Community Partnership Advancing Health Equity for Women

The Community Fund for Women & Girls has awarded its single-largest and first-ever multi-year grant to Women’s Health Research at Yale, signaling the start of a new partnership advancing health equity for women. The Community Fund for Women & Girls is a component fund of the Community Foundation for Greater New Haven. The Fund promotes the advancement of women and girls, including physical and emotional health as well as social and economic well-being, through strategic philanthropy, advocacy and collaboration.

The contribution from the Fund will help sustain our ongoing work. Our program, which raises its own research funds to initiate biomedical studies on women’s health, focuses on gender differences in health and disease. A growing body of evidence, including our own research findings, demonstrates the critical importance of considering the effects of sex and gender on health.

Support for our Program also allows the translation and dissemination of our research findings, enabling community members to become more knowledgeable about their health.

“This new grant is an investment in the long-term aspirations of both of our programs,” said Dr. Carolyn M. Mazure, Director of Women’s Health Research at Yale. By design, the grant must be matched by our Program’s supporters. “Through this matching initiative, we hope to prompt increased philanthropic efforts by women who wish to play a role in science that is advancing the development of gender-specific medicine,” Mazure said.

“The core missions of our organizations are aligned. Together we can help improve the well-being of women and girls, champion the cause of health equity for women, and help inform the community about the practical benefits of our Program’s latest research findings,” Mazure said. “We are grateful for the generous support from the Community Fund for Women & Girls, and look forward to the success that will come from joining together to multiply our efforts.”

— Helene Robbins, Chair Community Fund for Women & Girls’ Advisory Committee
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 in support of our endowment fund and our annual general operating costs for research and education are welcome at all levels.

To join the Society of Friends 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...
Denise Adams  Annie Ducmanis Adams
Dr. Hilary Blumberg  Patti Russo
Anne Worcester

In memory of...
David Evans  Dr. Letty Russell
Karene Person  Ann Schpero Kaplan
Herbert Pearce

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
Each of the four parathyroid glands, located in the neck behind the thyroid, is about the size of a grain of rice. Despite their small size, however, these endocrine glands play a large role in maintaining good health.

They secrete parathyroid hormone, which regulates calcium balance in the body. This balance is essential to the smooth running of the nervous system and muscles, including the heart. Calcium balance also helps ensure healthy bones and teeth, and plays a key role in the blood clotting process, as well as in maintaining a balanced mood.

A condition known as hypoparathyroidism occurs when there is a deficiency of parathyroid hormone. This condition occurs in children with particular genetic disorders. More commonly, this condition affects adults, primarily women.

Because of their close proximity to the thyroid gland, the parathyroid glands often are removed or injured when surgeons are removing a cancerous thyroid. Sometimes surgeons must remove the parathyroid glands to treat other ailments, or these glands can malfunction. The resulting calcium imbalance can cause significant medical problems and calcium replacement can be difficult in some patients, requiring daily or even hourly oral calcium administration.

Dr. Julie Ann Sosa, Associate Professor of Surgery and Medicine and an endocrine surgeon, has become keenly aware of patients’ complications with hypoparathyroidism through her own clinical experience, and has long sought a new, more effective way to treat this condition.

In one of the latest Pilot Project Program studies funded by Women’s Health Research at Yale, Sosa and a carefully-assembled team are trying to create parathyroid cells that would replace lost or malfunctioning cells. Specifically, they are attempting to induce human embryonic stem cells to develop into parathyroid cells. Embryonic stem cells are not embryos, and the use of the cells being studied in this project is consistent with federal and state rules and guidelines.

This pilot project represents an entirely new approach to dealing with hypoparathyroidism that will not have the problems engendered in calcium supplementation. If the project is ultimately successful, Sosa envisions supplying patients with newly created parathyroid hormone-secreting cells that could conceivably be injected into muscle tissue anywhere in the body where there is blood supply to nourish them. This technique would be a more “organic” approach to replacing parathyroid function and thus would induce fewer side effects.

