RNA modification is important factor in smooth muscle contraction

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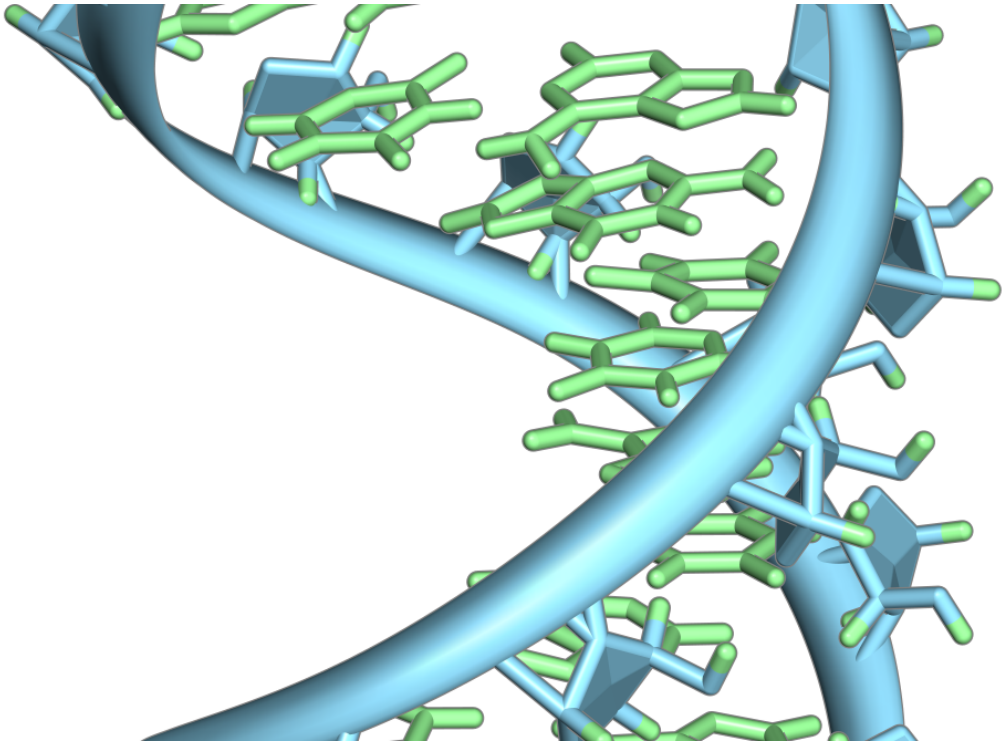

A hairpin loop from a pre-mRNA. Highlighted are the nucleobases (green) and the ribose-phosphate backbone (blue). Note that this is a single strand of RNA that folds back upon itself. Credit: Vossman/ Wikipedia

Genetic information is stored in DNA and is passed on in a very stable manner from one cell to the next or from one generation to the next. On a cellular level, genetic information is transcribed from DNA into RNA

(ribonucleic acid) and then mostly "translated" into proteins, which carry out cellular functions. This normally involves modifying the RNA so that this information can be "read" correctly or used appropriately – in order to adapt to changes in prevailing conditions. Researchers from the Division of Cell and Developmental Biology at MedUni Vienna have now shown that defects in this RNA modification can result in altered smooth muscle contraction, cardiovascular diseases and high blood pressure.

The main finding of the study by lead author Mamta Jain supervised by Franz-Michael Jantsch of MedUni Vienna's Division of Cell and Developmental Biology is that if a particular RNA modification in smooth muscle is defective or inadequate in the mouse model, there is a greater likelihood of high blood pressure and cardiovascular problems developing as a result of over-contraction. Working with MedUni Vienna's Division of Anatomy, this finding was further corroborated by post-mortem tests on bodies donated to science: defective RNA modification in the aortic muscles was observed in those who had died with a hypertrophic, or enlarged, heart: This vital modification was around 50% lower than in most people. Normally, RNA modification of 90% can be read in the proteins but, in the affected individuals, it was below 40%.

"Defective RNA modification, which is also referred to as adenosine deamination, results in a decline in smooth muscle contraction," explain the MedUni Vienna researchers. Consequently, the actin-binding protein filamin A, which plays an important role in organisation of the cytoskeleton and hence muscular contraction, cannot be produced in the correct form (variant R). "At the same time, we were able to show, for the first time, that adenosine deamination plays an important role in smooth muscle, not only in the central nervous system as previously believed" says Jantsch.

It is not yet known what causes RNA modification defects in smooth muscle and this will be the focus of follow-on studies. These might potentially lead to the development of new therapeutic options for improving the treatment of high blood pressure or certain forms of cardiovascular disease that are attributable to defective RNA modification.

Smooth muscle is one of three types of muscle found in humans and animals. It occurs in the walls of all hollow organs (apart from the heart), which are able to contract. For example, these include blood vessels, organs of the digestive tract (bladder, bowel) and the respiratory tract. It is called smooth muscle because of its microscopic structure—whereas skeletal muscle and cardiac muscle exhibit visible horizontal stripes when viewed under the microscope, smooth muscle has no such stripes. Unlike skeletal muscle, it cannot be contracted at will. Instead, its contraction is controlled by muscular mechanisms and also by the nervous system, by hormones, neurotransmitters and other messenger substances.

More information: Mamta Jain et al. RNA editing of Filamin A pre-mRNA regulates vascular contraction and diastolic blood pressure, *The EMBO Journal* (2018). DOI: 10.15252/embj.201694813

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