Women’s Health Research at Yale awards four pilot study grants

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This year’s Pilot Project Program grants from Women’s Health Research at Yale [1] target some of today’s most critical areas of women’s health: smoking cessation, which is more difficult for women than men; breast and ovarian cancers, the second and fifth leading causes of cancer death among American women; breast ultrasound screening, which is increasingly being used as supplemental screening in women with dense breast tissue, and neurodegenerative disorders, such as Alzheimer’s disease, which are more common in women than men.

“Smoking, breast, and ovarian cancers, and Alzheimer’s disease exact a huge toll on the health of women,” said Carolyn M. Mazure, director of Women’s Health Research at Yale, and professor of psychiatry and psychology. “The investigations by this year’s awardees, like all of our previously funded studies, are designed with the goal of translating new scientific findings in these important areas into real-world benefits for women.”

The four 2012 Women’s Health Research at Yale pilot grant recipients are:

- **Irina Esterlis,** assistant professor of psychiatry. Smoking quit rates for women have been lower than those for men in every single year for decades, and the most commonly used treatments to aid quitting — nicotine replacement therapies — are not as effective for women as for men. Thus, in order to improve smoking cessation therapies for women, there is a critical need to investigate whether the neurobiology of smoking in women is different from that targeted by nicotine replacement therapies. By using PET scanning (a technology that produces visual images of cellular and molecular level functioning), Esterlis will take the first steps in investigating whether treatments targeting brain receptors—called metabotropic glutamate receptors (mGluR5)—may be a better option for helping women quit smoking. She believes glutamate receptors are excellent candidates because evidence from animal studies suggests there are gender differences in the role of mGluR5 in nicotine addiction, and because glutamate, a key chemical messenger in brain cells, has been shown to be compromised in mood disorders such as depression, one of the reasons that women smoke or relapse to smoking after quitting.

- **Dr. Peter M. Glazer,** professor and chair of therapeutic radiology. This study will begin moving a powerful new antibody (a protein made by immune cells to attack disease agents such as cancer cells) toward clinical application for improving breast and ovarian cancer treatments. Glazer discovered that this antibody, 3E10, can increase the vulnerability of various

types of cancer cells to radiation and chemotherapy. Early evidence shows this effect is greater in breast and ovarian cancer cells related to mutations of two particular genes, BRCA1 and BRCA2. Inherited mutations involving these genes increase risk for breast and ovarian cancers, and many non-familial breast and ovarian cancers are associated with cell-repair defects involving mutations of these two genes. The 3E10 antibody is distinguished from all other antibodies currently in use for cancer treatment by its abilities to penetrate cells and affect cell-repair. The ultimate goal is to provide new, more effective treatments for women with breast and ovarian cancers.

- **Dr. Regina J. Hooley,** assistant professor of diagnostic radiology. Mammography screening can reduce breast cancer mortality through early detection, but has limited ability to detect cancers in women with dense breast tissue. Because of this limitation, other screening methods, including breast ultrasound, have also been used to detect breast cancer. In this study, Hooley will investigate the performance of breast ultrasound since the 2009 implementation of a Connecticut law mandating that radiologists inform women with dense breast tissue that they may benefit from supplemental screening with ultrasound, after the mammography. Through her review and analysis, Hooley and colleagues can determine the usefulness of ultrasound plus mammography in detecting tumors not revealed by mammography alone. As other states and the federal government consider adoption of laws similar to Connecticut’s, the outcome of this study could inform the medical community, legislators and women worldwide about the value and cost-effectiveness of breast ultrasound screening.

- **Dr. Flora M. Vaccarino,** professor of neurobiology and the Harris Professor in the Child Study Center. Women have a higher incidence of disorders involving degeneration of nerve cells such as Alzheimer’s disease. Although studies have examined the role of estrogen in these neurodegenerative diseases, little research has focused on the cellular mechanisms underlying gender differences in aging. Further, no research has examined the role of cells called astroglial cells in gender differences and aging, despite a clear role for these cells in the generation and preservation of nerve cells, and evidence that these astroglial cells facilitate estrogen’s role in supporting healthy nerve cells. Astroglial cells, the most abundant cells in the brain, play roles in key areas including maintenance of the blood-brain barrier, transmission of electrical signals, and repair of nerve cells. Vaccarino will take initial steps toward understanding the cellular mechanisms that underlie gender differences in aging, and will identify genes expressed in astroglial cells involved in aging. Gene identification may enable the targeting of particular cellular genes that control growth and play roles in determining gender differences in neurodegenerative diseases and aging. Thus, this study represents first steps at identifying new targets in developing interventions for neurodegenerative diseases, particularly those which are more common in women.

Women’s Health Research at Yale is funding the studies by professors Esterlis and Glazer in conjunction with the Yale Comprehensive Cancer Center.

Women’s Health Research at Yale was founded in 1998 to address historic gender disparities in medical research by initiating and supporting innovative studies on women’s health and gender differences in health. Since inception, the center has awarded more than $4.4 million in annual pilot grants to more than 60 Yale investigators who have used their results to obtain nearly $50 million in new external grants to further their work.

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[1] http://medicine.yale.edu/whr/index.aspx