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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, visit our website:
- www.yalewhr.org

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Foundations Fuel our Work with Sustained Support
- Maximilian E. & Marion O. Hoffman Foundation Renews Partnership
- Werth Family Foundation Continues Commitment

2013 Pilot Project Grants Target Breast Cancer, Autoimmune Diseases, HIV Prevention and Viral Infections

Supporting vibrant, new research designed to uncover solutions to health conditions affecting women today is the goal of Women’s Health Research at Yale’s Pilot Project Program. The four projects selected for funding this year target:

- Breast cancer, the second leading cause of cancer deaths among women.
- Autoimmune diseases, more common in women than men, including antiphospholipid antibody syndrome, (or APS), which can cause stroke, heart attack and pregnancy-related problems, and lupus.
- HIV prevention for young black women, given an infection rate higher than among other young women.
- Sexually transmitted viral infections that affect more women than men and currently have no cure or intervention to prevent recurring outbreaks.

“As with all of our pilot grants since our founding 15 years ago, the investigations by this year’s awardees are designed to generate findings that can be translated as soon as possible into practical benefits for women affected by or at risk for serious health conditions that are unique or more

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JOIN THE SOCIETY OF FRIENDS

Consider a donation to Women’s Health Research at Yale in celebration of a birthday, a special occasion, or to honor 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

Educational and outreach activities are made possible through the generous support of
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Seymour L. Lustman Memorial Fund
The Werth Family Foundation
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Women’s Health Research at Yale was founded in 1998 with initial funding from The Patrick and Catherine Weldon Donaghue Medical Research Foundation.
Werth Family Foundation Reaffirms Strong Partnership

One of our Center’s most generous donors, the Werth Family Foundation, has stepped forward to provide another major gift.

“By strengthening our partnership with Women’s Health Research at Yale, together we are helping bring meaningful health improvements to our communities,” said Suzanne K. Werth, Werth Family Foundation Board Member.

The Werth Family Foundation’s generous commitment this year will help fund our four key missions: jumpstarting innovative research on women’s health; sharing our findings with the community through outreach; facilitating scientific collaborations in our interdisciplinary Research Cores, and training the next generation of women’s health investigators.

Since initiating support of Women’s Health Research at Yale seven years ago, the Werth Family Foundation has helped us dramatically expand our efforts to improve health through scientific discovery.

“The Werth Family Foundation’s vital support of our key missions ensures that we remain mission driven – namely, that we generate and implement new health findings to advance health care,” said Dr. Carolyn Mazure, Director of Women’s Health Research at Yale.

The Werth Family Foundation began supporting our center in 2006 when it helped sponsor a benefit concert that featured Judy Collins. Since then the foundation has renewed its commitment with gifts to fund our Center’s overall operations and particular investigations, including a very timely study of gender differences in treatment of pain in military veterans seeking treatment for Post-Traumatic Stress Disorder (PTSD).

Hoffman Foundation Continues Decade-Long Commitment

The Maximilian E. and Marion O. Hoffman Foundation Inc. renewed its strong, decade-long partnership with our Center this year, providing a very generous grant to support our Pilot Project Program.

This program funds relevant, inventive studies on women’s health and gender differences, allowing Yale investigators to generate findings that can be used immediately to improve health and health care. As importantly, the investigators need these pilot study findings to apply for and obtain external grants from funding agencies such as the National Institutes of Health.

“Continuing support from the Hoffman Foundation is helping propel our vital mission of studying key health conditions affecting women today and rapidly translating our findings into solutions that benefit the community,” said Dr. Carolyn Mazure, Director of Women’s Health Research at Yale. “We are truly grateful for this longstanding, renewed partnership.”

This year’s contribution is the fourth major gift to Women’s Health Research at Yale from the Hoffman Foundation since becoming a partner in our mission in 2003.

Previous generous grants from the Hoffman Foundation have supported the work of our investigators in a wide array of women’s health areas, as well as our Center’s educational outreach efforts to share our findings and health information with the community.
Ultrasound Can Detect Cancers Missed by Mammography: WHRY Research at Center of National Debate

The American Cancer Society recommends yearly mammography beginning at age 40. This is because a mammogram, an X-ray picture of the breast, is the only screening method proven in clinical trials to reduce the number of deaths from breast cancer through early detection. When caught early, most tumors are still small and highly treatable.