Sosa’s team still has a way to go before stem cells could be turned into replacement parathyroid cells. But not long ago this possibility was little more than a notion. About two years ago, Sosa and
Dr. Sanziana Roman, also Associate Professor of Surgery, were talking with their colleague, Dr. Diane Krause, Professor of Laboratory Medicine, Cell Biology, and Pathology, and Associate Director of the Yale Stem Cell Center, about this “out-of-the-box idea” of creating parathyroid cells from stem cells, and asked her opinion.

Krause, an M.D., Ph.D., and an internationally recognized stem cell researcher, did not say much initially. However, not long after, she told Sosa and Roman to their surprise that their idea might work.

Led by Sosa, who has since completed laboratory training to become a Yale Stem Cell Center member, the three began working together and ultimately found a stem cell scientist who they needed to complete the study team. This fourth member of the team is Betty Lawton, Ph.D., who came to Yale in December from the University of Connecticut.

“Steering” Stem Cells

Dr. Lawton’s specialties as a stem cell scientist are working with human embryonic stem cells, and the intricate “turning on” of genetic information that drives undifferentiated cells to become specialized cells. Knowledge and experience in this area made her the right person to complete the research team. “It is such a unique set of skills that we needed,” Sosa said.

Embryonic stem cells are primitive, undifferentiated cells derived from pre-implantation stage embryos, capable of dividing when cultured for a prolonged period and known to develop into cells and tissues of three primary “germ,” or cell, layers: ectoderm, mesoderm and endoderm.

Ectoderm cells give rise to the nervous system, sensory organs, skin, and brain. Mesoderm cells become the muscles, connective tissues, kidneys, and other organs. The endoderm cells give rise to the lungs, liver, pancreas, esophagus, digestive system, thyroid, and, importantly for this pilot study, the parathyroid glands.

The embryonic stem cells must be steered by the addition of factors to the growth medium to “turn on” certain genes at just the right time to first become endodermal cells, then ultimately parathyroid cells. One of the major challenges is that these cells grow very slowly and are difficult to manipulate using techniques that most cell types respond to readily. They must be monitored in the laboratory and each variable relating to their development – temperature, medium in which they are growing, the time at which cells are propagated, and chemical stimuli – must be precisely maintained, Sosa said. “These cells require care seven days a week,” added Lawton.

With Dr. Krause’s guidance, Sosa’s team also forged a collaborative relationship with a molecular geneticist in the Stem Cell Center, Yibing Qyang, Ph.D., who has donated materials and expertise that will enable the team to turn a piece of genetic material called a BAC (Bacterial Artificial Chromosome) into a key tool needed in the initial step of the project. This tool is a marker which will allow the investigators to observe the
transformation of the cells into the appropriate types.

“We are working on this step right now and are making good progress,” Lawton said.

After the team has demonstrated that the appropriate cells can be created, the resulting cells will be expected to follow a development pattern that occurs normally in humans when parathyroid cells are created.

Using Patients’ Own Cells

The next steps, expected later this year and next year, will be to consistently “turn on” the genes that develop the embryonic stem cells into parathyroid cells, then demonstrate they can survive and function normally in an animal model of hypoparathyroidism.

When human embryonic stem cells have been successfully turned into functional parathyroid cells, the research team hopes to repeat this process using embryonic-like cells – known as human-induced pluripotent stem cells – that can be made in the lab from skin cells and other mature cell types found in all adults. These cells could be taken from an individual patient, differentiated with the same protocol used for embryonic cells, and returned to the patient as functional parathyroid cells, minimizing the risk of immune rejection by using the patient’s own cells during the process.

First, the team will need to test the safety and ongoing function of the created parathyroid cells before they can be implanted into patients. Sosa and her team, a fine example of both the interdisciplinary collaboration and translational research that Women’s Health Research at Yale fosters, say they are not deterred. As Sosa says, “Improving patients’ quality of life makes it all worthwhile.”

The Discovery of the Parathyroid Glands

Why the Rhinoceros?

When the Zoological Society of London acquired its first Great Indian Rhinoceros (Rhinoceros unicornis) in 1834, it could not have foreseen the importance of the scientific discovery that would flow from this purchase.

