

Macro Roles of microRNAs in Rett Syndrome?

They were overlooked for decades, dismissed out of hand as the flotsam and jetsam of cellular degradation. But over the past few years, molecular biologists have discovered that the tiny segments of RNA once thought to be random pieces of genetic material actually do something—several things, in fact. These small RNAs are known as microRNA (miRNA for short). MiRNAs were first described more than a decade ago by scientists working with *Caenorhabditis elegans*, a species of nematode worm favored by researchers because of the simplicity of its genome. In typical cell development, double-stranded DNA is “read” by single-stranded messenger RNA which translates (“codes”) the genetic information into proteins that drive cell development. The nematode discovery revealed that some genes instruct the RNA not to code for proteins, but for other, non-translating, RNA. Small bits of non-coding RNA had been observed inside cells for years, but scientists thought they were just evidence of cell aging or environmental damage.

From 1998 to 2002, different groups of researchers found indications that these microRNAs play a vital role in cell development. These short segments of microRNA interact with the longer strands of messenger RNA, intervening in its coding and translation process to influence the degree to which certain proteins are expressed. Scientists now believe miRNAs are a key force controlling gene expression, stem cell differentiation, and tissue development.

The work from Peng Jin’s (Emory University) and Xinyu Zhao’s (University of New Mexico) shows that microRNAs could also play a role in Rett syndrome as well. They found that MeCP2 could regulate the expression of specific microRNAs, particularly miR-137. The absence of functional MeCP2 leads to the increased expression of miR-137, which affects neurogenesis and neuronal maturation. These findings demonstrate that besides protein-coding mRNAs, MeCP2 could also directly regulate the expression of noncoding RNAs, particularly microRNAs. Identification of miR-137 as a target of MeCP2 also provides us a new target for therapeutic development. In summary microRNAs could play macro roles in the pathogenesis of Rett Syndrome.

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