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Golgi trafficking controlled by G proteins

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A family of proteins called G proteins are a recognized component of the communication system the human body uses to sense hormones and other chemicals in the bloodstream and to send messages to cells. In work that further illuminates how cells work, researchers at University of California, San Diego School of Medicine have discovered a new role for G proteins that may have relevance to halting solid tumor cancer metastasis.

The study is reported online April 9 in *Developmental Cell*.

"Our work provides the first direct evidence that G proteins are signaling on membranes inside cells, not just at the cell surface as has been widely believed for several decades," said Pradipta Ghosh, MD, associate professor and senior author. "This is significant because the G-protein pathway is a target of at least 30 percent of all current drugs on the market."

Specifically, the UC San Diego-led team used live cell imaging of fluorescent proteins and other biological assays to show that G proteins in cultured human cells are active on a series of pancake-shaped membranes, called the Golgi body. The Golgi body sorts, packages and directs the distribution of newly synthesized proteins to various locations within a cell. It also secretes enzymes, including matrix metalloproteases that enable cancer cells to digest surrounding tissue, escape and spread.

In addition to documenting G protein activity on the Golgi, scientists also identified the protein that turns on G proteins as GIV, widely

recognized in the cancer research community for its role in facilitating metastasis. When GIV was inhibited, G proteins were shown to remain inactive on the Golgi and secretion of enzymes and other proteins was delayed.

"We've identified a new mechanism that may contribute to the progression of chronic diseases like cancer," Ghosh said. "Prior to the study, the role of GIV in mediating cancer metastasis was ascribed to its ability to activate G proteins near the cell surface. We now know that targeting GIV and G proteins is a double whammy that inhibits key cancer-driving signals near the cell surface as well as secretion from the Golgi that may contribute to metastasis."

Provided by University of California - San Diego