

ALZHEIMER'S SCIENCE NEWS

SUMMER 2022



PROTEINS MAY EXPLAIN COGNITIVE RESILIENCE IN PEOPLE WITH ALZHEIMER'S PATHOLOGY

In Alzheimer's disease, the abnormal buildup of toxic proteins damages brain cells involved in memory and other mental abilities. Yet some adults are cognitively resilient, meaning their brain scans show Alzheimer's pathology but they have no significant cognitive decline. On the other hand, some people do have cognitive impairment without Alzheimer's pathology, a condition known as frailty.

An Alzheimer's Disease Research grantee, Becky Carlyle, PhD, of Oxford University, was part of a team investigating what causes these differences.

Scientists analyzed brain tissue samples from two prior studies of people with varying levels of Alzheimer's pathology and cognitive function. They studied hundreds of proteins involved in cell signaling, metabolism, protein degradation, and DNA damage. They also recruited 100 people with varying levels of cognitive function and pathology.

The researchers found that resilient adults have increases in energy production, as well as synaptic signaling—a process that allows cells to



Becky Carlyle, PhD

communicate with each other. They also have less damage to waste clearance and antioxidant proteins. By contrast, frail adults display metabolic shifts similar to patients with Alzheimer's, and they show increases in DNA repair proteins, indicating higher DNA damage.

Dr. Carlyle and her team suggest that these newly identified proteins could serve as biomarkers to help measure people's risk for Alzheimer's. Additionally, the dysregulated proteins seen in frail individuals could potentially serve as therapeutic targets in the future.

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PRESIDENT'S CORNER

We're making critical progress in the fight against Alzheimer's disease—and you help make that possible.

I'm excited to share this issue of our newsletter with you. You'll read about scientists we fund who are identifying how bacteria in the gut can help program brain cells toward health or disease. Others are unlocking genetic secrets to understand why certain risk factors for Alzheimer's impact people differently based on their ancestry, which could lead to new treatments.

Advances like these offer so much hope to people living with Alzheimer's and their families.

With help from friends like you, we will one day defeat this mind-stealing disease. Thank you for your commitment and generosity.

Stacy Pagos Haller

RESEARCHER SPOTLIGHT: LAURA COX, PHD

Little is known about why certain cells in the brain become dysfunctional in Alzheimer's disease, but new studies suggest that gut bacteria may play a role.

Alzheimer's Disease Research grantee Laura Cox, PhD, at Brigham and Women's Hospital in Boston, is trying to identify microbes and metabolites that affect brain aging and to understand how microbes program brain cells toward health or disease.

There are four major cell types in the brain which can be affected by gut bacteria: neurons, microglia, astrocytes, and oligodendrocytes. Dr. Cox is studying whether gut bacteria can affect the programming of these cell types to switch them from a healthy to a dysfunctional state.

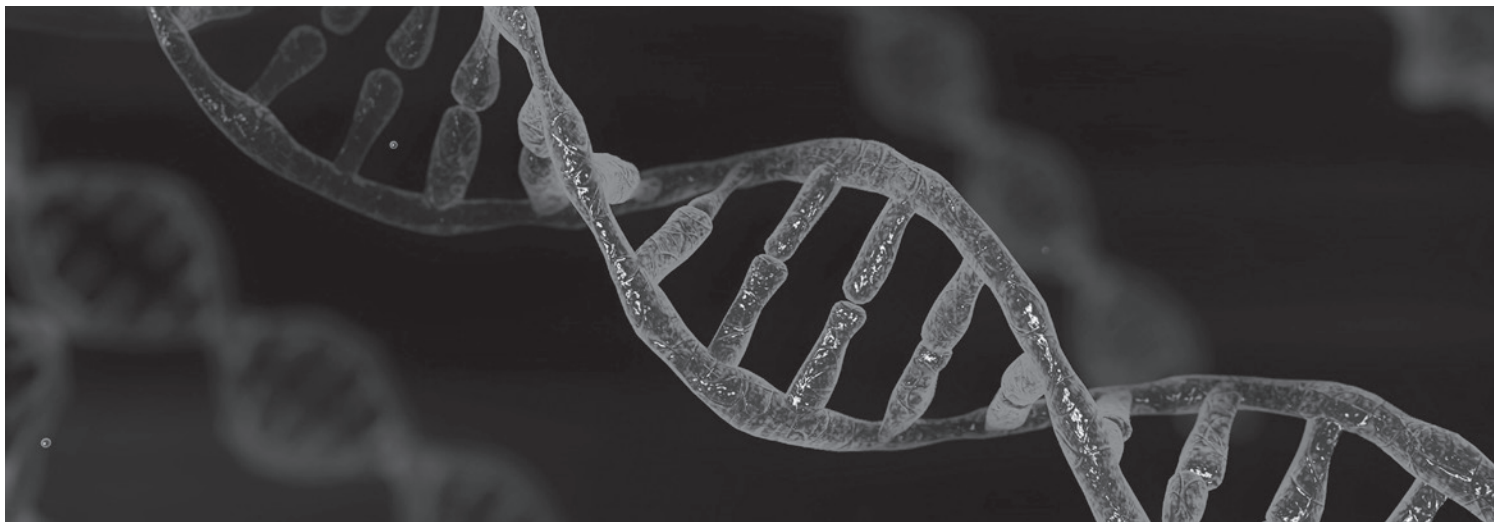
She is also searching for microbial metabolites that may affect brain cells, in hopes of uncovering novel therapeutics that could protect the brain in aging and in Alzheimer's disease.



