

-大学院歯学独立研究科-

第 132 回 大学院 研究科 発表会 プログラム
第 150 回 中 間 発表会 プログラム

大学院学生等が、これまでの研究成果を発表します。
どなたでも聴講できますので、多数の参加をお待ちしております (聴講申込不要)

場 所：実習館 2 階 総合歯科医学研究所セミナー室

日 時：2026 年 10 月 28 日 (水) 17 時 30 分 開会

—2026 年 10 月 28 日 (水) —

No.	発表区分・予定時間	演題名・発表者	審査委員
1	[大学院] 17:30~18:00 司会:小林 教授	「Lepr ⁺ bone marrow stromal cells protect Inflammaging and immune-senescence through Wnt secretion」 朱 徳超 硬組織疾患制御再建学 硬組織機能解析学	主査:村上教授 副査:中村特任教授 :芳澤教授
2	[中 間] 18:00~18:30 司会:樋口 教授	「無歯顎欠損患者に対する補綴治療介入効果の検証」 秋山 洋 顎口腔機能制御学 臨床機能評価学	主査:黒岩教授 副査:川原良美教授 :増田特任教授
3	[中 間] 18:30~19:00 司会:李 特任教授	「NRF2 upregulation in MSC spheroids suppresses SASP and promotes osteogenesis (MSC スフェロイドにおける NRF2 発現上昇は SASP を抑制し、骨形成を促進する)」 孔 晶晶 硬組織疾患制御再建学 臨床病態評価学	主査:山下教授 副査:石田講師 :川原一郎教授
4	[中 間] 19:00~19:30 司会:栗原 教授	「Effects of bioabsorbable materials in combination with spontaneous spheroids transplantation on bone repair microenvironment (生体吸収性材料と自発的スフェロイドの併用により骨修復微小環境に及ぼす影響)」 岳 磊 硬組織疾患制御再建学 硬組織疾患病態解析学	主査:平賀教授 副査:上原准教授 :亀山教授

発表内容の要旨(課程博士)
Abstract of Presented Research (For the Doctoral Course)

学 籍 番 号 Student ID No.	ID # G 2408	入 学 年 Entrance Year	2024 年 Year
(ふりがな)	シュ・トクチョウ		
氏 名 Name in Full	朱 徳超		
専 攻 分 野 Major Field	硬組織機能解析学		
主 指 導 教 員 Chief Academic Advisor	小林 泰浩		
発 表 会 区 分 Type of Meeting	中間発表会 ・ 大学院研究科発表会 ・ 松本歯科大学学会 Midterm Meeting / Graduate school research meeting presentation / The Matsumoto Dental University Society		
演題名 / Title of Presentation			
LepR ⁺ bone marrow stromal cells protect Inflammaging and immune-senescence through Wnt secretion			
発表要旨 / Abstract			
Wnt ligands activate both canonical and non-canonical signaling pathways and play important roles in regulating bone metabolism to maintain bone mass. However, it remains unclear whether Wnt ligands derived from bone cells suppress bone phenotypes associated with aging. To address this question, we generated leptin receptor (LepR)-Cre; Wntless conditional knockout mice (LepR-Wls cKO), in which LepR-expressing cells are unable to secrete Wnt ligands, and analyzed their phenotypes. LepR-Wls cKO mice exhibited decreased bone mass and increased bone marrow adipogenesis. Notably, survival analysis from 20 to 80 weeks of age revealed that LepR-Wls cKO mice had a 3.48-fold (males) and 4.15-fold (females) higher risk of mortality compared with heterozygous controls. Frailty assessment further demonstrated that LepR-Wls cKO mice developed systemic aging phenotypes beginning at middle age (35 weeks). Immunohistochemistry, western blotting, and qPCR analyses of senescence markers, including p21, p16, SA-β-Gal, γH2AX and inflammatory cytokines, suggested that LepR-Wls cKO mice develop bone marrow inflammaging, characterized predominantly by senescence in monocyte/macrophage lineage cells. Consistently, lipopolysaccharide (LPS) challenges showed that LepR-Wls cKO mice also exhibited increased mortality, indicating accelerated immunosenescence in these mice. Taken together, these findings suggest that bone marrow stromal cell-derived Wnt ligands protect against bone marrow inflammaging, thereby delaying age-associated immunosenescence.			

