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Encouraging Breakthrough for Future Alzheimer's Treatment

Crossing the Blood-Brain Barrier

A research team led by BrightFocus grantee Matthew Campbell, PhD, has discovered a potentially new way to get medications into the brain to help clear it of a buildup of the toxic amyloid beta that leads to Alzheimer's.

The brain's circulation is tightly controlled to keep out damaging substances. This is often referred to as the blood-brain barrier (BBB). Researchers are focusing on getting excess amyloid beta out of the brain before it creates problems. However, because of the BBB, it's not possible to send medications through the bloodstream to do so.

"As clearance mechanisms slow down with age," Campbell explains, "amyloid and plaques build up in the brain. Regulating these tight junctions and getting them to open up using drugs could potentially allow the amyloid beta to diffuse out of the brain."

Campbell continues, "Working with a mouse model of Alzheimer's, we've taken mice at a very young age, pre-symptomatically, injected them with drugs that open up the barrier transiently, and followed the same mice for one year. At the end of that year, the mice have better cognitive function, better memory, and higher levels of amyloid beta in their circulation, which means that it's coming out of the brain."

Future research may lead to human use and, one day, by modulating tight junctions in this fashion, oral agents could be absorbed and delivered through the bloodstream to the brain to treat Alzheimer's.

Campbell's research is already being widely discussed in the field, and appears poised to drive further advances to finding effective treatments and cures for Alzheimer's.



Matthew Campbell, PhD

President's Corner



HOPE FOR THE FUTURE

In 2025, just nine years from now, an estimated 7 million

Americans will suffer with Alzheimer's disease – and that's not counting the family members and caregivers affected by it.

The good news is, the National Institutes of Health has set a goal of curing Alzheimer's disease by 2025.

So there is hope.

Hope that's within reach, thanks to scientists around the world, including those you'll read about in this newsletter, who are dedicated to solving this disease. They are working diligently toward a cure. And, with the help of our incredible donors, they will get there.

This was evident at the most recent Society for Neuroscience (SfN) meeting. More than 30,000 neuroscientists from more than 85 countries gathered together in Chicago, Illinois, to present emerging science, learn from experts, forge collaborations with peers, and explore new tools and technologies to defeat Alzheimer's.

To be a presenter at SfN is an honor among peers, and a recognition of important scientific discovery. I'm so thrilled that BrightFocus-funded researchers, like Dr. Maya Koronyo-Hamaoui (featured on page 3), had that opportunity, showcasing their promising Alzheimer's research.

Together with our loyal donors and the dedicated researchers, we are moving closer to a cure.

Stacy Pagos Haller

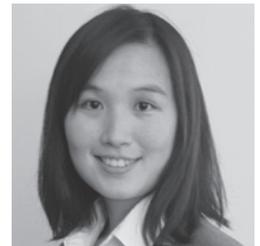
Meet 2015 Grantee Ming-Hsuan Ou-Yang, PhD

Ming-Hsuan Ou-Yang developed an interest in neurodegenerative diseases while studying for her PhD at the State University of New York, Stony Brook. She then began working with Robert Vassar, PhD, at Northwestern University in Chicago, continuing her Alzheimer's research by studying the roles of Beta-secretase 1 (BACE1), the enzyme that starts the production of the toxic amyloid beta peptide in Alzheimer's disease.

"With Alzheimer's, people lose the capability to perform day-to-day tasks required for independent living, but they're also deprived of their memories, a very important part of being human that we use to define who we are," Ou-Yang says. "So for me, the ultimate goal of researching Alzheimer's disease is to develop a treatment to maintain the integrity of our life to the end."

Ou-Yang's BrightFocus-funded research explores how BACE1 regulates learning and memory. While drugs that block BACE1 to prevent amyloid beta production are currently

being tested in clinical trials as treatments, Ou-Yang's research team has found that mice lacking the BACE1 gene have impaired memory. They hypothesize that BACE1 is important for normal memory. Their research is testing this hypothesis in order to gain a better understanding of how BACE1 functions and whether there may be potential side effects of future BACE1 drugs, thus devising ways to ensure the safety and effectiveness of such agents.



Ming-Hsuan
Ou-Yang, PhD

"I believe that with every failure, we are one step closer to the solution," Ou-Yang shares. "But no great achievement can be made without support from society at large. Philanthropy has always been a driving force for scientific discoveries, and the generosity of your support will continue to motivate and inspire our research."

Recruiting Fresh Immune Cells

BrightFocus-Funded Research Presented at Society for Neuroscience 2015

BrightFocus grantee Maya Koronyo-Hamaoui, PhD, is exploring how it may be possible to “recruit” fresh immune cells to replace or invigorate the brain’s existing immune cells that have become depleted and flawed during the preclinical stage of Alzheimer’s disease. She recently presented her research at the Society for Neuroscience conference (SfN).



