Researchers Uncover Cell Fusion Mechanism

October 8 2006

In a study that could shed light on disorders that occur in skeletal muscles, bone, the placenta, and other organs where fused cells are common, researchers at the Technion-Israel Institute of Technology and at the US National Institute of Child Health and Human Development have identified a protein in worms that encourages two or more normal-sized cells to fuse into a single giant cell with multiple nuclei—a normal but little understood phenomenon in biology. The study is published in the October 2 issue of the journal *Developmental Cell*.

The findings could aid researchers looking for ways to fuse therapeutic stem cells or cells carrying replacement genetic parts to cells that are damaged or diseased, according to lead researchers Professor Benjamin Podbilewicz of the Technion and Leonid V. Chernomordik of the NICHD.

“If you could deliver a necessary protein or gene to diseased muscle cells by fusing cells that carry this gene, in theory you could use this technique to fix these muscles,” said Podbilewicz.

Although researchers previously uncovered fusion proteins that help viruses latch on to their target cells and proteins that promote fusion between cells, the study by the combined Technion-NICHD team is one of the first to identify a protein that drives fusion between cells in normal animal and plant development.

Podbilewicz and colleagues first identified a cell membrane protein called EFF-1 as a possible fusion protein in their studies of the nematode worm C. elegans. In the skin of worms with mutated EFF-1, “where most fusion takes place in C. elegans, cells sort of get lost, and start making very funny structures,” Podbilewicz explained.

To clarify EFF-1’s cellular role, the researchers inserted the protein in insect cells grown in the lab. They quickly discovered that EFF-1 encourages cells to fuse together, forming giant cells with more than one cell nucleus. The cell nucleus contains a cell’s genes wrapped up in chromosomes.

Both cells must contain EFF-1 to fuse together, the researchers found. Cell fusion aided by EFF-1 also includes a “half-fused” step where the cell membranes blend together but the contents of each cell do not mingle. This half-fusion step is a trait shared by viral fusion and fusion inside cells.

The finding could help researchers understand the development of some important organs in humans. “One of the biggest examples—one third of all our body weight—is the long fibers of our skeletal muscles, which form by cell fusion,” Podbilewicz said.

In theory, researchers could also try to harness the natural mechanisms of cell fusion to deliver cell therapies—by fusing regenerative stem cells to diseased cells, for instance.

But Podbilewicz warned that giant cells with multiple nuclei have also been found in certain types of cancer. “If cells fuse, they will get more chromosomes than usual, and more chromosomes than usual can cause defects” in diseases such as cancer, he said.

So far, researchers have not found a human equivalent of EFF-1. Podbilewicz said researchers would have to search for the human version by looking for proteins that have a structure similar to that of EFF-1, since the DNA sequence that encodes the fusion protein is probably quite different between worms and humans.

The study authors included Evgenia Leikina of the NICHD and Amir Sapir, Clari Valansi, Meital Suissa and Gidi Shemer of the Technion-Israel Institute of Technology.

Source: American Technion Society