Sphingolipid imbalance can take out an eye

Yonamine et al. report that the relative amounts of two sphingolipids control the breakdown of light-sensing proteins and determine whether eye cells survive.

Sphingolipids aren't just building blocks of membranes. Some of the molecules, such as sphingosine 1 phosphate (S1P) and dihydrosphingosine 1 phosphate (DHS1P), take part in signaling pathways that manage everything from heart development to immune cell migration. Yonamine et al. found that these sphingolipids also control endocytosis of rhodopsin and another light-sensitive eye protein, the transient receptor potential (TRP) channel. After exposure to light, receptor cells in the fly that overproduces a fl y that overproduces

Annexin keeps tau on a short leash

Gauthier-Kemper et al. identify tau’s membrane tether and show how the protein breaks free in a form of dementia.

Some cases of frontotemporal dementia (FTD) and Alzheimer’s disease (AD) have similar symptoms and a common molecular malfunction. Microtubule (MT)-binding tau proteins that normally settle in axons bunch up in the cell body, which can kill the neuron. One difference between the diseases relates to tau phosphorylation. In AD, tau is hyperphosphorylated, which might allow the protein to abscend to the cell body by breaking its connection to MTs. But in one of the most common inherited forms of FTD, mutant tau carries fewer phosphate groups than normal. Researchers haven’t explained how this hypophosphorylated form of the protein gets loose.

Tau links to the cell cortex and adjusts MT dynamics during processes such as axonal growth. Gauthier-Kemper et al. found that the extensions that sprouted from neuronal cells carrying a form of mutant tau from FTD patients were fragile and highly dynamic, rapidly elongating and then collapsing. In the brain, such behavior might cause synapses to disconnect. However, Gauthier-Kemper et al. showed that this version of tau can still attach to MTs, ruling out one possible explanation for its mislocalization to the cell body.

Instead, the problem appears to be tau’s connection to the cell cortex. The researchers determined that the protein annexin A2 normally fastens tau to the plasma membrane. But mutant tau didn’t bind annexin A2 and could thus escape from the axon tip, perhaps because the mutant’s reduced phosphorylation prevents it from making the connection.


Natural killer cells commute death sentence

Natural killer (NK) cells sometimes target a friend instead of a foe. Abeyweera et al. reveal how healthy cells call off a misdirected attack.

An NK cell hunts down and destroys tumor cells and cells infected by viruses. Once it detects the characteristic surface proteins that betray one of these abnormal cells, an NK cell delivers the kiss of death, glomming onto its target and forming a cytolytic synapse. But the killer checks for an additional form of ID—the class I MHC protein, which is mainly expressed by healthy cells. A mystery is how an NK cell’s inhibitory receptors, which halt an attack in response to class I MHC, override the activating receptors that spur the cell to kill.