A muscular path to quiescence

Muscle stem cells called satellite cells can pull back from the brink, according to Zammit et al. (page 347). When activated by muscle damage, the cells divide and start uniformly down a differentiation path. Only at the last minute do some of the cells split off to revert to a quiescent, stem cell phenotype.

Satellite cells sit quietly underneath the basal lamina of myofibers until a muscle is damaged. Either mitogens leaking into a damaged muscle or signals from a deinnervated muscle may wake up the satellite cells, which then divide and supply new cells that fuse to repair or replace damaged myofibers.

Zammit et al. isolated intact myofibers and placed them in mitogen-laden cultures to activate the satellite cells. The activated cells, which when quiescent make the transcription factor Pax7 but not the muscle determinant MyoD, turned on MyoD. Most of the doubly positive cells then turned off Pax7 and differentiated, but some turned off MyoD instead and reverted to a quiescent phenotype.

The Pax7+MyoD− cells could not have arisen from a persistent, fast-dividing pool of Pax7+, MyoD− cells because at intermediate times such cells were found on only a few myofibers. The authors also noted that recently replicated cell pairs may have provided evidence for a recent switch, as in some cases only one of the daughter cells expressed MyoD.

Thus, the cells are capable of shutting off MyoD, which was thought to mark an irreversible commitment to the skeletal muscle lineage. Using this divergent pathway, satellite cells can replenish themselves, with no need to invoke an outside supply of new stem cells. Heterogeneity may still exist in the starting population of satellite cells, predisposing some cells to the eventual loss of MyoD. Alternatively, the satellite cells may progress to the MyoD+ state as a truly homogenous population, with loss of MyoD in certain cells relying on communication both with the myofiber and between multiplying satellite cells.

Do yeast apoptose?

Suicide in a unicellular organism might sound like a lousy idea, but there are several possible justifications. Budding yeast cells that are sickly, mating-incompetent, or stuck in the middle of a colony might do better to go out with a messy bang, thus releasing all their nutrients for their nearby relatives, than to fade away with energy sources locked behind a cell wall.

Yeasts do die of causes other than old age, but it remains unclear whether this death is like mammalian apoptosis, and to what extent it is controlled rather than a direct result of an insult to the cell. Apoptosis was put forward as a possibility when a caspase-like protein, Yca1p, was discovered, and dying cells were found to bind a caspase substrate.

But on page 311, Wysocki and Kron bring these conclusions, and the whole concept of yeast apoptosis, into doubt. Using yeast that are irreversibly arrested because of exposed telomeres, they find that it is the fluorophore, not the attached caspase substrate, that is binding the dying cells. Death does not require either Yca1p or the production of reactive oxygen species (ROS). Wysocki and Kron conclude that the cells are probably popping because of extended cell cycle arrest, although runaway autophagy remains a possibility.

The authors emphasize that apoptosis or other forms of programmed cell death may well occur, but that better evidence is needed. Kron says he would be convinced by a pathway that is activated before the onset of death and that can cause death when turned on in the absence of any cellular insult. Otherwise, he says, we are stuck with death via explosion—“the ultimate disappointing, dumb answer.”