SOUTHWESTERN NEWS

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MAIN REGULATOR OF MEMBRANE TRAFFICKING NOT WHAT RESEARCHERS ONCE THOUGHT, SCIENTISTS DISCOVER

DALLAS – Aug. 8, 2003 – Researchers at UT Southwestern Medical Center at Dallas have identified a main regulator of the system that controls membrane trafficking, debunking what scientists for a decade had thought controlled this process.

The Golgi – described as the "grand central sorting station" of the cell by scientists – is regulated by phosphatidylinositol 4 phosphate (PI4P) instead of phosphatidylinositol 4,5 bisphosphate (PIP2), which was believed to be the main regulator of this system. Both lipids are essential for recruiting proteins to the membrane.

The findings appear in today's issue of *Cell*.

"PI4P has been overshadowed by PIP2 as one of the major regulators of the Golgi because PI4P is made into PIP2. It is the immediate precursor of PIP2," said Dr. Helen Yin, professor of physiology and the study's senior author. "It was thought that PIP2 was important for all aspects of membrane trafficking in the Golgi, but we have found that PI4P is very abundant in the Golgi and without PI4P the Golgi can't function."

PI4P acts as a zip code by directing proteins to the Golgi. An understanding of this system gives researchers insight into membrane trafficking, a vital process for cell survival.

"If the Golgi does not have PI4P it can't perform vital functions necessary for cell survival," Dr. Yin said. "If this system is interrupted, cells will go through apoptosis, or cell death."

Diseases like Alzheimer's and Parkinson's are a result of problems associated with protein trafficking, Dr. Yin added.

"Every time a protein is made, there is the possibility that something can go wrong," Dr. Yin said. "There is a checking mechanism from the endoplasmic reticulum (where proteins are

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made) to the Golgi, and then the protein is released. If this checking mechanism is disrupted, you will have a traffic jam that will result in misfolded proteins."

Other UT Southwestern researchers contributing to the study include Dr. Ying-Jie Wang, lead author and a postdoctoral researcher in physiology; Dr. Joseph Albanesi, professor of pharmacology; Manuel Martinez, research assistant in physiology; Dr. Michael Roth, professor of biochemistry; Dr. Hui-Qiao Sun, assistant professor of physiology; Dr. Yuxiao Sun, postdoctoral researcher in molecular biology; and Jing Wang, a student research assistant in physiology. Researchers at Harvard Medical School also contributed to the work.

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