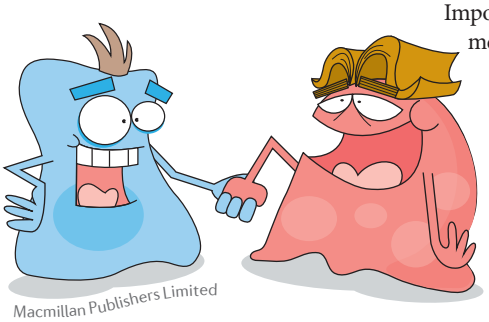
Nature Reviews Rheumatology | Published online 15 Feb 2018; doi:10.1038/nrrheum.2018.16

BONE

Direct contact between mature osteoblasts and osteoclasts

> mature osteoblasts attenuate the bone-resorbing activity of mature osteoclasts via cell-cell contact

Bone remodelling takes place in specialized modelling units spread throughout the skeleton and involves bone resorption by mature osteoclasts, followed by differentiation of osteoblast precursors to mature osteoblasts to replace the resorbed matrix. Mature osteoblasts and mature osteoclasts are therefore thought to be spatially and temporally separated and, unlike their precursors, direct communication between the two has been questioned. Furuya et al. now show that mature osteoblasts and osteoclasts can be in direct contact in living bone and that this contact is associated with a reduction in osteoclast activity.



Macmillan Publishers Limited

To visualize mature osteoblasts and osteoclasts in vivo, the authors created a reporter mouse line expressing two different fluorochromes under the control of the 2.3 kb fragment of rat *Col1a1* promoter and the *Trap* promoter, followed by intravital two-photon bone imaging of the endosteal surface of the skull.

As previously suggested, mature osteoblasts and osteoclasts were mainly present in distinct colonies and direct contact was limited even when cells were in close proximity. Nevertheless, the researchers observed dendritic projections extending from the mature osteoclasts in direct contact with the osteoblasts.

Importantly, resorptive activity, measured using a pH-sensing chemical probe, was lower in osteoclasts in direct contact with osteoblasts than in unconnected osteoclasts. Consistent with this effect, the decrease in bone resorption following 3 weeks of intermittent parathyroid hormone treatment was associated with a spatial redistribution of and more direct contact between mature osteoblasts and osteoclasts, when compared with placebo or 1-week treatment. The increase in osteoclast and osteoblast proliferation, which occurred early during treatment, did not require cell–cell contact.

Thus, this study demonstrates that mature osteoblasts attenuate the bone-resorbing activity of mature osteoclasts via cell–cell contact. "The event of bone cell coupling would be an interesting therapeutic target for several disorders," reveals Masaru Ishii, corresponding author, adding that his research group is currently looking into several candidate molecules.

Liesbet Lieben, Senior Editor,
Nature Reviews Disease Primers

ORIGINAL ARTICLE Furuya, M. et al. Direct cell–cell contact between mature osteoblasts and osteoclasts dynamically controls their functions in vivo. *Nat. Commun.* **9**, 300 (2018)