

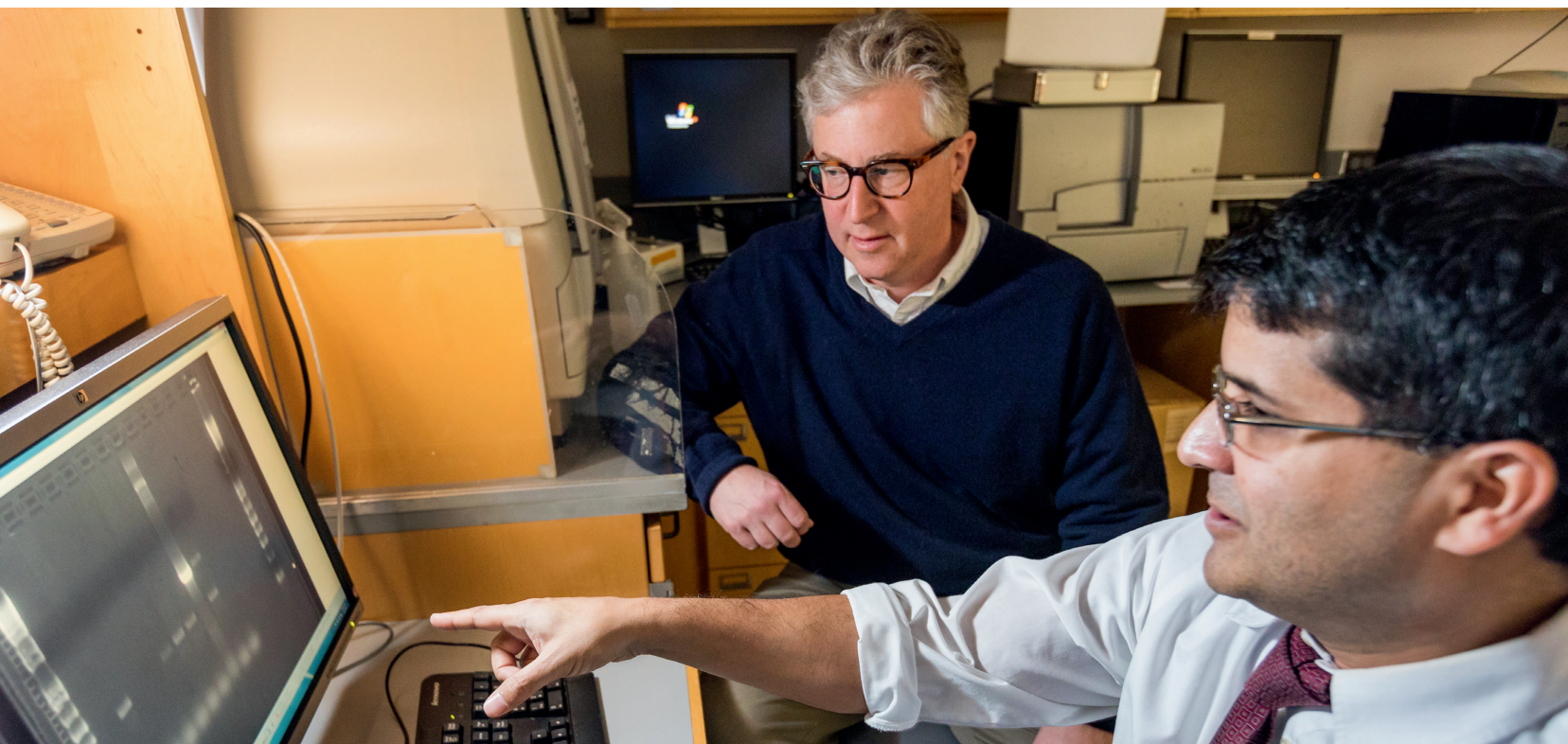
INNOVATIONS

► in Women's Health

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Fighting Breast and Ovarian Cancer with a Lupus Antibody

Of the 1.5 million people living with lupus in the United States, 90% are women. This disease turns the body's immune system against itself, potentially causing extreme pain, fatigue, difficulty thinking clearly, and cardiovascular disease.

Officially known as systemic lupus erythematosus, lupus is distinct among autoimmune diseases in the way circulating antibodies — proteins that when functioning properly help to protect against disease — react against DNA, the body's instructions for building cells and passing traits from parents to children.

Drs. Peter M. Glazer and James Hansen discovered that one specific lupus antibody, known as 3E10, can penetrate cancer cells and make them sensitive to and killed by standard radiation and chemotherapy methods. Notably, this technique has shown significant effectiveness in killing cancer cells with DNA repair deficiencies, such as those with mutations in the tumor-suppressing BRCA2 gene that lead to higher rates of breast and ovarian cancer.