Laura Cox, PhD, is investigating how gut bacteria can program brain cells toward Alzheimer's disease.



STUDY EXPLAINS WHY IMPACT OF GENETIC RISK FACTOR VARIES BY ANCESTRY



Understanding how genetic risks impact populations differently could help scientists find ways to prevent Alzheimer's.

Scientists have long known that people with a variation of the apolipoprotein E gene, called APOE ϵ 4, are at higher risk of developing Alzheimer's. However, it doesn't affect all populations the same way.

Previous research has shown that people of European ancestry are at greater risk. They have higher levels of APOE ϵ 4 gene activity in their brains, as well as RNA and protein released due to that gene, than those of African descent. But the reasons for this were unclear.

Now, with help from an Alzheimer's Disease Research grant, Jeffery Vance, MD, PhD, at the University of Miami, has discovered key differences in nearby portions of DNA.

His research team looked at gene regulatory units known as "enhancer regions" which can influence

APOE ϵ 4 expression. They identified regions with higher enhancer activity in European/Japanese samples compared with samples from African descent. These regions also interact with APOE in microglia and astrocytes, which play an integral role in the progression of Alzheimer's disease, indicating that these interactions can mitigate or exacerbate Alzheimer's risk.

These findings provide a critical area for further study, as scientists translate how genetic variations affect Alzheimer's risk among people of different ancestries.

In an era of personalized medicine, understanding differences in APOE ϵ 4 expression could help researchers develop treatments that target these enhancer regions to decrease APOE ϵ 4 expression and protect against Alzheimer's.

TAKING CARE OF YOURSELF AS AN ALZHEIMER'S CAREGIVER

Caring for a person with Alzheimer's can be stressful and demanding. If you or someone you know is looking after a family member with this disease, it's important to remember that you have needs of your own—and that you must take care of yourself as well as your loved one.

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CREATE A LEGACY OF HOPE

When you include Alzheimer's Disease Research in your will or estate plan, you ensure that innovative, mind-saving research will continue to advance for years to come.

Making a gift by bequest allows you to leave a lasting legacy of hope that will benefit future generations as we continue discovering treatments for this mind-stealing disease—and one day a cure.

It may also lessen the burden of taxes on your family, and there may be estate tax savings as well.

In addition to a gift in your will, there are many other planned giving opportunities you can use to help win the fight against Alzheimer's disease. Visit brightfocus.org/plannedgiving to learn more or contact Charlie Thomas, our Planned Giving Manager, at 301-556-9362 or plannedgiving@brightfocus.org.



You can continue to support groundbreaking research for years to come.



brightfocus.org/stopAD

TAKING CARE OF YOURSELF... CONTINUED FROM PAGE 3

To help cope with the strain of caregiving, give yourself permission to feel your full range of emotions—both positive and negative. This enables you to express them and deal with them. It is all right to:

- **Be angry:** Turn your energy into positive action. Clean a closet, take a walk, or talk with someone.
- **Be frustrated:** Stop what you are doing, take a deep breath, and begin a different activity.
- **Take time out:** Sit in a favorite chair in a quiet room, take a trip to the store, or spend a few hours out with friends.
- **Ask for help:** Explore family, friends, and local agencies for resource services. Many doctors' offices and clergy provide referrals.
- **Recognize your limits:** You are a valuable person. Take care of yourself, too!
- **Make mistakes:** No one is perfect, and mistakes help you learn.
- **Grieve:** It is normal to be sad over the loss of the way things used to be.
- **Laugh and love:** Now more than ever, it's important to have meaningful connections.
- **Hope:** Tomorrow, the day may go smoother, a friend may call, and new treatments may be found.

To learn more, visit: brightfocus.org/alzcaregiving

Please share this newsletter with someone you know who might be interested in learning about some of the latest advancements in research to diagnose, prevent, treat, and cure Alzheimer's disease.

This newsletter is published by Alzheimer's Disease Research, a program of BrightFocus Foundation.

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