

Direct cell-cell contact between mature osteoblasts and osteoclasts dynamically controls their functions *in vivo*

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Bone homeostasis is regulated by communication between bone-forming mature osteoblasts (mOBs) and bone-resorptive mature osteoclasts (mOCs). However, the spatial-temporal relationship and mode of interaction *in vivo* remain elusive. Here we show, by using an intravital imaging technique, that mOB and mOC functions are regulated via direct cell-cell contact between these cell types. The mOBs and mOCs mainly occupy discrete territories in the steady state, although direct cell-cell contact is detected in spatiotemporally limited areas. In addition, a pH-sensing fluorescence probe reveals that mOCs secrete protons for bone resorption when they are not in contact with mOBs, whereas mOCs contacting mOBs are non-resorptive, suggesting that mOBs can inhibit bone resorption by direct contact. Intermittent administration of parathyroid hormone causes bone anabolic effects, which lead to a mixed distribution of mOBs and mOCs, and increase cell-cell contact. This study reveals spatiotemporal intercellular interactions between mOBs and mOCs affecting bone homeostasis *in vivo*.

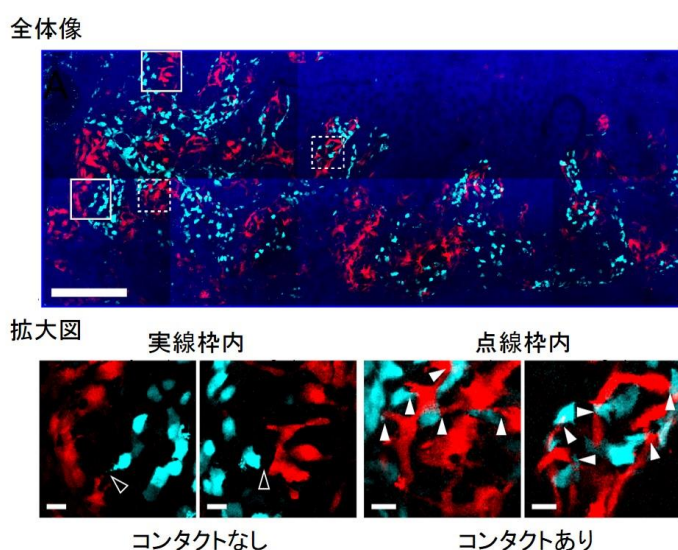


図 1. 生体骨組織内部のイメージング画像

骨芽細胞(水色)と破骨細胞(赤色)が直接接触しコミュニケーションをとる瞬間を捉えることに成功。青色は骨組織。スケールバー:全体像 300 μ m、拡大図 20 μ m

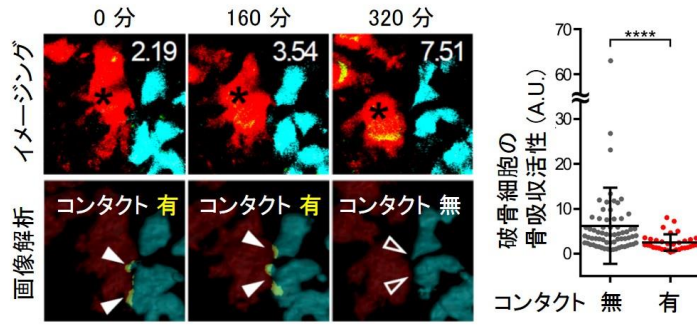


図 2. pH 応答性蛍光プローブを用いた骨吸収活性の解析
骨芽細胞(水色)と接触している破骨細胞(赤色)は、骨を溶かす機能が抑制されている。緑色は pH 応答性蛍光プローブ。

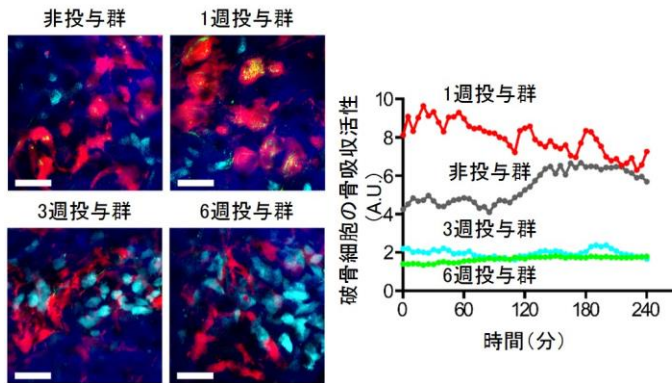


図 3. PTH 製剤の薬効評価

PTH 製剤は、骨芽細胞(水色)と破骨細胞(赤色)の細胞間接触を増加させ、破骨細胞の骨吸収を抑制する。