Now, nearly a decade since this amazing discovery and the help of a grant from Women's Health Research at Yale, researchers are close to

After discovering a specific lupus antibody that can penetrate cancer cells and, with a grant from Women's Health Research at Yale, showing it makes cancer cells vulnerable to standard treatments, Dr. Glazer and colleagues are moving a treatment to clinical trials.
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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. Women's Health Research at Yale is a program within Yale School of Medicine. Yale University is a 501(c)(3) nonprofit organization.

Fighting Breast and Ovarian Cancer... (Continued from front cover)

advancing a treatment toward clinical trials while learning more about how this lupus antibody penetrates and kills cancer cells.

“This discovery has unlocked promising new pathways for treatment of BRCA-related cancers that affect so many women around the world,” said Glazer, the Robert E. Hunter Professor of Therapeutic Radiology, professor of genetics, and chair of the Department of Therapeutic Radiology. “We have learned a great deal about how 3E10 interacts with DNA, and we continue to explore how this knowledge could be used to create therapies for other types of difficult-to-treat cancers.”

Dr. Glazer and his colleague Dr. James E. Hansen, associate professor of therapeutic radiology, licensed the rights for their antibody discovery to a company that has validated the work and developed 3E10 as a cancer therapy for human use. An earlier human study in Switzerland attempting to use 3E10 as a vaccine for lupus had already demonstrated that it is nontoxic. Phase 1 clinical trials could begin as early as next year, Dr. Glazer said, likely for patients with cancers related to mutations of BRCA1/2 genes or of another tumor suppressing gene known as PTEN.

“This is very promising,” Glazer said. “I think it will be important to identify the right subgroup of patients for which this is most effective.”

After publishing the results, Dr. Glazer and his colleagues leveraged the data to obtain a pair of large multiyear grants from the National Institutes of Health. With this funding and the help of Yale graduate student Audrey Turchick, the team has discovered that inside a cancer cell, 3E10 sticks to a DNA repair protein called RAD51. This causes the lethality for cancer cells that are deficient in BRCA1 and BRCA2 genes by preventing the cells from conducting the routine DNA repair necessary to sustain themselves.

With ongoing funding from the NIH, Dr. Glazer’s team, including structural biologist Dr. Franziska Bleichert, is building on these findings to enhance the anti-cancer potency of 3E10 and develop therapeutic strategies by identifying ways for the antibody to stick more strongly to RAD51.

In addition, an MD/PhD student in the lab, Elias Quijano, helped identify the capacity of 3E10 to bind with RNA – a type of molecule used to carry out DNA instructions – and carry RNA into a cancer cell, potentially with instructions that can kill the cell. Quijano and Drs. Glazer, Stephen Squinto, and Bruce Turner co-founded Gennao Bio, a company seeking to develop this method of cancer-fighting therapy.

“This was an unexpected discovery that turns out may be very useful,” Glazer said. “We have some data

showing the efficacy of this method against tumors in a laboratory model. It is a versatile platform, because it can deliver different types of RNA in a similar way to how the COVID-19 mRNA vaccines work.”

The research continues, thanks in large part to the investment WHRY made so many years ago.

“I think that type of funding is extremely valuable,” Glazer said of his WHRY grant. “It allowed us to do the sets of exploratory experiments we needed to do to demonstrate our approach was viable and get the larger grants. We showed this is feasible, this is promising.” ◀

ABOUT THE INVESTIGATOR

Dr. Peter M. Glazer received his MD and PhD from Yale University, an MSc from the University of Oxford, and a BA from Harvard University. He is currently the Robert E. Hunter Professor of Therapeutic Radiology, a professor of genetics, and chair of Yale School of Medicine’s Department of Therapeutic Radiology.

As a radiation oncologist, Dr. Glazer makes it his priority to provide patients seeking care at Smilow Cancer Hospital and its Care Centers with the most advanced technologies and evidence-based treatments. His research focuses on new therapeutic strategies for treating cancer and the role of altered DNA repair in tumor progression. His research was recently recognized by the National Cancer Institute with a prestigious Outstanding Investigator Award that supports his efforts to develop novel DNA repair inhibitors for cancer therapy.





Dr. Carolyn Fredericks, seen here with her research team, is seeking to understand the functional impact of a genetic variant on the brains of women who develop Alzheimer's disease and create new opportunities for targeted therapies. © Anthony DeCarlo.

Building a Brain Map for Alzheimer's Disease

What's Behind a Greater Genetic Risk for Women

Like many labs in the early stages of the COVID-19 pandemic, Yale School of Medicine's Clinical Neurosciences Imaging Center temporarily stopped bringing in patients for research. Like many researchers without new subjects to scan, Dr. Carolyn Fredericks and her team took advantage of the pause by taking a closer look at publicly available data.

