Sarcospan, a little protein for a big problem

November 3 2008

The overlooked and undervalued protein, sarcospan, just got its moment in the spotlight. Peter et al. now show that adding it to muscle cells might ameliorate the most severe form of muscular dystrophy.

In Duchenne muscular dystrophy (DMD), the mutated dystrophin protein fails to anchor correctly to its membrane glycoprotein complex. And without this anchoring, muscle cells experience severe contraction-induced damage. Sarcospan is part of the anchoring complex, but because mice without sarcospan don't seem any worse for its absence, it hasn't received much attention. Sarcospan's structure, however, suggests it might help stabilize the membrane complex, so the authors decided to test the effects of increasing sarcospan expression in a DMD mouse model.

The increase did not improve the dystrophin–glycoprotein interaction, but instead, the team was surprised to find sarcospan coaxed a dystrophin relative called utrophin to spread out on the muscle membrane. Utrophin is normally restricted to the neuromuscular junction, where it serves a role similar to that of dystrophin.

The extra sarcospan prompted higher levels of utrophin in the cell, but not by increasing its expression. Sarcospan instead stabilized extrajunctional utrophin complexes, which normally form early in development and then disappear after the first few weeks of life.

Mouse muscle cells were protected by sarcospan, but the true importance of this discovery will lie in its potential for human therapeutics,

specifically gene therapy. In that regard, sarcospan's small gene size is significant—at 600 bp, it is easily packaged into the safest viral vectors, unlike either dystrophin or utrophin, which are about 700 times larger and require more immunogenic vectors.

Citation: Peter, A.K., et al. 2008. *J. Cell Biol.* doi:10.1083/jcb.200808027.

Source: Rockefeller University Press