発表内容の要旨(課程博士)
Abstract of Presented Research (For the Doctoral Course)

学 籍 番 号 Student ID No.	ID # G 2301	入 学 年 Entrance Year	2023	年 Year
(ふりがな)	あきやま ひろし			
氏 名 Name in Full	秋山 洋			
専 攻 分 野 Major Field	顎口腔機能制御学講座 臨床機能評価学ユニット			
主 指 導 教 員 Chief Academic Advisor	樋口大輔			
発 表 会 区 分 Type of Meeting	中間発表会 ・ 大学院研究科発表会 ・ 松本歯科大学学会 Midterm Meeting / Graduate school research meeting presentation / The Matsumoto Dental University Society			
演題名 / Title of Presentation				
義歯治療患者における自由咀嚼と片側咀嚼の違いが咀嚼能力評価に及ぼす影響				
発表要旨 / Abstract				
現在, グミゼリー咀嚼時のグルコース溶出量分析による咀嚼能率検査法では, まず, 被験者にグミゼリーを任意に咀嚼させて主咀嚼側(習慣性咀嚼側)を判定し, 次いでその主咀嚼側のみを用いた場合の咀嚼能力を評価している. しかし, 本来の咀嚼は両側性に行われるものであるため, 片側のみを指定した咀嚼は検査のための通常とは異なる負担(ストレス)を与える可能性や, 患者が本来有している咀嚼能力を正確に反映していない可能性が考えられた. そこで本研究では, 入れ歯治療(補綴治療)を受ける患者を対象に, 片側咀嚼だけでなく自由咀嚼による咀嚼能力検査も実施し, 咀嚼方法の違いが治療効果の評価に与える影響について検証することとした. 2023 年 12 月～2026 年 8 月に欠損補綴治療を希望し, 甲府市の診療所を受診した患者のうち, 研究への参加について同意が得られた患者を連続サンプリングした. 対象は, 上下顎無歯顎患者, または上顎もしくは下顎無歯顎患者で, 術前の咀嚼機能検査におけるグルコース溶出量が 100 mg/dL 未満の者とした. なお, 本研究は松本歯科大学研究等倫理審査委員会の承認を得て実施した(承認第 368 号). 期間中に欠損補綴治療を希望して来院した患者は 66 名であり, そのうち, 上下顎無歯顎または上顎もしくは下顎無歯顎患者は 43 名であった. さらに, 術前の咀嚼機能検査におけるグルコース溶出量が 100 mg/dL 未満であった 23 名を本研究の対象とした. 補綴治療前後に, グミゼリーを主咀嚼側, 非主咀嚼側および自由咀嚼で咀嚼させ, それぞれのグルコース溶出量を測定した. また, 併せて Short-Form Oral Health Impact Profile (OHIP-14) を用いて口腔関連 QOL も評価した. 主評価項目は補綴治療前後におけるグルコース溶出量の変化量, 副次評価項目は OHIP-14 による口腔関連 QOL のサマリースコアとした. 対象患者は 23 名(男性 9 名, 女性 14 名, 平均年齢 80.8 歳)であった. 主咀嚼側のグルコース溶出量の平均は, 補綴治療前 46.9mg/dL から治療後 70.0mg/dL へ上昇した. 非主咀嚼側では, 42.7mg/dL から 85.9mg/dL へ上昇し, 自由咀嚼では 45.9mg/dL から 79.5 mg/dL へ上昇した. 補綴治療前後の比較では, 主咀嚼側および非主咀嚼側, 自由咀嚼, いずれにおいてもグルコース溶出量が有意に上昇した.				

