Discovery of a Protein Quality Control System for Selenoproteins

A research group led by Dr. Hsueh-Chi Sherry Yen, Assistant Research Fellow at the Institute of Molecular Biology in collaboration with Dr. Kay-Hooi Khoo, a Distinguished Research Fellow at the Institute of Biological Chemistry has recently identified a novel protein quality control system mediated by a CRL2 ubiquitin ligase. The system controls the fidelity of selenoproteins. Selenium is an essential trace element that executes its biological function in the form of selenoproteins, and is closely related to many human diseases. The article was published in July 3, 2015 issue of *Science.*

Proteins represent the basic cellular machinery that make possible all processes necessary for life, and ensuring utmost fidelity during protein synthesis is essential for cell survival. During the production process, a string of amino acid building blocks is laced together to form a unique protein, which then folds into a unique structure necessary to fulfill the role of the individual protein. Nevertheless, problems encountered during this process can result in malformed proteins lacking vital functional units, which can cause problems for the entire organism if not discovered. Cells have quality control systems, but it is unclear how abnormal proteins are identified and how effectively problems are recognized.

Selenoproteins contain an unusual amino acid building block, selenocysteine. Proteins containing this amino acid frequently encounter premature termination of synthesis, resulting in a smaller protein that lacks functionality. In the article, Dr. Yen's group reported that a special protein called CRL2 is a gatekeeper in selenoprotein quality control. CRL2 recognizes the exposed tails of these shortened selenoproteins and marks it for of degradation. Dr. Yen developed a highly sensitive, novel cellular system to examine protein stability throughout the cell. Using this technique, they identified what may be the most stringent protein quality control system ever documented, where a change in protein length by just a single amino acid block is sufficient to signal degradation of the protein.

Defective proteins have been implicated in aging, neurodegenerative diseases, and cancer, making understanding the quality control mechanisms of the cell crucial. Dr. Yen's work paves the way for clinical strategies based on the cell's own machinery to improve overall human health. Following on from this discovery, Dr. Yen's group has begun to examine the possible quality control functions of CRL2 beyond selenoproteins.

The current article is the third study by Dr. Yen to appear in the prestigious journal *Science*. The first two articles, published in 2008, detailed the invention and application of a global protein

stability (GPS) profiling technique. The first author of the current article, Hsiu-Chuan Lin, is a graduate student of the Genome and Systems Biology Degree Program at National Taiwan University.

The full article entitled “CRL2 Aids Elimination of Truncated Selenoproteins Produced by Failed UGA/Sec Decoding” is available at Science website at:
http://www.sciencemag.org/content/349/6243/91.short

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