

Remodeling the nucleus

Daniel Colón-Ramos, Mariano A. García-Blanco (Duke University, Durham, NC), and colleagues demonstrate in a recent article that *Chlamydomonas* nuclear architecture changes to accommodate cytoplasmic needs.

Chlamydomonas is a highly polarized cell that offers a unique system to study changes in nuclear shape. Loss of this algae's flagella (after certain chemical or mechanical stresses) causes the nucleus to adopt a pear-like shape and take an anterior position in the cell, nearer where the flagella once sat.

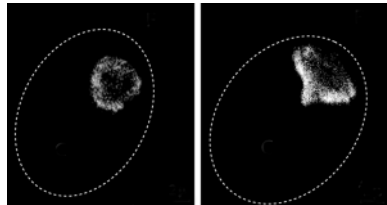
García-Blanco wondered whether sites of transcription of the β tubulin gene, which is strongly up-regulated upon deflagellation, move closer to the flagella to expedite their rebuilding. Immunocytochemistry and electron microscopy revealed that the β tubulin gene did not move from its posterior

nuclear position. But the experiments did uncover an unexpected asymmetry of nuclear pore complex distribution.

Even in flagellated cells, the complexes were preferentially located at the posterior side of the nucleus, near a polysome-rich portion of the cytoplasm. Deflagellation further exaggerated the asymmetry. The changes correlated with accumulation of β tubulin transcripts near the concentrated translation machinery. Says García-Blanco, "what we don't know yet is what causes what." He hopes to find mutants that uncouple events following

deflagellation to determine whether nuclear architecture directly targets mRNA cytoplasmic localization. ■

Reference: Colón-Ramos, D., et al. 2003. *Dev. Cell.* 4:941–952.



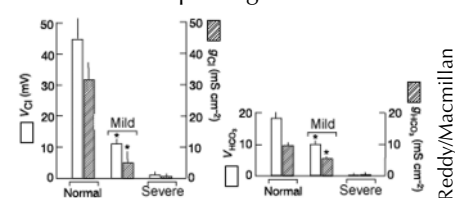
NPCs (white) move to the posterior side of the nucleus after deflagellation (right).

García-Blanco/Elsevier

Glutamate in unusual places

Glutamate has a critical physiological function unrelated to its job as a neurotransmitter, according to results from M.M. Reddy and Paul Quinton (University of California, San Diego, CA). The duo find that glutamate activates an epithelial ion channel that is mutated in patients with cystic fibrosis.

Cystic fibrosis is caused by mutations in the CFTR anion channel, which is found in various epithelial tissues, including the lungs. A long-standing assumption that CFTR is activated by phosphorylation and ATP has recently been challenged by observations that the channel is open regardless of kinase activity in sweat glands.



Mild CFTR mutations mainly affect Cl^- transport (left), but severe forms also perturb bicarbonate conductance (right).

activated CFTR. CFTR is activated by glutamate only from the cytoplasmic side, however, and thus is distinguished from standard glutamate receptors, which respond to extracellular glutamate. Reddy does not yet know whether glutamate binds to CFTR directly or activates it indirectly.

Cl^- may not be the only CFTR-conducted ion important for normal gland function. Reddy found that bicarbonate ions also passed through the CFTR channel in the presence of both glutamate and ATP. Mutant versions of CFTR found in patients with severe forms of cystic fibrosis were deficient in both Cl^- and bicarbonate transport. Milder CFTR mutations spared bicarbonate transport. The findings suggest that defects in bicarbonate transport should not be ignored in the search for treatments for cystic fibrosis. ■

Reference: Reddy, M., and P. Quinton. 2003. *Nature.* 423:756–760.

Epithelial cells, including sweat glands, seem to express glutamate receptors, although their function is not known. Reddy studied the effect of glutamate on epithelial transport and found that it

Reddy/Macmillan

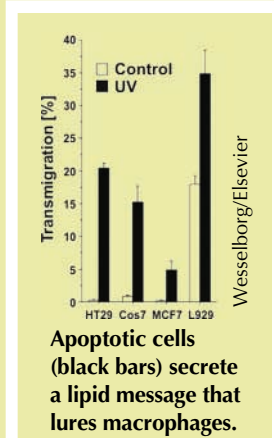
Dying cells say come-hither

Apoptotic cells are swallowed whole by phagocytes before they can release intracellular molecules that might produce inflammatory responses. Phagocytes get their instructions from cell surface markers on the dying cells. But in an entire organism the chances that the scavengers will encounter a dying cell in time are low. In a recent report, Kirsten Lauber, Sebastian Wesselborg (University of Tübingen, Tübingen, Germany), and colleagues show that apoptotic cells ensure their discovery by sending a long-distance chemotactic message to phagocytes. The new discovery reveals an additional signaling pathway that may be impaired in patients with autoimmune diseases.

The attractive signal for phagocytes was identified as lysophosphatidylcholine (LPC), a hydrolysis product of a plasma membrane phospholipid. LPC was released from apoptotic cells of various types via caspase-3-mediated activation of the calcium-independent form of phospholipase A_2 (iPLA $_2$). Inhibition of either caspase-3 or iPLA $_2$ blocked chemotaxis of macrophages in vitro. The group also showed that culture supernatants of apoptotic cells injected under the skin of mice caused macrophages to invade the injected area.

The phagocyte side of the story has yet to be worked out. For instance, it is not clear which receptors recognize LPC. Possibilities include G-protein-coupled receptors such as G2A, which binds to LPC and stimulates migration of blood cells. ■

Reference: Lauber, K., et al. 2003. *Cell.* 113:717–730.



Apoptotic cells (black bars) secrete a lipid message that lures macrophages.

Wesselborg/Elsevier