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日 時: 2011 年 6 月 3 日(金) 17 時 30 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

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タイトル: ポドソーム形成と細胞融合におけるアダプター分子 Tks5 の機能解析

(Tks5-dependent formation of circumferential podosomes mediates cell-cell fusion)

Abstract: Multinucleation of osteoclasts during osteoclastogenesis requires dynamic rearrangement of the plasma membrane and cytoskeleton, requiring numerous previously characterized factors. However, the mechanism underlying osteoclast fusion remains obscure. Here, we show that the adaptor protein Tks5 functions as part of the fusion machinery downstream of PI3-kinase and Src in osteoclasts. Tks5 expression was induced during osteoclastogenesis, and reducing its expression impaired both formation of circumferential podosomes and osteoclast fusion without altering differentiation. Tyrosine phosphorylation of Tks5 was reduced in *Src*^{-/-} osteoclasts, likely accounting for defects in podosome organization and multinucleation seen in these cells. Circumferential podosome formation in B16 melanoma cells in the presence of RANKL, TGFβ and TNFα also required Tks5 phosphorylation. Co-culture of B16 melanoma cells with osteoclasts in an inflammatory milieu promoted increased formation of melanoma-osteoclast hybrid cells. Our results revealed a previously unappreciated regulation of Tks5 in both circumferential podosome formation and cell-cell fusion.

担当: 硬組織疾患制御再建学 宇田川信之