Maya Koronyo-Hamaoui, PhD

removing amyloid beta, and ultimately they’re believed to become pro-inflammatory themselves.

What does the research show? In mice, Koronyo-Hamaoui and her team at Cedars-Sinai Medical Center in Los Angeles have experimented with different methods of invigorating the brain’s host defense against amyloid beta plaques. These include weekly immunization with a drug that is known to enhance natural recruitment of blood-borne immune cells to diseased parts of the brain and therapeutic injections of bone marrow-derived immune cells into the peripheral bloodstream. They also tried therapies together.

Results were successful, and showed that in 13-month-old mice exhibiting Alzheimer’s symptoms, these interventions helped rescue and preserve synapses (the ends of neurons through which nerve signals pass), and helped to maintain cognitive function. In addition, treatment helped reduce overall amyloid burden.

Why do we need fresh immune cells?

Growing evidence shows that, in the earliest stages of Alzheimer’s, an army of immune cells are responsible for clearing neurotoxic amyloid beta protein from the brain.

But over the course of a decades-long battle, as brain tissue succumbs to chronic Alzheimer’s-associated inflammation, the host defenses get worn down. They become less and less efficient at

Knowledge Is Power

BrightFocus Urges the FDA to Expand Neurodiagnostic Tools

BrightFocus President and CEO Stacy Pagos Haller was recently invited to speak at a public medical devices workshop convened by the U.S. Food and Drug Administration (FDA). The purpose of this workshop was to get feedback and address the need for neurodiagnostic tools that could help assess cognitive function in patients with dementia or other conditions.

Speaking on a panel of key stakeholders, Haller called on the FDA to support the development of much-needed cognitive tools and devices. She said that these tools can give important information to families affected by diseases such as Alzheimer’s, and provide valuable data to researchers studying the effectiveness of drugs and other treatments.

“Knowledge is power,” Haller reminded the FDA. “It is critically important to help people monitor their own brain health and take steps to manage their risk.”

Haller pointed out that these tools could also help caregivers, who are often the “second victims” of these diseases. Caregivers could monitor their own health, provide observations about the health of the person with the disease, and offer other data to researchers.

Haller called on the FDA to support an environment that encourages continued research and the development of much-needed tools and devices. She urged the agency to “embrace the uncertainty” in order to keep pace with a rapidly changing field.

Brain Food

A Healthy Recipe Contest Winner

This dish from Roxie C. is quick and easy to prepare, nutritious, and delicious!

Santa Fe Chicken Salad Scoops

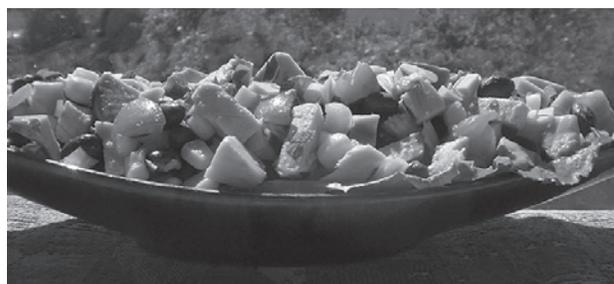
Ingredients:

- 2 cups diced cooked chicken breast
- 1/3 cup small diced avocado
- 1/3 cup frozen yellow corn kernels, cooked
- 1/3 cup chopped tomato
- 1/4 cup chopped sweet onion
- 1/2 cup drained and rinsed canned black beans
- 2 Tbsp. snipped parsley
- 2 tsp. lime juice
- 1 tsp. chopped chipotle pepper in adobo sauce
- 4 romaine lettuce leaves

Directions:

1. Combine all ingredients except lettuce; mix well.
2. Fill lettuce leaves, dividing equally, and serve.
3. Serves 4.

Tip: Prepare filling ahead of time and then spoon into lettuce leaves just before serving.



TIPS FOR FIGHTING ALZHEIMER'S DISEASE

Exercise, nutrition, and mental stimulation are part of a healthy lifestyle and a possible way of managing this devastating disease.

Stay Active

- Go for a walk
- Take a dance class
- Go swimming

Enjoy a Healthy Diet

- Fresh fruits
- Green leafy vegetables

- Whole grains
- Fish, nuts, seeds, and oils high in omega-3 fatty acids

Exercise Your Mind

- Read newspapers or books
- Work on puzzles
- Learn a new hobby



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. The *Alzheimer's Disease Research Review* is published by Alzheimer's Disease Research, a program of BrightFocus Foundation, located at 22512 Gateway Center Drive, Clarksburg, Maryland 20871, 301-948-3244, 855-345-6237, www.brightfocus.org.

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