PRESS RELEASE

RNA modification important for brain function

8 Dec 2016, Mainz, Germany. *Researchers at the Institute of Molecular Biology (IMB) and Johannes Gutenberg University (JGU) in Mainz have shown that a new way of regulating genes is vital for the activity of the nervous system. They found that this form of regulation, a chemical modification on RNA called m^{6}A, is also important in influencing whether flies become male or female. This study clearly shows that RNA modifications play an important role.*

In their study, published in *Nature* today, the scientists show that the m^{6}A RNA modification occurs at high levels in the developing fly's nervous system and that it is important for this system to function. When they disrupted the molecular pathway that modifies the RNA, the flies behaved abnormally: they had problems folding their wings correctly, could not orientate themselves anymore and moved more slowly than flies whose RNA modifications were normal. The effect on locomotion results from an impaired function of the brain. The researchers also show that m^{6}A is important to fine-tune sex determination (i.e. whether a fly develops as male or female).

Jean-Yves Roignant, a group leader at IMB and corresponding author on the study, says, "The discovery that RNA modifications are so abundant on messenger RNAs was not anticipated until a few years ago and to my view this is one of the most exciting discoveries in the field in the last 15 years. Our study now sheds light on what they do in living organisms. We show that the m^{6}A modification plays an important role in the function of the nervous system and in sex determination in the fruit fly, *Drosophila*. As this modification is also enriched in the vertebrate nervous system, it is conceivable that it has similar roles in humans."

In order for our bodies to function normally, it is important for genes to be turned on or off in the right cells at the right times. It is already well established that DNA modifications are important to regulate the activity of genes. These molecular marks on the DNA act as signals to the cell machinery that converts the information contained within a gene into a proteins, and help determine how a particular gene is regulated. These signals can be added and removed, which changes whether genes are active or inactive. Many different modifications have also been identified on RNA, but what they do *in vivo* was not well understood. m^{6}A is the most prevalent of these RNA modifications, and scientists have shown that it can be added and removed in an analogous way to DNA modifications. The present publication is the first comprehensive study investigating the role of all components involved in the biogenesis of the m^{6}A RNA modification in a multicellular organism.

Besides finding an important role for m^{6}A in embryonic development, Dr Roignant and his team also identified a new component of the molecular machinery that regulates this RNA modification - *Spenito*. They next intend to investigate how this machinery works in more detail.

Tina Lence, a PhD student in the Roignant lab at IMB and first author of the paper, says "now we have found that m^{6}A is there and that it's important for neuronal functions, we want to understand more

about its precise role. For example, is it important in all circumstances, or is it more involved in the fine-tuning of gene expression, or in response to changes in the environment?"

This emerging field of RNA modifications, also called epitranscriptomics, is likely to yield many more exciting findings in the future.

Researchers involved in the study are based at the IMB, JGU's Institute of Pharmacy and Biochemistry and the university's Institute of Zoology, in Mainz, Germany, and at the Kimmel Center for Biology and Medicine of the Skirball Institute in New York, USA.

Further details

Lence T, Akhtar J, Bayer M, Schmid K, Spindler L, Hei Ho C, Kreim N, Andrade-Navarro MA, Poeck B, Helm M & Roignant JY. m^{6}A modulates neuronal functions and sex determination in *Drosophila*. *Nature*, 540, 242-247

Further information about research in Jean-Yves Roignant's lab can be found at www.imb.de/roignant.

About the Institute of Molecular Biology gGmbH

The Institute of Molecular Biology gGmbH (IMB) is a centre of excellence in the life sciences that was established in 2011 on the campus of Johannes Gutenberg University Mainz (JGU). Research at IMB concentrates on three cutting-edge areas: epigenetics, developmental biology, and genome stability. The Boehringer Ingelheim Foundation has dedicated 100 million euros for a period of ten years to cover the operating costs for research at IMB, while the state of Rhineland-Palatinate provided approximately 50 million euros for the construction of a state-of-the-art building. For more information about IMB, please visit: www.imb.de.

About the Boehringer Ingelheim Foundation

The Boehringer Ingelheim Foundation is an independent, non-profit organisation committed to the promotion of the medical, biological, chemical and pharmaceutical sciences. It was established in 1977 by Hubertus Liebrecht (1931-1991), a member of the shareholder family of the company Boehringer Ingelheim. With the PLUS 3 Perspectives Programme and the Exploration Grants, the foundation supports independent group leaders. It also endows the internationally renowned Heinrich Wieland Prize as well as awards for up-and-coming scientists. In addition, the foundation pledged to donate 100 million euros to finance the scientific running of the IMB at Johannes Gutenberg University Mainz for ten years. In 2013, the Boehringer Ingelheim Foundation donated a further 50 million euros to Johannes Gutenberg University Mainz. www.boehringer-ingelheim-stiftung.de.

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