Stayin’ alive, without antigen

When a T cell meets a dendritic cell that carries an antigen, the meeting activates the T cell to battle pathogens. Less certain is what happens when the dendritic cell doesn’t have antigen. Now, two reports bolster the controversial hypothesis that this kind of antigen-free cell-to-cell contact is necessary for the survival of T cells.

Roland Martin and colleagues of the National Institute of Neurological Disorders and Stroke in Bethesda, MD, found that contact with an antigen-free dendritic cell provokes dramatic changes in human memory T cells—though not as profound as activation by an antigen. Gene expression shifts, boosting production of cytokines such as interferon gamma, and some T cells begin to divide slowly. Most importantly, the meeting lengthens the life of memory cells, more than doubling the percentage that survive five days in culture.

Working with naive mouse T cells, a team led by Alain Trautmann of the Institut Cochin de Génétique Moléculaire in Paris, France, saw similar results: greater survival and low-level proliferation in the T cells. “In the normal life of a lymphocyte, it will interact repeatedly with dendritic cells,” Trautmann says. “These repeated meetings are essential for survival.” To their surprise, the authors also detected a structure known as an immunological synapse at the junction between the cells.

Both groups agree that cellular contact may boost the immune system’s readiness in two ways. By stimulating survival and slow reproduction, the interaction may help maintain stocks of T cells. And the low level of stimulation provided by dendritic cells seems to prime lymphocytes for action. However, Martin believes that the work also exposes a possible downside. He thinks that the surge in cytokine production may increase the risk of autoimmune diseases like multiple sclerosis in susceptible individuals. “The interaction may set up a certain environment that is conducive to the pro-inflammatory reactions that you see in autoimmune diseases,” he says.


A mobile transcription factor

Location, location, location—the mantra of real estate also holds true for plant development, where the fate of a plant cell depends largely on its position rather than its lineage. In the core of a growing root, cells learn their position from their neighbors through the actions of a transcription factor that travels between cell layers, according to a study conducted at New York University, NY. This protein is novel because of its dual function: it both induces cell division and signals cell identity.

Philip Benfey and colleagues report that the SHORT-ROOT protein (SHR) is made only in the innermost layer of the Arabidopsis root, but it travels to the adjacent layer. There, it stimulates cell division by turning on a growth-promoting gene called SCARECROW, and it helps establish the identity of endodermal cells, which arise from this layer. So far, only plants have been shown to pass transcription factors like SHR from cell to cell, Benfey says.

In a mysterious twist, SHR’s advance stops at this second layer. Benfey says this pattern raises two burning questions he and his coworkers are hoping to answer. First, how does SHR get from one layer to the next? It may travel through the plasmodesmata, but there is no firm evidence for this yet. And second, what prevents the protein from moving farther? If SHR is passing through the plasmodesmata, then these channels or something associated with them may be acting as border guards to limit SHR’s movements.

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 resoriously 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.


Leaf starter

To grow a new leaf, a plant just needs to relax—it’s 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 relaxes the cell wall and conquers 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 the 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.


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 Nyström 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? Nyström 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.