As a clinician-scientist with a long-standing interest in studying neurodegenerative disease, Dr. Fredericks focused her attention on how brain circuitry changes in women and men as they age. What she and a research associate found surprised her.

Distributed across the brain is a circuit known as the default mode network (DMN), important for episodic memory and what is known as self-referential processing, such as mulling over previous conversations. Studies have shown that this network is specifically targeted by Alzheimer's Disease (AD).

Dr. Fredericks was intrigued to discover that as women age, this circuit begins to look more like people

who are at higher risk for developing AD, even if they show no cognitive symptoms. This circuit in the brains of men, on the other hand, tends, over time, to look more like what has been observed in past studies of brain aging.

"The back parts of the DMN seem to be more connected to the rest of the DMN in women than men," said Dr. Fredericks, an assistant professor of neurology and a clinician specializing in neurodegenerative disorders. "And this is also something we've seen in people with preclinical Alzheimer's disease or an increased genetic risk for the disease. But nobody has explored the impact of this sex difference."

Now, with a grant from Women's Health Research at Yale, Dr. Fredericks is employing a cutting-edge neuroimaging technique to do just that.

"It's very easy to see that women have more cases of Alzheimer's disease than men," Fredericks said, noting that two-thirds of all people affected in our country are women. "But it's more complicated to understand why women are at increased risk."

Examining a Genetic Variant

Women on average live longer than men and so have greater incidence of age-related dementias. In addition, gender-based factors can influence cognitive decline. For example, women tend to have less access to education, physical activity, stimulating employment, and other social determinants of health shown to protect against the cognitive effects of aging.

However, research has also shown a growing biological basis for the different rates of AD in women and men. For example, the disease often advances more quickly in women than men. Dr. Fredericks's new study focuses on the genetic variant that is more likely to affect the development of AD in women than men.

This variant, known as the APOE-ε4 allele, is a mutated form of the apolipoprotein E (APOE) gene on chromosome 19, which helps to create a protein involved in carrying cholesterol and other types of fat through the bloodstream.

Everyone inherits one APOE allele from each parent. For women who carry one copy of the APOE-ε4 variant, the risk of developing Alzheimer's disease can be as high as 12 times as great as someone without this variant. But men with one APOE-ε4 allele have little or no increased risk.

Researchers estimate that 25% of the U.S. population possesses at least one APOE-ε4 allele, and little is known about what might be happening inside the brains of women with this variant to make them so much more susceptible to developing Alzheimer's disease.

“
It's very easy to see that women have more cases of Alzheimer's disease than men ...

”
A High-Powered Model to Make Predictions

Dr. Fredericks is using an extensive database of individuals who have a large buildup in their brains of a protein associated with Alzheimer's disease but no cognitive symptoms. With data from magnetic resonance imaging (MRI) and abundant health information, her team will apply a new technique developed at Yale called connectome-based predictive modelling to identify the specific signature of abnormal brain network connectivity in women and men who carry the APOE-ε4 allele.

This technique divides the brain map into about 268 clusters based on the type of functions carried out in each cluster. The researchers then create a 268 x 268 matrix showing the strength of the connection between each pair of clusters and examine which connections predict the outcomes under investigation. In this study, they are looking to see if the patterns predict the presence of the APOE-ε4 allele as well as short-term memory performance and then comparing the results for women and men.

Based on the size of the dataset and the power of this technique, the researchers anticipate being able to apply what they learn in one group of individuals to predict an outcome in an entirely different set of individuals.

For example, if they notice that women with a particular pattern of brain connections have the APOE-ε4 allele, they expect to see those same brain connections predict the presence of the APOE variant in another randomly assembled group of people.

If, as hypothesized, a specific set of connections only appears in women and not men, they can begin to investigate the functional impact of APOE-ε4 on the brains of women who develop Alzheimer's disease and create new opportunities for therapies aimed at a specific molecular or anatomical target.

While still early in the long process of exploring one of the most devastating diseases within the most complicated biological structure on earth, Dr. Fredericks expressed great hope for this new technique.

“As we move toward an era of tailoring medicine to the individual, we need to recognize there is not always a one-size-fits-all cure,” she said. “Pathology can move differently, and genes can impact health differently for people depending in part on their sex or gender. I think the future of understanding Alzheimer's disease is looking very hopeful. But understanding the specific mechanisms of the disease for individuals will be important to target treatments the right way.” ◀



ABOUT THE INVESTIGATOR

Dr. Carolyn Fredericks earned her MD from Stanford University School of Medicine and her BA and BS degrees from Brown University. At Yale School of Medicine, she is an assistant professor and a member of the Clinical Neuroscience Imaging Center (CNIC), a multidisciplinary group applying innovative imaging methods to the study of brain disease. Her research focuses on preclinical Alzheimer's disease and on less common Alzheimer's variants, using advanced imaging tools to better understand how Alzheimer's disease progresses through functional networks in the brain. Clinically, Dr. Fredericks sees patients with a variety of cognitive and behavioral concerns, specializing in the diagnosis and treatment of neurodegenerative disorders.

