Enzyme shapes mitochondria

TP synthase bends the mitochondrial membrane to improve its performance, say Mike Strauss, Werner Kühlbrandt, and colleagues (Max Planck Institute of Biophysics, Frankfurt, Germany).

Kühlbrandt is interested in the structure of membrane proteins, which are normally extracted from their surroundings before examination. But with the recent emergence of electron tomography, Kühlbrandt realized, “if a protein is large enough, it should be possible to visualize it in situ without taking the whole thing apart.” His team tried its luck on ATP synthase embedded in bits of mitochondrial membrane.

The images revealed long ribbons of ATP synthase dimers in highly curved membranes. Previous work suggests that the curvature is created by the dimers: yeast mutants lacking dimerization subunits are missing the elaborate mitochondrial membrane invaginations called cristae. And the massive synthase leaves little room for anything else to do the bending.

The curves, the group suggests, make the synthase more efficient by increasing the local pH gradient, which helps drive ATP synthesis. The gradient is created by the pumping of protons into the inner membrane space. Mathematical calculations revealed that those protons can be more densely packed along membrane curves, thereby increasing the pH gradient there, where ATP synthase is situated. Bacteria get by with only monomeric ATP synthase in flat membranes. But eukaryotes probably evolved dimers rapidly, as they are found in yeast, unicellular ciliates, and mammals. JCB Strauss, M., et al. 2008. EMBO J. doi:10.1038/emboj.2008.35.

Stem cells sport longest telomeres

Adult stem cell hideouts can be identified by the presence of extra long telomeres, according to findings from Ignacio Flores, Maria Blasco (Spanish National Cancer Center, Madrid, Spain), and colleagues.

Because of their location at chromosome tips, telomeres shorten with every cell division. Stem cells divide more slowly than other cell types, so Blasco’s group reasoned that they might have the longest telomeres. Using a precise, quantitative version of FISH with telomere sequences, the group found that cells with the longest telomeres corresponded to known stem cell niches in skin, brain, testis, and other tissues.

The approach bypasses the need to identify distinguishing stem cell markers in each tissue type. Until now, the only other generally applicable method was the slower label-retaining technique. The authors will now test other tissues to identify unknown stem cell populations or resolve controversial ones.

Telomeres in the stem cell niches and elsewhere were dramatically shorter in two-year-old mice than in those just a year younger. The group hypothesizes that telomere maintenance mechanisms may go awry in old age. If stem cells with stubby telomeres are unable to function normally, this shortening may be a cause of aging. The group would now like to try to extend lifespan in mice by delaying telomere shortening. JCB Flores, I., et al. 2008. Genes Dev. 22:654–667.

Myosin and kinesin collaborate

Molecular motors each have their favorite tracks. Kinesin tugs cargo along microtubules for long distance transport, and myosin continues the haul on actin at the cell edges. But recently the group found that myosin also diffuses along microtubules. “At the time,” says Trybus, “we supposed that the diffusion might help myosin hook up with kinesin and its cargo, but the idea wasn’t very satisfying.” They now find a more gratifying explanation.

Using an in vitro system, the group showed that myosin’s interactions with microtubules enhanced kinesin’s processivity. When both motors were hooked to a cargo, kinesin took longer trips made up of several short runs linked by pauses. Dual-motor cargo might exist in vivo, given that large cargos such as melanosomes harbor dozens of motors.

The improved kinesin run lengths stemmed from electrostatic interactions between myosin and microtubules. Adding more positively charged residues to myosin further improved kinesin’s performance, whereas removing them blunted its effects. The findings suggest that myosin tethers a detached kinesin near the microtubule while it finds a site to rebind. “Without the tether,” says Trybus, “kinesin and the cargo are more likely to simply diffuse away.”

Kinesin returned the favor by increasing myosin’s run lengths, again through electrostatic effects. If charge is the decisive characteristic, any positively charged cargo can lend a hand to its own transport. JCB Ali, M.Y., et al. 2008. Proc. Natl. Acad. Sci. USA. 105:4691–4696.