Text by Nicole LeBrasseur
lebrasn@rockefeller.edu

Wnt for adhesion

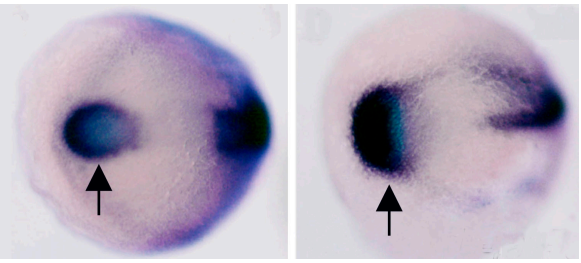
Wnt signaling keeps a group of migrating cells together, say Florian Ulrich, Michael Krieg, Carl-Philipp Heisenberg (Max Planck Institute, Dresden, Germany), and colleagues. Wnt achieves this by promoting the recycling of adhesion molecules.

Signaling via Wnt11 is needed during vertebrate gastrulation, when the group of cells that will form the axial mesendoderm migrate en masse to the animal pole. Heisenberg's group finds that these cells are uncoordinated and migrate in various directions in the absence of Wnt11.

The authors found that Wnt11 mutants adhered less tightly, both to each other and to matrix proteins. "The ability to cohere," says Heisenberg, "allows cells to align their [migratory] processes better. Loose clusters can project processes in all sorts of directions. Coherent ones can only put processes where there aren't any cells in the way."

Adhesion in these cells is mediated by E-cadherin, which the authors show is properly recycled only in the presence of Wnt. The activation of endocytosis corrected the migratory problems of Wnt11 mutants, whereas loss of endocytosis weakened cell adhesion strengths. Wnt might induce endocytosis via its known ability to activate actomyosin contraction.

Though more surface cadherin should result from a block in endocytosis, Heisenberg thinks the total amount is less important than its dynamicity. "For cells to form cohesive clusters," he says, "they need to undergo a lot of junctional remodeling, which might be dependent on E-cadherin recycling." JCB



HEISENBERG/ELSEVIER

The prechordal plate (arrows) is posteriorly displaced and elongated in a Wnt11 mutant (left). Activating endocytosis (right) corrects the defects.

Reference: Ulrich, F., et al. 2005. *Dev. Cell.* 9:555–564.

Presenting lipid antigens

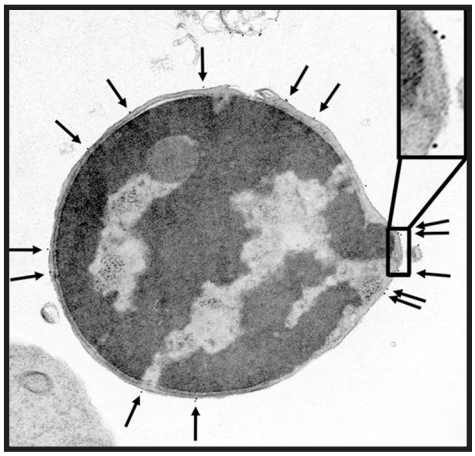
Immune cells inspect not just protein but also lipid antigens, thanks to presentation by the MHC relative CD1. Now, results from Peter van den Elzen, Michael Brenner (Harvard Medical School, Boston MA), and colleagues show that immune cells co-opt normal pathways of fat metabolism to deliver these lipid antigens to CD1.

Lipids circulate as part of large particles containing apolipoproteins such as ApoE. Cells that need more lipids secrete ApoE, which grabs onto fats and is then recaptured via receptor-mediated endocytosis. Brenner noticed that dendritic cells were dumping out much more ApoE than is required for their metabolic needs for fats.

But much of this ApoE is probably used to search for foreign lipids, according to the findings. The authors show that ApoE binds directly to lipid antigens and brings them into dendritic cells much more efficiently than does macropinocytosis (which dendritic cells use to engulf foreign peptides). Endocytosis "deposits the lipids in endosomal compartments," says Brenner, "right where CD1 is waiting. Then they come to the surface, where they can activate T cells."

In the absence of ApoE, dendritic cells required hours rather than minutes in contact with lipid antigens to activate T cells. This lag is precious lost time during which a pathogen might be rapidly multiplying. Blocking ApoE-dependent endocytosis might be beneficial, however, in preventing lipid-filled macrophages from initiating autoimmune disorders such as atherosclerosis. JCB

Reference: van den Elzen, P., et al. 2005. *Nature.* 437:906–910.



NAGATA/MACMILLAN

PtdSer (arrows) on an extruded nuclei (shown) signals to macrophages to digest it.

Marks of death on nuclei

Mammalian red blood cells get rid of their nuclei as they mature. Now, Hideyuki Yoshida, Shigekazu Nagata (Osaka University Medical School, Osaka, Japan), and colleagues show that the extruded nuclei cover themselves with the marks of dying cells. As a result, macrophages engulf and degrade the nuclei, as they do apoptotic cells.

The mark of an apoptotic cell that calls in macrophages is phosphatidylserine (PtdSer). Macrophage receptors such as MGF-E8 initiate phagocytosis when they sense this phospholipid in the dying cell's plasma membrane. Yoshida et al. found that PtdSer also appears on the plasma membrane surrounding an extruded nucleus. Masking PtdSer prevented macrophages from engulfing the nuclei.

PtdSer is normally retained in the inner leaflet of the plasma membrane by an ATP-dependent mechanism. But once separated from their cell body, the extruded nuclei were unable to generate their own ATP. PtdSer thus rapidly appeared on the outer surface of the membrane. Since ATP levels remain high in apoptotic cells, lone nuclei and dying cells must generate the PtdSer marks via different means.

Autoimmune problems in mice expressing a mutant MFG-E8 have been attributed to persistent apoptotic cells. But since at least tenfold more red blood cells than dying cells are generated per day, the unscavenged nuclei are probably the bigger issue. JCB

Reference: Yoshida, H., et al. 2005. *Nature.* 437:754–758.