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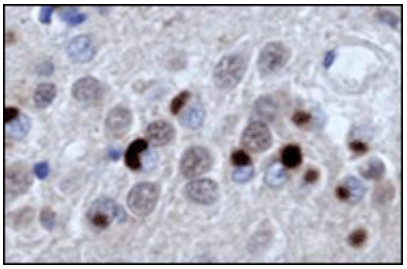
Common Protein Found in Dementia and ALS

By JR Minkel | October 5, 2006



IN THE CLUMPS: A long-sought protein that forms deposits (*dark spots*) in the brains of people with a common dementia also clumps up in people with ALS, meaning the disorders may have related routes to cell death. Image: VIRGINIA M-Y. LEE, Ph.D. *University of Pennsylvania School of Medicine*; SCIENCE

Globs of malformed protein are conspicuously present in many degenerative disorders of the brain and nervous system. A number of these possibly damaging proteins have been isolated and studied, but researchers have struggled to characterize certain protein deposits in the brains of people with frontotemporal dementia (FTD), the second most common type of dementia after Alzheimer's disease. Scientists have now revealed the offending molecule and discovered that it also shows up in those with Lou Gehrig's disease, a debilitating neuromuscular disorder, suggesting that the two conditions might have intersecting routes on the pathway to cell death.

In people with FTD, the frontal and temporal lobes of the brain shrink and their behavior changes. They may become fixated on sex or engage in criminal behavior, and they eventually die from the disorder. Lou Gehrig's disease, or amyotrophic lateral sclerosis (ALS), would seem like a different beast, given that it causes degeneration in motor neurons. But in recent years neurologists have observed that people with one of the conditions tend to get the other.

Researchers have long known that in about half of FTD cases, brains are speckled with protein clumps containing tau, a protein implicated in Alzheimer's and other brain diseases. In the other fraction of FTD cases, the deposited protein was unknown. To identify the mystery molecule, neurobiologists Virginia Lee and John Trojanowski of the University of Pennsylvania and their colleagues isolated a group of proteins from brain samples of people with FTD. They injected the molecules into mice to create antibodies capable of recognizing the various suspect proteins, and then searched through the antibodies to find those that stuck only to the clumps in brain samples of FTD patients. The search turned up an obscure protein, TDP-43, they report in the October 6 *Science*.

The antibodies also clung to protein deposits in motor neuron samples from ALS patients, indicating that TDP-43 was present there, too.

"What that strongly suggests," says neurobiologist Michael Hutton of the Mayo Clinic in Jacksonville, Fla., who was not involved in the research, "is that in each of these diseases there is at some point a common pathway to neuronal cell death. We've long suspected this might be the case; we just didn't realize it was the same major protein accumulating." From here, he explains, researchers can begin studying how TDP-43 deposits arise in, and maybe contribute to, the diseases.