ALZHEIMER’S DRUG TRIAL PROVIDES SOME HOPE

Medication appears to slow accumulation of brain plaque

BY MELISSA HEALY

In the search for a treatment capable of changing the course of Alzheimer’s disease, new findings are offering a new glimmer of hope. In a preliminary trial of subjects suffering from memory and thinking problems or diagnosed with early Alzheimer’s, a disease-modifying medication called aducanumab has demonstrated the ability to clear accumulations of beta-amyloid protein—a hallmark of Alzheimer’s—from brain cells.

And compared with subjects receiving a placebo medication, those who get monthly infusions of aducanumab in high doses appeared to experience less progressions in a minimal function. The results of the early clinical trial reported Wednesday in the journal Nature offer new evidence that clearing amyloid plaques might be an effective strategy for preventing, halting or even reversing the degenerative brain disorder that is detected and diagnosed with early Alzheimer’s.

ROGER TSIEH • 1952-2016

UCSD Nobel laureate made vital discovery

BY GARY ROBBINS

Roger Tsien, the eminent and versatile UC San Diego researcher who shared the 2008 Nobel Prize in chemistry for helping to find a more effective way to peer inside cells and organisms, died on Aug. 24. He was 64.

Tsien is credited with helping to find a more effective way to peer inside cells and organisms, such as green fluorescent protein (GFP), used as a biological marker.

MEXICO CITY

Donald Trump, who has made deporting unauthorized immigrants from Mexico a cornerstone of his campaign, met with Mexican President Enrique Pena Nieto on Wednesday — striking a cordial and cooperative tone as he faced a world leader who forcefully opposes his signature proposal.

Yet just hours later in a major speech on immigration in Phoenix, the Republican presidential nominee returned to the aggressive tone that has defined much of his campaign. Repeatedly raising his voice, he said that “anyone who has entered the United States illegally is subject to deportation,” and he vowed to crack down especially hard on unauthorized immigrants who have committed other crimes.

TRUMP, PEÑA NIETO SPLIT OVER PAYMENT FOR WALL

Conciliatory tone contrasts with hard-line immigration policy speech later

BY JOSHUA PARNLOW & SEAN SULLIVAN

Mexican President Enrique Pena Nieto and Donald Trump met Wednesday in Mexico City, where the GOP presidential candidate defended the right of the United States to build a massive border wall to block illegal immigration.

“I kind of admire his courage,” Mix, a Pro Football Hall of Fame inductee, said of Kaepernick, with whom he worked in San Diego.

“I don’t have to agree with him politically, but I respect his courage and his ability to stand up for what he believes,” he said. Mix also said he was inspired by Kaepernick’s protest because it was done “in a peaceful and non-violent way” rather than “in a violent and illegitimate way.”

“Shimomura and Martin Chalfie revealed that it glowed bright green under ultraviolet light. Chalfie showed how it could be used as a biological marker. Combining his deep skills in molecular biology and chemistry, Tsien found ways to make GFP glow more brightly and consistently. Then he created a full palette of fluorescent proteins that scientists could use to track different cellular processes at the same time.”

“GFP has become a fundamental tool in life sciences laboratories around the world, allowing researchers to look inside cells or whole animals, to watch molecules interact in real-time and to turn green fluorescent proteins interact in real-time,” the campus community on Wednesday. The precise cause of death has yet to be determined.

“Tener — a first-generation American who began to explore chemistry at age 8 — was hailed Wednesday for “illuminating” the study of such diseases as cancer and HIV. He learned about Shimomura and Martin Chalfie in 1994 at the University of Wisconsin.

“I am so honored to be here today,” Shimomura said. “I thought this would be a dream come true.”

Shimomura and Martin Chalfie also received the Nobel Prize for Chemistry in 2008 for their work on fluoroescence proteins.

BY PHILLIP MOLNAR

It’s a dream house raffle without a dream home. For 12 years, the local Ronald McDonald House Charities has held a “Dream House Raffle” in which a lucky mansion is advertised as the game’s grand prize for the price of a ticket.

But this year, the raffle’s nonprofit partner announced it would no longer sponsor the house because it often doesn’t sell enough tickets to make it a “winning ticket.”

“It’s a jarring contrast for voters and send a confusing message about the kind of president he would be,” Trump said at the joint news conference in Mexico that he and Pena Nieto didn’t discuss Wednesday. In Phoenix, he outlined his plan for building along the U.S.-Mexico border, despite his long-standing vow to compel Mexico to foot the bill. "He and Pena Nieto avoided direct confrontation in front of the cameras, using their differences on immigration, border security and trade in cordial tones. But later, Pena Nieto tweeted: ‘All the best to President Trump.’"

“Tener appears to have passed away while on a bike trial in Eugene, Ore., said UC San Diego Chancellor Pradeep Khosla, who broke the news to the campus community on Wednesday. The precise cause of death has yet to be determined.

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An increase in paralysis seen in Zika outbreak areas

Infections may bring on Guillain-Barré cases, study says

In seven countries that recently experienced Zika outbreaks, there were also sharp increases in the number of people suffering from a form of temporary paralysis, researchers reported Wednesday.

The analysis, published online in The New England Journal of Medicine, adds to substantial evidence that Zika infections — even asymptomatic ones — may cause by a number of other factors, including infection with other viruses. Researchers studying the Zika epidemic in French Polynesia had estimated that roughly 1 in 4,000 people infected with the virus could develop the syndrome.