Yet mammography is an imperfect screening tool that can miss breast cancers in some women, particularly those with dense breast tissue. In fact, mammograms can miss up to half the cancers in women with dense breasts. Moreover, having dense breast tissue increases breast cancer risk and approximately 40 percent of women have dense breast tissue.

Mammography’s limitations led to a debate in recent years about whether other imaging technologies should supplement mammography to improve the early detection of breast cancer. One technology at the center of this debate is screening with ultrasound, which uses sound waves to produce an image of the breast.

Connecticut became the first state to enact a law mandating that radiologists inform women who undergo mammography if they have dense breast tissue and that they may benefit from supplementary screening tests.

Even before the Connecticut law took effect in October 2009, Dr. Regina Hooley, M.D., Assistant Professor of Diagnostic Radiology and a clinician at the Smilow Breast Center, knew she wanted to study the performance of screening ultrasound to begin exploring the key question for both patients and scientists: Can breast ultrasound screening after mammography effectively improve the cancer detection rate and find cancers missed by mammography?

“When I decided to do the study, I had no idea there was going to be a national movement,” Hooley said.

At least 10 other states – Alabama, California, Hawaii, Maryland, Nevada, New York, Oregon, Tennessee, Texas and Virginia – have enacted laws requiring breast density notification after mammography. As more women become aware of breast density and opt for ultrasound screening, the need for research data on the technology’s usefulness increases.

Against this backdrop, Hooley was awarded a 2012 Women’s Health Research at Yale Pilot Project Program grant to study the performance and value of supplementary breast screening with ultrasound, following mammography. Given Connecticut’s head start on experience with supplemental ultrasound screening, compared to other states, Hooley’s WHRY-funded research is at the forefront of a heated medical debate that has spilled into legislatures across the country.

Critics of the notification laws say that the breast density information requirements are premature because supplemental screening with ultrasound has not been proven to be beneficial. They point to a high rate of false positives with ultrasound screening, leading to unnecessary biopsies.

Supporters of the laws say providing information about breast density and supplementary screening options are positive steps for women who want to
know if they have cancer or reassurance that they do not. They say that finding cancers at a smaller size and stage can reduce breast cancer deaths, and say that false positives with ultrasound can be reduced.

Hooley had mixed opinions initially and now is among the supporters, though she remains committed to following her research data wherever it leads.

Specifically, Hooley’s study is designed to determine the rate at which ultrasound screening can detect breast cancers not found through mammography screening, patients’ opinions about ultrasound screening, and Connecticut physicians’ referral patterns related to ultrasound screening after mammography.

She expects to survey 1,000 patients about their opinions on ultrasound screening after mammography. So far, questionnaires completed by more than 200 women indicate:

- 91 percent said ultrasound screening was important in finding cancers that were not detectable with mammography.
- 45 percent reported anxiety due to awareness of breast density.
- 89 percent said they chose ultrasound screening despite the increased chance of needing additional testing after the ultrasound.

Hooley is circulating a questionnaire to 500 physicians locally and about 800 physicians across the state through the Connecticut Medical Society, and is waiting for an adequate number of responses.

The central component of her study is a review of the records of nearly 4,000 women who underwent mammography and supplementary breast ultrasound screening in the first three years, 2009-2012, after Connecticut’s mandate took effect. Hooley is exploring breast ultrasound’s weaknesses as well as strengths, and seeking ways to improve its medical effectiveness. Although the study will not be completed until next year, Hooley’s preliminary conclusion is that supplementary ultrasound screening after mammography can benefit women with dense breast tissue.

“There is increasing demand for improved breast cancer detection by both patients and their physicians,” Hooley said. “Mammography has its limitations, especially for women with dense breast tissue. Screening ultrasound is a reasonable supplemental screening tool that can detect breast cancer at a rate of 3.5 new cases per thousand (women screened).”

