Unconventional Secretion of Transmembrane Protein

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Most eukaryotic secretory or membrane proteins reach the plasma membrane through the conventional endoplasmic reticulum (ER)-Golgi pathway. However, evidence suggests that many cytoplasmic, nuclear, and signal-peptide-containing proteins also can reach the cell surface via a Golgi-bypassing route. These pathways are collectively referred to as unconventional protein secretion (UPS). A number of transmembrane proteins including CFTR, CD45, voltage-gated potassium channel Kv4, the yeast protein Ist2, the *Drosophila melanogaster* alpha-integrins, Mpl, and pendrin are known to reach the cell surface via UPS under specific conditions. Understanding the UPS pathways is important not only to elucidate the mechanisms of intracellular trafficking pathways, but also has important ramifications for human health because many proteins undergo UPS are associated with human diseases. For example, our group recently found that the selective activation of the UPS pathway would be a potential therapeutic strategy for the treatment of diseases arising from the transport defects of misfolded proteins, such as cystic fibrosis and Pendred syndrome. In this talk, I will introduce the molecular machineries involved in the UPS of transmembrane proteins, particularly those related to human diseases, and discuss the potential for new therapeutic strategies for the treatment of UPS-associated diseases.