

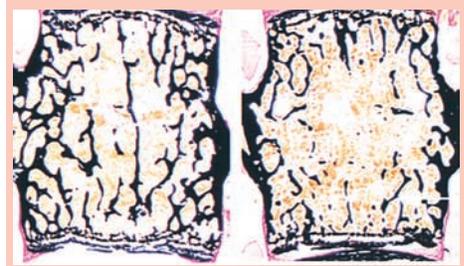
AIR-2 (green) breaks down the last links between chromosomes (red).

Knowing when to let go

During meiosis I, some mechanism must allow homologous chromosomes to separate while keeping sister chromatids paired until meiosis II. How does a cell make this distinction? On page 219, Rogers et al. propose that in *C. elegans* the aurora-B kinase AIR-2 is largely responsible for ensuring that cohesion between chromosomes breaks down at the proper place and time. The authors also identified additional components in what is likely to be a conserved pathway controlling chromosome cohesion.

When AIR-2 activity is inhibited by RNAi, meiotic cells in the worm do not separate homologous chromosomes or sister chromatids. In metaphase I in normal meiotic cells, AIR-2 localizes distal to chiasmata, corresponding to the last points of contact between homologous chromosomes. In metaphase II, AIR-2 localizes to the last points of contact between sister chromatids. AIR-2 phosphorylates the cohesin protein REC-8 at a specific site in vitro, and inhibition of the CeGLC-7 α or - β phosphatases causes AIR-2 to localize nonspecifically along chromosomes.

The authors suggest that CeGLC-7 α / β phosphatases restrict AIR-2 localization temporally and spatially on meiotic chromosomes. AIR-2 phosphorylates REC-8 in its vicinity, causing the cohesin to be degraded and releasing chromosomal cohesion only in the appropriate location. ■



Mice lacking Lrp5 (right) have low bone mass in their vertebrae.

For healthy eyes and bones: got Lrp?

The Wnt family of secreted proteins controls several crucial developmental processes, some of which are apparently mediated by Wnt coreceptors from the LDL receptor-related protein (Lrp) family. Now, on page 303, Kato et al. report that the targeted disruption of Lrp5 in mice causes a phenotype virtually identical to that seen in humans with osteoporosis-pseudoglioma syndrome. In addition to identifying a long-sought genetic component for bone mass determination, the work identifies Lrp5 as a critical component for controlling both osteogenesis and eye vascularization during late stages of development.

Mice lacking functional Lrp5 exhibit lower rates of bone formation than wild-type mice, and fail to achieve normal bone mass early in life. This happens despite normal expression of Cbfa1, a protein thought to be the principal controller of osteogenesis, suggesting that Lrp5 functions in an independent osteogenesis pathway. In addition, Lrp5 knockout mice retain part of the embryonic eye vascularization network, which regresses postnatally in wild-type mice by macrophage-mediated apoptosis. Since normal ocular macrophages are present in the mutant mice, Lrp5 appears to be specifically required for macrophage-mediated apoptosis. The authors are now trying to determine whether other aspects of bone biology are governed by the Lrp5-mediated osteogenesis pathway, and which Wnt proteins signal through this pathway. ■

Adapting to the pit

Cell surface receptors that are internalized generally interact with the endocytic machinery through adaptor proteins. On page 315, Howard et al. describe the first example of a protein involved in recognizing endocytic targeting signals in yeast. The work links together several earlier observations about yeast actin dynamics and endocytosis, and suggests that an analogous system may exist in mammalian cells.

The authors found that a sequence containing the amino acid motif NPF_(1,2)D, previously characterized as an endocytic targeting signal in yeast, is sufficient to direct the uptake of a truncated cell surface receptor. A two-hybrid screen for NPF_(1,2)D-binding proteins yielded Sla1p, which is known to interact with the endocytic machinery and regulate actin dynamics. Disrupting Sla1p expression inhibited NPF_(1,2)D-mediated endocytosis.

Combined with previous findings, the results imply that Sla1p is part of

a complex that links cargo bearing the NPF_(1,2)D motif to the actin and clathrin-based endocytic machinery. By analogy, a similar complex in mammalian cells might provide a Sla1p-like adaptor function in endocytosis. Searches of the yeast genome database suggest that NPF_(1,2)D directs endocytosis of a subset of cell surface proteins, and may also mediate other types of protein sorting. ■

