Medical Xpress

Noncoding RNA may promote Alzheimer's disease

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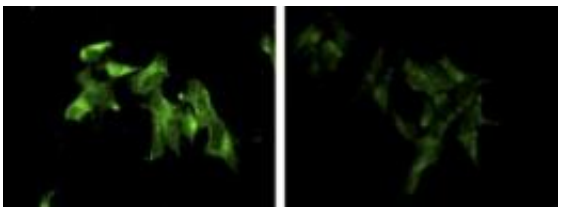

Researchers show that the small RNA 38A spurs cells to manufacture Var IV, a splice variant of a key neuronal protein, and potentially promote Alzheimer's disease. In this image, Var IV (green) is prevalent in cells that make extra 38A (left) but rare in control cells (right). Credit: Massone, S., et al. 2011. J. Cell Biol. doi:10.1083/jcb.201011053.

Researchers pinpoint a small RNA that spurs cells to manufacture a particular splice variant of a key neuronal protein, potentially promoting Alzheimer's disease (AD) or other types of neurodegeneration. The study appears in the May 30 issue of The *Journal of Cell Biology*.

Like a movie with an alternate ending, a protein can come in more than one version. Although scientists have identified numerous proteins and RNAs that influence alternative splicing, they haven't deciphered how cells fine-tune the process to produce specific protein versions. Four years ago, researchers identified a set of 30 small, noncoding RNAs that they suspected help regulate gene expression.

Italian researchers have now determined the function of one of the RNA snippets, known as 38A, that hails from a noncoding part of the gene that encodes the protein KCNIP4. KCNIP4 helps ensure that neurons fire impulses in a characteristic slow, repeating pattern. The researchers found that 38A spurs cells to produce an alternative splice variant of KCNIP4, Var IV, that disrupts this current, potentially leading to neurodegeneration.

KCNIP4 normally interacts with gamma-secretase, the enzyme complex that helps generate beta-amyloid (Abeta), a protein that accumulates in the brains of AD patients. But Var IV can't make the connection, possibly disturbing Abeta processing. Supporting that notion, the researchers found that levels of 38A were more than 10 times higher in brain cells from AD patients than in controls and that 38A hiked output of the more dangerous Abeta isoform Abeta 1-42.

More information: Massone, S., et al. 2011. J. Cell Biol. doi:10.1083/jcb.201011053

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