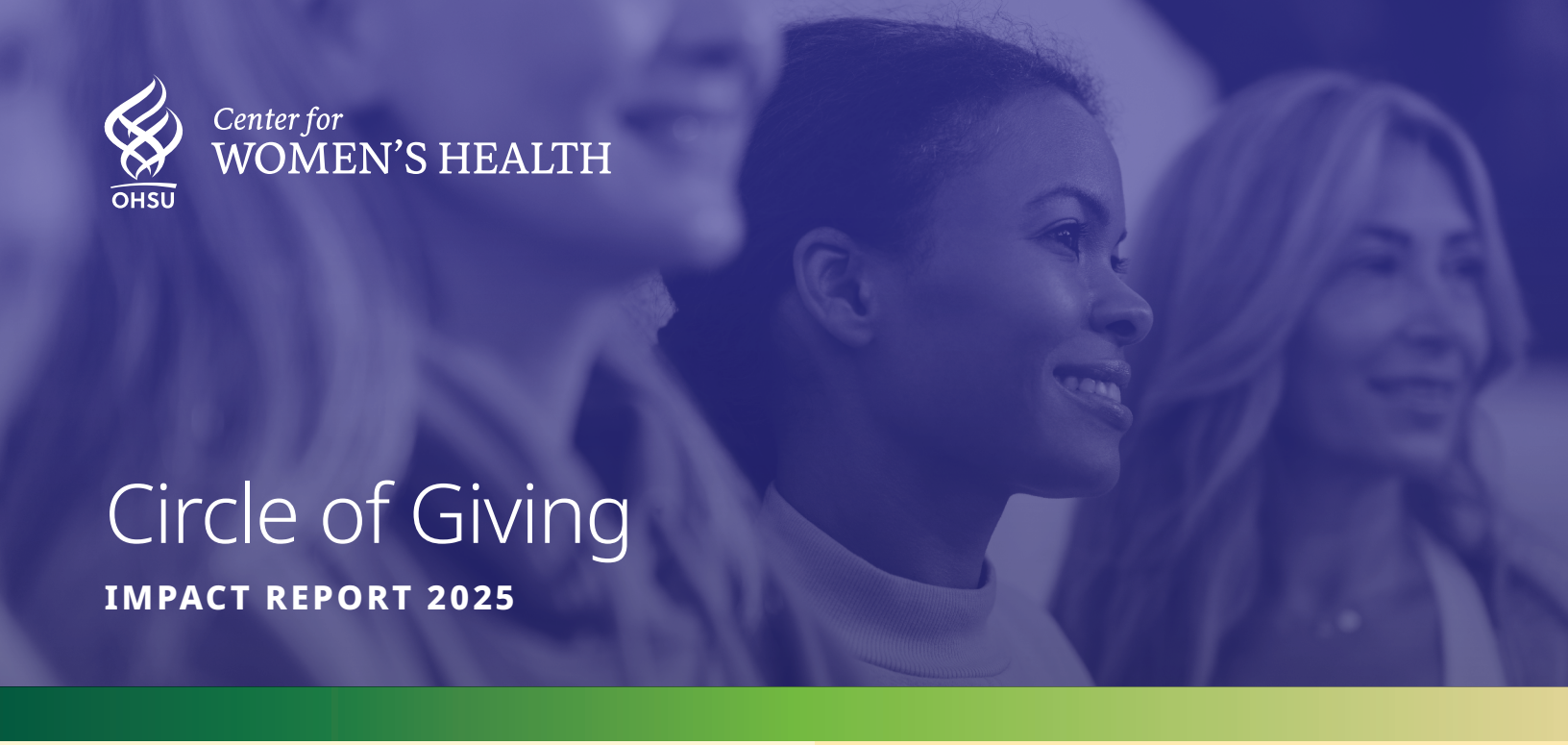

Center for WOMEN'S HEALTH
OHSU

Circle of Giving

IMPACT REPORT 2025

This year, the OHSU Center for Women's Health Circle of Giving continues to show that intentional, early investment in women's health research transforms lives. Thanks to your generosity, OHSU researchers are asking bold questions, testing new ideas and turning discoveries into meaningful care for women everywhere. This year's report will also highlight groundbreaking projects related to Alzheimer's disease — a condition that disproportionately affects women — underscoring the Circle's role in tackling urgent health challenges.