Terminology

Dementia: A general term for loss of memory and other mental abilities severe enough to interfere with daily life. It is caused by physical changes in the brain. Alzheimer's disease is the most common type of dementia, but there are many kinds. *Source: The Alzheimer's Association*

Ensuring Bone Health for Adolescents Identifying as Transgender

About 1.4% of American adolescents report identifying as transgender.

That figure comes from a report released in June by the University of California, Los Angeles School of Law's Williams Institute, after analyzing data from the U.S. Centers of Disease Control and Prevention. This estimate almost doubles the organization's previous figure for that age group from 2017 and contributes to an estimated total of 1.6 million persons in the country who identify as transgender.

"For many people, to have one's physical characteristics not align with their own internal sense of their gender is highly distressing," said Dr. Stuart Weinzimer, a professor of pediatrics at Yale School of Medicine and the research director of the Yale Gender Program. "We call it dysphoria – feelings of extreme discomfort with one's own self, that your body and identity are not in sync."

This discomfort can grow at puberty, a time when physical changes can trigger initial concerns about a gender assigned at birth or amplify longstanding distress.

"One of the main jobs of adolescence is to develop one's identity, including gender identity," Weinzimer said. "Most people don't really think twice about their gender identity because they don't have to, just like you don't have to think about breathing. You just do it. However, for people who are not



Drs. Stuart Weinzimer and Christy Oleski are studying how a hormone treatment for a growing population of adolescents might affect their long-term bone health. © Anthony DeCarlo

physically in sync with the way they feel inside, this disconnect can become a barrier to mental health. A barrier to one's own formation of personhood."

Gender dysphoria can present serious, even life-threatening risks, including anxiety, depression, and suicidality. The Yale Pediatric Gender Program provides thorough psychosocial evaluations for those who are experiencing this "disconnect" in their gender identity and seeking help. Individuals considering or already pursuing a social transition are seen with their parents or caregivers and provided the opportunity to discuss and better understand these experiences. After comprehensive consultation, next steps based on individual goals are discussed. In this context, gender-affirming hormone therapy (GAHT) may be offered as a possible option.

As is true of many medications, GAHT may present risks as well as benefits to the individual. For example, patients undergoing GAHT with testosterone can develop unfavorable cholesterol profiles that may increase long-term risk to heart health. Patients undergoing GAHT with estrogen may have an increased risk for blood clots. GAHT can also present other health risks that have not yet been fully explored. Yet, despite knowing potential risks, the experience of gender dysphoria may be so clear and overwhelming, GAHT may be chosen.

Hormones and Bone Strength

Bones are a live organ. On an ongoing basis, bones respond to weight stressors by strengthening themselves, like a computerized bridge programmed with the sense and capacity to somehow reinforce

Terminology

Cisgender: A term used to describe an individual whose gender identity aligns with the one typically associated with the sex assigned to them at birth.

Transgender: A term that may be used to describe people whose gender expression does not conform to cultural norms and/or whose gender identity is different from their sex assigned at birth. Transgender is also considered by some to be an "umbrella term" that encompasses

a number of identities that transcend the conventional expectations of gender identity and expression. People who identify as transgender may or may not decide to take hormones and/or undertake surgical interventions to match their gender identity.

itself and support the load of traffic above. Bones also work a little like an individual retirement plan, in that people make contributions (via minerals deposited in their bones) throughout their lives so when they are older, they can make withdrawals to support themselves. The most rapid period of such investments for increasing bone strength occurs in late adolescence before typically plateauing through an individual's 20s and 30s and generally starting to diminish in the 40s.

"You build up bone strength in your early years, so you have that reserve," said Dr. Thomas Carpenter, a professor of pediatrics and of orthopedics and rehabilitation at Yale School of Medicine. "The presence of sex hormones in puberty plays a significant role in building that strength."

Under the influence of the male hormone testosterone, the strong cylinder around the outside of bones, known as the periosteum, grows in thickness. This is why cisgender adult men (assigned male at birth and identifying as male) tend to have larger, thicker, and stronger bones.

