Molecular motor works by detecting minute changes in force

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Researchers at the University of Pennsylvania School of Medicine discovered that the activity of a specific family of nanometer-sized molecular motors called myosin-I is regulated by force. The motor puts tension on cellular springs that allow vibrations to be detected within the body. This finely tuned regulation has important implications for understanding a wide variety of basic cellular processes, including hearing and balance and glucose uptake in response to insulin. The findings appear in the most recent issue of *Science*.

"This is the first demonstration that myosin-I shows such dramatic sensitivity to tension," says senior author E. Michael Ostap, Ph.D., Associate Director, Pennsylvania Muscle Institute and Associate Professor of Physiology. "It is surprising that a molecular motor can sense such small changes in force."

Myosin-I is a biological motor that uses the chemical energy made by cells to ferry proteins within cells and to generate force, powering the movement of molecular cargos in nearly all cells.

In two specific cases, myosin I puts tension on the specialized spring-like structures in human ears that enable hearing and maintenance of balance, and also has a role in delivering the proteins that pump glucose into cells in response to insulin. "However, why a tension-sensing molecular motor is needed for this function is unknown," says Ostap.

In collaboration with Henry Shuman, PhD, Associate Professor of

Physiology, the research team used optical tweezers -- a combination focused laser beam and microscope, of sorts -- to measure incredibly small forces and movements (on the piconewton and nanometer level) to discover that myosin I motors are regulated by force. The motors pull on their cellular cargos until a certain tension is attained, after which they stop moving, but will hold the tension. If something happens in the cell to decrease this tension, the motor will restart its activity and will restore the lost tension.

Myosins use the energy from ATP to generate force and motion. Humans have 40 myosin genes that sort into 12 myosin families. Members of the myosin family have been found in every type of cell researchers have examined. The Ostap lab is investigating the biochemical properties of several members of the myosin family to better understand movement in cells, which is important in development, wound healing, the immune response, and the spread of cancer, among other functions. These new findings shed light on the role of myosin I in cells, supporting the notion that this molecular motor is more important in generating and sustaining tension rather than transporting protein cargo.

The research team will now apply these results to better understand how cells use these tension sensors to carry out their physiological functions.

Source: University of Pennsylvania