Sir Richard Owen, an anatomist in the Royal College of Surgeons of England, was offered the carcass of the animal after it died in 1849. During his post-mortem examination of the two-ton rhinoceros, he discovered in the animal’s neck “a small compact yellow glandular body attached to the thyroid,” a structure we now know as a parathyroid gland.

Owen’s dissection of the rhinoceros and his discovery are considered pivotal to the history of endocrine surgery. For this reason, endocrine surgeons have taken the Indian Rhinoceros to be their international mascot.

A Swedish medical student, Ivar Viktor Sandstrom, is credited with naming the parathyroid glands in humans in 1880. The parathyroid glands are among the last major organs discovered in the human body, and they are vitally important to maintaining good health.

Women's Health Research at Yale's Pilot Project Program provides funding to Yale researchers to generate feasibility data for innovative ideas that can advance medical care. These findings are necessary to apply for and obtain larger external grants so the researchers can continue their investigations. The two studies featured in this newsletter edition are among our recent pilot projects.
Reducing Obesity in Women with Schizophrenia: Pilot Study Shows Promise

People with schizophrenia, especially women, are particularly at risk of becoming obese because many medications necessary to manage the psychotic symptoms of this disorder and improve quality of life are known to induce weight gain.

On average, people with schizophrenia live 25 years less than those in the general population, largely as a result of obesity-related illnesses. These ailments include cardiovascular disease and high blood pressure; diabetes; and endometrial, ovarian and breast cancers in women. Clearly, life span can be extended and health improved for women with schizophrenia if reductions in weight can be achieved and maintained.

Using a Women’s Health Research at Yale Pilot Project Program grant, Dr. Cenk Tek devised a clinical trial to determine whether a medication commonly prescribed to treat addictive behaviors, naltrexone, could be used for a different purpose. In this trial, he wanted to determine if naltrexone could be used to counter the weight gain that can be induced by medications that are prescribed for control of psychotic symptoms.

Naltrexone has been used for years as an intervention approved by the U.S. Food and Drug Administration to help individuals recovering from alcohol and opioid dependence reduce their cravings for these substances. This medication has a higher affinity to bind to the “reward-response” receptors in the brain and works by effectively blocking these receptors, preventing a response to the alcohol or illicit drugs.

It was noticed in this population that naltrexone suppressed appetite. Naltrexone also has been used in laboratory studies of eating behaviors and in a small number of clinical trials for treatment of obesity. The emerging data appear to show it may be particularly effective in women. Dr. Tek hypothesized that naltrexone might be effective at limiting weight gain in women taking antipsychotic medications for symptoms of schizophrenia.

His pilot study was designed as a randomized clinical trial. In such a study, half of the volunteers are randomly placed into one of two groups. Half of the 24 subjects who participated in Dr. Tek’s study were placed in a group that received a daily oral dose of 25 milligrams of naltrexone for eight weeks. The other 12 subjects received a placebo daily for eight weeks.

On average, the women who enrolled in the study weighed about 220 pounds, and all were diagnosed with schizophrenia and experienced weight gain related to the antipsychotic medication they were taking. Each of the women underwent a baseline physical examination and blood analysis at the start of the study to determine overall health and eligibility to participate. The women then made weekly visits to be weighed and complete questionnaires. Follow-up visits included blood work at the midpoint and endpoint of the study.

The results, according to Dr. Tek, Assistant Professor of Psychiatry, have been promising, in that the women in the study who received a placebo showed a modest weight gain of about one pound.
while the women in the study who received the low dose of naltrexone showed arrested weight gain and, surprisingly, modest weight loss of about five pounds.

“We would have been happy to just stop the weight gain,” Dr. Tek said. “This is terrific that we saw even modest weight loss.”

Encouraged by these feasibility data, Dr. Tek is using the results of the Women’s Health Research at Yale-funded pilot study to apply for a National Institutes of Health grant to conduct a more comprehensive study. The expanded study would be designed to confirm the findings of the pilot investigation, determine whether men with schizophrenia could expect similar results with naltrexone, and generally increase understanding of how such an intervention might help people with schizophrenia who often must also deal with obesity.

