# 'Cut-and-paste' gene defect hints at cause of developmental disease

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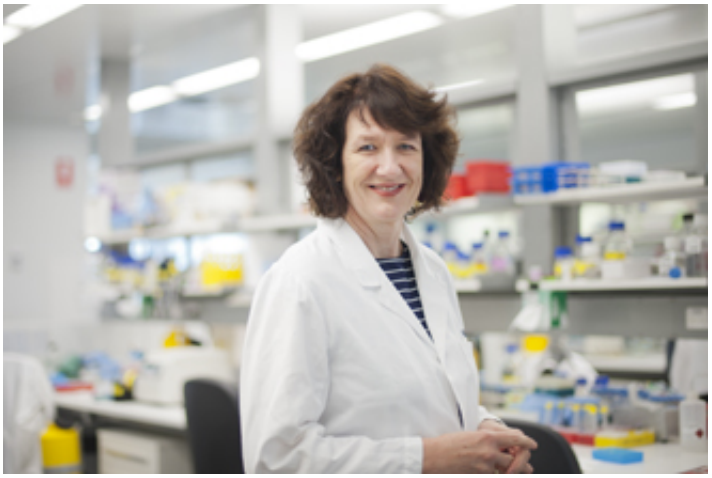

Associate Professor Joan Heath has uncovered a new way that protein production is regulated in development. Credit: Walter and Eliza Hall Institute, Australia

Melbourne researchers have made a major step forward in understanding how changes in an essential cellular process, called minor class splicing, may cause a severe developmental disease.

Using zebrafish, which is a popular laboratory model for studying development, the researchers discovered that the action of a protein called Rnpc3 is critical for the growth of many organs. Rnpc3 functions to regulate protein production through a process called minor class messenger RNA splicing.

Messenger RNA is a molecule that is required to convert the genetic information encoded in DNA into proteins. RNA splicing is a 'cut and paste' process that cuts unwanted sequences, called introns, out of messenger RNA, and pastes the remaining pieces back together again.

Without splicing, proteins cannot be made correctly from genes. Ludwig Member and Associate Professor Joan Heath at the Walter and Eliza Hall Institute and Dr Sebastian Markmiller, now at the University of California, San Diego, showed that the protein Rnpc3 is required for the rapid growth of organs, including the intestine, liver, pancreas and eye, during zebrafish development. The findings are published today in the journal *Proceedings of the National Academy of Sciences*.

Associate Professor Heath said the finding was important because it helped to shed light on how defects in minor class splicing cause a severe human developmental disorder known as Taybi-Linder syndrome.

"Altogether there are about 200,000 introns in the genome and most of these are removed by a process known as major class splicing," Associate Professor Heath said. "Minor class splicing is much rarer and is used to remove only a few hundred introns. Why this minor class splicing pathway exists at all, and how important it is, has eluded geneticists for more than two decades.

"We have discovered that minor class splicing is critical for the proper expression of genes that are themselves important for regulating gene expression. This means that defects in minor class splicing can have widespread effects on which genes are switched on. This is particularly crucial during development when rapid changes in gene expression and protein production are required," Associate Professor Heath said.

"In the long-run, we anticipate that our research will show that minor class splicing contributes to other diseases that are currently not fully

understood," she said.

**More information:** Minor class splicing shapes the zebrafish transcriptome during development, www.pnas.org/cgi/doi/10.1073/pnas.1305536111

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