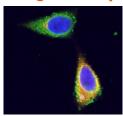
In This Issue

MagT1 helps a glycosylase gain acceptance



MagT1 (red) localizes to the ER (green) in HeLa cells.

herepanova et al. describe how an oxidoreductase enzyme promotes the glycosylation of newly synthesized proteins in the ER.

Two different oligosaccharyltransferase (OST) complexes glycosylate asparagine-containing acceptor sites in secretory proteins. Complexes containing the catalytic subunit STT3A target nascent polypeptides as

they feed into the ER through the protein translocation channel. STT3B-containing complexes subsequently glycosylate acceptor sites ignored by STT3A, but, by this point, the target proteins are beginning to fold into their native conformation and forming disulfide bridges that could limit the complex's access to the glycosylation acceptor sequence.

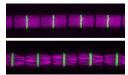
Cherepanova et al. were interested in a protein called MagT1, which is mutated in patients with X-linked mental retardation and

Sperm's sensitive steering machinery ichlo et al. describe how sea urchin sperm respond to tiny

amounts of chemoattractant. Sea urchin sperm are incredibly sensitive, being able to detect and respond to single molecules of chemoattractant as they navigate toward the egg. The guanylyl cyclase (GC) chemoreceptor localizes to the sperm flagellum where, upon binding to chemoattractant, the GC synthesizes the second messenger cGMP; in turn, the rise of cGMP activates ion channels in the flagellar membrane. Ca²⁺ ions flow into the flagellum, which alters the sperm's swimming path. But how the chemoreceptor manages to respond to picomolar chemoattractant concentrations is unknown.

Pichlo et al. estimated that each sperm flagellum contains \sim 300,000 GC chemoreceptors, enough to cover about 15% of the flagellum surface. Bacteria, in contrast, have a much lower density of chemoreceptors on their cell membrane and can only respond to micromolar concentrations of chemoattractant.

Lasp brings a giant down to size



Actin (magenta) and the titin family protein kettin (green) are disorganized in muscles lacking Lasp (bottom) compared with a wild-type myofibril (top).

ernandes and Schöck reveal that Drosophila make do with a much shorter version of the actin-binding muscle protein nebulin.

Nebulin is a giant protein that contains 185 actin-binding repeats and aligns with muscle thin filaments by extending from the Z-discs at the ends of sarcomeres. Mutations in nebulin reduce thin filament length and cause the muscle disease nemaline myopathy. Lasp, the only

nebulin-related protein in *Drosophila*, is a much smaller protein that contains just two nebulin repeats. Lasp controls the actin cytoskeleton in germline cells, but its function in fly muscles is unknown.

Fernandes and Schöck found that flies lacking Lasp showed several defects in sarcomeric structure: their thin filaments has been proposed to act as a magnesium transporter at the plasma membrane. The protein is, however, homologous to a budding yeast OST subunit, and the researchers found that it localizes to the ER in human cells. MagT1 associated with STT3B-containing OST complexes, and knocking down the protein inhibited the glycosylation of STT3B-dependent, but not STT3A-dependent, target sites. Many of these sites contained, or were located next to, cysteine residues. MagT1 was no longer required for the glycosylation of these sites when the researchers inhibited disulfide bond formation.

MagT1 contains a domain similar to the oxidoreductase enzyme thioredoxin. Mutating the catalytic cysteine residues in this domain impeded MagT1's ability to support STT3B-dependent glycosylation, suggesting that the protein forms temporary disulfide bonds with substrate proteins, thereby opening up some of their acceptor sites to STT3B. Author Reid Gilmore now wants to investigate how MagT1 promotes the glycosylation of STT3Bdependent sites that aren't located near cysteine residues.

Cherepanova, N., et al. 2014. J. Cell Biol. http://dx.doi.org/10.1083/jcb.201404083.

Not surprisingly, the GC chemoreceptor binds to its ligand with extremely high affinity. But Pichlo et al. found that this affinity decreases as more receptors become occupied. This allows sperm to dial down their sensitivity as they near the egg, preventing the chemoreceptors from becoming saturated so that they can continue to operate in the presence of higher chemoattractant concentrations.

The receptor's high ligand-binding affinity might cause the chemoattractant to activate the receptor for extended periods, disrupting the sperm's ability to navigate up the chemotactic gradient. Pichlo et al. found that each chemoreceptor is deactivated by dephosphorylation within 150 milliseconds of binding to its ligand. This deactivation may be permanent, but ample chemoreceptors remain to guide the sperm further along its path. Senior author Benjamin Kaupp now wants to investigate how the \sim 300,000 chemoreceptors are organized within the sperm flagellum.

Pichlo, M., et al. 2014. J. Cell Biol. http://dx.doi.org/10.1083/jcb.201402027.

were shorter, their thin and thick filaments were spaced further apart, and the I-band region around the Z-discs was disorganized. Compensating for its smaller size, Lasp controlled these different aspects of muscle structure by localizing to two distinct regions of the sarcomere. The protein bound to α -actinin in the Z-discs, stabilizing I-band architecture by anchoring a member of the titin family of elastic muscle proteins, and also localized to the A-band, where thin and thick filaments overlap.

Lasp therefore makes do with just two nebulin repeats, and Fernandes and Schöck found that each repeat has a different function. The first is involved in binding to α -actinin, whereas the second binds to myosin, recruiting Lasp to the A-band to regulate filament spacing. Author Frieder Schöck now wants to analyze this latter interaction in more detail.

Fernandes, I., and F. Schöck. 2014. J. Cell Biol. http://dx.doi.org/10.1083/ jcb.201401094.