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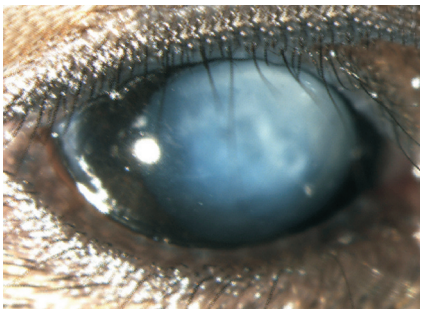
Cataracts and NrCAM

The Ig superfamily member NrCAM is believed to help orchestrate neuronal development, so Moré et al. (page 187) were surprised at the phenotype of their recently generated NrCAM −/− mice; the animals appear to have nearly normal nervous systems, but develop cataracts.

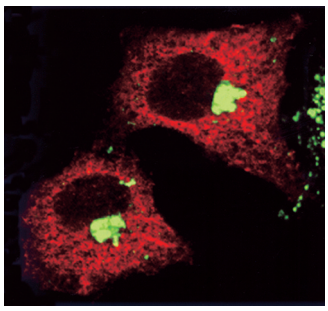
The mice are slightly smaller than their heterozygous littermates and show a slight motor defect, but are viable and fertile, and lack any histological abnormalities in any neural tissues. Their commissural axons cross the spinal cord midline normally, an unexpected result because previous work had suggested a requirement for NrCAM in directing commissural axon growth.



Cataracts form in mice lacking NrCAM.

While the absence of NrCAM does not appear to cause serious problems in neuronal tissue, NrCAM -/- mice develop cataracts because of a failure in establishing contact between lens fiber cells, and thus presumably a failure in forming normal water channels. Flow through these channels appears to be important for lens clarity, and defects in communication between lens fiber cells in the eye leads to the breakdown of the cells. Mice lacking ankyrin-B display a similar disorganization in the lens fiber, providing genetic evidence that NrCAM function requires a link to the cytoskeleton via ankyrin. The new work is also the first demonstration of NrCAM expression in the lens.

Cataracts are the most common cause of visual impairment in humans. If mutations in human NrCAM or ankyrin-B are also involved in the formation of cataracts, then drugs or gene therapy strategies targeting these proteins might be medically important. ■



Overexpression of human Vam6p (red) promotes clustering and fusion of lysosomes (green).

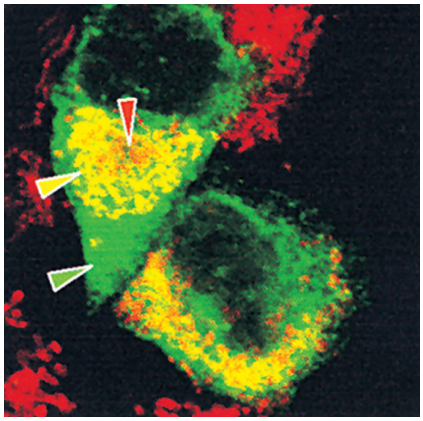
Clumping lysosomes

Caplan et al. (page 109) find evidence that human Vam6 protein is a mammalian tethering or docking factor with the intrinsic ability to promote lysosome fusion in vivo. The protein is related to a member of a vacuole-fusion complex in budding yeast, but has a unique citron homology domain that is required for lysosome clustering and fusion. Although Rab7 can induce lysosome fusion in yeast, dominant-negative Rab7 does not block hVam6p activity, suggesting that the human protein operates either downstream of, or in parallel to Rab7. ■

How *Toxoplasma* hooks up

The intracellular parasite *Toxoplasma gondii* hides out in a specialized compartment surrounded by the parasitophorous vacuole membrane (PVM). The PVM associates with host cell organelles, possibly as a way of scavenging lipids from the host cell. On page 95, Sinai and Joiner describe a protein that mediates this association. The new work illuminates a poorly understood aspect of parasite biology, and may be relevant for understanding organelle interactions in eukaryotic cells.

Sinai and Joiner focused on the *T. gondii* ROP2 protein, as this protein appears on the PVM around the time that the PVM associates with mitochondria, and it contains a domain with characteristics of a mitochondrial targeting signal.



ROP2 localizes to both mitochondria (yellow) and ER (green).

In vitro, they find that the N-terminal domain of ROP2 partially translocates into the mitochondrial outer membrane, and appears to stably integrate there. The same domain also contains a motif that promotes a high-affinity interaction with the endoplasmic reticulum (ER). In vivo, an expressed N-terminal domain of ROP2 targets both organelle systems.

The results suggest that one organelle might use a protein such as ROP2 to "capture" other organelles. Because PVM–organelle interactions are morphologically similar to normal interactions between organelles, such as ER–mitochondria interactions, the authors propose that this type of tethering mechanism may be a general phenomenon. ■