Where mtDNA is made

On page 503, Meeusen and Nunnari show that yeast mitochondria harbor self-sustaining DNA replication factories. The mitochondrial genome (mtDNA) is packaged into nucleoids, some of which attach to the mitochondrial membrane at sites that contain the outer membrane protein Mmm1. Mmm1 binds to the actin cytoskeleton, and mitochondrial movement depends on actin, so one obvious hypothesis is that this DNA–protein structure segregates mtDNA into buds. But Meeusen and Nunnari suggest that Mmm1 and associated proteins replicate, rather than actively segregate, the genome.

The authors find that Mmm1-linked nucleoids are associated with both replicating mtDNA and proteins necessary for its duplication, including Mgm101, an essential DNA repair protein, and Mip1, the mtDNA polymerase. These proteins make up an independent structure, spanning two membranes, that is replicated and inherited even in the absence of mtDNA, indicating that the association is not simply a byproduct of DNA-binding abilities. It is not yet clear which components are needed for its replication.

The structures do not seem to segregate DNA actively, as they had limited movement except in concert with the organelle as a whole. However, they might still ensure faithful mtDNA inheritance by anchoring nucleoids throughout the organelle. This model is consistent with the uniform spacing of the complexes seen in vivo.

Quick cartilage transformation

On page 661, Holmbeck et al. identify a new mechanism of cartilage remodeling. This quick remodeling system bypasses time-consuming steps to bone formation that are required in the previously known pathway.

In the well-known pathway to bone formation, a cartilage scaffold must be mineralized before it is degraded by osteoclasts and replaced with bone. But some bones seem to be formed without cartilage mineralization. Holmbeck et al. find that this process relies on the matrix metalloprotease MT1-MMP, which degrades unmineralized cartilage.

The authors examined bone formation in MT1-MMP–deficient mice, which have skulls that are misshapen by cartilage. They find that in wild-type mice this same cartilage is not mineralized, but rather expresses MT1-MMP before its removal and replacement with bone. Without the protease, the cartilage remains, and adult bone layers do not form correctly.

Cartilage leftovers were also found in joints and at bone–tendon interfaces. As the mice have a dwarf phenotype, the authors suggest that growth of limb bones (a mineralization-dependent process) must be accompanied by the remodeling of cartilage into ligaments and tendons. This could be done quickly by the MT1-MMP pathway, which avoids the mineralization step. Its speed is also well-suited to keeping up with the rapid growth of the skull that occurs after birth.

A few cells within the cartilage remnants expressed bone markers. Thus, some bone may be formed by differentiating cartilage cells rather than immigrating osteoblasts. If so, this hints at a mammalian version of metamorphosis—an MMP-dependent replacement of transient with definitive organs.