Since its founding in 2007, the Circle of Giving has awarded $3.85 million in grants to 33 projects that would not have advanced without your support. Collectively, these projects have secured more than $75 million in additional funding — a return of more than 20 to 1. In other words, every dollar contributed has sparked more than twenty additional dollars in research and clinical advancements, proving the ripple effect your commitment creates.

This extraordinary return reflects more than numbers — it represents lives changed and futures reimagined. The stories in this report illustrate how your partnership accelerates innovation, closes critical gaps in care and advances health equity. Together, we are shaping a future where every woman has access to the highest standard of care.

On behalf of the OHSU Center for Women's Health and the many lives touched by your generosity — thank you for your vision, dedication and belief in what is possible.

Maria I. Rodriguez, M.D., M.P.H.
Julie Neupert Stott Endowed Professor in Women's Health
Director, OHSU Center for Women's Health
Director, OHSU Center for Reproductive Health Equity

Circle of Giving by the Numbers

33 grants awarded

$3.85M total funds awarded by the Circle of Giving

$75M+ additional research funds from projects initially supported by the Circle of Giving

110+ papers related to research fueled by their Circle of Giving grant have been published

70+ additional funds received for projects that received seed stage funding from the Circle of Giving

2007 the year the first Circle of Giving grant was awarded

130 people have supported the Circle of Giving since inception

For every $1 donated to the Circle of Giving, **$20** comes back to OHSU in additional investment in scientific discovery

Research Focus: New Discovery Sheds Light on Why Women Face Higher Alzheimer's Risk

Award year: 2018

Julie A. Saugstad, Ph.D.
Professor of Anesthesiology and Perioperative Medicine, OHSU School of Medicine
Professor of Molecular and Medical Genetics, OHSU School of Medicine
Molecular and Medical Genetics Graduate Program, OHSU School of Medicine
Neuroscience Graduate Program, OHSU School of Medicine
Program in Molecular and Cellular Biosciences, OHSU School of Medicine

Ursula Sandau, Ph.D.
Instructor of Research in Anesthesiology and Perioperative Medicine, OHSU School of Medicine

Initial breakthrough: Of the 7.2 million Americans living with Alzheimer's disease (AD), nearly two-thirds are women. A woman's estimated lifetime risk of developing AD at age 65 is 1 in 5. Women in their 60s are about twice as likely to develop Alzheimer's during the rest of their lives as they are to develop breast cancer.

One key suspect is the APOE4 gene. Women who carry it face faster cognitive decline, more brain shrinkage and higher risk of developing AD than men of the same age. Researchers have discovered that tiny cellular messengers called exosomes may play a role. In women with AD, these exosomes contain unique miRNAs that target a protein called Intersectin1 (ITSN1) — a key player in brain cell communication and memory — causing levels of this protein to drop. Both APOE4 and ITSN1 are linked to a brain signaling pathway triggered by reelin, another protein that helps neurons "talk" to each other. In 2018, Dr. Saugstad and Dr. Sandau received funding from the Circle of Giving to explore whether APOE4 and exosomes disrupt reelin's signal, potentially worsening memory loss in women.

Ripple effect: Fueled by momentum from the Circle of Giving grant, Dr. Saugstad and Dr. Sandau received an additional $4.05 million in funding to advance their research. At the heart of this support was the highly competitive $3,758,962 R01 grant from the National Institutes of Health. R01 grants are one of the most prestigious and sought-after awards in medical research, reserved for projects with exceptional promise and impact. In addition, they also received $267,194 from the JTMF Foundation to acquire two pieces of medical equipment and $30,000 from the Collins Medical Trust to further strengthen their efforts.

Subsequently, the duo published two papers and headed up a task force initiative. With a team of fellow scientists, they published a paper in *Frontiers in Cell and Developmental Biology: Special Research Topic*.

Update: Dr. Saugstad and Dr. Sandau have forged a dynamic partnership unraveling the complexities around the impact of AD on women, blending mentorship with groundbreaking science. Their collaborations have sparked new avenues of inquiry and launched them into new independent research ventures.