Combined with lifestyle interventions including exercise and optimal nutrition, an approach using naltrexone to stop and reduce weight gain in women with schizophrenia could provide obvious practical benefits, including reduced illness and longer life span, according to Dr. Tek. Overall, the health and quality of life for women with schizophrenia could be improved with such interventions.

As this was a pilot investigation, the study was not large enough to make definitive conclusions about the efficacy of the possible intervention, especially over the long term. This is why Dr. Tek is seeking to conduct a larger investigation with a longer period of study. However, the clinical significance of the pilot results, he said, is important because this group of women receiving medications to control the symptoms of schizophrenia had been gaining weight at an annual rate of about 10 percent prior to the study.

Schizophrenia is a chronic, severe and disabling brain disorder. The symptoms of this disorder fall into three categories: positive, negative and cognitive symptoms. Positive symptoms include delusions and hallucinations, such as hearing or seeing things that others cannot. People with positive symptoms also may exhibit paranoia and falsely believe others are plotting to harm them. Antipsychotic medications are used to treat the positive symptoms of schizophrenia.

Negative symptoms, which are often more difficult to recognize, are associated with disruptions to normal emotions and behaviors. People suffering from these symptoms often do not find pleasure in everyday life, lack the ability to begin and sustain planned activities, and may speak little even when forced to interact. Cognitive symptoms also may be difficult to recognize, and include trouble focusing or paying attention, and an inability to understand information and use it to make decisions.

An individual with schizophrenia may have any combination of symptoms, and the symptoms can change over time. Ultimately, this disorder is one of the most devastating mental illnesses, sometimes making it difficult to hold a job or sustain personal relationships.

About 2.4 million Americans suffer from schizophrenia, a disease which has significant personal costs and consumes more than $60 billion a year in direct treatment costs, according to a study published in 2005 in the Journal of Clinical Psychiatry.

As documented by the National Institute of Mental Health, the onset of this disorder often occurs early in life, but men usually experience the first symptoms earlier than women. Onset generally occurs in the late teens or early twenties in men, and in the mid twenties or early thirties in women.

Studies conducted before the advent of antipsychotic medications reveal that people with
schizophrenia often were underweight compared to the general population, and had difficulty gaining weight even when adequately nourished, according to Dr. Tek.

The first antipsychotic medications were discovered in the 1950s and introduced in clinical practice in the 1970s. A second generation of these medications was introduced in the 1990s. Scientists now believe that people who take certain antipsychotic medications to control their symptoms, including commonly prescribed drugs such as clozapine, olanzapine and risperidone, gain weight partly because the medications effectively stimulate the desire for food.

“Weight loss is difficult for anyone,” Dr. Tek said. “It’s even more difficult when you are on a medication that increases appetite.”

The specific mechanisms at work here are not fully understood. However, Dr. Tek believes that the antipsychotic medications blunt chemical receptors in the brain that are integral to deriving pleasure from food. When these receptors are blocked, the so-called “reward response” that results particularly from eating rich, high fat or sweet foods is minimized. Thus, these medications essentially cause us to eat more than would be otherwise necessary to get the pleasurable reward. As Dr. Tek explains, there is no stop signal to “reward” eating, and not surprisingly, the overeating causes weight gain.

Dr. Tek’s study was funded by The Ethel F. Donaghue Women’s Health Investigator Program at Yale, the initial grant making arm for Women’s Health Research at Yale.

Obesity: A National Epidemic

Adult obesity, a condition characterized by excessive body fat, is a problem not just for women or men with schizophrenia. It is a national epidemic, causing widespread health problems, a lower quality of life and higher medical costs. Consider this information from the U.S. Centers for Disease Control and Prevention:

- During the past 30 years, rates of obesity have more than doubled, to nearly 34 percent of adult Americans, though the percentage of people who are obese appears to have topped off in recent years.
- Women in the general population appear to have a slightly higher rate of obesity than men, though the gap between rates has declined in recent years.
- Obesity increases risks for many other health problems, including cardiovascular disease; stroke; diabetes; liver and gall bladder disease; sleep apnea and respiratory problems; osteoarthritis; gynecological problems (abnormal menses and infertility), and endometrial, breast and colon cancer.

