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Watch out, Alzheimer's! Big new grant at UCI, new drug trial at Hoag coming for you

'We remain in our infancy in our field compared to other fields of medicine, but we're learning at an incredible rate.'





(File photo by Mark Rightmire, Orange County Register/SCNG)

By **TERI SFORZA** | tsforza@scng.com | Orange County Register
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Do you make a lot of lists so you don't forget stuff? Blank on the name of a colleague you've worked with for 20 years? Lose track of what day it is?

We do too, but are cautioned not to panic — that's normal as we age.

But getting lost driving to a familiar place, or failing to remember the name of that colleague later, or losing track of what season it is, can signal a more serious memory condition: Alzheimer's.

Alzheimer's is characterized by abnormal deposits of proteins throughout the brain, impairing the function of once-healthy neurons. It's the No. 3 cause of death in Orange County and about 84,000 people in O.C. are either living with, or at risk of developing, the condition, according to county statistics and the Alzheimer's Orange County association.

Nationwide, some 6.2 million people aged 65 and older have Alzheimer's, and that's expected to more than double by 2050.

So it's with some hopeful, enlightened self-interest that we tell you how busy this last week has been for Orange County researchers probing a condition known as "the long goodbye":

- UC Irvine, a longtime hub of Alzheimer's investigation, has been awarded a \$47 million grant from the National Institute on Aging to support a team developing next-generation mouse models for studying late-onset Alzheimer's.





Alzheimer's is the No. 3 cause of death in Orange County, and there are some 84,000 people in O.C. living with, or at risk of developing, the condition, according to county statistics and the Alzheimer's Orange County association.(iStockphoto)

"This grant for UCI is really going to be the power ball that hits it out of the park," said Jim McAleer, president and CEO of Alzheimer's Orange County.

"It's bigger than people may think it is on the face of it. It will allow them to lay the groundwork for research, so scientists can count more on what they're seeing in animal trials as they relate to humans."

And while the Hoag trial is a Phase 1 study, focused on the new drug's safety profile, it presents an opportunity for people to get in on the ground floor, so to speak, for later phases on its efficacy. The drug, ACU193, takes a different approach than currently approved medications, seeking to halt the neural toxicity that seems to be at the core of the disease.

"What if it works?" McAleer said. "That would be pretty spectacular. People can be reluctant to raise their hands for Phase 1 trials, but without them, you don't get anywhere. If it were me, and I were eligible, I would certainly raise my hand and try whatever might work."

Hoag: New drug



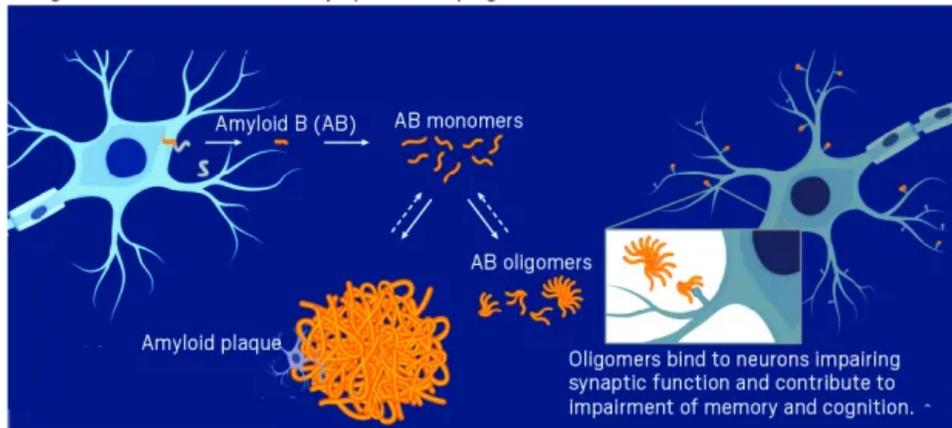
The drug being tested, ACU193, does *not* target the infamous *amyloid plaques* that people who closely follow Alzheimer's research have heard so much about; the tangles of misfolded proteins that form in the spaces between nerve cells and seem tied to the disease.

Instead, it targets, and binds to, *amyloid-beta oligomers*, sort of an earlier stage toxin that builds up in the brain.

Oligomers might or might not become plaques, said Dr. Gustavo Alva, psychiatrist at Hoag and principal investigator of the study. But they appear to be quite toxic, and possibly an underlying cause of the neural degeneration that is characteristic of Alzheimer's.

A new drug to halt Alzheimer's?

Hoag Hospital is seeking participants for a clinical trial of Acumen Pharmaceuticals' ACU193, which takes a different approach to treating Alzheimer's disease. ACU193 is designed to locate and bind to abnormal proteins (amyloid, monomers and oligomers) that build up in the brain. These proteins are thought to be involved in disease symptoms and progression.



