PRESS RELEASE

Molecular biologist Helle Ulrich receives ERC Proof of Concept Grant for her research on ubiquitin

Mainz-based research team forges a new tool for manipulating ubiquitin chains and thus protein behaviour

19th March 2018. *Prof. Helle Ulrich from the Institute of Molecular Biology and Johannes Gutenberg University Mainz (JGU) has been awarded a Proof of Concept Grant from the European Research Council (ERC). This grant will go towards exploring the development of a new experimental tool called "Ubiquiton," which will enable researchers to specify the type of ubiquitin modification on any protein inside a living cell. The system will allow biologists to identify linkage-specific interaction partners, control the fate of proteins, and determine the consequences of such modifications in health and disease.*

As the name suggests, the protein ubiquitin is everywhere in our cells. And attaching ubiquitin to other proteins is one of the fundamental ways in which cells control the behaviour of the millions of proteins produced in each cell daily. Ubiquitin can be thought of as the instructions of a theatre director who tells the players, i.e., the proteins, what to do and when to leave the stage. These instructions can be quite complex since ubiquitin can be added to proteins either singly, multiply, or in the form of variable ubiquitin chains. The specific type of modification is what determines the function, location, or ultimate fate of a protein.

Scientists in the laboratory of Prof. Ulrich are currently developing a new tool to manipulate ubiquitin chains at will, which will open up entirely new ways to understand how ubiquitin controls proteins. Until now, the ability to study the effect of different ubiquitin chains has been severely limited since there are no good tools that allow for their easy manipulation. This is crucial as different ubiquitin assemblies can radically change the behaviour of a protein, and misguided or deregulated ubiquitylation is known to underlie diseases, such as cancer, neurodegeneration, and inflammation.

The tool developed by researchers in the laboratory of Prof. Ulrich is termed the "Ubiquiton" system. It uses an innovative set of tailor-made, inducible ubiquitylation enzymes that combine with substrate- and linkage-specific tags to form custom polyubiquitylated chains on desired proteins. Essentially, it allows the researcher to attach any one set of ubiquitin chains to any protein and look to see what happens. This is a major advance for signalling biologists, as Prof. Ulrich explains. "The Ubiquiton system enables us, for the first time, to examine the consequences of different ubiquitin signalling events across a whole new landscape of cells, tissues, and organisms. Up until now, researchers have known how to analyse what type of polyubiquitin chain a given protein naturally carries or how to inhibit the process altogether, but it has been impossible to purposefully induce the modification or even alter the type of chain. Our system allows exactly that. It removes the guesswork and allows us to identify the specific effects of each type of modification in each system individually. The Ubiquiton system will serve as an innovative research tool for any biologist wishing to investigate the physiology of polyubiquitylation in health and disease."

The European Research Council (ERC) has recognised the significance of this development and awarded Prof. Ulrich one of its Proof of Concept Grants to further develop her research. These prestigious grants are given to researchers to explore the possibility of turning ideas developed as part of other ERC-funded projects into a commercial or socially valuable proposition. Prof. Ulrich will use this funding to explore the development of the Ubiquiton system for use as a molecular biology discovery toolkit. With her lab, she will design expression constructs for a range of experimental systems and subcellular compartments and demonstrate the versatility of the method in different cell types. When this project is completed, it is envisioned that the techniques and enzymes will be shared with the wider scientific community.

Prof. Helle Ulrich is a Scientific Director at IMB and a Professor in the Faculty of Biology at the Johannes Gutenberg University, Mainz. Further information about research in Prof. Ulrich's lab can be found at www.imb.de/ulrich.

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 institute is a prime example of a successful collaboration between public authorities and a private foundation. The Boehringer Ingelheim Foundation has dedicated 100 million euros for a period of 10 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 Johannes Gutenberg University Mainz

Johannes Gutenberg University Mainz (JGU) is a globally renowned research university with about 32,500 students. With its PRISMA Cluster of Excellence and the MAINZ Graduate School of Excellence, JGU has successfully demonstrated its research capacity in the German Excellence Initiative. Thanks to its outstanding researchers and the establishment of vibrant research networks specifically in the fields of particle and hadron physics, materials sciences, the life sciences as well as translational medicine, Mainz University is in the international top league of research and maintains close ties with regional, national, and international partners in the scientific, cultural, and business sectors.

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 Perspectives Programme "Plus 3" and the Exploration Grants, the foundation supports independent junior group leaders. It also endows the internationally renowned Heinrich Weiland Prize as well as awards for up-and-coming scientists. In addition, the foundation pledged to donate a total of 100 million euros over ten years to the University of Mainz for the scientific running of the Institute of Molecular Biology (IMB) and a further 50 million euros for the development of the life sciences. www.bistiftung.de

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