

DISEASE

Two of a Kind

The similarities between Alzheimer's disease and Down syndrome draw attention

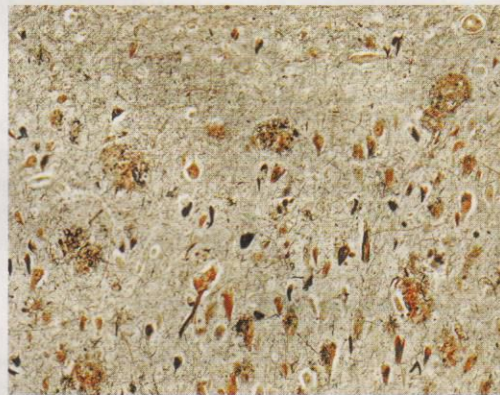
Is Alzheimer's disease an acquired form of Down syndrome? When neurobiologist Huntington Potter first posed the question in 1991, Alzheimer's researchers were skeptical. They were just beginning to explore the causes of the memory-robbing neurological disease. Scientists already knew that by age 40, nearly 100 percent of patients with Down syndrome, who have an extra copy of chromosome 21, had brains full of beta-amyloid peptide—the neuron-strangling plaque that is a hallmark of Alzheimer's. They also knew that the gene that codes for that protein lives on chromosome 21, suggesting that people acquire more plaque because they get an extra dose of the peptide. Potter, though, suggested that if people with Down syndrome develop Alzheimer's because of an extra chromosome 21, healthy people may develop Alzheimer's for the same reason. A quarter of a century later mounting evidence supports the idea.

“What we hypothesized in the 1990s and have begun to prove is that people with Alzheimer's begin to make molecular mistakes and generate cells with three copies of chromosome 21,” says Potter, who was recently appointed director of Alzheimer's disease research at the University of Colorado School of Medicine, with the express purpose of studying Alzheimer's through the lens of Down syndrome.

He is no longer the only one exploring the link. In recent years dozens of studies have shown Alzheimer's patients possess an inordinate amount of Down syndrome-like cells. One 2009 study by Russian researchers found that up to 15 percent of the neurons in the brains of Alzheimer's patients contained an extra copy of chromosome 21. Others have shown Alzhei-

mer's patients have 1.5 to two times as many skin and blood cells with the extra copy as healthy controls. Potter's own research in mice suggests a vicious cycle: when normal cells are exposed to the beta-amyloid peptide, they tend to make mistakes when dividing, producing more trisomy 21 cells, which, in turn, produce more plaque. In August, Potter and his team published a paper in the journal *Neurobiology of Aging* describing why those mistakes may occur: the inhibition of a specific enzyme.

Meanwhile University of Kentucky researchers have been collecting brain scans, blood tests and lifestyle surveys from dozens of adults with Down syndrome over the past five years. They aim to understand why—even though nearly all patients develop plaque—only 60 to 80 percent develop dementia.



Plaque buildup in the brain is a hallmark of Alzheimer's disease.

National Institutes of Health director Francis Collins recently told a Senate subcommittee that there is “intense interest” in studying the two conditions together. And in 2013 the Alzheimer's Association teamed up with the Linda Crnic Institute for Down Syndrome to fund work examining the link.

In general, by studying Alzheimer's in a smaller population guaranteed to develop the pathology, scientists can learn more, faster, says Dean Hartley, director of science initiatives for the Alzheimer's Association. He and others say it is too early to conclude that Alzheimer's is indeed a form of Down syndrome: “But we need new ideas like this in the field to help us better understand the underlying pathways of the disease.”

—Lisa Marshall

THOMAS DEERINCK/Science Source