



Press Release
For Immediate Release
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Complex that Removes Damaged Cellular Proteins Discovered

Baltimore, MD— A research team of investigators from the University of Maryland Biotechnology Institute (UMBI) and the National Institutes of Health (NIH) have identified a new complex involved in removing damaged proteins from cells, the discovery of which could lead to novel therapies for treating human disorders, especially neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, Huntington's disease and amyotrophic lateral sclerosis, all of which are linked to an accumulation of misfolded proteins in the brain.

The discovery of the complex is published in the October 18th online issue of *The Journal of Cell Biology*. The article is titled "Ubiquilin and p97/VCP Bind Erasin, Forming a Complex involved in ERAD" and is authored by Precious J. Lim, Rebecca Danner, Jing Liang, Howard Doong, Christine Harman, Deepa Srinivasan, Cara Rothenberg, Hongmin Wang, Yihong Ye, Shengyun Fang, and Mervyn J. Monteiro

The team, led by Dr. Mervyn J. Monteiro from UMBI's Medical Biotechnology Center (MBC), discovered the new complex in the endoplasmic reticulum (ER), the factory where many important proteins are made. However, just like any typical factory, proteins made in the ER sometimes contain flaws, or they may be missing parts for correct assembly, and if so, they must be removed; otherwise

they can wreak havoc on cells. Fortunately, there is a strict quality control system that inspects proteins in the ER for such defects. Those that pass the inspection are released for export, whereas those that are defective are channeled out of the ER and degraded by the proteasome, a giant “protein-eating machine” of the cell. Defects in this clearance pathway induce ER stress, which if not alleviated can cause cell death. In fact, recent evidence suggests that mutant proteins that cause amyotrophic lateral sclerosis and Huntington’s disease block the clearance pathway, but efforts to prevent this from happening are hampered by a lack of understanding of the pathway.

The new complex that the team identified functions to remove damaged proteins from the ER. Two of the chief components of the complex are ubiquilin and erasin, both of which were discovered by the Monteiro lab in 2000 and 2006, respectively. Using a variety of techniques, including testing with known damaged proteins, the authors confirmed the existence and function of the complex. Furthermore, they found that loss of ubiquilin or erasin expression leads to a buildup of ER stress and reduces lifespan in animals. They believe that insight obtained from the study could be exploited to modulate the function of the complex in order to prevent ER stress that is thought to cause several different human diseases.

The work was funded by the National Institute of General Medical Sciences and the National Institutes on Aging of NIH.

Further information on the paper can be found at:

<http://jcb.rupress.org/cgi/content/abstract/jcb.200903024v1>

With research centers in Baltimore, Rockville, and College Park, UMBI, the University of Maryland Biotechnology Institute, is the newest of 13 institutions forming the University System of Maryland. UMBI has more than 50 ladder-ranked faculty and a mandate to advance the biotechnology economy while preparing a well-equipped workforce.

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