The Centers for Disease Control and Prevention has said that the Zika virus is “strongly associated” with Guillain-Barre, but has stopped short of declaring it a cause of the condition.

The new data suggest a telling pattern. Each country in the study saw unusual increases in Guillain-Barré that coincided with peaks in Zika infections, the researchers concluded.

“It’s pretty obvious that in all seven sites there is a clear relationship,” said Dr. Marros Espinal, the study’s lead author and the director of communicable diseases at the Pan American Health Organization, which collected data on confirmed and suspected cases of Zika infection and on the incidence of Guillain-Barré.

“Something is going on.”

In Venezuela, officials expected roughly 70 cases of Guillain-Barré from December 2015 to the end of March 2016, as mosquitoes were spreading the virus. Instead, they were 684 cases.

During five months in which the Zika virus was circulating in Colombia, officials recorded 520 cases of Guillain-Barré when there should have been about 100. From September 2015 to March 2016, while Zika infections peaked in El Salvador, cases of Guillain-Barré doubled to 184 from 92.

The researchers included patients with both suspected and confirmed Zika infections, as reported by national health officials.

Dr. Kenneth C. Gorson, professor of neurology at Tufts who was not involved with the new analysis, called it compelling.

“This is a substantial public health burden for countries that may not have well-developed health systems in place,” he said.

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ALZHEIMER’S • Amyloid plaque accumulation cut

FROM A1 treated early.

“It is a hopeful sign,” said Dr. James Hendrix, director of global science initiatives for the Alzheimer’s Association.

“This is a small trial, but it still is exciting for a number of reasons.

“I am cautiously optimistic,” he said.

The new study reflects the findings of a trial designed primarily to test the safety of aducanumab at a range of doses. The drug’s developer, Washington, D.C-based Biogen Inc., is soon to launch a pair of much larger trials designed to test aducanumab’s effectiveness as a treatment for Alzheimer’s.

“We hope to see these findings confirmed,” Hendrix said.

Although aducanumab holds promise as a potential Alzheimer’s drug, it is for now an early answer to a more basic question about Alzheimer’s disease: What role do clumps of beta-amyloid protein play in the disease?

As long as 25 years ago, scientists suspected a role for amyloid plaques — accumulations in the brain of beta-amyloid protein — in Alzheimer’s disease. When they examined the brains of people who died after suffering a progressive loss of memory and reasoning skills, scientists typically found clumps of beta-amyloid surrounded by destroyed synapses and brain cells that had long since died.

But whether those clumps were a cause of Alzheimer’s dementia or just another symptom of the mysterious disease process wasn’t clear.

If a cure to this scourge were found, that unanswered question was important: If accumulating amyloid plaques in the brain precipitated a patient’s decline in memory and thinking, developing or discovering drugs that cleared those aggregations — or prevented them in the first place — could be key. But if amyloid plaques were incidental to other processes causing memory loss, then fighting them was probably a distraction.

Over the last decade or so, the amyloid hypothesis has been put to the test often, without clear results. Many experimental therapies have sought and failed to prevent or clear amyloid plaques. Where a few therapies have succeeded in doing so, patients benefit with dementia symptoms failed to improve, and their loss of memory and function continued unabated.

In the meantime, improvements in brain-imaging methods have at least made it possible to measure amyloid deposits in living brains. In the current study, subjects were all people who had substantial amyloid brain clumps — just one factor that put them at risk for a progressive loss of memory. The other factor was that their memory loss was already evident: All had been diagnosed either with mild Alzheimer’s or with mild cognitive impairment — a more subtle level of confusion and forgetfulness that frequently precedes an Alzheimer’s diagnosis.

In these preliminary findings on aducanumab, treatment not only reduced the accumulation of amyloid plaques; it also appeared to slow the inexorable slide into dementia that most subjects were expected to suffer.

After a year of monthly infusions of aducanumab therapy, the brains of subjects who got the highest dose had significant reductions in their baseline levels of amyloid plaque accumulation. Their scans showed a level of amyloid plaques very near the cutoff point for normal protein accumulation. Those who got a placebo drug showed, on average, no change in amyloid plaque above the levels shown on baseline scans.

And on a key test of mental function, subjects who got the experimental drug showed less progression toward dementia at the one-year mark than did those who got placebo. How much less progression was proportional to the dose they got.

“The dose-related reduction in brain amyloid with aducanumab is dramatic and convincing,” said Dr. Paul Aisen, director of the Keck School of Medicine’s Alzheimer’s Therapeutic Research Institute at the University of Southern California.

Aisen, who has consulted extensively with Biogen but was not involved in the newly published clinical trial, said that if confirmed by further trials, the benefits of a therapy like aducanumab “would represent a true breakthrough” in the treatment of Alzheimer’s disease.

The clinical trial did raise a safety concern. About 41 percent of those getting the highest dose and 37 percent of those getting the second-highest dose developed a complication of brain-fluid accumulation that hampered brain imaging and was sometimes linked to headaches, visual disturbances and confusion.

The complication tended to disappear four to 12 weeks after treatment. But it prompted 46 percent of those who developed it to drop out of the clinical trial.

Healy writes for the California News Group, publisher of the Union-Tribune and the L.A. Times.