Acceptance speech

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Kazutoshi Mori, awardee in the Biology and Biomedicine category (16th edition)

Proteins are responsible for the activity of life. We humans use approximately 20,000 proteins, and each protein has its own three-dimensional structure to fulfill its function. This protein folding is assisted by a special type of proteins, called molecular chaperones. Drs. Hartl and Horwich nicely showed how chaperones work. This means, in other words, that protein misfolding constitutes a fundamental threat to all living things. Protein misfolding is particularly acute in the endoplasmic reticulum (ER), an organelle where ligand-like secretory protein and its receptor-like transmembrane protein are folded and assembled, because they play a critical role in intercellular communication. Protein misfolding in the ER is called ER stress. Importantly, we have developed a way to cope with ER stress, which is called the unfolded protein response (UPR). Dr. Walter and I elucidated the molecular mechanism of the UPR and showed how molecular chaperones are induced to cope with ER stress.

ER stress and the UPR have been considered to be associated with the development and progression of various diseases. For example, cancer cells survive under stressful conditions by activating the UPR. Therefore, UPR inhibitors can be used as anti-cancer drugs, some of which are now in phase II clinical trial. Other examples are neurodegenerative diseases. The chemical chaperone is a small molecule capable of stabilizing protein folding status. Quite recently, chemical chaperones have been approved to treat patients with amyotrophic lateral sclerosis (ALS) in the USA and Canada.

Peter and I have shared 5 international awards and this is my first award from Europe. I believe that real understanding of ER stress and the UPR will develop new therapies and I promise I will keep working in this direction.