The female hormone estrogen tends to inhibit or suppress the breakdown of bones, which are regularly remodeling as some cells deposit calcium and other minerals and other cells chew up bone cells and dissolve them. In this way, estrogen slows the degradation of bones. This is why cisgender women experiencing lower levels of estrogen through menopause are at greater risk for osteoporosis and fractures.

The typical patterns and timing of pubertal development are altered in those who undergo GAHT during adolescence, and the effects of these hormonal regimens on the process of bone development are not fully understood.

A Better Picture of Bone Health

Standard bone density measurements use an X-ray machine (commonly called DXA), which cannot detect variability in the microstructures that affect bone quality.

"Bone structure is like having a strong chain with a lot of links," Carpenter said. "But if you have one link that is thin, that is where your chain is likely to break. You have to determine if there are those weak spots."

With a grant from WHRY, Dr. Weinzimer, in collaboration with Dr. Carpenter and Yale Pediatric Gender Program Director and founder Dr. Christy Oleszki, is using more sophisticated methods to obtain a picture of the dynamic process of bone development including bone density, quality, and architecture, and they are assessing bone changes over the first year of GAHT in adolescents who identify as transgender.

In addition, the study, based on work begun by former post-doctoral fellow Apoorva Ravindranath Waikar, will catalog metabolic markers of bone health and identify demographic, clinical, and behavioral variables such as diet and exercise that may facilitate or interfere with normal skeletal health in this population as they age.

"This study represents an important step to be able to see for the first time how these metrics change in people undergoing gender-affirming hormone therapy," Weinzimer said. "We don't know what that looks like yet and may find these variability measures are very different in this population. If we find that, we then need to look at ways to mitigate risk in this population."

Possible strategies could include changes to diet and exercise or adjusting hormonal regimens.

The study will ultimately help to inform central clinical questions in GAHT during adolescence, including:

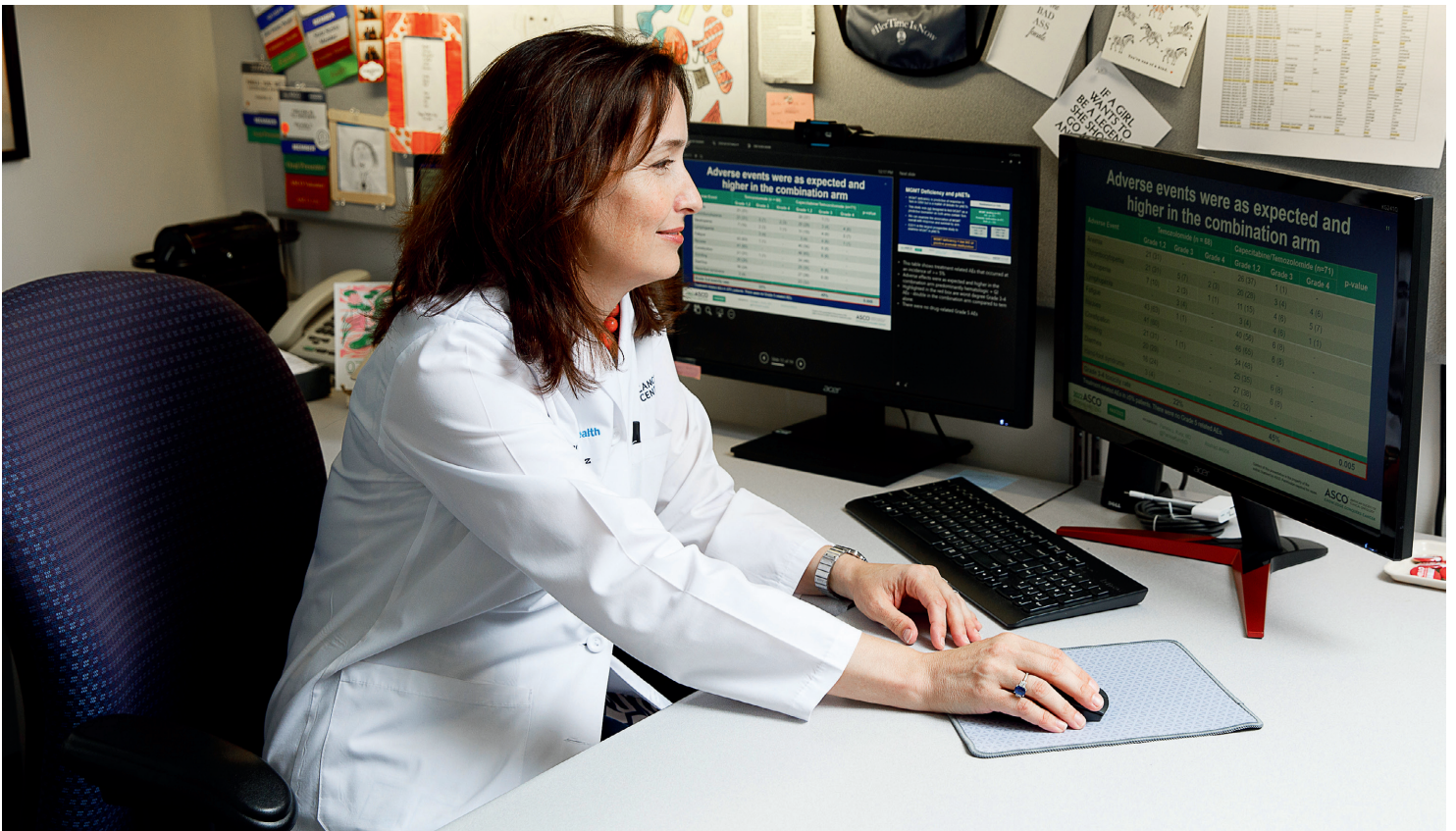
Are current treatments effective in optimizing skeletal health when initiating these hormone therapies? What role do non-pharmacological influences, such as physical activity and diet play in the trajectories of these metrics over time? And, how can we use these data to counsel individuals and their families so the healthiest decisions are made about timing the initiation of these treatments?

