

Progress in understanding Alzheimer's disease genetics, hope remains for drugs in testing

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What is happening with Alzheimer's disease research and treatment? We



heard from Maria Carrillo, chief science officer of the nationwide Alzheimer's Association, during a recent visit to San Diego. Here are some questions and answers from the interview, edited for space and clarity.

Q: There have been several failed clinical trials of monoclonal antibody drugs designed to stop or remove toxic proteins. Is that approach dead?

A: I would say it is not dead in the water—yet—because there still are a couple of trials that have not reported negatively, and we have to wait to see what happens.

There's a monoclonal antibody used in the A4 study (a4study.org). It's being tested in a population that is very early in the disease. So we need to see the evidence in that population, and in those who have inherited Alzheimer's disease.

The next few years will tell us if <u>monoclonal antibodies</u> are still a viable option.

Q: What have we learned about the role of genetics in Alzheimer's disease? And can we do anything about it?

A: What we're learning is that there are more and more genes associated with dementia than we ever thought before. What we're looking for is an algorithm that measures all the risk genes you have, because they're going to be different from mine.

How much of that risk can you mitigate? Epigenetics (DNA modifications that turn genes on or off) sits on top of genetics. And you may be able to change your epigenetics with <u>lifestyle changes</u>.

So I have a predisposition to diabetes in my family. My brother is



younger than me and he already has diabetes. With my lifestyle, I am trying to make sure I don't get diabetes. The hope is that we can do the same thing for dementia.

But what exactly should be recommended? We have launched the U S. POINTER study (www.alz.org/us-pointer/) in order to find out what that recipe could be.

The National Institute on Aging has supported a \$47 million add-on to include tau and amyloid imaging (toxic brain proteins linked with Alzheimer's). And on top of that we are going to be adding a sleep study, because sleep is incredibly important. And that's also paid for by the National Institute on Aging.

Q: Blood tests for Alzheimer's are reportedly on the way. How can they help?

A: These <u>blood</u> tests are able to detect the proteins that are changing, specifically amyloid beta. They correlate with PET scans. Those are the gold standard, and they're very expensive. Instead of having to screen 10,000 people with an expensive PET scan, you might be able to screen them with a <u>blood test</u>, which is a lot cheaper.

But these blood tests have only been used in about 100 people so far, so they're not ready for your doctor's office. However, they can be very useful in a study like the A4 trial. A blood test doesn't have to be perfect as a potential screening tool in the clinic.

Q: Why should people want a blood test if there's no effective therapy?

A: It's going to be quite a few years before this blood <u>test</u> is available in your doctor's office. And we need to develop these therapies alongside as we develop those early detection markers so we can be ready when we



have a therapy.

You can bet your bottom dollar that the earlier you get therapy, the potentially better your outcome might be.

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