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National Tsing Hua University Scientists Published Novel Primary Proton Pump Result in *Nature*

Hsinchu, March 28, 2012. A research team from the College of Life Science of National Tsing Hua University led by Professors Yuh-Ju Sun and Rong-long Pan unraveled the first crystal structure of a membrane-embedded H^+-pyrophosphatase (H^+-PPase) and revealed a unique proton translocation mechanism.

According to Professor Yuh-Ju Sun, "*this work illustrates how plant cells efficiently hydrolyze metabolic by-product to generate the proton gradient as energy source for other metabolism. It is a significant breakthrough and sets an important milestone in the field of membrane proteins*!"

The paper entitled "**Crystal Structure of a membrane-embedded H^+-translocating pyrophosphatase**" is reported in the March, 28, 2012 edition of the magazine *Nature*.

H^+-PPase, which was widely found in plants, bacteria and archaea, has been studied for many decades. This novel enzyme exhaustively uses a metabolite, pyrophosphate, to drive other transporter systems in a way similar to trash treatment plant in our daily life.

In plants, H^+-PPases enhance their resistance to cold, drought, salt and many other stresses. It is also a key enzyme for the development and improvement of economic crops. On the other hand, pathogens such as tetanus and periodontal bacteria contain these enzymes on their cell surface. It is thus suitable for pharmaceutical development as specific drug target. Therefore, this study has a great economic potential in the environment, green energy, agriculture and medicine etc.

Professors Yuh-Ju Sun and Rong-long Pan cooperated with Prof. Chwan-Deng Hsiao of Academia Sinica in discovering the mystery of this proton transporter. Using X-ray crystallography and the light source provided by Taiwan's National Synchrotron Radiation Research Center (NSRRC,) Mr. Shih-Ming Lin, the first author of the Nature publication, successfully determined the high-resolution structure of H^+-PPase. Mr. Lin tactfully employed crucial protocols in purification and crystallization of the membrane protein. H^+-PPase consists of two molecules and each contains sixteen transmembrane helices forming a very complex transmembrane region. By delineating this structure, the team found that each protein molecule has a highly acidic catalytic site for the hydrolysis of pyrophosphate, and a unique translocation pathway for the proton transport. This new discovery helps us to understand the reaction mechanism, ion transport, and possible coupling reaction of the enzyme.

The membrane protein accounts for about 30% of all proteins in the cell. However, only about 1% structures of membrane proteins have so far been solved. Due to the insolubility of membrane proteins and the complexity of their structures, it is difficult to purify and crystallize membrane proteins for the structural determination. Since membrane protein locates on the cell surface where it is suitable for drug attack, more than 50% pharmaceutical drug target proteins are membrane proteins.

"*The structural and functional studies of H^+-PPase is enormously helpful in drug designs, improvement of economic crops, and biomass energy supply*," according to Professor Rong-long Pan. "*This work reported in Nature provides a paradigm for the membrane protein study, and has received much attention by academic circles worldwide*," concluded Pan.

http://www.nature.com/nature/journal/vaop/ncurrent/full/nature10963.html