PRESS RELEASE

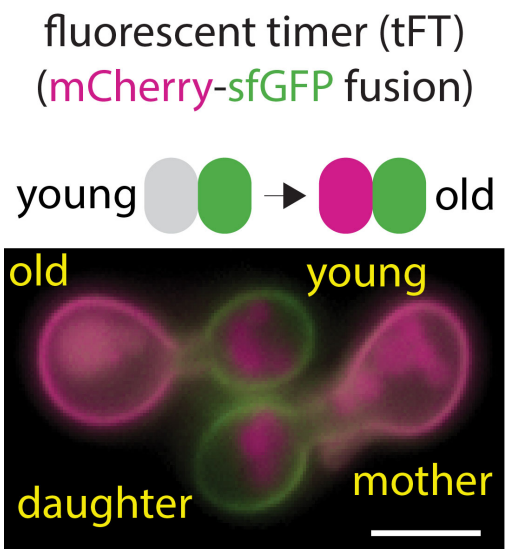
Protein quality control under the microscope as IMB appoints new group leader

16th November 2018. *In a new appointment, IMB is delighted to welcome Dr Anton Khmelinskii to the institute as a Junior Group Leader. Dr Khmelinskii studies the way living organisms ensure only functional proteins are present in cells and how abnormal proteins are recognised and degraded.*

Anyone familiar with manufacturing knows just how important it is to ensure that end products are produced to spec and sent to the right places; damaged or mislabelled products need to be identified and removed before shipping for a company's survival. As with so many other things we have learnt in the last 100 years, typically, biology has been doing the same thing for millions of years before us, just on a microscopic scale. Our cells produce proteins at a speed and accuracy to rival any modern production line. To ensure that these proteins are folded properly and sent to the correct compartment, our cells employ a series of quality control checks to refold or degrade proteins that are not up to scratch. Failures in these systems are associated with numerous diseases, including neurodegenerative diseases, and ageing.

It is within this field of protein quality control that Dr Khmelinskii will bring his expertise to IMB, starting in January 2018. He will perform research on the ubiquitin-proteasome system (UPS), which is responsible for the selective degradation of proteins. As Dr Khmelinskii explains "we will continue using the budding yeast *Saccharomyces cerevisiae* to work on identifying substrates for all UPS components and explore the functions of this system in replicative ageing and genome stability in cancer." In a similar vein of research, he will advance his work on the quality control of mislocalized proteins where he identified the Asi pathway (*Nature,* 2014). Describing the goals of his research, Dr Khmelinskii explains that "despite the prevalence of protein mislocalization, the systems performing quality control of mislocalized proteins are unknown for most of the proteome. Our immediate future work will tackle the limitations in identifying these systems." To this end, Dr Khmelinskii is the recipient of an ERC starting grant on the topic of quality control of mislocalized proteins. This prestigious award will enable him to drive his research in this field into new and exciting directions.

Dr Khmelinskii highlights that good quality control of proteins is required for healthy ageing. As cells age, there is a "gradual collapse of proteome homeostasis and accumulation of damaged or otherwise abnormal proteins." One of the mechanisms that cells have devised to overcome this issue is to divide in an asymmetric fashion, segregating the older, damaged proteins into one cell and having only the younger more efficient proteins



Fluorescent timer for protein age. *By labeling a protein with two fluorescent tags with different rates of maturation, protein age can be visualised. Here in yeast cells, we see that during cell division older proteins (magenta) are retained in the mother cell, while the younger recently produced proteins (green) are shuttled to the budding daughter cell.*

reside in the new cell. Dr Khmelinskii has developed a unique fluorescent timer approach to study this phenomenon whereby old and young proteins are differently labelled and their inheritance in cell division can be studied (see figure). Using this system, he hopes to understand how factors that drive the ageing process are retained in one cell in preference to the newly synthesised daughter cell.

Further details
Further information can be found here https://www.imb.de/research/khmelinskii/research/

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 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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