CERTAIN TYPES OF FATS LINKED WITH DEMENTIA

When scientists study the impact of diet on the development of disease, they often rely on an individual’s self-reported information. To obtain more objective data, Alzheimer’s Disease Research grantees Majken Jensen, PhD, and Manja Koch, PhD, both of Harvard University, examined collected blood samples from 1,252 older adults who took part in a clinical trial on memory. Of these, 498 later developed dementia.

Drs. Jensen and Koch looked for 45 different types of fat particles and found that individuals with higher levels of saturated fats in their blood were more likely to experience cognitive losses and develop Alzheimer’s disease than those with higher levels of linoleic acid, a polyunsaturated omega-6 fatty acid found in many plant oils.

Scientists had already begun to link diets higher in saturated fat to a higher risk of cognitive decline, but this study, published in a leading scientific journal, is one of the first to use such a high number of subjects’ blood tests to understand the link between diet and later brain health.

Experts have long recommended the Mediterranean diet for brain health. Past research has shown that it is prudent to choose olive, canola, grapeseed, avocado, sunflower, peanut, and other vegetable oils, and to avoid partially hydrogenated oils, which contain trans fats. This study did not find a direct link between trans fats and cognitive decline, but artificial trans fats have been banned in the U.S. due to their link to type 2 diabetes and cardiovascular disease, which are themselves risk factors for dementia.

This study helps confirm that saturated fats—found in many foods, such as butter, cheese, red meat, and coconut oil—are best consumed in moderation to protect both brain and overall health.

IN THIS ISSUE

- President’s Corner
- Deciphering the Alzheimer’s Disease Glyco-Code
- Restoring Immune Function to Treat Alzheimer’s
- “Zinc Fingers” Gene Therapy Reduces Toxic Tau in Mice
- Breaking News: FDA Approves New Alzheimer’s Drug
- Sweet and Spicy Tofu Pad Thai
The fight against Alzheimer’s has never been more urgent.

Today, over 6 million Americans have this disease, with 500,000 new people developing Alzheimer’s every year. Each person is someone’s husband or wife, father or mother, sibling or friend. And the heartbreak they face is immeasurable.

That’s why we are so committed to stopping Alzheimer’s. Your support helps us fund critical advances that increase our understanding of it and pave the way for new therapies. In this issue of our newsletter, you’ll learn how scientists we support are restoring immune function to treat this disease. Another group is testing “zinc fingers” to reduce toxic tau. Plus, you’ll read about a new drug recently approved by the FDA to treat Alzheimer’s.

I have never been more hopeful than I am now that we can one day make Alzheimer’s a thing of the past. Thank you for supporting our mind-saving work.

Stacy Pagos Haller

---

Alzheimer’s disease is the most common cause of dementia. However, the current understanding of its pathology isn’t sufficient to provide new ways to prevent or treat it. It is crucial to understand its molecular alterations to decode the underpinning disease mechanisms, discover new biomarkers, and improve treatment strategies.

Emerging evidence suggests a connection between extracellular matrix (ECM) molecules and the incidence of Alzheimer’s. The extracellular matrix provides structural support for cells and is made up of large molecules like collagen, enzymes, proteins, and groups of carbohydrates called glycans.

ECM molecules facilitate cell-to-cell communication and support the attachment and interaction with neighboring cells. Changes in brain ECM molecules are associated with Alzheimer’s disease pathology. With help from an Alzheimer’s Disease Research grant, Manveen Sethi, PhD, of Boston University, is investigating the structure and biology of proteins and glycans in patients with the disease.

Dr. Sethi will extract glycans from tissue specimens and perform detailed structural analysis using mass spectrometry to establish functional relationships and explore their critical roles in Alzheimer’s.

Her study has two goals. First, to identify the structural differences in the glycans that occur in Alzheimer’s pathology to understand the underlying molecular mechanisms. And second, to use this information to develop clinical markers for early detection of Alzheimer’s and assess if they could be a potential area for drug development.

This project will generate the fundamental knowledge required to improve the diagnosis and treatment of patients with this memory-robbing disease.

Manveen Sethi, PhD
“ZINC FINGERS” GENE THERAPY REDUCES TOXIC TAU IN MICE

Scientists we fund were able to reduce tau protein levels in animal models, which could offer hope for new treatments for Alzheimer’s disease.

Tau is a protein that misfolds in Alzheimer’s, causing it to accumulate in the brain and contribute to cognitive decline.

