Medical Xpress

Newly discovered long noncoding RNA plays critical role in brain growth and signaling

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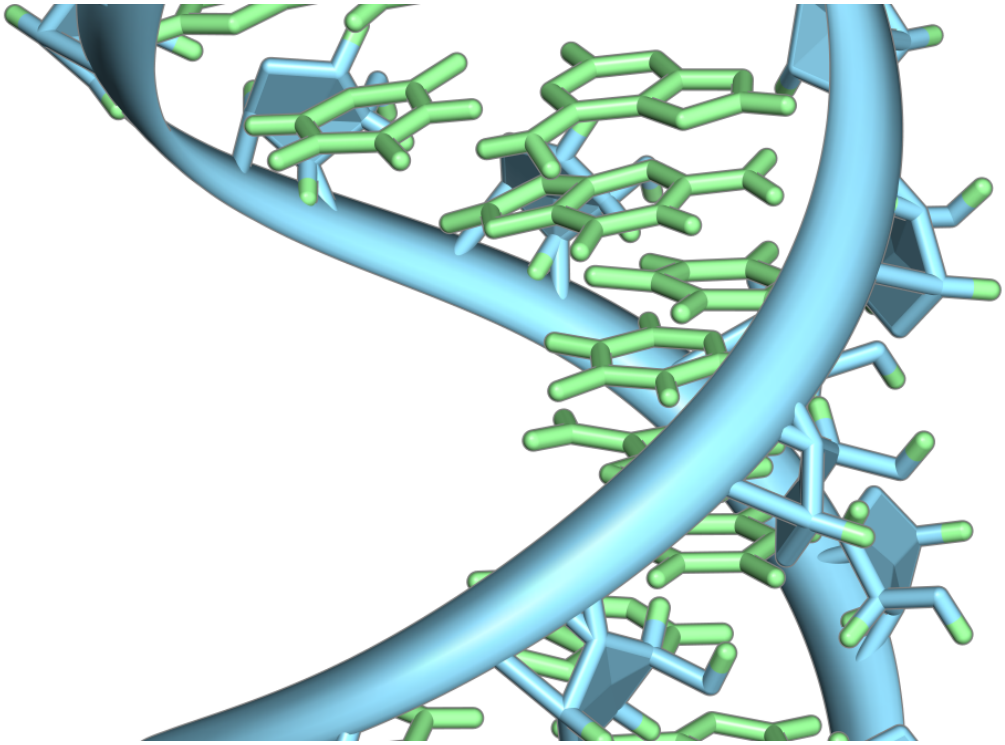

A hairpin loop from a pre-mRNA. Highlighted are the nucleobases (green) and the ribose-phosphate backbone (blue). Note that this is a single strand of RNA that folds back upon itself. Credit: Vossman/ Wikipedia

A new study from the Scripps Research laboratory of Sathyanarayanan Puthanveettil, Ph.D., peers deep within the nucleus of developing brain cells and finds that long noncoding RNAs play an important role in the

healthy functioning and maintenance of synapses, the communication points between nerve cells in the brain.

"Long noncoding RNAs are often described as 'the dark matter of the genome.' So, systematic interrogation of their function will illuminate molecular mechanisms of brain development, storage of long-term memories and degradation of memory during aging and dementia," Puthanveettil says.

RNA are the master regulators of the cell, tiny chains of nucleotides that read, transcribe and regulate expression of DNA, and build proteins. While scientists have gained great insights recently into the genetics underpinning how brain cells reach out and communicate with each other, the role of noncoding RNA is poorly understood. Research suggests that the longest of these noncoding RNA, those over 200 nucleotides long, help determine which genes are activated and operating in brain cells at various times. But which ones?

Writing in the journal *Proceedings of the National Academy of Sciences*, Puthanveettil and his colleagues on Scripps Research's Florida campus report that a specific long non-coding RNA, GM12371, controls expression of multiple genes involved in nervous system development and functioning. Furthermore, it affects the developing neurons' shape and ability to signal.

In mouse hippocampal cells, learning-related signaling upregulates GM12371, while its reduction produces inactive neurons, ones with sparse branches.

Together, the results suggest that healthy growth and development of brain cells and brain circuits depends not just upon specific proteins but also upon specific long noncoding RNAs, which scientists are now beginning to explore.

What role GM12371 dysfunction may play in diseases of the brain and nervous system demands further study, Puthanveettil says.

"Both coding and noncoding RNAs are increasingly viewed as druggable targets. Identifying their specific roles in the fundamental biology of functioning of neural circuits might eventually open new ways of treating neuropsychiatric disorders, such as autism and Alzheimer's disease," Puthanveettil says.

More information: Bindu L. Raveendra et al, Long noncoding RNA GM12371 acts as a transcriptional regulator of synapse function, *Proceedings of the National Academy of Sciences* (2018). DOI: 10.1073/pnas.1722587115

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