While this detection rate may seem low, it is close to the cancer detection rate for screening with mammography, approximately 5 new cases per 1,000 women screened, Hooley said.

Smilow Breast Center, the clinic where Hooley practices, did not offer ultrasound screening before Connecticut’s breast-density notification requirement took effect. With the law’s implementation, the clinic immediately began offering ultrasound screening by trained technologists using hand-held devices. Radiologists review the images. Connecticut is one of the few states requiring health insurance to cover the cost of supplemental breast cancer screening, and demand for ultrasound screening has kept the clinic very busy, Hooley said.

In the first year after the law took effect, 953 women who were informed about their dense breast tissue after mammography chose to have the extra ultrasound screening and were included in Hooley’s study population. The supplementary screening with ultrasound detected three cancers that were not found by mammography, for a cancer detection rate of 3.2 per 1,000, in this first year population.

Hooley is now reviewing the records of 1,046 women who underwent supplementary ultrasound screening in the third year after the law took effect. She will eventually review the records for the second year, but decided to review the third-year records first. This is because, in the third year, the clinic began

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Involving a new, more sophisticated mammography (tomosynthesis mammography, which provides three-dimensional images) in conjunction with regular mammography.

Hooley wanted to immediately investigate whether this change would affect the rate at which supplementary ultrasound screening detects cancers not seen in mammography. As she expected, the 3-D mammograms revealed cancers at a higher rate than regular mammograms, so the detection rate for supplementary screening with ultrasound not surprisingly decreased from 3.2 to 2.0 new cases per 1,000, in this third-year population.

As radiologists in her clinic gain more experience looking at and interpreting ultrasound images, according to Hooley, the rate of false positives that require follow up tests or biopsies is being reduced. When she and her colleagues first started using ultrasound, they were seeing cysts and other masses that had not been detected with mammography. These findings initially caused concern. However, with more experience the clinicians are learning to recognize benign masses that do not need additional testing, Hooley said.

While she continues to gather evidence about the value of supplementary screening with ultrasound, Hooley thus far views the technology as beneficial, despite limitations and a need to continue improving its effectiveness. Ultimately, she said, research data will help clinicians identify which patients will benefit the most from supplementary screening, and which patients will not need follow-up tests.

“The bottom line is that, with the state notification law in place, patients want to know their options if they are informed they have dense breast tissue. Supplementary screening with ultrasound is a test that can actually give patients more reassurance that they don’t have cancer, or the test can find cancers missed by mammography,” Hooley said. “And this pilot study is helping us understand and improve the use of the technology.”

Q & A with Dr. Regina Hooley

Q: Why is screening with mammography an imprecise tool for detecting cancers in dense breast tissue?

A: Breasts consist of fat and glandular tissue. On mammography, fat is grey while glandular tissue and cancers are white. If a woman’s breast consists of mostly fat, it is easy to see the white cancer in a background of grey fat. However, if a woman’s breast consists of mostly glandular tissue, it can be very difficult to see a white cancer surrounded by white glandular tissue, like searching for a polar bear in the snow. With dense breast tissue, the mammogram is less accurate and can miss more cancers compared to non-dense breasts.

Q: Although your study is not completed, your preliminary conclusion is that supplementary screening with ultrasound after mammography can benefit women with dense breast tissue. Which of your findings lead you to this view?

A: Early results show the cancer detection rate of supplemental screening ultrasound in the general population is approximately 3 per thousand women screened, similar to the cancer detection rate of mammography. Some of these cancers are not seen with the new 3D tomosynthesis mammograms and are generally small, invasive tumors with very good prognoses. As screening with ultrasound is optional and controversial, it is important to be aware of women’s knowledge and opinions regarding this test. Early patient survey results indicate that women are amenable to screening ultrasound because it provides additional information regarding their breast health.
prevalent in women or have gender differences,” said Dr. Carolyn M. Mazure, Director of Women’s Health Research at Yale.

