In This Issue

**Homing therapy**

Skeletal muscle becomes much more efficient at muscle repair if they first get a boost of cytokines and migratory adhesion molecules, report Galvez et al. (page 231). The improved repair stems from better homing abilities.

Skeletal muscle can be repaired by a class of stem cells known as mesangioblasts, which reside within blood vessels. Injection of mesangioblasts into the femoral artery of mice improves muscle function in a mouse model of muscular dystrophy. Only a small fraction of the injected cells enters the tissue after injection, however. With their new findings, the authors report how to increase this fraction.

The authors found that mesangioblasts efficiently crossed endothelium-coated filters in vitro when the other side held either mature myotubes or muscle-associated cytokines, such as SDF-1. Immature myoblasts, which secrete less of these cytokines, did not induce strong migration.

In addition to cytokines, adhesion molecules also improved migration. Transfection of mesangioblasts with L-selectin or α4 integrin increased the cells’ migration efficiency across the endothelium-coated filters. L-selectin and α4 integrin are not normally expressed by mesangioblasts, but are known to help leukocytes migrate through vessels walls into nearby tissues.

In vivo experiments demonstrated that both strategies improved the stem cells’ homing ability in a mouse model of muscular dystrophy. When cytokine-pretreated cells were injected in the femoral artery, ~20% of the cells migrated to the thigh muscle, compared with 10% of untreated control cells. A similar improvement was detected for α4 integrin–expressing stem cells.

Both modifications together made an even better improvement. Approximately 50% of the mesangioblasts that were pretreated with SDF-1 and that expressed α4 integrin entered the muscle.

After receiving the juiced-up stem cells, the mice had improved muscle function. Galvez et al. are now testing the same strategy in a dog model of muscular dystrophy. Moreover, they hypothesize that, with the right cytokines, a similar experimental approach could be used to improve the homing ability of other stem cell types. JCB

**Scattering synaptic vesicles**

Synaptic vesicles get dispersed to new sites, according to Bamji et al. on page 289, via neurotrophin-induced disruption of adhesion complexes. The dispersal increases synaptic density, number, and size.

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As synapses communicate via the secretion of neurotrophin-containing presynaptic vesicles, the authors studied BDNF’s effect on vesicle behavior. They found that treatment of hippocampal neurons with BDNF dispersed synaptic vesicles into the region surrounding the original synapse. The dispersal of synaptic vesicles might help to form new synapses as the clusters of mobile vesicles populate new territories, although this theory remains to be tested.

The authors next addressed how the vesicles were released by BDNF. A likely target for this neurotrophin is the cell adhesion complex formed by cadherin and catenin proteins, which the authors had shown helps to localize synaptic vesicles to the presynaptic terminals. Indeed, BDNF caused a transient increase in β-catenin phosphorylation and a decrease in the amount of β-catenin bound to cadherins, resulting in adhesion complex disruption.

Expression of a nonphosphorylatable mutant of β-catenin eliminated both disruption of the cadherin–catenin complex and synaptic vesicle dispersion. The β-catenin mutant also blocked the formation of new synapses after BDNF treatment.

Bamji et al. speculate that the mechanism they uncovered may be a general model for how other ligands and tyrosine kinase receptors influence synaptic plasticity in various neuronal cell types, such as the ephrins and Eph receptors that influence synaptogenesis and axon guidance. Given the prevalence of both tyrosine kinase receptors and cadherin–catenin complexes, they think that tyrosine kinases might regulate other cell behaviors as well through β-catenin phosphorylation. JCB