Dr. Saugstad has a new partnership with Dr. Aleksandar Milosavljevic, Director of the Program in Quantitative and Computational Biosciences at Baylor College of Medicine, to study the contribution of extracellular RNA genomic loci to AD.

Dr. Sandau has received her own Circle of Giving grant in 2025 for another AD-related project, "Establishing the impact of APOE4 on brain extracellular vesicles in females with AD." She and her colleague, Randy Woltjer, M.D., Ph.D., will use these funds to study the relationship between changes in cerebrospinal fluid EVs and changes that occur in the brain of women with AD. Dr. Sandau will use the data from this investigation to support an R01 NIH application to identify new therapeutic targets best suited to treat AD in women.

> *"We are honored to share that our Circle of Giving project has been so fruitful and brought so many excellent returns to us in funding, research and publications."*
>
> **— Julie A. Saugstad, Ph.D., Ursula Sandau, Ph.D.**

Research Focus: Advancing Safer Hormone-based Treatments for Alzheimer's in Women

Award year: 2016

Phillip Copenhaver, Ph.D.
Professor of Cell, Development and Cancer Biology, OHSU School of Medicine
Director, Cell and Developmental Biology Graduate Program, OHSU School of Medicine
Neuroscience Graduate Program, OHSU School of Medicine
Program in Molecular and Cellular Biosciences, OHSU School of Medicine
Cancer Biology Graduate Program, OHSU School of Medicine

Initial breakthrough: Menopause marks a significant shift in a woman's life that brings not only hormonal and physiological changes but elevates the risk of developing Alzheimer's disease (AD). A key factor in this increased vulnerability is the decline of estrogen, which plays a protective role in brain health. Without it, women are more susceptible to the build-up of toxic amyloid proteins, a hallmark of AD. However, giving women experiencing menopause estrogen increases their risk for blood clots and cancer. There is an urgent need for therapies that replicate estrogen's benefits to the brain without its harmful side effects. Researchers are studying an experimental drug, STX, that copies some of the helpful effects of estrogen, including shielding brains from amyloid toxicity. But scientists still don't fully understand how it works. In 2016, Dr. Copenhaver received a Circle of Giving award to investigate how STX protects brain cells from amyloid damage. Safety testing in mice with AD-like symptoms would determine if STX offers protection without the harmful effects of estrogen.

Ripple effect: As a result of the Circle of Giving award, Dr. Copenhaver received $1.17 million in additional funding to support this research. This includes $75,000 from Coins for Alzheimer's Trust (Rotary Foundation), $600,000 over 4 years from the Veterans Administration and $499,991 from NIH.

In addition, Dr. Copenhaver's research resulted in the publication of two papers inn *Neurobiology of Disease* (2022) and *Journal of Alzheimer's Disease* (2016).

Update: Using a combination of cell culture assays and mouse AD models, Dr. Copenhaver and his team have shown that STX does protect neurons against the toxic effects of amyloid in different contexts. The results strongly suggest the model STX could be used to prevent decline in brain function in women at risk for AD.

Dr. Copenhaver's team has added a new collaborator to the team, Nora Gray, Ph.D., who brings her expertise in investigating how modulating antioxidant response and mitochondrial function impact neural and cognitive health and how these pathways can be altered with plant-based interventions.

> *"Using mouse models, we have been developing a new advanced imaging method to visualize how STX protects against Alzheimer's pathology in the brain, which has been quite promising — all we need now is funding!"*
>
> **— Phillip Copenhaver, Ph.D.**

Research Focus: Exploring How Metabolic Health Influences Alzheimer's Risk

Award year: 2020

Martin Kelly, Ph.D.
Professor of Chemical Physiology and Biochemistry, OHSU School of Medicine
Neuroscience Graduate Program, OHSU School of Medicine
Graduate Program in Biomedical Sciences, OHSU School of Medicine

Oline Ronnekleiv, Ph.D.
Professor of Chemical Physiology and Biochemistry, OHSU School of Medicine
Neuroscience Graduate Program, OHSU School of Medicine
Graduate Program in Biomedical Sciences, OHSU School of Medicine