The Women’s Health Research at Yale 2013 Pilot Project Program studies are:

**Distinguishing Between Harmful and Harmless BRCA Mutations to Guide Treatment**
Ryan B. Jensen, Ph.D.
Assistant Professor of Therapeutic Radiology

Genetic tests for BRCA or breast cancer susceptibility gene mutations are becoming widely available. While certain mutations have been specifically linked to cancer risks, these genetic tests are increasingly showing thousands of mutations and variations that have not been characterized. The standard of care for women with harmful BRCA mutations, known to dramatically increase cancer risk, can involve preventive double mastectomy. However, when genetic tests show mutations not yet known to be definitively linked to cancer risks, these ambiguous findings leave patients and health care providers with no clear options.

Capitalizing on the latest biochemical, analytical tools, Dr. Jensen will characterize a multitude of BRCA variations and mutations. His ultimate goal is to develop a high-speed test, a biochemical assay, to distinguish between harmful mutations and innocuous, routinely occurring genetic variations.

This test will be invaluable in guiding decisions for patients who undergo genetic tests, and potentially for designing new treatments to specifically target tumor cells related to BRCA mutations.

**Identifying Bacteria That May Be at the Root of Autoimmune Disorders**
Martin Kriegel, M.D., Ph.D.
Assistant Professor of Immunobiology and Internal Medicine

Autoimmune diseases such as antiphospholipid antibody syndrome (APS) and lupus are more common in women than men, and share an underlying pathological process – proliferation of antibodies that cause harm. In lupus, these antibodies can lead to a variety of symptoms in various parts of the body. In APS, these antibodies can lead to the formation of blood clots that can cause stroke, heart attack, deep vein thrombosis and pregnancy-related problems, such as recurring miscarriages or premature birth.

Focusing on the cause of this underlying pathological process in APS, Dr. Kriegel hypothesizes that normally benign bacteria in the digestive tract trigger the production of the harmful antibodies. His preliminary data from laboratory work has identified a possible antibody-producing trigger among a vast array of different bacteria. While the cause of APS is unknown, patients typically are treated lifelong with anti-clotting medications with adverse side effects that include bleeding.

Now, in what is believed to be the first study to identify such triggers among APS patients, Kriegel will determine which bacteria may be at the root of the disease. His ultimate goal is to identify biomarkers for development of new diagnostic and treatment options to target and stop initiation of the antibodies rather than mitigating the harmful effects of antibodies after production.

**Creating a Video Game for HIV Prevention Among Young Black Women**
Kimberly D. Hieftje, Ph.D.
Associate Research Scientist in Internal Medicine
&
Lynn E. Fiellin, M.D.
Associate Professor of Internal Medicine

Taking advantage of contemporary technologies to communicate with and among young people, Drs. Hieftje and Fiellin will develop a prototype for a video
Current Research

A video game that will be played and shared among women on social media networking sites. The video game will be designed to promote prevention of human immunodeficiency virus (HIV) transmission among young black women (18 to 24 years old).

This population has far higher rates of acquiring HIV and sexually transmitted infections than other young women. The investigators will conduct focus groups with young black women in New Haven to understand barriers to avoiding risk and how these women engage their friends and social networks to gain support for taking steps to reduce risk. Hieftje and Fiellin will then use this community input to create the prototype for a video game to increase understanding of risk-benefit ratio and HIV awareness, promote safe sex practices and encourage partner testing for HIV.

The ultimate goal is to develop an appealing social media/social network video game that young black women will play using a mobile device “app” or via computer download on a social network, making the game widely available to maximize public health benefit.

Developing Immune Therapy for Controlling Genital Herpes Outbreaks in Women
Akiko Iwasaki, Ph.D.
Professor of Immunobiology

Genital herpes, caused by the herpes simplex virus (HSV-2), is a global health threat affecting a fifth of women worldwide and is more common in women than men. Currently, there is no cure and no therapy to prevent or control recurring symptoms or transmission of the virus, which can cause fatalities in children if transmitted from the mother during birth. In addition to a physical burden, women with the infection bear a social and emotional burden, as many feel they cannot marry or bear children as a result of this disease.