Alzheimer’s Disease Research grantee Sarah DeVos, PhD, of Harvard-affiliated Massachusetts General Hospital, used genetic engineering to lower tau expression with a hybrid protein called a zinc finger protein transcription factor. It has two domains: the zinc finger protein and the transcription factor. Dr. DeVos and her colleagues designed the zinc finger protein to recognize the tau gene and engineered the transcription finger to suppress the transcription of tau protein.

Using animal models, they injected a virus that targets the tau-making gene. The virus was either targeted to the hippocampus, a part of the brain involved in learning and memory that is affected by tau pathology, or to the blood to determine if the virus would cross the blood-brain barrier and have beneficial effects on the brain.

In both cases, a single dose reduced tau protein levels by 50%-80% in the brain within two weeks, and the effect lasted for the duration of the study, which was almost one year. The mouse models treated with zinc fingers developed fewer dystrophies, and their neurons were protected from toxicity.

While more research is needed, this provides further evidence that reducing harmful tau protein could help people with Alzheimer’s disease, even after neurodegeneration has begun.

RESTORING IMMUNE FUNCTION TO TREAT ALZHEIMER’S

Scientists have discovered a potential new treatment approach for Alzheimer’s—restoring the function of regulatory T cells (Tregs) to control the body’s immune response and suppress brain inflammation associated with this disease.

For his study funded by Alzheimer’s Disease Research, Alireza Faridar, MD, of Houston Methodist Research Institute, hypothesized that Tregs—important immune modulators that suppress the immune response—might lose their function in Alzheimer’s, leading to increased inflammation.
BREAKING NEWS
FDA APPROVES NEW ALZHEIMER’S DRUG

The Food and Drug Administration (FDA) recently approved the clinical use of a new drug, aducanumab, to slow the cognitive decline in Alzheimer’s. Marketed under the name of Aduhelm, it removes the brain amyloid protein associated with this disease. The FDA’s accelerated approval, while further testing takes place, can continue to help validate the drug’s efficacy in modifying the disease’s effects.

This news fuels great hope for the future of Alzheimer’s research. There are currently at least 29 potential treatments in late-stage Phase III clinical trials. In addition, Alzheimer’s Disease Research recently announced funding for 59 new research grants to jump-start promising new studies.

RESTORING... CONTINUED FROM PAGE 3

Dr. Faridar detailed continuing results from this clinical study where he and his colleagues showed that the number of Tregs were decreased in people with Alzheimer’s. To determine whether these Tregs could suppress inflammation, they were co-cultured with pro-inflammatory immune cells. Results showed that Tregs from people with Alzheimer’s were unable to elicit an appropriate immune response compared to people with mild cognitive impairment.

To restore their immunogenic properties, Tregs from people with Alzheimer’s were expanded in a dish with factors to amplify their suppressive activity. This increased immunoregulatory genes, suppressed the proliferation of response T cells, and increased suppression of pro-inflammatory immune cells.

Restoring Treg cell function has been successful in treating other neurodegenerative diseases. As a result of key early funding from Alzheimer’s Disease Research to get this idea off the ground, larger organizations, including the Gates Foundation, are providing Dr. Faridar with new and greater resources to continue to pursue whether this could lead to a safe and effective treatment for people with Alzheimer’s.

SWEET AND SPICY TOFU PAD THAI

Studies show that eating a nutritious diet is a simple way to help protect your brain’s health.

Ingredients:
1 tablespoon peanut oil
2 garlic cloves, minced
1 small jalapeño, seeds and membranes removed, minced
1/2 cup sliced mushrooms
1 package tofu, drained and cut into cubes
1 package pad thai rice noodles
1/4 cup lime juice
1/4 cup low-sodium soy sauce
1 tablespoon honey
1/2 cup chopped nuts
1/2 cup shredded carrots
2 tablespoons cilantro

Directions:
Using a wok or deep saucepan, sauté oil, garlic, jalapeño, mushrooms, and tofu over a medium-high heat until tofu is toasted brown and vegetables are tender. Prepare noodles according to package instructions, then add to the tofu-vegetable mixture.

In a small bowl, whisk together lime juice, soy sauce, and honey. Toss together with the tofu and vegetables. When thoroughly heated, remove from stove. Place into dishes and top each with nuts, carrots, and cilantro.

Yield: 6 servings

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. The information in Alzheimer’s Science News is provided as a public service and should not in any way substitute for the advice of a qualified health care professional, nor is it intended to constitute medical advice. BrightFocus Foundation does not endorse any medical product or therapy. Copies of Alzheimer’s Science News are available upon request.

Alzheimer’s Disease Research is a BrightFocus Foundation Program
22512 Gateway Center Drive, Clarksburg, Maryland 20871 • 855-545-6237 • brightfocus.org/stopAD
© BrightFocus Foundation, 2021