MedicalXpress

Molecular motors may speed nutrient processing

May 30 2007

Matthew Tyska, Ph.D., recalls being intrigued, from the first day of his postdoctoral fellowship in 1999, with a nearly 30-year-old photograph. It was an electron micrograph that showed the internal structures of an intestinal cell microvillus, a finger-like protrusion on the cell surface. Microvilli are common features on the epithelial cells that line the body's cavities.

At the time, Tyska knew that the core bundle traveling up the center of the microvillus was an array of the structural protein actin, and that the ladder-like "rungs" connecting the actin bundle to the cell membrane were composed of the motor protein myosin-1a. This myosin, though related to the myosin involved in muscle cell contraction, was thought to serve a purely structural role. "The textbook thinking for decades was that microvilli serve as a passive scaffold, a way to amplify the membrane surface area," said Tyska, assistant professor of Cell and Developmental Biology at Vanderbilt University.

In the intestines, an expanded cell surface increases the space for nutrient-processing enzymes and transporters, offering greater capacity for nutrient handling. But it didn't make sense to Tyska that a motor protein – a protein with the potential to generate force and move cargo around in cells – would play a passive structural role. "When I looked at that image, the near crystalline arrangement reminded me of actin and myosin in a muscle fiber," Tyska said. "I kept returning to the same question: why would the microvillus have this beautiful structure packed with motor proteins. The concentration of myosin motors in a single

microvillus is very high; there's serious force-generating potential there."

Tyska and Russell McConnell, a student in his laboratory, tested the idea that these motor proteins are more than molecular glue binding the cell membrane to the actin bundle" The investigators purified the intestinal "brush border" – the layer of densely packed microvilli – from the intestines of rats or mice, and added ATP, the chemical fuel for myosin-1a. Through the microscope, they watched the cell membrane move toward the tips of the microvilli and pop off the ends in the form of vesicles, tiny bubble-like packets.

Their findings, reported in the May 21 Journal of Cell Biology with one of their images featured on the issue cover, have implications for nutrient processing and other aspects of gastrointestinal physiology. Tyska is excited about the group's unexpected discovery. "What we're showing is that the microvillus is more than just a scaffold to increase the amount of cell membrane," Tyska said. "It's a little machine that can shed membrane from the tips." The team confirmed that myosin-1a is the motor that moves membrane up the microvillus. Brush borders isolated from knockout mice lacking the myosin-1a gene shed membrane at only five percent of the level of brush borders from wild-type animals.

The investigators are working now to understand why intestinal cells might launch vesicles from their microvilli. They know from ongoing vesicle sorting and mass spectrometry studies that the vesicles contain nutrient-processing enzymes and transporters, like the microvillar membrane. "One idea is that these vesicles operate remotely to speed nutrient processing, before the nutrients even get to the brush border to be absorbed by the (intestinal epithelial cell)," Tyska said.

The team is also exploring other possibilities for the role of membrane shedding: that it offers protection against microbes and pathogens by

expelling them from the surface before they can enter the cell; that it provides a mechanism for altering the composition of the microvillar surface to handle changes in "what comes down the pipe;" and that it serves a role in cell-cell communication by launching vesicles that contain signaling proteins. Tyska and his team also plan to explore whether myosin-1a is serving a similar membrane-moving role in its other known location: the hair cells of the inner ear, and if other microvilli also use myosin motors to jettison vesicles from their tips.

Source: Vanderbilt University Medical Center