Yeast dies for a noble cause

The yeast Saccharomyces cerevisiae is a popular model for studying apoptosis, raising an obvious mystery: why would a unicellular organism ever initiate programmed cell death? On page 501, Herker et al. elegantly demonstrate that under conditions simulating growth of yeast in the wild, suicide is an appropriate altruistic response.

After finding that cells in old yeast cultures die with the typical membranous and nuclear markers of apoptosis, the authors looked for a motive. Cells overexpressing Yap1p, which mediates the yeast stress response, enjoy prolonged survival in aging cultures, indicating that the death response is triggered by stress. Deleting the caspase YCA1 improves short-term survival, but YCA1 deletants fail to regrow when transferred from an old culture to fresh medium, and wild-type cells out-compete YCA1 deletants in cocultures. Yeast cells undergoing apoptosis release low molecular weight substances that improve the growth of old cultures.

Herker et al. argue that, in the wild, apoptosis allows a clonal population of yeast to ensure the survival of its genes through lean times, by killing off less fit individuals to conserve nutrients, and promoting the survival of only the healthiest descendants. The results also explain why yeasts die in minimal medium, but survive in distilled water. In the complete absence of any nutrients, apoptosis is presumably inhibited.

Boning up on JunB

Transcription factor JunB negatively regulates proliferation in several cell types. But Kenner et al. (page 613) show that JunB, which acts as one-half of an AP-1 dimer, is a positive regulator of both osteoblast and osteoclast proliferation and differentiation. In the process they have produced a new animal model for studying osteoporosis.

As JunB is essential for placenta formation, the authors conditionally deleted the gene in embryonic tissues. The resulting mice were viable, but soon developed severe bone loss resembling human senile osteoporosis, and later a condition resembling chronic myelogenous leukemia.

A separate strain of mice, lacking JunB only in the macrophage and osteoclast lineage, but not in osteoblasts, developed severe osteopetrosis and increased bone mass. The leukemia is consistent with earlier results suggesting a tumor-suppressor function for JunB, which negatively regulates the proliferation of myeloid progenitor cells. Osteoblast and osteoclast proliferation, however, seem to be boosted by JunB, and ex vivo experiments confirm that this effect is cell autonomous. Thus, JunB is a key regulator of bone growth and affects bone formation more strongly than resorption.

Apoptotic mitochondria blow a fuse

Mitochondrial networks fragment during apoptosis, and it is known that fission increases. Any fission increase is usually accompanied by a fusion increase, but on page 493 Karbowski et al. find that activating apoptosis blocks mitochondrial fusion.

The authors came up with a clever new technique to track individual organelles using a photoactivatable form of GFP with a mitochondrial targeting sequence. Aiming a laser at individual mitochondria in tagged cells activated the fluorescent tag, and the dilution of fluorescence provided a quantitative readout of organelle fusion and fission. Inducing apoptosis blocked mitochondrial fission to a degree that could fully account for apoptotic mitochondrial fragmentation. The block in fusion occurs around the same time as Bax translocation to mitochondria and mitochondrial permeabilization, and before caspase activation.

The data suggest that a complete block in mitochondrial fusion is a normal part of apoptosis, and that this block is either fully or partially responsible for mitochondrial fragmentation. The authors are now adapting their assay to study mitochondrial fragmentation in more detail, and suggest that it could be used for high-resolution studies on the dynamics of other organelles.