

## Zfp521 works its zinc fingers to the bone



The clavicle (arrow) is underdeveloped in mice lacking one copy of *Runx2* (left) but is partially restored when *Zfp521* expression is also reduced (right).

The zinc finger protein *Zfp521* also controls bone formation and is a binding partner of *Runx2*. Hesse et al. examined how the two proteins combine to regulate osteogenesis *in vivo*.

Mice lacking one copy of *Runx2* have underdeveloped bones similar to cleidocranial dysplasia patients. This phenotype was largely rescued by removing one copy of *Zfp521*, whereas overex-

A zinc finger protein controls two stages of bone formation by opposing the master regulator of osteogenesis, Hesse et al. report.

*Runx2* is a transcription factor essential for the differentiation of mesenchymal precursors into bone-forming osteoblasts. Mutations in human *Runx2* cause the skeletal disorder cleidocranial dysplasia, in which certain bones are

underdeveloped. The zinc finger protein *Zfp521* also controls bone formation and is a binding partner of *Runx2*. Hesse et al. examined how the two proteins combine to regulate osteogenesis *in vivo*.

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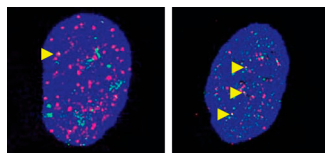
pressing the zinc finger protein exacerbated the bone defects. Accordingly, Hesse et al. found that *Zfp521* inhibits *Runx2* to limit the differentiation of mesenchymal cells into osteoblasts. *Zfp521* blocked *Runx2* by recruiting the histone deacetylase HDAC3 to switch off *Runx2*-mediated transcription. *Zfp521* was unable to inhibit *Runx2* activity in the absence of HDAC3.

Some evidence suggests that *Runx2* itself has an inhibitory function at later stages of bone development, preventing osteoblasts from reaching their fully mature state. Indeed, overexpressing *Runx2* in adult mice resulted in reduced bone density and the accumulation of immature osteoblasts. This was reversed by simultaneously overexpressing *Zfp521*, suggesting that the zinc finger protein antagonizes *Runx2* at this stage of bone development as well.

*Zfp521* therefore maintains the correct balance of *Runx2* activity for osteoblast commitment and maturation. The authors now want to identify other transcription factors regulated by *Zfp521*.

Hesse, E., et al. 2010. *J. Cell Biol.* doi:10.1083/jcb.201009107.

## Telomeres get SIRT-ified



A cell lacking *SIRT1* (right) shows increased DNA damage (green) at chromosome ends (red).

Budding yeast telomeres are partly maintained by a deacetylase called *Sir2*, but whether the mammalian orthologue of this protein, *SIRT1*, has a similar function is unclear. Mice overexpressing *SIRT1* have an increased healthspan—remaining healthy for longer than wild-type littermates. Palacios et al. examined telomeres from these mice, as well as from animals that lack *SIRT1* entirely.

*SIRT1*-deficient mice had shorter telomeres, whereas *SIRT1* overexpression boosted telomere length, preventing them from short-

A protein that protects against aging-related diseases maintains telomere length and integrity, Palacios et al. reveal.

Telomeres protect chromosome ends but grow shorter with age, potentially contributing to several age-associated illnesses.

*SIRT1* therefore maintains telomere length and integrity, which may explain why *SIRT1*-overexpressing mice stay healthier for longer. Telomeres re-grow when differentiated cells are reprogrammed into an embryonic stem cell–like state. Palacios et al. found that *SIRT1* binds to the elongated telomeres of these induced pluripotent stem cells. Senior author Maria Blasco now wants to investigate whether *SIRT1* contributes to telomere extension during reprogramming.

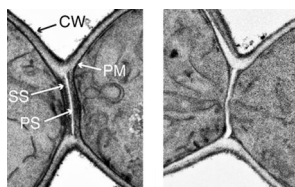
Palacios, J.A., et al. 2010. *J. Cell Biol.* doi:10.1083/jcb.201005160.

ening as the mice grew older. This latter effect required the activity of telomerase enzyme, a major contributor to telomere production. Yet *SIRT1* may also influence a second maintenance pathway called alternative lengthening of telomeres, or ALT. *SIRT1* overexpression increased the amount of homologous recombination at chromosome ends, a key step in the ALT pathway. *SIRT1* boosted homologous recombination along the rest of chromosomes as well, suggesting that the deacetylase promotes DNA repair. On the other hand, *SIRT1*-deficient cells showed increased damage at their chromosome ends.

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## Myo1 provides a ring in the tail



Yeast expressing the *Myo1* tail (right) still form a primary septum (PS), which promotes cytokinesis in the absence of *Myo1* motor activity.

lacks the actin-binding and motor activity of *Myo1*'s head domain.

By constructing a series of deletion mutants, Fang et al. discovered two separate mechanisms that localize the tail of *Myo1* at different points in the cell cycle. Before cytokinesis, *Myo1* local-

Fang et al. describe two distinct pathways that target the tail of yeast myosin II to the bud neck to direct cell division.

Myosin II motors drive cytokinesis by assembling a contractile actomyosin ring at the site of cell division. The budding yeast myosin II, *Myo1*, is targeted to the bud neck by its C-terminal tail, and this domain alone is sufficient to separate mother and daughter cells, even though it

ized to the bud neck by binding *Bni5*, a protein that in turn binds to septin GTPases. During cytokinesis, however, *Myo1* targeting depended on the actin-binding protein IQGAP instead.

The *Myo1* tail was sufficient to assemble an actomyosin ring at the bud neck, perhaps because IQGAP can compensate for the loss of *Myo1*'s actin-binding head. But how does the *Myo1* tail promote cytokinesis in the absence of any motor activity? Fang et al. found evidence to suggest that the “headless” actomyosin ring directs the deposition of vesicles around the bud neck to form the primary septum—a specialized cell wall region that pushes the cytokinetic furrow inward. Senior author Erfei Bi says that the actomyosin ring therefore coordinates membrane deposition and contractile force during cytokinesis. He now wants to investigate how *Myo1* and IQGAP promote actomyosin ring assembly and how the ring is coordinated with septum formation.

Fang, X., et al. 2010. *J. Cell Biol.* doi:10.1083/jcb.201005134.