Sizing up cell division

How does a growing cell know that it’s big enough to divide? Challenging a long-held view, a new study argues that the decision depends mainly on external factors that stimulate growth and division rather than an internal mechanism for assessing size.

The standard take on the relationship between growth and division envisions a "size checkpoint" during the cell cycle, where the cell somehow gauges its girth before advancing further. However, Ian Conlon (University College London, England) and colleagues found that they could separate growth from progression through the cell cycle by manipulating the concentrations of insulin-like growth factor-1 (IGF-1) and glial growth factor (GGF). Of the two, only IGF-1 incited growth in rat Schwann cells, while GGF drove cell cycle progression without speeding growth. Applying that discovery, the researchers used GGF to accelerate the cell cycle and gradually shrink cultured cells. The cells grown in high GGF concentrations were ~20 percent smaller than cells grown in low GGF.

According to Conlon, the findings demonstrate that the decision to divide doesn’t hinge on reaching a set size. Instead, the relative concentrations of several growth factors and mitogens probably provide the crucial cues, and as a result cell size is variable. However, he cautions, the results don’t discount the influence of size. "It’s reasonably clear that growth does have an effect on cell cycle progression, but it’s usually not the limiting factor," he says.

Mutations can alter cell size at division, but this is the first study to show that manipulating external factors has the same effect, says developmental biologist Thomas Neufeld of the University of Minnesota in Minneapolis. Now, we need to determine how widespread this mechanism is, he says.

Reference: Conlon, I.J., et al. 2001. Nat. Cell Biol. 3:918–921.

Death by mistake

A new study implicates a novel culprit in the accumulation of oxidative damage in aging cells. Increased protein oxidation may stem not from increased activity of free radicals or decreased levels of antioxidants, but from the higher error rate of ribosomes, according to a team led by Thomas Nystrom of Göteborg University in Sweden.

The study delivers a blow to the popular rate-of-living hypothesis—the idea that lifespan and metabolic rate are negatively correlated. When the authors examined Escherichia coli cells that were in a starvation-induced state of senescence, they found no relationship between metabolic rate and protein oxidation. Instead, the numbers of misfolded or malformed proteins surged in the senescent cells, suggesting that ribosome fidelity might influence the rate of protein oxidation. Mutants with sloppy ribosomes had higher levels of oxidized proteins, whereas mutants with super-accurate ribosomes showed much lower levels of these proteins.

How would more errors during translation increase oxidative damage? Nystrom and colleagues hypothesize that error-prone ribosomes make more malformed proteins that may be particularly susceptible to oxidative damage. They also suggest that a decline in ribosome fidelity, perhaps triggered by a shortage of charged tRNAs in older cells, might spur age-related oxidation in eukaryotic cells.

Reference: Ballesteros, M., et al. 2001. EMBO J. 20:5280–5289.

Leaf starter

To grow a new leaf, a plant just needs to relax—its cell wall, that is. This conclusion comes from a new study on the regulation of leaf formation. The authors report that a protein called expansin loosens the cell wall also sparks the growth of normal leaves.

To stimulate expansin production within the meristem that makes new leaves, a group led by Andrew Fleming of the Swiss Federal Institute of Technology in Zurich, Switzerland, created transgenic tobacco plants in which expansin gene was coupled to a tetracycline-dependent promoter. Induction of expansin expression caused a leaf to sprout at the site. As far as they could determine, the resulting leaves were normal internally and externally, says Fleming—unlike the results from a prior experiment in which dabbing expansin on nontransgenic plants produced only spindly growths.

The authors do not yet know how expansin relaxes the cell wall or how it triggers leaf formation. It may seem surprising that what seems like a small change could unleash a complex process like leaf development. However, says Fleming, the study lends credence to a much-debated hypothesis that cells are not only attuned to their chemical environment, but also to the forces that impinge upon them. “It’s possible that the cell responds to the biophysical forces around it and can change its gene expression accordingly,” he says.

Reference: Pien, S., et al. 2001. Proc. Natl. Acad. Sci. USA. 98:11812–11817.