PRESS RELEASE

How to read R-loops, a bookmark in DNA for gene expression

(Mainz, 08 Jan 2019) *Scientists from the Institute of Molecular Biology (IMB) in Mainz, Germany, have uncovered a new way in which cells control gene activity. In a paper in* Nature Genetics, *the group of Prof. Christof Niehrs describe a mechanism for how R-loops regulate gene expression. R-loops are interwoven strands of RNA and DNA and the Niehrs' group show how R-loops are read and interpreted by the protein GADD45A as an important mechanism for gene regulation.*

R-loops are formed when RNA slides between the two strands of DNA, binding to one and pushing the other out into a single-stranded loop. Until recently, R-loops have often been thought of only for their negative aspects, such as disrupting genome stability or mutating DNA. However, in a paper published in *Nature Genetics* today, the group of Christof Niehrs describe how this tête-à-tête is a regular part of the cell's repertoire for controlling gene activity. Using a gene that suppresses tumour formation as an example, they show that R-loops can act as homing beacons for proteins needed to switch the gene on.

The activating region of a gene—the promoter—is often modified in such a way that proteins needed for the gene's expression can no longer bind. This "off" state can be converted to an "on" state by the removal of these modifications. As Prof. Niehrs explains, "R-loops form continuously in many genes. However, when they form near the promoter region, they can act as a platform for other proteins to come along and remove repressive modifications. Essentially, the cell is reading the R-loop and using it to activate genes at the correct time and place." At the heart of their discovery is a 'reader' for R-loops, a protein called GADD45A, which specifically recognises these structures and recruits further gene regulators. This research emphasizes that R-loops do not only have negative effects but are part of a cell's normal biology. It illustrates that R-loops are yet another tool cells use to control the activity of its genes—a process crucial for e.g. cell differentiation during development and cellular function.

Further details
Further information about Christof's work can be found at www.imb.de/research/niehrs/research/ and the paper in which this research is presented can be found at www.nature.com/articles/s41588-018-0306-6.

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.

Boehringer Ingelheim Foundation
The Boehringer Ingelheim Foundation is an independent, non-profit organization 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 Perspectives Programme "Plus 3" and the Exploration Grants, the foundation supports independent junior group leaders. It also endows the internationally renowned Heinrich Wieland Prize as well as awards for up-and-coming scientists. In addition, the Foundation is donating a

total of 154 million euros from 2009 to 2027 to the University of Mainz for the Institute of Molecular Biology (IMB). Since 2013, the Foundation has been providing a further 50 million euros for the development of the life sciences at the University of Mainz. www.bistiftung.de

Press contact for further information
Dr Ralf Dahm, Director of Scientific Management
Institute of Molecular Biology gGmbH (IMB), Ackermannweg 4, 55128 Mainz, Germany
Phone: +49 (0) 6131 39 21455, Fax: +49 (0) 6131 39 21421, Email: press@imb.de