

In the news

THE LASKER PRIZE UNFOLDS

The 2014 Albert Lasker Basic Medical Research Award goes to Kazutoshi Mori (Kyoto University, Japan) and Peter Walter (University of California, San Francisco, USA) “For discoveries concerning the unfolded protein response — an intracellular quality control system that detects harmful misfolded proteins in the endoplasmic reticulum and signals the nucleus to carry out corrective measures.”

([Lasker Foundation](#)).

Proteins that are secreted or destined for the cell surface must enter the endoplasmic reticulum (ER), where they undergo maturation and folding. The unfolded protein response (UPR) detects damaged or misfolded proteins, both in stress conditions and during normal homeostasis, and signals to the nucleus to bolster the cells’ protein folding capacity. In the mid-1990s, Mori and Walter identified core components of the yeast UPR, revealing unexpected aspects of its mechanism.

Earlier studies suggested that cells monitor the abundance of unfolded proteins in the ER and signal to the nucleus to promote the synthesis of BIP, a yeast protein that promotes folding. In 1993, Mori and Walter independently discovered the key factor that transduces the unfolded signal: the ER transmembrane kinase IRE1. They showed that IRE1 detects unfolded proteins inside the ER, and its cytoplasmic domain modifies *HAC1* mRNAs so that active HAC1 protein enters the nucleus to activate the gene encoding BIP.

Mori, Walter and others later identified other UPR pathways in mammals and future studies will continue to peel back the layers of this complex system and how it can be manipulated to treat diseases such as cancer; cancer cells that accumulate misfolded proteins are kept alive by the UPR. As Walter says, “At a clinical level we need to understand where we can interfere or intervene with the signaling pathway to the benefit of the patient.” ([Scientific American](#), 9 Sept).

Kim Baumann