"We know that GAHT saves lives," Weinzimer said. "Even though it is effective, we know there are risks. The way to address the risks is not to say, 'It's dangerous — don't do it.' It is to identify what those risks are, understand the physiology, and learn how to counteract the negative effects." ◀



ABOUT THE INVESTIGATOR

Dr. Stuart Weinzimer earned his BA in molecular biochemistry and biochemistry at Yale and his MD at the Albert Einstein College of Medicine in New York. He returned to Yale in 2002 to focus his research on the continuous glucose sensors and insulin pumps toward the development of an artificial pancreas. As the Research Director of the Yale Gender Program, he conducts studies investigating the effects of gender-affirming hormone therapy on skeletal and cardiometabolic health and qualitative studies examining the decision-making processes around fertility preservation.



Dr. Pamela Kunz is analyzing a large U.S. database of multiple completed clinical trials in patients with neuroendocrine neoplasms to identify sex-based differences in treatment-related side effects. © Anthony DeCarlo

Sex Differences in Treating Gastrointestinal Cancer

Dr. Pamela Kunz understands that workplace equity for health care systems employees and health equity for patients share a goal: improving care.

“If we are going to give everyone an opportunity to achieve their full health potential, we need people who think differently in our hospitals and other care facilities – people who come from different backgrounds, different genders, and different races,” said Kunz, an associate professor of medicine and the vice chief of diversity, equity, and inclusion for the medical oncology section at Yale Cancer Center. “I like to think about solutions. About how I can use a scientific lens to overcome historic knowledge gaps about sex, gender, race, and ethnicity. And advance patient health equity.”

With this year’s Wendy U. and Thomas C. Naratil Pioneer Award

and co-funding from Yale Cancer Center, Dr. Kunz is achieving that goal. An oncologist, associate professor of medicine at Yale School of Medicine, and director of the Center for Gastrointestinal Cancers at Smilow Cancer Hospital and Yale Cancer Center, Dr. Kunz is conducting one of the first studies to examine sex differences in treating neuroendocrine neoplasms (NENs), a rare form of cancer often found in the gastrointestinal tract.

“There have been very few studies about sex differences in many types of cancers,” Kunz said, noting how much research dating back decades involved exclusively studying males. “I think the assumption has been that there wouldn’t be sex differences, so it wasn’t deemed relevant to look for them. But in many fields, we are seeing how much sex and gender can play a role in

how diseases develop and respond to treatment.”

Research has found sex differences in the 12,000 Americans diagnosed with an NEN every year, including where the cancer starts and survival rates. But few studies have been dedicated to examining sex differences in the side effects caused by treating this type of cancer.

The most common chemotherapy and radiation therapy treatments for NENs can produce toxic side effects that contribute to poor quality of life, worse outcomes, and increased costs for both patients and the health care system. These challenges are especially important in chronic cancers such as NENs, particularly if treatments are interrupted or doses reduced.

One small, retrospective study on this subject found that female patients with the disease receiving two multikinase

inhibitors, a type of anti-tumor drug, were more likely than men to develop liver toxicity, headaches, fever, nausea and vomiting, hair disorders, skin disorders, and dizziness. Another small study of a combination of two chemotherapy pills for treating NENs showed that female patients had twice the rate of low platelets (cells that help blood clot) and five times the risk of low white blood cells (the cells that fight infection).

While it remains unclear why females have higher rates of these treatment-related toxicities, Dr. Kunz said this difference could stem from how some of these medications are given at fixed doses or doses based on height and weight – measurements that do not account for differences in metabolism and body fat, nor the different systemic effects of female and male sex hormones.

