THE MULTITUDES OF NONCODING RNA

The term “noncoding RNA” is a catch-all for sequences in the genome that are transcribed but typically not translated. These molecules, which account for the majority of the transcribed sequences in the genome, are now thought to play key roles in brain evolution and function. Noncoding RNAs, classified based on their size, structure, location, or function, include dozens of different kinds described to date. Here are four types of noncoding RNA frequently studied in brain tissues.

LONG NONCODING RNAs

Long noncoding RNAs (lncRNAs) are generally defined as any noncoding RNAs greater than 200 nucleotides in length. Because of their variable size and composition, they can have diverse shapes and perform a variety of cellular activities, though most await functional investigation.

Example: The human and chimpanzee versions of a lncRNA called HAR1 differ by 18 nucleotides, which impacts the molecule’s secondary structure. The human version is predicted to be more stable, but exactly how that translates into differences in brain form or function isn’t yet clear.

CIRCULAR RNAs

As the name suggests, circular RNAs (circRNAs) are noncoding RNAs with joined ends, creating a more stable, circular molecule. Many questions remain as to the functions of circRNAs, but some are known to bind miRNAs, likely acting as sponges to modulate the miRNAs’ translation-suppressing effects.

Example: The circRNA CDR1-AS fine tunes neuronal development in humans, binding microRNAs (teal) highly expressed in secretory neurons that regulate developmental gene expression.

MICRORNAS

MicroRNAs (miRNAs) are small noncoding RNAs of just ~20–26 nucleotides (teal) that are cleaved from larger precursors. Their most well-described function is the regulation of gene expression by binding to messenger RNAs, where they generally inhibit translation and, therefore, reduce the amount of protein produced from a given gene.

Example: Overexpression of miRNA-124 leads to Alzheimer’s-like pathologies in mice, and elevated levels of the miRNA are found in the brains of people who died from the disease.

TRANSFER RNAs

Transfer RNAs’ primary job is to shuttle amino acids to growing peptide chains during translation. In the brain specifically, there’s emerging evidence that modifications to tRNAs play important roles in neuronal health and disease. Furthermore, tRNA fragments—small chunks from tRNA breakdown—seem to have their own functions, including in neurodegeneration.

Example: When researchers exposed Drosophila neuron cultures to synthetic tRFGln-CTG (teal)—a fragment of the tRNA for glutamine—the cells swelled and died, suggesting the fragment could play a role in neuronal necrosis.

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