Dr. Iwasaki will develop a two-step “prime and pull” intervention for controlling recurrence of the infection. In laboratory models, she will test a potential vaccine, designed to prevent initial onset of genital herpes, as a method in the first step to activate or “prime” anti-viral immune cells to combat already established genital herpes. These anti-viral cells will be recruited to the infection site in the second step via the use of a vaginal ring. The ring will be coated with particular proteins that will “pull” the anti-viral cells to the infection site to establish and prolong the cells’ presence for greater protective effect.

Women’s Health Research at Yale is funding Dr. Jensen’s study in conjunction with the Yale Comprehensive Cancer Center, and Dr. Kriegel’s study in conjunction with a Yale Rheumatic Diseases Research Core Center award to the Section of Rheumatology in the Department of Medicine.

Our Center’s annual Pilot Project Program awards allow Yale investigators to generate previously unavailable data on crucial areas of women’s health. The investigators then use the pilot results from these studies to apply for and obtain much larger external grants to further their research. Since our founding in 1998, we have awarded more than $4.5 million in these “seed” grants and our funded investigators have used their findings to obtain over $52 million in new external grants.

The Women’s Health Research at Yale Pilot Project Program is supported in part by the Maximilian E. and Marion O. Hoffman Foundation, the Seymour L. Lustman Memorial Fund, The Seedlings Foundation, The Werth Family Foundation, and anonymous donors.
Fippinger Grant Drives Inventive New Study: Restructuring Mood to Treat Trauma and Substance Abuse

Patients seeking substance abuse treatment have very high rates of trauma. “To be to able treat either of these disorders it is important to treat both simultaneously,” said Associate Research Scientist Dr. Lindsay Oberleitner.

However, treating these co-occurring disorders can be difficult because individuals who abuse substances often do so to avoid negative moods related to traumatic events rather than confronting these emotions. And patients exposed to trauma often have difficulty engaging intimacy-based emotions, such as expressions of love.

Now, thanks to a recent grant from the Grace J. Fippinger Foundation supporting our Research Core on Women and Trauma, Oberleitner has begun a vibrant study to evaluate a new “mood-exposure” approach to treating substance abuse in patients with co-occurring trauma. Though this new approach may be more effective in women, the intervention is expected to benefit male and female patients.

This group-therapy intervention is designed to improve outcomes for trauma and substance abuse treatment by helping patients recognize, express, accept and change their experience of moods and stress reactions in a controlled and therapeutic manner.

Working with Dr. Sherry McKee, Associate Professor of Psychiatry, Oberleitner will recruit 15 women and 15 men in smaller same-gender groups. She will investigate whether this intervention, drawing from techniques used successfully in behavioral medicine, is more effective for either gender, and expects to complete the study by year’s end.

Our Center has been very fortunate to have the Grace J. Fippinger Foundation as a generous, dedicated partner since 2006.
Council News...

Connecticut Women's Hall of Fame to Induct Linda Lorimer and Congresswoman Rosa DeLauro

Linda Koch Lorimer, J.D., Vice President of Yale University and Special Advisor to our Council, and U.S. Representative Rosa DeLauro of New Haven, an Honorary Member of our Council and longtime advocate of support for research on women’s health, will be inducted into the Connecticut Women’s Hall of Fame this fall.

Founded in 1994, the Connecticut Women’s Hall of Fame honors the achievements of extraordinary Connecticut women, preserving their stories, informing the public and inspiring continued achievements by women and girls. Lorimer and DeLauro will be among four women to be honored at the organization’s 20th anniversary induction ceremony on November 6th, focusing this year on “Women’s Education – Women’s Empowerment.”

Linda has led Yale’s efforts to contribute to revitalizing New Haven and in recent years developed an ambitious strategy and numerous programs to increase the University’s global presence. Recognizing these roles, the Hall of Fame will honor her as a “leader in higher education, spearheading strategic partnerships locally and abroad.” She is a graduate of Hollins University and Yale Law School.

