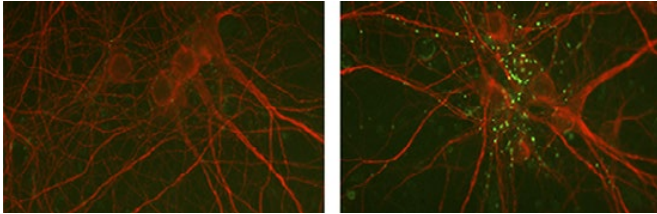


# Decrypting a collagen's role in schizophrenia

14 March 2016



Cortical neurons (red) form few inhibitory synapses (green) in the absence of collagen XIX (left), but synapse formation is restored by a signaling peptide derived from the protein's C-terminal region (right).  
Credit: Su et al., 2016

A small peptide generated from a collagen protein may protect the brain from schizophrenia by promoting the formation of neuronal synapses, according to a paper published in *The Journal of Cell Biology*. The study, "Collagen-Derived Matricryptins Promote Inhibitory Nerve Terminal Formation in the Developing Neocortex" by Jianmin Su and colleagues, may lead to new approaches to treating the mental disorder.

The [collagen](#) family of [extracellular matrix proteins](#) performs numerous functions in the brain, and mutations in several family members cause neurological diseases in humans. How collagen XIX promotes normal brain function is unknown, but loss of the gene encoding this collagen has been linked to familial schizophrenia.

A team of researchers led by Michael Fox at Virginia Tech Carilion Research Institute has been closely examining collagen XIX. They found that collagen XIX-deficient mice display a number of schizophrenia-related symptoms, including an abnormal startle response and an increased susceptibility to seizures. Schizophrenia has previously been linked to defects in a particular type of interneuron. This interneuron dampens

neuronal activity in the brain's cortex by forming [inhibitory synapses](#) with the cell bodies of other neurons. These inhibitory synapses were lost in collagen XIX-deficient mice.

Like similar types of collagen, collagen XIX can be cleaved by extracellular protease enzyme to generate a small signaling peptide called a matricryptin. Jianmin Su and colleagues found that this peptide was sufficient to rescue the formation of inhibitory synapses in neuronal cultures prepared from collagen XIX-deficient mice, apparently by binding and activating a cell adhesion receptor called integrin  $\alpha 5 \beta 1$ .

Fox and colleagues now want to learn more about how collagen XIX's matricryptin fragment promotes synapse formation. "We also want to investigate whether the peptide holds any therapeutic potential for any diseases that result from malformed or malfunctioning cortical interneurons," Fox says.

**More information:** Su, J., et al. 2016. *J Cell Biol.* [dx.doi.org/10.1083/jcb.201509085](https://doi.org/10.1083/jcb.201509085)

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