PRESS RELEASE

Dealing with new neighbours: Keeping genes active after transposon insertion

(Mainz, 07 Dec 2018). *The group of Falk Butter at the Institute of Molecular Biology (IMB) in Mainz, Germany, in collaboration with the group of Steven Jacobsen from the University of California Los Angeles (UCLA), have discovered how cells prevent the accidental silencing of critical genes. In an article published today in* Science*, they describe how a group of proteins protect genes from the silencing effects of nearby transposable elements. This research highlights how an epigenetic modification, DNA methylation, which usually silences genes, can also be used to enhance gene expression.*

The DNA in the cells of all complex organisms contain so called "jumping genes" that can insert new copies of themselves back into the DNA at different locations. These transposable elements can be beneficial as they are a source of evolutionary diversity across organisms. They are also important in determining the architecture of DNA in a cell and in regulating gene activity. However, they can also pose a problem for the host in which they transpose. When reinserted into DNA, these elements can disrupt the function of genes. This happens through changes in what triggers gene activation, how strongly a gene is activated or by disrupting a gene entirely. To counteract these effects, cells have developed sophisticated methods to prevent transposable elements from interfering with the activity of nearby genes after they jump into a new location. This is achieved by using a chemical modification to DNA known as methylation, a form of epigenetic regulation. Methylation encourages DNA to condense and become less accessible to proteins that read genes. Thus, the genes become "silenced". A problem in this context is, when transposable elements are inserted near a gene, the cell's silencing mechanism may also inadvertently inactivate the gene itself. This can lead to crucial genes not being active anymore and can be very detrimental to the health of an organism. Thus the question has been around for some time, just how do cells deal with this problem?

When investigating which proteins bind to methylated DNA in plants, Marion Scheibe, the co-first author of the paper and a postdoc in the group of Falk Butter at IMB, identified several proteins whose functions were not well characterised. In particular the SUVH proteins. These proteins have been shown to activate methylated genes but it is not understood how they achieve it. This is where the expertise of Steven Jacobsen's group at UCLA came into play. They uncovered that the SUVH proteins were recruiting two other proteins, DNAJ1 and DNAJ2, to enhance gene transcription near methylated sequences, in particular those of transposable elements. Thus, genes close to transposable elements, that might otherwise have been accidentally silenced, stay active. As Falk Butter explains, "Steven's group were able to show that the recruitment of DNAJ1 to DNA was sufficient to induce gene expression. The SUVH and DNAJ proteins are binding to the DNA in silenced regions, including many transposable elements. What's really interesting is that they can keep the transposable elements switched off while still activating genes that are often very close by."

These findings help explain how DNA methylation can limit the detrimental effects of "jumping genes", while allowing them to remain in the genome as a source of evolutionary diversity and positive gene regulation. It is another step in understanding the puzzle of how evolution has let so

many of these elements become critical features in the DNA of most organisms but still managed to avoid their nastier side effects.

Further details
The research paper used as the basis for this article can be found here.

Falk Butter is a group leader at IMB and head of the Proteomics Core Facility. Further information about research in the Butter lab can be found at www.imb.de/butter.

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 focuses on three cutting-edge areas: epigenetics, developmental biology, and genome stability. The Institute is a prime example of successful collaboration between a private foundation and government: The Boehringer Ingelheim Foundation has committed 154 million euros to be disbursed from 2009 until 2027 to cover the operating costs of research at IMB. The State of Rhineland-Palatinate has provided approximately 50 million euros for the construction of a state-of-the-art building and will give further 52 million in core funding from 2020 until 2027. For more information about IMB, please visit: www.imb.de.

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