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Better understanding of cell renewal and cellular quality control

Approval for Collaborative Research Centre (CRC) on selective autophagy led by Frankfurt scientists

FRANKFURT. The German Research Foundation (Deutsche Forschungsgemeinschaft/DFG) has approved 11 million Euro for the next four years for establishing a CRC on selective autophagy under the lead of Goethe University. Autophagy literally means "self-eating" and refers to a sophisticated system in which cellular waste is specifically detected and removed. It contributes to regular cell renewal, secures quality control and protects against diseases. Defects in this pathway can promote cancer development and neurodegenerative diseases like Parkinson, and contribute to infectious diseases and inflammatory reactions. The objective of the CRC is a better understanding of autophagy at the molecular and cellular level. In future, the researchers hope to be able to specifically target autophagy for improving the therapy of diverse diseases.

Professor Birgitta Wolff, President of the University, congratulated the researchers: "Well done to Ivan Dikic and his team for achieving this important milestone. The research planned within the CRC forms a promising basis for the development of new and more effective therapies. We are particularly pleased that we will be joining forces with Mainz University, the Institute of Molecular Biology in Mainz and the Georg-Speyer-Haus in the CRC – a further sign of the vitality of our regional partnerships."

Autophagy is conserved from simple organisms such as yeast up to complex ones like humans. Typical targets for autophagy are harmful or superfluous proteins - it degrades for example aggregated proteins, which can otherwise lead to severe damage and cell death, as observed in numerous neurodegenerative diseases. Even entire cell organelles and invading pathogens such as bacteria or viruses can be eliminated via this pathway. The building blocks generated through this degradation process are recycled, which is why autophagy also functions as a survival strategy in times of low energy supply.

Autophagy is a highly complex and precisely regulated process which requires a concerted action by numerous players: The target substrate needs to be specifically recognized and surrounded by membranes to form what is known as the autophagosome. Autophagosomes fuse with lysosomes, which are cell organelles filled with digestive enzymes, finally enabling the breakdown of all cargo into the individual building blocks.

"The enormous significance of autophagy for the pathophysiology of diseases has only been recognized in the past decade. As a result, research activity in this field has increased rapidly", explains Professor Ivan Dikic, CRC Speaker and Director of the Institute of Biochemistry II at Goethe University. "By strategic recruitments over the past five years, we have succeeded in developing Frankfurt into a centre for autophagy research. Now we are in a position to address many of the unanswered questions: What triggers autophagy? How does the cell select targets for autophagy? How does this pathway crosstalk to other cellular mechanisms and how is it involved in the pathogenesis of human diseases?"

Meanwhile it is known that the role of autophagy strongly depends on the cellular context: In healthy tissues, it prevents the emergence of cancer cells. At the same time, however,

cancer cells capitalize on autophagy to overcome bottlenecks in nutrient supply, which occur as a result of rapid tumour growth. The researchers are now analysing this complex interaction. So far, little is known about the interplay of autophagy with other mechanisms, such as cellular trafficking (endocytosis), programmed cell death (apoptosis) and the ubiquitination system, which marks proteins for degradation in the proteasome.

Within the newly established CRC, researchers will study autophagy at the level of molecules, cells and model organisms. It is the first large-scale collaborative project in this field in Germany and allows scientists in Frankfurt and Mainz to position themselves in an internationally highly competitive field. A broad line-up of disciplines is needed to tackle the open questions, and therefore, within the CRC, structural biologists have teamed up with biochemists, cell biologists and clinicians. New insight into the molecular mechanisms underlying autophagy will be directly transferred to model systems for human diseases.

At Goethe University, the three faculties of Biological Sciences, Biochemistry, Chemistry and Pharmacy, and Medicine, and the cross-disciplinary Buchmann Institute for Molecular Life Sciences (BMLS) are participating in the CRC. Partners outside the University are the Institute for Pathobiochemistry at the University Medical Center of Johannes Gutenberg University Mainz (Prof. Dr. Christian Behl is Vice Speaker of the CRC), the Georg-Speyer-Haus in Frankfurt and the Institute of Molecular Biology gGmbH in Mainz.

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Die Goethe-Universität Goethe University is a research-oriented university in the European financial centre Frankfurt founded in 1914 with purely private funds by liberally-oriented Frankfurt citizens. It is dedicated to research and education under the motto "Science for Society" and to this day continues to function as a "citizens' university". Many of the early benefactors were Jewish. Over the past 100 years, Goethe University has done pioneering work in the social and sociological sciences, chemistry, quantum physics, brain research and labour law. It gained a unique level of autonomy on 1 January 2008 by returning to its historic roots as a privately funded university. Today, it is among the top ten in external funding and among the top three largest universities in Germany, with three clusters of excellence in medicine, life sciences and the humanities.

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