■一般演題（口演）

日時：9月5日（金）16:00-16:40
会場：F会場（会議場3階　32会議室）
座長：宇佐美 悠（阪大　院歯　口腔病理）

一般演題（口演）骨1（O1-PM-F1 ～ 4）

O1-PM-F1 「AI and Bioinformatics Reveal Organelle Remodeling in O-GlcNAcylation-mediated Osteoblast Differentiation」

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To understand how O-GlcNAcylation affects bone formation, we re-analyzed public RNA-seq data and found that mitochondria and the cytoskeleton are key targets in osteoblasts differentiation. While their roles have been studied, their specific involvement in osteogenesis remains unclear. Using Ogt-knockout osteoblast cells, we observed reduced differentiation, movement, growth, Mito-ER coupling, ER size, nuclear tubulin levels, and oxygen metabolism. Live-cell imaging and AI modeling linked these changes to disrupted Mito-ER interaction. Further analysis suggested that Ezh2 and its downstream genes (Opa1, Gsk3a, Wnt3a, Hif1a, Hspa9) may mediate this regulation. Overall, O-GlcNAcylation influences osteoblast differentiation by altering mitochondria, cytoskeleton, and ER structure, with Ezh2 playing a key role.
Non-member collaborative researcher: Ziyi Wang (Department of Molecular Biology and Biochemistry, Okayama University)

O1-PM-F2 「Regulation of Osteoblast Differentiation by VGLL3 Through DAPK2-Mediated Autophagy」

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Our previous work found that Vestigial-like family member 3 (Vgll3) regulates osteoblast differentiation. To further clarify the function of Vgll3, we analyzed RNA-seq data of Vgll3-knockdown (shVgll3) MC3T3-E1 cells and found Death-associated protein kinase 2 (Dapk2) as one of the down stream factors of Vgll3. Dapk2 is known to be an important factor in autophagy, which has been reported as a critical process in osteoblast differentiation. Therefore, we examined the autophagic activity in shVgll3 cells by TEM and WB. The number of autophagosomes and the protein expression level of LC3 were decreased in shVgll3 cells, indicating that autophagy activity was decreased by the suppression of Vgll3. Next, the effect of Dapk2 knockdown on osteoblast differentiation was assessed using qPCR, WB, ALP staining and Alizarin red staining. Dapk2 knockdown in MC3T3-E1 cells reduced the expression of key osteogenic markers and intensity of ALP/Alizarin red staining. Then we found rapamycin treatment partially restored both autophagic activity and osteoblast differentiation in shVgll3 cells. Our findings reveal a new role for Vgll3 in osteoblast differentiation via Dapk2-mediated autophagy.

O1-PM-F3 「Osteoblast-specific p65 deficiency enhances bone formation and confers resistance to estrogen deficiency-induced bone loss」

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Nuclear factor κB (NF-κB) pathway regulates inflammation and immune responses and plays crucial role in bone biology. This study elucidates role of p65, a major NF-κB subunit, in osteoblast differentiation and bone formation. Since global p65 knockout is embryonic lethal, osteoblast-specific p65-conditional knockout (p65cKO) mice were generated using tamoxifen-inducible Cre recombinase under the type I α collagen promoter. Tamoxifen administered at 6 weeks of age, and analyzed after 4 weeks. p65cKO mice showed increased trabecular bone and bone formation compared to control, with no change in osteoclast numbers. After ovariectomy (OVX) induced estrogen deficiency, control mice exhibited high bone turnover with increased formation and predominant resorption, leading to bone loss. In contrast, p65cKO mice showed low bone turnover and resistance to OVX-induced bone loss. These findings indicate p65 deficiency in osteoblasts promotes osteoblast differentiation and bone formation via cell-autonomous mechanisms under physiological conditions, while suppressing osteoclastogenesis through osteoblast-mediated paracrine regulation during estrogen deficiency, thereby maintaining bone mass.

O1-PM-F4 「高ビタミンD症および慢性腎臓病両病態モデルにおいて、骨芽細胞系列細胞のビタミンD受容体(VDR)は、翻訳後糖鎖修飾を介して循環スクレロスチン量と骨形成を調節する」

中道 裕子[1・2]、劉 子洋[2]、何 治鋒[1]、宇田川 信之[1・2・3]
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高ビタミンD症（HVD）は、医原性または内因性に発症する。HVDおよび慢性腎臓病(CKD)はともに、ビタミンD恒常性破綻によるカルシウム・リン代謝性疾患であり骨代謝カップリング破綻が認められる。我々は、HVDにおける骨吸収亢進、軟組織石灰化、骨形成抑制は、骨芽細胞系列（OB）細胞のVDRを介して誘導されることを報告した（Endocrinology 2020, JSBMB 2023, 2025)。HVDを誘導した野生型マウスでは、骨形成阻害因子Sclerostinの血中濃度上昇を伴う骨形成低下を認め、OB特異的VDR-cKOマウスでは、これらの表現型は認められなかった。最近、糖転移酵素B4GALNT3が、Sclerostinの糖鎖末端にGalNAcβ1→4GlcNAcを転移（LDN化）することで、血中Sclerostinのクリアランスを促進する可能性が提起された（eBioMedicine 2023)。HVDを誘導した野生型マウスでは、B4galnt3 mRNAの骨における発現は低下し、OB特異的VDR-cKOマウスでは低下しなかった。OB細胞株の活性型ビタミンD（1,25D）処理は、B4galnt3 mRNAの発現とSclerostinのLDN化率を減少させた。次に1,25D欠乏性疾患であるCKDモデルマウスを解析したところ、予想に反してHVDマウスと同様に、B4galnt3 mRNAの骨における発現減少を伴う血中Sclerostin濃度上昇と著明な骨形成低下が観察された。以上、カルシウム・リン代謝性疾患においてOB細胞のVDRがB4GALNT3発現調節によりSclerostin分解を制御し、骨形成調節の要として働く可能性が示された。