“Any one of these things can affect how females metabolize medications” Kunz said. “And can result in increased side effects.”

In her WHRY pilot project, unlike the earlier smaller sample studies, Dr. Kunz and her team are analyzing a large U.S. database of patient information and four large completed clinical trials to benchmark the extent of sex differences in NEN treatment outcomes and adverse events and to better design future studies that include sex as a key variable.

For example, one of the categories of increased side effects in female patients involves lower counts of red and white blood cells and platelets in bone marrow. If the study confirms an increase in treatment-related toxicities for female patients with NENs, oncologists could administer boosters for these immune system cells, possibly even preventatively. Or, researchers could conduct studies to determine if lowering doses for female patients taking certain medications

could reduce negative effects without lowering the medication's effectiveness at targeting cancer cells.

Importantly, Dr. Kunz also is identifying candidate genes or common gene variations to help determine which patients are at risk for a single toxicity from treatment or a cluster of related toxicities. The overall goal is to optimize treatment selection for all patients to better predict outcomes and mitigate toxicity, perhaps by conducting a genetic test before treatment to tailor the therapy to the patient.

Because patients with NENs typically have chronic, slow growing cancer that spreads to other sites, Dr. Kunz wants to make sure these patients can tolerate treatments that can extend for a decade or more.

“Our number one goal is to improve the lives of patients when they are on long-term treatments,” she said.

Dr. Kunz expressed her appreciation for WHRY's funding, which, with guidance from WHRY, has led to supplementary funding from a private foundation.

“This is an example of how contributions can multiply,” she said. “By stringing together smaller amounts of money, it can grow into a lot more. Not just additive – it's synergistic.”

That synergy extends to her team, which includes Dr. Maryam Lustberg, associate professor of medicine (oncology) and director of the Center for Breast Cancer at Yale Cancer Center; Dr. Namrata Vijavergia, assistant chief of gastrointestinal medical oncology at Fox Chase Cancer Center in Philadelphia; and Dr. Stephen T. Sonis, a professor at the Harvard School of Dental Medicine and senior surgeon at the Dana-Farber Cancer Institute. She has also recruited a pair of internal medicine residents, Dr. Wan Ying Tan from Norwalk

Hospital and Dr. Caroline Gordon from Yale New Haven Hospital.

“I love teaching and mentoring,” Kunz said. “As I transition from mid-career to someone more senior, I want to inspire the next generation to do research on how sex and gender influence health. And to broaden health equity for everyone.” ◀



ABOUT THE INVESTIGATOR

Dr. Pamela Kunz earned her MD from Dartmouth Medical School and her BA from Dartmouth College. At Yale School of Medicine, she is an associate professor of medicine in the Division of Oncology and director of the Center for Gastrointestinal Cancers at Yale Cancer Center (YCC) and Smilow Cancer Hospital. She is also the chief for gastrointestinal medical oncology and the vice chief of diversity, equity, and inclusion for the medical oncology section at YCC. Dr. Kunz is an international leader in the treatment and clinical research of patients with neuroendocrine neoplasms and is advancing the field through clinical trials and translational science that are defining the next generation of therapies for patients with this rare diagnosis.

Building Momentum **WHRY's Undergraduate Fellows Advance Women's Health**

Changing medical research and practice is a team effort. Women's Health Research at Yale mentors undergraduate students as well as graduate students and rising junior faculty members to ensure that the next generation of scientists and medical providers fully account for the health needs of women and sex-and-gender differences affecting health. Here are a few examples of what our former undergraduate fellows are up to now:



Milana Bochkur Dratver, '18

Milana Bochkur Dratver, '18

After graduating from Harvard Medical School in the spring, Milana began a residency in obstetrics and gynecology at the Hospital of the University of Pennsylvania. Inspired by the experiences of her mother and grandmothers navigating the health care system, Milana is the first member of her family to become a doctor.

"I always knew I wanted to practice medicine, but I did not know what area or specialty," she said. "It is one of the reasons I signed up for the WHRY fellowship. Once I learned about the dearth of attention to women's health and data on sex-and-gender differences, it became clear to me. There are a lot of questions still to answer.

At medical school, Milana gained a new appreciation for how sex and gender inform health beyond the reproductive system.

"That's something that medical school curriculums are starting to focus on," she said. "When I started, the topic of sex and gender in health was covered in a day. Now it gets discussed more holistically."

At WHRY, Milana worked in the human laboratory of Dr. Lynn Fiellin at the Yale Center for Health and Learning Games, helping to design and develop video game interventions and assessments for adolescents and young adults. At Harvard, she conducted research on gestational diabetes and obesity in pregnancy and would like to continue pursuing research to benefit women.

