One step closer to a drug treatment for cystic fibrosis

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A University of Missouri researcher believes his latest work moves scientists closer to a cure for cystic fibrosis, one of the world's most common fatal genetic diseases.

The Journal of Biological Chemistry has published findings by Tzyh-Chang Hwang, a professor in the School of Medicine's Department of Medical Pharmacology and Physiology and the Dalton Cardiovascular Research Center. The publication has been recognized as the "paper of the week" for the journal, meaning Hwang's work is considered to be in the top 1 percent of papers reviewed annually in terms of significance and overall importance.

Hwang's work focuses on the two most common genetic mutations among approximately 1,500 mutations found in patients with cystic fibrosis. These two mutations cause specific chloride channels in the cell, known as the Cystic Fibrosis Transmembrane conductance Regulator (CFTR) chloride channels, to malfunction. This ultimately leads to repeated pneumonia, the primary cause of most deaths associated with cystic fibrosis.

"The normal function of a cell is to pass chloride ions across the cell membrane at a very fast speed," Hwang said. "We know some signaling molecules elicit this reaction, much like a hand signals an automatic water faucet to dispense water. But in the case of cystic fibrosis, that signal is no longer detected by the mutated channel protein. Through some mechanisms we still don't quite understand, malfunction of this

channel protein eventually leads to bacterial infection in the lung, which is believed to be responsible for the most severe symptoms of cystic fibrosis."

The most recent study found that manipulating the sensor of the channel protein can significantly rectify the malfunction of the mutated channel, thus opening the door to a drug design that may eventually be a "real cure," Hwang said.

"We could help a lot of patients if we can utilize the power of computer simulations and structure-based drug design to discover new therapeutical reagents for cystic fibrosis, but it's very expensive to do this kind of research in an academic institute," Hwang said.

Provided by University of Missouri-Columbia