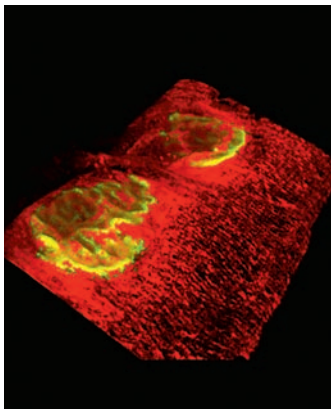


Tag-Team Proteins

A COMPLEX OF PROTEINS PROTECTS MUSCLES FROM COLLAPSING DURING CONTRACTION.

A protein important for maintaining the heart's rhythm also helps muscle cells retain their structure during stress. The discovery has broad implications for other cell types and for human diseases, including muscular dystrophy, says Vann Bennett, an HHMI investigator at Duke University Medical Center.

Bennett's group is studying a family of three proteins called ankyrins, which Bennett discovered in red blood cells in 1979. In many cell types, ankyrins anchor membrane-spanning proteins.



The surface of a muscle cell, with ankyrin proteins (red) and neuromuscular junctions (yellow).

The current study—published in the December 26, 2008, issue of *Cell*—focuses on two ankyrins: ankyrin-B, which the Bennett group established as important to heart rhythm, and ankyrin-G.

Mice that lack ankyrin-B die soon after birth. But Gai Ayalon, a postdoctoral fellow in Bennett's lab, found a way to study its effects by suppressing it in the leg muscles of adult mice. In the ankyrin-B-deficient cells, two other

proteins known to support cell structure were missing from the cell membrane. One, dystrophin, is key to cellular structure and support (mutations in the human dystrophin gene cause some types of muscular dystrophy). Another, beta-dystroglycan, forms a complex with dystrophin to protect the cell membrane during muscle contraction. Both proteins were still made but were not where they needed to be.

Without the protective proteins, the ankyrin-deficient muscle cells broke apart during exercise, a phenomenon similar to what occurs in muscular dystrophy.

When the group suppressed ankyrin-G in leg muscle cells, dystrophin and beta-dystroglycan were transported to the membrane but were not organized properly.

"These two ankyrins are a tag team," Bennett says. "Ankyrin-B mediates transport of newly synthesized proteins, and ankyrin-G retains them in the right place."

Researchers knew that, without dystrophin, the entire muscle-protecting complex was lost, but nobody knew why. The group found that dystrophin binds directly to ankyrins, and that gave them the beginning of an answer. "We have found the outlines of a pathway through which dystrophin assembles this [protective] complex," Bennett says. The missing piece of the puzzle was the ankyrin proteins. ■ —NANCY VOLKERS

IN BRIEF

somehow they trigger similar stress responses, causing the bacteria to produce free radicals and destroy themselves. The researchers are working to better understand how that occurs. Collins' results appear in the November 14, 2008, issue of *Cell*.

TRAFFIC ON CELLULAR ROADWAYS

To know what a living cell is doing, one needs to know what proteins it makes. Most often, scientists try to elucidate a cell's plans by sequencing its DNA to see what proteins can potentially be made. Then they analyze messenger RNAs (mRNAs)—the intermediate step between DNA and proteins—to see what proteins the cell was preparing to make.

But the method doesn't always tell the full story of what each cell is doing, says Jonathan Weissman, an HHMI investigator at the University of California, San Francisco. According to their needs, cells decide which genes to translate into mRNA, but they also control which mRNA to translate into proteins.

Now, Weissman and colleagues have developed a method to follow the deci-

sions a cell makes at that second step. To translate mRNA to proteins, cells rely on complexes called ribosomes. By identifying which pieces of a cell's mRNA are attached to ribosomes, the scientists can observe which proteins are really being made—not just which mRNA is being made.

Weismann says the new technique, called ribosome profiling, allows researchers to follow what DNA is being turned into protein much more directly. This procedure could lead to a better understanding of how cells work, and how various diseases affect the proteins made by a cell.

"The complement of proteins made by a cell may provide the precise signature of the pathologies and disease states," he says. The findings were published online on February 12, 2009, in *Science Express*.

HEY SUGAR, SUGAR

It's not just the insides of cells that change when a cell needs to do different jobs: on the outer surfaces of cells reside complex sugars, called glycans, that move and change.

A team of researchers led by HHMI investigator Carolyn Bertozzi, of the

University of California, Berkeley, has developed a way to monitor these changes. The method can check how glycan numbers, compositions, and positions in living cells and organisms change over time. To capture these changes, Bertozzi's group first chemically modifies sugars to incorporate a small, nontoxic component. Cells eat these sugars and use them to build glycans. Next, the researchers expose the cells to chemical probes that react only with the modified sugars and make the glycans visible with imaging techniques. They have used the method in a variety of ways, including watching the changes in glycans inside developing, transparent zebrafish.

Bertozzi hopes that eventually glycan imaging will be used to detect cancer in humans. Cancer cells exhibit changes in glycan composition and distribution that could not be imaged in living systems before.

Bertozzi and Scott Laughlin, a Berkeley chemist, published an overview of glycan imaging in the January 6, 2009, issue of *Proceedings of the National Academy of Sciences*.