Rosa, who has represented Connecticut’s 3rd congressional district since 1990, is being honored by the Hall of Fame as a “champion of women’s causes.” Throughout her service in Congress, she has sponsored legislation aimed at improving health care and policies related to women, and supporting women’s health research. She helped lead support for doubling the National Institutes of Health’s budget between 1998 and 2003, and has repeatedly introduced legislation on pay equity for women. She earned a bachelor’s degree from Marymount College and a master’s degree in international relations from Columbia University.

Diane Young Turner Helps Connect Community-Yale Jobs

New Haven residents looking for employment are finding jobs at Yale thanks to the efforts of Council member Diane Young Turner, who is Director of a new Yale office called the New Haven Community Hiring Initiatives.

Diane’s role was featured in a YaleNews article on the June 5th grand opening of New Haven Works, a non-profit joint venture of the city Board of Alderman, local employers including Yale, labor unions and local residents. Her office connects job candidates from New Haven Works directly with the University’s Human Resources staff.

“Yale’s goal in developing this internal ‘pipeline’ is to provide laser focus on our effort to reduce the unemployment rate of residents in the city of New Haven,” she told YaleNews. “We are committed to working tirelessly with New Haven Works, community agencies, colleges, and universities, as well as the high school populations to insure that there are pathways and job opportunities here at Yale.”

As exemplified by the extraordinary activists featured above, our Center’s advisory Council consists of community leaders who share our dedication to advancing women’s health research. Members provide advice, raise awareness about our mission, and lead efforts to ensure Women’s Health Research at Yale exists forever.
Press Notes...

Supreme Court Ruling A Victory for Women’s Health Research

Anyone interested in promoting innovative, unfettered research on women’s health and making health care for women more affordable and available should take note of the U.S. Supreme Court’s June 13th ruling on patenting human genes.

In the unanimous decision, the court invalidated five patents held by Utah-based Myriad Genetics on two of the breast cancer susceptibility genes, BRCA1 and BRCA2. The patents had allowed the company to have a monopoly on BRCA genetic testing – important for women to understand their inherited risk of breast and ovarian cancers.

Patient advocates, scientists and clinicians who challenged the patents in court said the genes are products of nature and thus not eligible for patenting. The court agreed, saying that even though Myriad had discovered the precise location and sequence of the genes, and isolated them from the human body, the company did not create or alter any of the genetic information encoded in the genes.

The immediate effect of the decision will be to give patients greater access to genetic testing and provide scientists assurance they can engage in research on these genes without fear of being sued. In a larger sense, as National Institutes of Health Director Francis Collins put it in a statement to the media, “the decision represents a victory for all those eagerly awaiting more individualized, gene-based approaches to medical care.”

To my mind, this ruling is a clear win for women’s health, medical research, personalized medicine, and common sense.

Investigation Update...

Out-of-Network Costs

Even patients who believe they are carefully following their insurance plan’s rules can still be charged for unexpected out-of-network medical costs, says Dr. Kelly Kyanko.

This is among the key findings of a new WHRY-sponsored survey of patients’ experiences published in June in the journal Health Services Research.

“Our data reveal that patient education may not be sufficient to reduce the prevalence and financial burden of involuntary out-of-network care,” Kyanko and her colleagues concluded, citing “system-level failures” as key factors.

The new study builds on a 2010 WHRY Pilot Project Program study that reviewed the experiences of more than 7,800 individuals in private insurance plans. The prior study showed that 8 percent of U.S. patients go out of their health care networks for care, and of those, 40 percent – representing 3 million patients a year – do so involuntarily. While women and men appear to be equally affected by involuntary use of out-of-network services, the study showed that women are more likely than men to face out-of-network charges overall, Kyanko said.

Kyanko was a Robert Wood Johnson Clinical Scholar at Yale when she was a co-investigator on our 2010 pilot study. (The clinical scholars program helped WHRY fund these studies.)

Now a researcher at New York University and primary care physician at Bellevue Hospital Center, Kyanko said in a statement announcing the new study, “We cannot and should not continue to put the onus on patients if our billing systems are not transparent, consistent, or fair.”
Learn how you CAN improve your health!

Our new “Your Health” page provides information on how you can take charge and improve your health.

Go to “Your Health” in the Community section of our homepage for the full details.

www.yalewhr.org