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第 330 回松本歯科大学大学院セミナー

日　時: 2015 年 7 月 21 日(火)　18 時 15 分～19 時 00 分

場　所: 実習館 2 階 総合歯科医学研究所セミナールーム

演　者: Thomas John Martin 氏(メルボルン大学
セントビンセント医学研究所・名誉教授)

タイトル: EphrinB2 signaling within the osteoblast lineage is necessary for normal bone formation.(骨芽細胞におけるエフリン B2 シグナルは正常な骨形成に必要である)

Eph/ephrin receptor tyrosine kinases regulate tumorigenesis, vascularization and axon guidance, and have the unique ability to signal both through Eph receptor (forward) and ephrin ligand (reverse). EphrinB2 expression by osteoblasts is rapidly stimulated by parathyroid hormone (PTH). Within these cells, ephrinB2 is the only family member whose production is stimulated by the bone formation stimuli, parathyroid hormone (PTH) and PTHrP. Pharmacological inhibition of ephrinB2/EphB4 interaction by receptor blockade *in vitro* impairs differentiation of osteoblasts, and *in vivo* impairs late stage osteoblast differentiation and stimulates osteoblastic support of osteoclast formation.

We examined the role of ephrinB2 in bone formation and anabolic PTH action using mice with conditional deletion of ephrinB2 from osteoblasts (using *Osx1.Cre*), and in cultured osteoblasts with ephrinB2 or EphB4 knockdown. Osteoblast differentiation and support of osteoclastogenesis was impaired when ephrinB2 (but not EphB4) was inhibited. *In vivo* this resulted in delayed osteoid mineralization, reduced bone stiffness, and impaired osteoblastic response to anabolic PTH treatment. Furthermore, ephrinB2 null mice exhibited greater levels of osteoblast and osteocyte apoptosis and caspase 8 activation. This indicates that ephrinB2 reverse signaling within the osteoblast lineage is required for PTH anabolic action, and maintains osteoblast differentiation by limiting apoptosis of the differentiated osteoblast, providing *in vivo* evidence for a role of ephrinB2 reverse signalling in cellular metabolism.

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Furthermore in mice in which ephrinB2 was deleted using *Ctsk.Cre,* osteoclast formation from precursors was the same as in controls, and the mice deficient on ephrinB2 in osteoclasts had no bone phenotype, indicating that reverse signaling within the osteoclast lineage does not restrain osteoclast formation.

担当:硬組織疾患制御再建学講座　宇田川 信之