PRESS RELEASE

Taking out the cellular "trash" – at the right place and the right time

Vienna, October 20th, 2016

New possibilities for the regulation of molecular processes

New insight about how cells dispose of their waste is now given by the group of Claudine Kraft at the Max F. Perutz Laboratories (MFPL) of the University of Vienna and the Medical University of Vienna. They show the necessity of a regulation in space and time of a key protein involved in cellular waste disposal. Dysfunctions in the waste disposal system of a cell are linked to cancer and Alzheimer's disease. The study is published in the renowned journal *Molecular Cell*.

A clean apartment and workplace, while certainly important, are not strictly necessary in order to survive. For cells, however, tidying up is absolutely vital. The responsible process is called autophagy, which has now become widely known due to Yoshinori Ohsumi's winning of the Nobel Prize in Medicine in October 2016. During autophagy, a defined set of proteins coordinates the removal of viruses, bacteria, and damaged or superfluous material from a cell. Autophagy also enables cells to survive times of starvation, by degrading the cell's own components to recycle their building blocks – similar to recycling stations in a town. This process needs to be tightly controlled to prevent the removal of structures that are still required in the cell. "You would not want to accidentally throw away your TV set while cleaning up your apartment, would you?" explains Raffaela Torggler, shared first author of the study. "For a cell, aberrant activation of autophagy could easily have lethal consequences".

The key regulator of autophagy is the protein Atg1. Its importance for the activation of autophagy has long been known to researchers, and details of its functions were described by the Kraft group in their 2014 *Molecular Cell* publication. However, how Atg1 activity and the process of autophagy are controlled in order to prevent their aberrant activation had remained elusive. Now, the team of Claudine Kraft at the MFPL of the University of Vienna discovered that Atg1 is regulated in both space and time. Only when precise requirements are met, Atg1 is activated and autophagy is initiated.

To start the process, both the key regulator Atg1 as well as the "waste" to be discarded are separately brought to the precise location where the waste is packed into cellular "garbage bags". The simultaneous presence of both Atg1 and the waste at this place is crucial for the activation of Atg1 and the initiation of autophagy. Claudine Kraft and her team showed that the cell allows Atg1 to meet the waste only at the site of waste packaging. This tightly restricts autophagy initiation in space and time and prevents its aberrant activation.

In a normal cell two coordinators bring Atg1 and the waste independently from each other to the waste packaging location. When these coordinators are removed from the cell, the waste and Atg1 cannot meet and autophagy is not induced. Daniel Papinski, shared first author of the study, explains: "In cells without these coordinators, we were able to promote waste removal by autophagy when Atg1 was artificially forced to meet the waste. This shows that the concurrence of Atg1 and waste at the right place is a key regulatory step to activate autophagy".

The detailed study of such fundamental cellular processes is crucial for the understanding of diseases that go hand in hand with these events – in the case of autophagy, Alzheimer's disease or cancer. In the long run, this will help to better treat or perhaps even prevent these illnesses.

MAX F. PERUTZ LABORATORIES

Vienna Biocenter (VBC,) Dr. Bohr-Gasse 9 | 1030 Wien | Austria
Tel: +43 1 4277 24014
communications@mfpl.ac.at | www.mfpl.ac.at

Claudine Kraft elaborates: “This work gave us important insight into the molecular events regulating autophagy in space and time. Only if we understand the molecular details, we will be able to design medication exclusively targeting autophagy in these diseases”.

Publication in "Molecular Cell"
Torggler R, Papinski D, Brach T, Bas L, Schuschnig M, Pfaffenwimmer T, Rohringer S, Matzhold T, Schweida D, Brezovich A and Kraft C (2016). **Two Independent Pathways within Selective Autophagy Converge to Activate Atg1 Kinase at the Vacuole.** Molecular Cell, doi:http://dx.doi.org/10.1016/j.molcel.2016.09.008

Scientific Contact
Assoc.-Prof. Dr. Claudine Kraft
Max F. Perutz Laboratories
Universität Wien
Vienna Biocenter
1030 Wien, Dr.-Bohr-Gasse 9
T +43-1-4277-528 77
M +43-664-602 77-528 77
claudine.kraft@univie.ac.at

Press Contact
Caterina Purini, MSc.
Max F. Perutz Laboratories
Communications
Vienna Biocenter
1030 Wien, Dr.-Bohr-Gasse 9
T +43-1-4277-240 14
caterina.purini@mfpl.ac.at

About the MFPL
The Max F. Perutz Laboratories (MFPL) are a center established by the University of Vienna and the Medical University of Vienna to provide an environment for excellent, internationally recognized research and education in the field of Molecular Biology. The MFPL are located at the Vienna Biocenter, one of the largest Life Sciences clusters in Austria, and host on average 60 independent research groups, involving more than 500 people from 40 nations.