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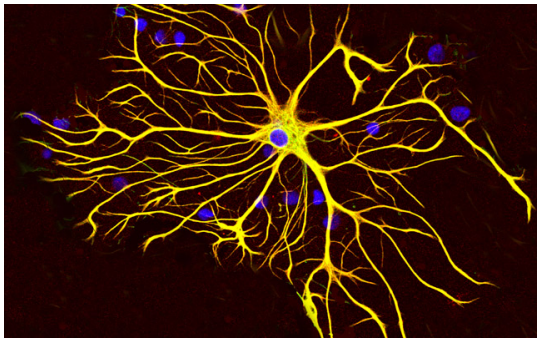
Inflamed Support Cells Appear to Contribute to Some Kinds of Autism

But researchers found that when glia cells were normal, they "rescued" autistic neurons in culture, causing the latter to behave normally

Modeling the interplay between neurons and astrocytes derived from children with Autism Spectrum Disorder (ASD), researchers at University of California San Diego School of Medicine, with colleagues in Brazil, say innate inflammation in the latter appears to contribute to neuronal dysfunction in at least some forms of the disease.



A confocal micrograph of a stained astrocyte grown in tissue culture. Blue indicates DNA, revealing the nucleus of the astrocyte and other cells. Image courtesy of EnCor Biotechnology.

The findings, published in the current issue of *Biological Psychiatry*, are the first to demonstrate that supporting brain cells, called astrocytes, may play a role in some subtypes of ASD. But more importantly, the research, using induced pluripotent stem cells, suggests the neuronal damage might be reversible through novel anti-inflammatory therapies.

To conduct the study, scientists took dental pulp cells from donated baby teeth of three children with diagnoses of non-syndromic autism (part of the on-going "Tooth Fairy Project") and reprogrammed the cells to become either neurons or astrocytes, a type of glia or support cell abundantly found in the brain. The cells were grown into organoids, essentially mini-brains in a dish.

Though genetically distinct, all three children displayed stereotypical ASD behaviors, such as lack of verbal skills or social interaction. When researchers examined the developed organoids in microscopic detail, they noted that the neurons had fewer synapses (connections to other

neurons) and other network defects. Additionally, some astrocytes showed high levels of interleukin 6 (IL-6), a pro-inflammatory protein. High levels of IL-6 are toxic to neurons.

The researchers co-cultured astrocytes derived from the ASD children with neurons derived from normal controls. The healthy neurons behaved like ASD neurons, said co-senior author Alysson R. Muotri, PhD, professor in the UC San Diego School of Medicine departments of Pediatrics and Cellular and Molecular Medicine, director of the UC San Diego Stem Cell Program and a member of the Sanford Consortium for Regenerative Medicine.

“But more importantly, the opposite was true. When we co-cultured ASD neurons with normal astrocytes, we could rescue the cellular defects. The neurons reverted to normal functioning and behavior.”

Muotri and colleagues say the data suggests there may be an intrinsic inflammatory reaction within a subgroup of persons with ASD. “What we are trying to do now is understand if we can predict this subgroup through genome sequencing and, perhaps, find a therapeutic opportunity to treat them with anti-inflammatory drugs.”

Co-authors of the study include: Fabiele Baldino Russo, Graciela Conceicao Pignatari, and Patricia Cristina Baleeiro Beltrao-Braga, University of Sao Paolo, Brazil; Beatriz Camille Freitas, and Jonathan Sebat, UC San Diego; and Isabella Rodrigues Fernandes, University of Sao Paolo and UC San Diego.

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Disclosure: Alysson Muotri is a co-founder and has equity interest in TISMOO, a company dedicated to genomic analysis and brain organoids focusing on therapeutic applications for Autism Spectrum Disorder and other neurological disorders. The terms of this arrangement have been reviewed and approved by the University of California San Diego in accordance with its conflict of interest policies.

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