MedicalXpress

'Alzheimer's in a Dish' model induces skin cells into neurons expressing amyloid-beta (w/ Video)

December 5 2014

The search for a living laboratory model of human neurons in the grip of Alzheimer's disease (AD)—the so-called "Alzheimer's in a dish"—has a new candidate. In work presented at the ASCB/IFCB meeting in Philadelphia, Håkan Toresson and colleagues at Lund University in Sweden report success in creating induced neurons that model Alzheimer's by starting with fibroblasts taken from skin biopsies. The differentiated cells express a full range of normal neuronal markers. Significantly, all the neurons derived from fibroblasts including those taken from patients diagnosed with AD, express the proteins classically associated with the neurodegenerative disorder including amyloid beta (Aβ) and the microtubule-associated protein tau, giving researchers a ready comparison between AD patients and the normal elderly.

All the fibroblast samples in Toresson's study came from patients enrolled in a large, long-term clinical research program on dementia called the Swedish BioFinder Study. The biopsies are linked to patient histories and results from batteries of longitudinal tests covering behavior, spinal fluid biochemistry, and brain imaging results including PET and MRI scans. The researchers subjected the fibroblast samples to growth factor treatment and transduction by three transcription factors, Ascl1, Brn2 and Myt1l, that induced differentiation into nerve cells. So far Toresson reports success in 12 out of 12 attempts to create induced neurons from the BioFinder samples, giving the researchers a cell biological library of neurons from elderly Swedes who exhibit signs of

sporadic AD, familial AD, or robust cognitive health.

The relationship of Aβ and tau in AD progression are still hotly disputed but accumulations of tau-based tangles and Aβ plaques in the brain at autopsy are currently the only clear diagnostic of the disease. But sampling AD-damaged neurons in living patients is impossible. Using animals to model human diseases such as cancer has been a powerful instrument in bioscience but no good animal model of AD, which is first seen as impairment of human cognitive function, has been found. "Alzheimer's in a dish" or, in Toresson's studies, a series of dishes could be that long-awaited model system.

Using a cell biology approach to AD, Toresson hopes to compare the cell phenotypes on induced neurons derived from sporadic AD patients with induced neurons from familial AD cases that have the characteristic APP, PSEN1, or PSEN2 mutations. Such an approach could pave the way for personalized treatments for dementia, allowing the use of a patient's accessible skin cells to assess what's happening inside the inaccessible neurons of the brain.

NOTE: A 19-second time lapse video showing the first six hours of neuronal conversion of skin fibroblasts from an AD patient is available.

Provided by American Society for Cell Biology