Source: Acumen Pharmaceuticals

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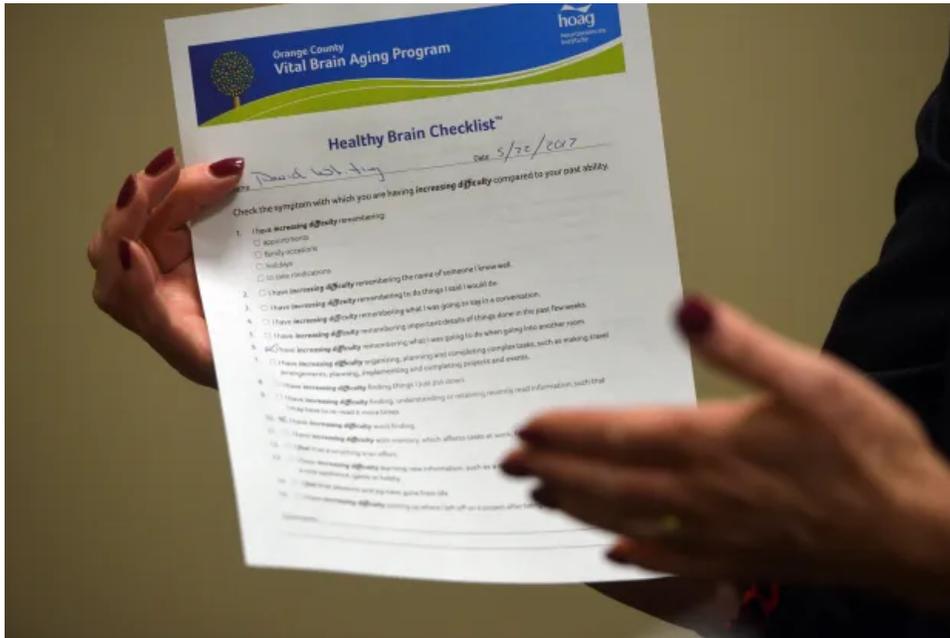
"The intercept study is exciting because it's literally a study to intercept the toxic oligomers," Alva said. "If we can prevent oligomers from binding to these neurons and dendritic spines, we may help preserve function."

If you think of Alzheimer's as a long line of dominoes, oligomers may be one of the first few standing in the queue. If you can stop it from toppling, the rest might never fall down.

Hoag is one of 16 sites nationally that will be testing the drug. The only other site in California is slated to be the Orange County Research Institute in Anaheim, which is not yet recruiting, according to clinicaltrials.gov.



Interested? Participants should be aged 55 to 90, with mild memory loss or mild dementia. For more information, call 949-764-6797, email clinicalresearch@hoag.org, and read the [study outline here: https://bit.ly/3R7bWNR](https://bit.ly/3R7bWNR).



A healthy brain checklist at Hoag Neurosciences Institute in Newport Beach, California in 2017.(Photo by Jeff Gritchen, Orange County Register/SCNG)

UCI: New money

A thousand brains have been donated to UCI to aid its investigations into Alzheimer's. And that work will get a big boost from the \$47 million coming to UCI from the National Institute on Aging, with the money to be parceled out over five years.

"It's an incredibly exciting time, and there's a lot of promise," said Joshua Grill, director of UCI's Institute for Memory Impairments and Neurological Disorders.

"We remain in our infancy in our field compared to other fields of medicine, but we're learning at an incredible rate."

The university houses one of just two U.S. groups working on late-onset



That approach contrasts with previous mouse models that mimic early-onset Alzheimer's. The project's next phase will be co-directed by Frank LaFerla, dean of the School of Biological Sciences; Andrea Tenner, a Distinguished Professor of molecular biology and biochemistry; and Kim Green, a professor of neurobiology and behavior.



The nonprofit Alzheimer's Orange County's annual Walk4ALZ & Run4ALZ at Angel Stadium drew more than 2,500 people and raised \$300,000. (Courtesy of Alzheimer's Orange County)

The project's highly collaborative nature is a particular point of pride. "This is a robust team that involves three principal investigators and lots of other scientists who all come together to do something huge and important," Grill said. "We're very successful, and we're generating important resources for the work."

The project began 12 years ago with a \$70,000 gift from the Pacific Life Foundation at the urging of Harry Bubb, a former CEO of Pacific Life Insurance Co., and officials said that initial donation illustrates the importance that private philanthropy can play in seeding science. In 2016, the researchers won a \$16 million grant from the National Institute on Aging, and this latest grant nearly triples that funding.



“Truly, because of that of that registry, we have accelerated research in a meaningful way,” he said.



Two unidentified study participants with the UCI MIND Alzheimer’s Disease Research Center meet with UC Irvine researchers, at left, Dr. Malcolm Dick and Dr. Gaby Thai. (Courtesy of Laurel Hungerford)

The next decade promises to be one of great progress in fighting Alzheimer’s, the experts said. There most likely will not be one magic bullet for “curing” Alzheimer’s, but multiple therapies that will address brain toxins, and their outfall, in multiple ways.

“Once you hit 50 and 60, you’re staring into the mouth of the lion and the research has a little more immediate impact,” said McAleer of Alzheimer’s Orange County. “If you can stop the first couple of dominos from falling, you’ll chip away at the larger problem.”

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Teri Sforza is one of the lead reporters on the OCR/SCNG probe of fraud, abuse and death in the Southern California addiction treatment industry. Our "Rehab Riviera" coverage won first place for investigative reporting from the California Newspaper Publishers Association, first place for projects reporting from Best of the West and is a finalist for the National Institute for Health Care Management Foundation's print award, competing with the New York Times, the Washington Post and ProPublica. Sforza birthed the Watchdog column for The Orange County Register in 2008, aiming to keep a critical (but good-humored) eye on governments and nonprofits, large and small. It won first place for public service reporting from the California Newspaper Publishers Association in 2010. She also contributed to the OCR's Pulitzer Prize-winning investigation of fertility fraud at UC Irvine, covered what was then the largest municipal bankruptcy in America's history, and is the author of "The Strangest Song," the first book to tell the story of a genetic condition called Williams syndrome and the extraordinary musicality of many of the people who have it. She earned her M.F.A. from UCLA's School of Theater, Film and Television, and enjoys making documentaries, including the OCR's first: "The Boy Monk," a story that was also told as a series in print. Watchdogs need help: Point us to documents that can help tell stories that need to be told, and we'll do the rest. Send tips to watchdog@ocregister.com.

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