Researchers Find 'Fusion' Protein

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Working with fruit flies, scientists at Johns Hopkins have discovered a protein required for two neighboring cells to fuse and become one "super cell."

Most cells enjoy their singular existence, but the strength and flexibility of muscles relies on hundreds or even thousands of super cells that make large-scale motion smooth and coordinated, such as flexion of a bicep.

The newly discovered protein, dubbed Solitary, coordinates the movement of tiny molecular delivery trucks to a cell's surface. Cells that lack Solitary stay, well, solitary. "They refuse to fuse," says Hopkins assistant professor of molecular biology and genetics Elizabeth Chen, Ph.D., whose report on the work is online this week in *Developmental Cell*.

Chen and her team studied fruit fly embryo muscles to find the molecular signals that tell two neighboring cells to join as one, plucking out for further study those embryos containing cells that refused to fuse.

They then compared the genetic sequences from healthy embryos with sequences from defective embryos to locate differences and identify the genes responsible for unfused muscle cells. In the process, they identified Solitary.

Chen's team next made a tool to see the Solitary protein, enabling them to track its localization under a fluorescent microscope. At each future fusion point between cells that they examined in the fly muscles, they saw concentrations of glowing clumps of Solitary protein.

"As we uncover more of the players in cell fusion, we get closer to manipulating fusion for our benefit," Chen adds. Muscular dystrophy, for example, might be treated by injecting into patients healthy muscle cells that are designed to fuse efficiently with the diseased muscles, saving the diseased cells from deteriorating.

They also discovered that Solitary protein is attached to the cell's skeleton. "It was so bizarre to see Solitary - something meant to regulate the cell's internal structure - to be involved in the external events of cell fusion," says Chen.

But in addition to structural support, the cell's "skeleton" provides an internal railway of sorts, along which other proteins and molecules can move. Indeed, the researchers saw that while normal cells were able to shuttle tiny storage compartments within the cell - presumably holding important molecular tools needed for cell fusion - to the fusion site, these storage compartments were scattered haphazardly, seemingly lost in the cellular wilderness, in cells lacking Solitary.

When two neighboring cells fuse, they need to break down the barrier between them, explains Chen. It turns out that the Solitary protein marks where that break is happening and subsequently tells the cell where to build its skeleton railway. "In this role, Solitary acts not like the delivery truck, but more like a construction site foreman," says Chen. "It's told where the cell barrier needs to be broken, then directs the building of a delivery road so that the molecular supplies can be brought to the fusion site."

Source: Johns Hopkins Medical Institutions