Scientists find how mysterious 'circular RNA' is formed, claim muscular dystrophy link

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Our genetic information is stored in DNA, tiny strands of nucleic acid that contain instructions for the functioning of our bodies. To express this genetic data, our DNA is copied into RNA molecules, which then translate the instructions into proteins that perform tasks in our cells.

Several years ago, scientists discovered a new type of RNA molecule. Unlike all other known RNAs, this molecule is circular, and was labeled circular RNA. Although circRNA molecules are abundant, little has been known about how they are produced. Moreover, little has been known about the role they play in our biology, and next to nothing has been known about the role they play in disease.

Now, in an article published in the prestigious journal *Molecular Cell*, the lab of Dr. Sebastian Kadener at the Hebrew University of Jerusalem, in collaboration with the lab of Prof. Nikolaus Rajewsky at the Max Dellbruck Institute in Berlin, has discovered how circRNAs are produced.

Kadener and his colleagues found that circRNAs not only compete with normal RNAs, but the body actually produces them at the expense of normal RNA. Therefore, the mere fact of circRNAs' production has an enormous impact on how our genes are expressed, which affects how our bodies develop and function.

The researchers also demonstrated that circular RNA molecules are highly produced in the brain, and in many cases from genes with very important functions. This strongly suggests that circRNAs play an important role in brain function—and likely in brain disease.

In addition, Dr. Kadener and colleagues identified the protein "muscleblind" as a factor involved in circRNA biogenesis, and showed that muscleblind can enhance and regulate the production of a subset of circular RNAs.

Importantly, defects in muscleblind function are known to cause a severe degenerative disease called myotonic dystrophy. Characterized by progressive muscle wasting and weakness, this is the most common form of muscular dystrophy that begins in adulthood. When considered together, the important role played by muscleblind in regulating circRNAs, combined with these molecules' abundance in the brain, suggests that circRNAs might be involved in development of myotonic dystrophy.

According to Dr. Kadener, "This research is significant from several perspectives. By mapping how circRNAs are produced, it helps advance our understanding of general molecular biology. In addition, it might be strongly relevant for understanding and eventually treating degenerative diseases both in muscle and the brain."

More information: The research is published in Molecular Cell as "CircRNA biogenesis competes with pre-mRNA splicing."

Provided by Hebrew University of Jerusalem

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