**In This Issue**

**Potential muscles everywhere**

Gerhart et al. report that stably committed muscle stem cells may wait in a quiescent state in mature non-muscle tissues like brain and liver, retaining the ability to differentiate into skeletal muscle if the opportunity arises (page 381). This discovery may provide both an important tool for developing regenerative therapies, and a challenge to the characterization of some stem cells as multipotential, an idea based on reported conversions of one cell type to another. Some of the conversion experiments were performed with non-clonal cell populations. The current work suggests that the varied phenotypes observed in the earlier experiments may have arisen from a heterogeneous population of mature stem cells committed to different lineages.

The authors found scattered cells expressing MyoD, a marker for skeletal muscle precursors, in a wide variety of fully differentiated organs in chicken fetuses. When cultured in vitro, some cells from the fetal organs gave rise to skeletal muscle, and when the MyoD-positive cells were isolated by fluorescence activated cell sorting, almost all were able to form skeletal muscle. The cells resemble skeletal myoblasts, and appear to be stem cells stably committed to forming muscle. Previous work suggests that some cells in the neuronal tissues of mice also express muscle-specific transcription factors, and Gerhart et al. believe that stably committed precursors of other lineages may also be distributed in mature organs.

Although the evolutionary utility of having muscle stem cells in nonmuscle tissues is not immediately obvious, one possibility is that they could be recruited to help the embryo recover from a loss of somite tissue. Medically, the presence of these cells may explain the origins of rhabdomyosarcomas, malignant tumors that express skeletal muscle proteins but often arise in non-muscle tissue. Because these cells are stably committed to a specific lineage, they might also be useful for regenerative therapies, particularly if they are able to induce multipotential stem cells to differentiate in damaged tissue.

**Shape up or ship out**

When proteins become misfolded in the ER, a quality control system targets them to the cytoplasm for degradation. On page 355, Vashist et al. have uncovered two separate sorting systems involved in ER quality control, and have identified a novel gene required for one of the two pathways. The findings indicate that ER quality control is more complex than previously believed.

By tracking the fates of several mutant proteins in *Saccharomyces cerevisiae*, the authors identified a sorting step in the ER in which misfolded proteins are targeted to one of two pathways. Some proteins are packaged into COPII transport vesicles, while others are excluded from vesicles and retained in the ER. Proteins packaged into vesicles are transported to the Golgi apparatus, then returned to the ER by retrograde transport, at which point the two pathways converge and both the retained and retrieved proteins are degraded.

Each mutant protein only follows one pathway, suggesting that the sorting system is highly selective. Although the results are consistent with a model in which membrane proteins are retained while soluble proteins follow the retrieval pathway, the authors stress that more extensive analysis will be required to identify the preferences of the sorting system.

A genetic screen uncovered a mutant allele of the *BST1* gene that blocks the transport of misfolded proteins from the ER to the Golgi without affecting most normal protein transport. Although the retrieval pathway is blocked in these cells, proteins targeted to the retention pathway by the ER are still degraded normally.

Vashist et al. are now identifying additional genes specifically involved in the retention and retrieval pathways.