

Retinal Neurons Research Could Lead to Regenerative Therapies for the Brain

Virginia Tech

Discovery may shed light on brain disease, development of regenerative therapies

Real estate agents emphasize location, location, and – once more for good measure – location. It's the same in a developing brain, where billions of neurons vie for premium property to make connections. Neurons that stake out early claims often land the best value, even if they don't develop the property until later.

Scientists at the [Virginia Tech Carilion Research Institute](#) [1] and the University of Louisville have discovered that during neurodevelopment, neurons from the brain's cerebral cortex extend axons to the edge of the part of the brain dedicated to processing visual signals – but then stop. Instead of immediately making connections, the cortical neurons wait for two weeks while neurons from the retina connect to the brain.

Now, in a study to be published in the Nov. 14 issue of the journal *Cell Reports*, the scientists have discovered how. The retinal neurons stop their cortical cousins from grabbing prime real estate by controlling the abundance of a protein called aggrecan.

Understanding how aggrecan controls the formation of brain circuits could help scientists understand how to repair the injured brain or spinal cord after injury or disease.

"Usually when neuroscientists talk about repairing injured brains, they're thinking about putting neurons, axons, and synapses back in the right place," said [Michael Fox](#) [2], an associate professor at the Virginia Tech Carilion Research Institute and lead author of the study. "It may be that the most important synapses – the ones that drive excitation – need to get there first. By stalling out the other neurons, they can get the best spots. This study shows that when we think about repairing damaged neural networks, we need to consider more than just where connections need to be made. We also need to think about the timing of reinnervation."

The researchers genetically removed the retinal neurons, which allowed the cortical axons to move into the brain earlier than they normally would.

"We were interested in what environmental molecular cues allow the retinal neurons to control the growth of cortical neurons," said Fox, who is also an associate professor of biological sciences in Virginia Tech's [College of Science](#) [3]. "After years of screening potential mechanisms, we found aggrecan."

Aggrecan is a protein that has been well studied in cartilage, bones, and the spinal

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cord, where it is abundant after injuries. According to Fox, aggrecan may be able to isolate damaged areas of the spinal cord to stop inflammation and prevent further destruction. The downside, however, is that aggrecan inhibits axonal growth, which prevents further repair from taking place.

"Axons see this environment and either stop growing or turn around and grow in the opposite direction," said Fox.

Although it is less studied in the developing brain, aggrecan appears in abundance there. In the new study, the researchers found that retinal neurons control aggrecan in a region that receives ascending signals from retinal cells as well as descending signals from the cerebral cortex.

Once the retinal neurons have made connections, they cause the release of enzymes that break down the aggrecan, allowing cortical neurons to move in.

Fox said it is interesting that the retinal axons can grow in this region of the developing brain, despite the high levels of aggrecan. He suspects that it may be because retinal neurons express a receptor – integrin – that cortical axons do not express.

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[1] <http://research.vtc.vt.edu/>

[2] <http://research.vtc.vt.edu/employees/michael-fox-phd/>

[3] <http://www.science.vt.edu/>