing gender-specific interventions that can improve the health of women after bypass surgery.

- only 54% of women hospitalized with a heart attack had a chief complaint of chest pain, compared with 69% of men. In addition, younger women were twice as likely to have respiratory symptoms as their chief complaint when hospitalized with a heart attack than men of the same age. Clarification of gender differences in clinical presentation demonstrated the need to recognize and treat acute coronary ischemia in women more promptly.
Annual Appeal Campaign Wrap-Up

We set an ambitious goal last year for the 2010 Annual Appeal that just ended on June 30th. It is with pure delight and sincere appreciation that we can announce that we not only reached our goal but exceeded it!

Thanks to your generosity and your concern for the well-being of women, we will be able to continue our efforts to gain valuable new information on breast cancer, heart disease, depression and a host of other vital areas of women’s health.

The landscape for federal research funding continues to be a difficult one. Yet, because of our Pilot Project Program, we continue to compete successfully for grant funding. With your continued support, our pilot projects will help us secure grants that illuminate key health issues for women.

We hope we can count on you once again, to join us in initiating important new research on women’s health. With our shared interest in gender-specific research, together we can put Women’s Health Research at Yale on a sound financial footing for years to come. Your support truly makes a difference.

Thank you!

Patti Russo, Chair
Philanthropy & Communications
Community Outreach...

“Your Health” – New website feature

In a continuing effort to make our community outreach and communications efforts more user-friendly, we have launched a new section on our website devoted to “Your Health.”

This page, found in the Community section of our Home Page, offers information on a particular women’s health concern in an easy to read format. We plan to update the topic periodically so we can bring you relevant information on a range of vitally important women’s health concerns. The page also will offer helpful links to informative sources on the topic.

This inaugural “Your Health” web page focuses on obesity, a timely topic as new national reports have recently put the spotlight on this epidemic health problem, and one of our just-awarded 2011 pilot grants is enabling a study to gain an understanding of the inner workings of cells that regulate the accumulation of diet-induced fat in women. (See Dr. Matthew Rodeheffer’s study p. 4)

To view the new “Your Health” page visit: www.yalewhr.org.

We want to hear what you have to say! Join us on Facebook and Twitter, and email us at whresearch@yale.edu.

Press Notes...

Obesity Epidemic Demands Constant Attention

This summer started off with a health report that offered a bleak assessment of obesity in America. In short, Americans are more obese today than they were 20 years ago.

The report, issued in July by Trust for America’s Health, a non-partisan advocacy group, and the Robert Wood Johnson Foundation, surveyed the level of obesity in the 50 states and the District of Columbia since 1990. Twenty years ago, no state had an obesity rate above 15 percent. Today, according to the report, 38 states have obesity rates above 25 percent. In the other 12 states, the rates are above 30 percent. The rising rates of two of the serious health problems that stem from obesity, diabetes and high blood pressure, also are documented in the report.

There are a couple of bright spots to speak of in the report. Close to home, Connecticut residents ranked as the third least obese, after residents of Colorado and Washington, D.C. In addition, obesity rates have begun to level off in several states. Overall, however, there is no end in sight to the U.S. obesity epidemic, which is particularly important to women as they suffer greater obesity-related health problems than men.

The new report, the fifth in an annual survey, includes policy recommendations for reversing the obesity epidemic, emphasizing prevention and the need to provide people with resources and opportunities to make healthier choices. We can turn this around. The way to start is to keep the focus on this issue as a top priority in women’s health, not simply a topic for a once-a-year report.
Training the Next Generation—Junior Faculty Scholars to Begin Training

With a $2.5 million grant from the National Institute on Drug Abuse and the National Institutes of Health Office of Research on Women’s Health, we have established a program to train junior faculty scholars to conduct interdisciplinary research on women’s health and addictive behaviors. This training program provides mentoring, coaching and team science experience for entry-level faculty to begin research careers focused on this important area of women’s health.

“The stark reality is that addictive behaviors in women currently rank among our most prevalent health concerns; disorders involving these behaviors are linked to some of the top causes of mortality and preventable disease. Our unique training program fills a great need for new researchers who can bridge many areas to fully understand addictive behaviors in women.”

- Carolyn M. Mazure, Ph.D.

Building Interdisciplinary Research Careers in Women’s Health (BIRCWH) Scholar Program

Faculty Leaders for the Yale BIRCWH:

Carolyn M. Mazure, Ph.D., Principal Investigator.

Samuel A. Ball, Ph.D., Research Director – Professor of Psychiatry, Director of Research for The APT Foundation. The APT Foundation is one of the largest providers of substance abuse treatment in Connecticut.

Jacob K. Tebes, Ph.D., Team Science Advisor – Professor of Psychiatry, Director of the Division of Prevention & Community Research and The Consultation Center. The Consultation Center, a unit within the CT Mental Health Center affiliated with the Department of Psychiatry, provides prevention and health promotion services to individuals and families, consults community and governmental agencies, and conducts prevention and community-based research.

Elise DeVito, Associate Research Scientist, Ph.D. from Cambridge University, U.K.

Research Area: Dr. DeVito will investigate the impact of sex and gender on the vulnerability to addictive disorders and responses to treatment.

Mentor: Kathleen M. Carroll, Ph.D., Professor of Psychiatry; Director of Psychosocial Research, Division of Addictions; Scientific Director, Psychotherapy Development Center for Drug Abuse.

Megan Smith, Assistant Professor of Psychiatry and Child Study, and Lecturer in Public Health, MPH from Yale School of Public Health and Dr.PH from Boston University School of Public Health.

Research Area: Dr. Smith will explore substance use, social context, and environment in pregnant, postpartum and parenting women.

Mentor: Linda C. Mayes, M.D., Professor in the Child Study Center, of Epidemiology, Pediatrics and of Psychology.

Azure Thompson, Associate Research Scientist, Dr.PH and MPH from Columbia University's Mailman School of Public Health.

Research Area: Dr. Thompson will study programs aimed at prevention of substance abuse among adolescent girls and young women, with a particular focus on African-American women.

Mentor: Jacob K. Tebes, Ph.D., Professor of Psychiatry.

Tomoko Udo, Associate Research Scientist, Ph.D. from the University of Medicine and Dentistry of New Jersey, School of Public Health, Health Education and Behavioral Science.

Research Area: Dr. Udo will work on the development of a human laboratory model for smoking relapse to assess gender differences in smoking cessation.

Mentor: Sherry McKee, Ph.D., Associate Professor of Psychiatry, Director of Yale Behavioral Pharmacology Laboratory.
“Your Health”

Our new “Community” section includes important, relevant information on women’s health.

Visit our homepage: www.yalewhr.org