Initial breakthrough: Many women who are experiencing Alzheimer's disease (AD) have completed menopause and no longer produce estrogen. On top of that, they often experience obesity and type 2 diabetes, which may increase their risk of developing AD. Researchers have been studying how hormones like estrogen and body conditions like being overweight and diabetes affect parts of the brain that control hunger, metabolism and reproduction. One of them is a natural form of estrogen called 17 beta-estradiol (E2). A group of brain cells called kisspeptin neurons help regulate both metabolism and reproductive functions. They live in the hypothalamus, a part of the brain that is the "control center" for the brain. Studies suggest that Hypothalamic neuronal dysfunction may be linked to AD. To help get close to an answer, Dr. Kelly and Dr. Ronnekleiv used their Circle of Giving funds to evaluate kisspeptin neuronal projections and functions in different brain nuclei. In addition, they discovered that neurons in a region of the hypothalamus called mammillary bodies became hyperexcited in a mouse model of AD.

Ripple effect: Propelled forward by this work, Dr. Kelly and Dr. Ronnekleiv received $1,965,692 in additional funding and published a paper in *eNeuro* (2021), "Arcuate and Preoptic Kisspeptin Neurons Exhibit Differential Projections to Hypothalamic Nuclei and Exert Opposite Postsynaptic Effects on Hypothalamic Paraventricular (PVH) and Dorsomedial (DMH) Nuclei in the Female Mouse." The PVH and DMH are regions of the brain that are important for many automatic functions including feeding and metabolism.

Update: In 2023, Dr. Kelly and Dr. Ronnekleiv made a surprising discovery in an area of the brain called the mammillary bodies: a substantial jump in a brain chemical called glutamate, which acts like a green light, telling brain cells to get active and communicate. They also noticed these brain cells were overstimulated, a possible early warning sign of AD. Portland State University student, Cole Martinson, assisted in this work, which became the focus of his honors thesis.

An article about their findings was published in the *Journal of Neurophysiology* in 2025.

> *"We are very grateful for this funding from the Circle of Giving members. It helped us at a critical time trying to reestablish funding in our labs and open new avenues of research."*
>
> **— Martin Kelly, Ph.D., Oline Ronnekleiv, Ph.D.**

Your support for the Circle of Giving goes beyond philanthropy — it is a powerful investment that will echo for decades. The breakthroughs you help make possible today will shape care, inform policy and improve outcomes for generations to come. Thank you for standing with us and keeping women's health at the forefront, fueling progress where it matters most.

Together, we are turning bold possibilities into lasting progress.

FOR MORE INFORMATION

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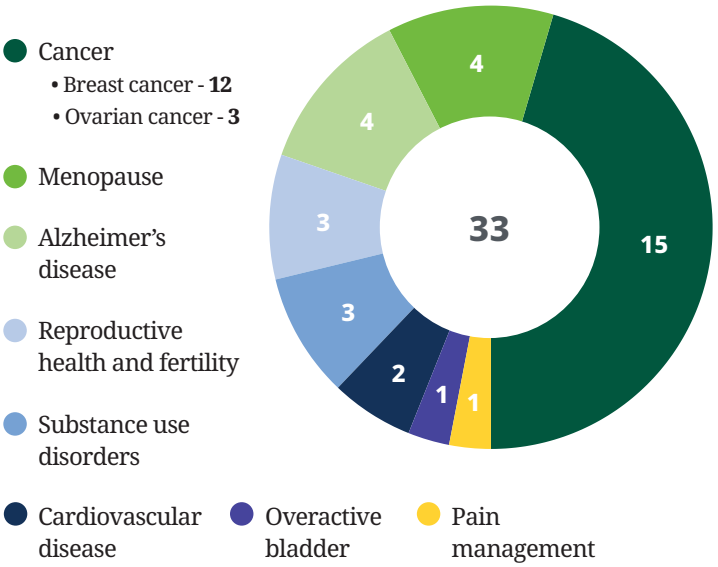
Circle of Giving Research by Clinical Area



Annual Circle of Giving Granting Cycle

October	Request for Proposals (RFP) opens
January	Applications due and review process begins
January – February	Independent peer reviewers evaluate each application
March	A panel of experts, called the Scientific Review Committee (SRC), meets to discuss and rank applications. The top five move on to the next round.
March – April	Circle of Giving selection committee volunteers review the top five proposals to select the three finalists that will present at Granting Day
May	Finalists present at Granting Day, and Circle Members vote to select the awardee