Molecular mechanism provides intra-cellular traffic signal

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City planners could learn a lesson or two from tiny cells on how to maximize traffic flow. Researchers at the University of Illinois at Chicago have found that intra-cellular trafficking is tightly coordinated for maximum flow through cellular compartments -- much as vehicles on a crowded road are allowed to pass quickly through a succession of green traffic lights.

The molecular mechanism that underlies this coordination is reported by lead researcher Nava Segev, UIC professor of biological sciences, in the November issue of *Nature Cell Biology*.

While the finding was made using yeast cells, intra-cellular mechanisms discovered in yeast almost invariably correspond to processes in mammalian cells, including humans, and the mechanism Segev described may find applicability in the biomedical field.

"Every system in our body depends on intra-cellular trafficking, because anything that goes from the inside of a cell to the outside, or from outside to inside, uses this process," Segev said. "Malfunctioning of this pathway can cause a variety of human diseases. For example, problems in insulin secretion or presentation of insulin-receptors on the cell membrane result in diabetes. Defects in growth factor secretion and presentation of their receptors on cells result in cancer. Defects in neurotransmitter release or internalization result in brain disorders."

A special set of proteins is responsible for the coordination. Molecular

switches that go by the letters Ypt allow membrane-enclosed vesicles to pass in and out of cellular compartments. Activator proteins flip the switches on. One activator protein, called TRAPP, coordinates two Ypt switches for quick entrance and subsequent exit from a central cellular compartment known as the Golgi apparatus.

"The Golgi is a central station in all cells, through which all intra-cellular traffic passes," Segev explained.

Specific subunits of TRAPP previously identified by the UIC researchers were found to be the key to coordinated switching and traffic flow through the Golgi. They have now shown that components of TRAPP act in sequence to direct the flow. One form of TRAPP turns on the first Ypt for entry into the Golgi, while at the other end of the Golgi, two subunits join TRAPP to activate the Ypt required for exit from the Golgi, Segev said.

Segev said the mechanism that her lab identified must now be shown to exist in mammalian cells. Her earlier discovery of the Ypt molecular switches in yeast and the subsequent finding of their homologues in mammalian cells, together with the fact that TRAPP is conserved in evolution from yeast to man, lead her to believe the entire coordinated switching mechanism is universal.

Source: University of Illinois at Chicago