"In order to be a good clinician, you need to constantly keep up with the latest research," she said. "I also want to be a part of it – make new discoveries and share them."



Kaveri Curlin, '19

Kaveri Curlin, '19

After graduation, Kaveri worked as a research assistant fellow at the National Institutes of Health in a laboratory

studying the social determinants of obesity. She is now a student at the University of California, Irvine School of Medicine.

"I am really enjoying my studies and its special concentration learning about health equity and access," she said. "I often think of my days as a WHRY undergraduate research fellow. I know that participating in the fellowship opened doors for me and allowed me to become the medical student that I am today."

Kaveri worked with WHRY on our project to integrate a focus on sex and gender into Yale School of Medicine's curriculum, providing evidence to support conversations with course directors, who have since agreed to address the issue. She presented this work at the 2018 Sex and Gender Health Education Summit in Utah, and the conference's organizers selected her work as one of the four best submissions. She was also a co-author of a published article on this work.

At UCI School of Medicine, Kaveri is a member of Leadership Education to Advance Diversity – African, Black and Caribbean (LEAD-ABC), a program designed to reduce health disparities among these communities.

Most recently, Kaveri was selected by the American Association for the Advancement of Science (AAAS) as a Mass Media Fellow, a program to provide hands-on science journalism experience for undergraduate or graduate science students. Kaveri is spending the summer as a health and science reporter for the Philadelphia Inquirer, seeking to make science more accessible to the general public.

"I care deeply about reducing health disparities in minority communities," she said. "And I believe that science communication and outreach are two important advocacy tools. ◀"

Women: What's in a Name? **by Carolyn M. Mazure, PhD**

It took women almost a century to secure the right to vote in our nation, from the Seneca Falls Convention in 1848 until the ratification of the 19th Amendment in 1920. An Equal Rights Amendment, asserting equity in employment and other opportunities, was first introduced in Congress in 1923. Despite being denied this legal protection in 1923 and subsequently, women in the twentieth century entered the paid workforce pursuing jobs that fed families and attained education that led to better jobs and increased autonomy in unprecedented numbers.

Beyond employment and education challenges, obtaining health care informed by scientific research also presented a serious obstacle for women. The National Institutes of Health (NIH), which traces its beginnings to 1798, grew to the world's largest single funder of biomedical research after World War II. Yet, it historically excluded women as study participants until an alliance of women from the public sector and one from Congress joined forces in the

1980s to change this practice. Needed change was accomplished through the 1993 NIH Revitalization Act, which required the inclusion of women in clinical studies funded by the NIH.

With clinical investigations finally considering women's health beyond reproductive health, research findings with data on women became a growing part of the scientific literature in the early years of the twenty-first century. Nonetheless, debate over the value of studying the biology of women's health and sex differences in health continued.

The terms sex and gender evolved during this period of debate to distinguish studying differences in biology – using the term sex (females and males), and in social experience – using the term gender (women and men). It was the NIH Office for Research on Women's Health that led the successful effort to establish a 2016 NIH requirement that biology-based laboratory studies, not only clinical studies, explore the underpinnings of health differences between women and men.

Today, as our scientific and cultural understanding expands, we have learned that sex and gender are not binary. And, in science, as our knowledge grows so must our efforts to welcome everyone in the identities they bring, and to enhance the precision of our language in adopting terms that value everyone.

Even so, we must not forget our history and the descriptive terms that serve us well.

Twenty-five years after the inception of our research center, we remain committed to advancing the health of women, studying how sex and gender influence health between and among groups of people, and successfully challenging historic inequities for the benefit of all. To my mind, maintaining the name “women” recognizes the historic obstacles surmounted by and enormous contributions made by those who came before us. Just as important, it embodies the continued relevance of challenges with us now and of those ahead as we advance health for women and all persons. ◀

A New Role for Mona Gregg

Having served Women's Health Research at Yale since its founding almost 25 years ago, Mona Gregg has been appointed as the center's newest special advisor. As she retires from her current position, we will be forever grateful for the immense impact she has had on advancing the health of women. We look forward to her counsel to ensure the continued success of our center in the years ahead.

Women's Health Research at Yale

► Better science, better lives ► ►

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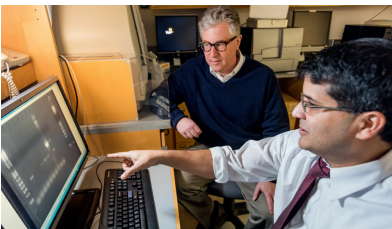
Women's Health Research at Yale is changing the landscape of medical research and practice by ensuring the study of women and examining health differences between and among women and men to improve the lives of everyone.

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