Josh Baxt
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Miller School Researchers Receive $1.86M Grant to Study Relationship between Menopause, DNA Damage, and Alzheimer’s

A research team at the University of Miami Miller School of Medicine, led by Claude-Henry Volmar, Ph.D., and Claes Wahlestedt, M.D., Ph.D., who are both in the Department of Psychiatry and Behavioral Sciences and the Center for Therapeutic Innovation, has received a $1.86 million National Institutes of Health/National Institute on Aging (NIH/NIA) R01 grant to study how menopause generates DNA damage and whether that increases a woman’s risks of developing Alzheimer’s disease. The ultimate goal is to identify biomarkers that could detect increased Alzheimer’s risk at an early age.

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(From left) Claes Wahlestedt, M.D., Ph.D.; Natalie Ricciardi, Ph.D. candidate; Jessica Dennison, Ph.D. candidate; and Claude-Henry Volmar, Ph.D.

“Alzheimer’s is a complex, polygenic disease, and once it takes hold, is extremely difficult to treat,” said Dr. Volmar, director of the research laboratory. “The solution is almost certainly prevention, and this grant will help us understand disease progression in women and hopefully lead to early interventions for those at greater risk.”

Researchers have long known that Alzheimer’s disease affects men and women differently. Almost two-thirds of Alzheimer’s patients are women, and quite often, the drugs being tested to fight the disease affect men and women differently. In addition, both menopause and aging can generate DNA damage. Nobody knows precisely how this damage impacts brain function, but the Miller School team is hoping to find out.

“There are major sex-dependent differences,” said Dr. Volmar. “Women show symptoms earlier and suffer longer. If we want to prevent Alzheimer’s, we need to figure out what's happening early, before post-menopause. Nobody else is doing that right now from the DNA damage and epigenetics perspective.”

Replicating Menopausal Changes

Previous animal studies in Alzheimer’s models have completely removed ovaries, abruptly changing hormonal dynamics. The Miller School team will instead take a more gradual approach, trying to replicate the changes that happen during menopause.

“If we remove the ovaries, the model goes straight to post-menopause,” said Dr. Volmar. “We want to know what's happening early and throughout that progression. If we find good biomarkers, and a woman in her 20s expresses those biomarkers, we could intervene early and hopefully have greater success.”

In addition to Drs. Volmar and Wahlestedt, two Ph.D. candidates will make major contributions to this research: Jessica Dennison in the neuroscience program and Natalie Ricciardi in the Department of Biochemistry and Molecular Biology. Dennison was recently awarded an F31 student fellowship from the NIH/NIA to study the role menopause plays in Alzheimer’s.

Catching Alzheimer’s Early

Once the team has collected data, in collaboration with Augur Precision Medicine, they will compare their results to a large U.K. biobank that has been collecting blood biomarkers from Alzheimer’s patients. By comparing the two datasets, they hope to pinpoint the molecular signals that could indicate a woman is at much higher risk for Alzheimer’s.

Catching the disease early could give clinicians greater opportunities to slow it down. Younger patients tend to have more robust DNA repair systems, and that could play an important role in keeping them healthy.

“We’d like to be able to prime the body’s repair mechanisms,” said Dr. Volmar. “Ideally, if someone had a molecular signature that showed increased risk for Alzheimer’s, we could boost their DNA repair enzymes and really slow the disease down.”

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