- Obesity results in more medical care, and increased cost.
- Societal and community changes accompanied the U.S. rise in obesity. People eat differently than in the past, driven by easy access to high-fat, sugary, salty foods that are highly advertised and marketed. Increases in sedentary activities also contributed to rising obesity rates.

Medical Complications of Obesity

- Pulmonary disease
- Idiopathic intracranial hypertension
- Nonalcoholic fatty liver disease
- Gastroesophageal reflux disease
- Gall bladder disease
- Gynecologic abnormalities
- Osteoarthritis
- Phlebitis
- Venous stasis
- Pulmonary hypertension
- Cataracts
- Nonalcoholic fatty liver disease
- Steatosis
- Steatohepatitis
- Cirrhosis
- Diabetes
- Hypertension
- Severe pancreatitis
- Cancer
- Breast, uterus, cervix, colon, esophagus, pancreas, kidney, prostate

Slide Courtesy of Dr. Cenk Tek (Nov 2010)
We are nearing the end of this year’s Annual Appeal.

There is still time for you to help us meet this year’s goal!

Please consider making a gift, and join us in initiating and sustaining important research on gender differences in health and disease.

Join our Society of Friends by visiting www.yalewhr.org or mail 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.

Help Us Fund Research that Makes a Difference!

We want to offer our sincere thanks to all of our supporters who have helped our Program as we hope to top the annual appeal goal we set this year.

Our program is self-supporting, meaning we raise our own funds to initiate new research that can help our daughters, mothers, sisters and friends. Please remember that a number of giving options are available to donors, such as the grant-matching initiative we have just begun with The Community Fund For Women & Girls (announced in our cover article).

We need your support to fund research on highly important areas of women’s health, such as breast and ovarian cancer, depression, smoking cessation, and much more, to increase scientific knowledge on gender-specific aspects of disease. As a recent report from the National Academy of Sciences’ Institute of Medicine notes, research on women’s health has contributed substantially to lessening the burden of disease over the past 20 years, but major gaps in knowledge remain.

We have raised an important part of the dollars that make our work possible, as we near the end of our annual appeal campaign. But there is still time to join our Society of Friends, help us top our goal, and aid in filling in the knowledge gaps. Together we can:

- Fund research to generate new knowledge on women’s health and gender differences that will provide real benefits.
- Inform community members about our findings to help them become more informed consumers of health information and healthcare.

We are grateful for the generous contributions we receive from our supporters, and continue to welcome new members to our Society of Friends for Women’s Health Research at Yale.

Thank you!
In the News

Council News...

Founding Council Member Roz Milstein Meyer Is Honored With Yale’s Elm Award

Roslyn Milstein Meyer, Ph.D., a founding member of our advisory Council, was honored by University President Richard Levin with a Yale Elm Award during the university’s 2010 Seton Elm and Ivy Awards ceremony on April 27th. These awards recognize outstanding individuals who strengthen the bonds between New Haven and Yale.

Roz is a member of the Yale College class of 1971 who went on to earn a master’s degree and a doctoral degree in clinical psychology at Yale. She co-founded Leadership, Education and Athletics in Partnership (LEAP), an educational program for inner-city youth, and co-founded the International Festival of Arts and Ideas, which seeks to enhance the cohesiveness of the community and spur economic development in New Haven.

Council members Diane Ariker and Diane Young Turner were previously honored with Ivy awards, in 1988 and 1993, respectively. University Secretary Linda Koch Lorimer, Special Advisor to our Program, was awarded a 1997 Special Elm and Ivy Award.

Girl Scouts of CT Honor Council Members

Two members of our advisory Council who have worked tirelessly for local philanthropic causes, Kim Healey and Diane Young Turner, were honored April 6th at the Girl Scouts of Connecticut’s annual Women of Achievement event.

Kim, Executive Director of the NewAlliance Foundation, and Diane, Yale’s Associate University Librarian for Human Resources and Chair of the United Way of Greater New Haven 2009 campaign, were recognized for their accomplishments and their commitment to the community.

Press Notes...

Look Closely and Take a Long View

The news in early April 2011 that some volunteers in the Women’s Health Initiative (WHI) hormone therapy trials had a markedly reduced risk of breast cancer surely had to come as a surprise to most women. After all, haven’t women heard alarming news about the risks of hormone therapy for years since the first two WHI studies ended nearly a decade ago?

The women who are the focus of the recent report were in the group that had a hysterectomy prior to receiving estrogen-only hormone therapy. Surprisingly, with new follow-up data, it was found that this group had a 23 percent lower risk for breast cancer compared to those who had taken a placebo.

Patti Russo in Forbeswoman

Patti Russo, Chair of our advisory Council’s Philanthropy & Communications Committee, was interviewed for a Forbes Magazine blog called Forbeswoman about her leadership of the Women’s Campaign School at Yale. The April 4th Q & A featured Patti’s succinct analysis of the underrepresentation of women in elected office and described the efforts of her non-profit organization to change this.

Daniel P. Jones
In the News

This is in contrast to the first group of women in the WHI trial who had received combined estrogen-progestin hormone therapy, and had a higher risk of breast cancer, according to the study.

Although the new findings, reported in the Journal of the American Medical Association, appear to challenge the conventional wisdom, they also demonstrate two important items from my perspective as a communicator and consumer of science news: the need for readers to pay attention to the details of each reported study development, and the value of pursuing a scientific inquiry over a long period.

Community Outreach...

Presentation for Social Work Month...

During the keynote address for the Yale Department of Social Work’s celebration of Social Work Month, Dr. Mazure focused on the innovative interdisciplinary research being conducted in our most recent Pilot Project Program studies. She highlighted, for instance, the development of a model of breast cancer that simulates the human immune system’s response to tumors and chemotherapy. Dr. Mazure also spoke about the need to fund research on women’s health and gender differences that can improve health care for all.

Lecture and Gathering at Yale Club of NYC...

...Yale alumni and guests gathered at the Yale Club of New York City to hear Dr. Mazure speak about the advancement of health information that comes from the biomedical studies funded by our Program. She focused on some of our ongoing investigations, including the use of nanoparticles as microscopic “shuttles” to strategically bind with ovarian cancer cells and deliver a potent chemotherapy agent.

Grand Rounds Presentation...

Depression & Heart Disease: Is There Gender-Specific Risk?

Viola Vaccarino, M.D., Ph.D., gave the annual Grand Rounds lecture sponsored by the Women’s Behavioral Health Research Division of the Department of Psychiatry on May 13th.

She spoke about the emerging science on the association between depression and heart disease, and whether heart disease confers greater risk for depression in women than men.

Depression, according to Vaccarino, is clearly a risk factor for cardiovascular disease for women and men. However, the risk is higher for young women, compared to older women and men. Causes for this difference that are under investigation include biological factors, such as genetic susceptibilities, and social factors, such as trauma in childhood, Vaccarino said.

Dr. Mazure invited Vaccarino to give this year’s lecture because of her significant contributions to the understanding of how women experience cardiovascular disease. Vaccarino is now Professor and Chair of Epidemiology at the Rollins School of Public Health at Emory University. Before leaving Yale in 2000, Vaccarino was a Women’s Health Research at Yale-funded investigator whose studies revealed gender differences in recovery after bypass surgery and pre-heart attack symptoms.

Vaccarino’s interest in psychological and biological health was fostered during her doctoral training in epidemiology at Yale, when she began investigating the interplay between psychological factors and physical conditions, particularly heart disease.
Send your email address to whresearch@yale.edu to receive updates, news and announcements.

Women's Health Research at Yale
135 College Street, Suite 220
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Understanding the complexities of women’s health...

“Factoring in Gender”

YouTube video visit: www.yalewhr.org

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