発表内容の要旨(課程博士)
Abstract of Presented Research (For the Doctoral Course)

学 籍 番 号 Student ID No.	ID # G 2405	入 学 年 Entrance Year	2024	年 Year
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氏 名 Name in Full	孔 晶晶			
専 攻 分 野 Major Field	臨床病態評価学			
主 指 導 教 員 Chief Academic Advisor	李 憲起			
発 表 会 区 分 Type of Meeting	中間発表会 ・ 大学院研究科発表会 ・ 松本歯科大学学会 Midterm Meeting / Graduate school research meeting presentation / The Matsumoto Dental University Society			
演題名 / Title of Presentation				
NRF2 upregulation in MSC spheroids suppresses SASP and promotes osteogenesis (MSC スフェロイドにおける NRF2 発現上昇は SASP を抑制し、骨形成を促進する)				
発表要旨 / Abstract				
Objective: Spontaneous MSC spheroids enhance stemness and osteogenic potential, but their effects on cellular senescence and bone regeneration in aged microenvironments remain unclear. This study aimed to investigate whether spontaneously bone marrow-derived mesenchymal stem cell (BM-MSC) spheroids suppress the senescence-associated secretory phenotype (SASP) and enhance osteogenic differentiation, and to elucidate the role of NRF2 in these effects. Materials and Methods: In vitro study, BM-MSCs were isolated from the femoral bone marrow of C57BL/6J mice and expanded under conventional two-dimensional culture conditions. Early-passage BM-MSCs were used as young control, whereas replicative senescence was induced by continuous passaging for more than 10 passages. Senescent BM-MSCs were subsequently cultured in low-attachment culture dishes to generate spontaneous spheroids. The cells were divided into three groups: young BM-MSCs, senescent BM-MSCs, and senescent BM-MSC spheroids. Cellular senescence was evaluated by analyzing the mRNA and protein expression of p53, p21, and p16 using RT-qPCR and Western blot, respectively. The mRNA expression levels of the senescence-associated secretory phenotype (SASP) factors IL-6, IL-1β, and TNF-α were quantified by RT-qPCR. NRF2 activation was assessed by examining the mRNA and protein expression levels of NRF2 and its downstream targets, including GCLC, HO-1, NQO1, and SOD2, using RT-qPCR and Western blotting. NRF2 expression was further evaluated by immunofluorescence staining. Furthermore, the NRF2 inhibitor was used to investigate the role of NRF2 in spheroids. For the in vivo study, a tibial bone defect model was established in 50-week-old male C57BL/6J mice. The mice were randomly assigned to four groups (n = 6): an untreated defect control group, scaffold group, scaffold loaded with monolayer-cultured BM-MSCs group, and scaffold loaded with BM-MSC spheroids group. Rat skin-derived type I collagen was used as the cell scaffold. Samples were collected at 1, 2, and 4 weeks after surgery. Bone regeneration was evaluated by micro-CT, HE staining, and Masson staining. The expression of NRF2 and osteogenesis-related proteins within the defect area was further evaluated by immunohistochemistry. Results: Compared with young BM-MSCs, senescent BM-MSCs showed increased expression of p53, p21, and p16 and elevated secretion of IL-6, IL-1β, and TNF-α. Spontaneous spheroids reduced these senescence and SASP related changes while increasing the expression of NRF2 and its downstream targets GCLC, HO-1, NQO1, and SOD2. NRF2 inhibition attenuated the inhibitory effects of spheroid formation on cellular senescence. In the aged mouse tibial defect model, BM-MSC spheroids enhanced new bone and collagen formation and increased the expression of NRF2 and osteogenesis-related proteins. Conclusion: Spontaneous BM-MSC spheroids suppress the SASP and enhance osteogenic differentiation by increasing NRF2 expression. Spheroids may therefore represent a promising strategy for improving the therapeutic and bone-regenerative potential of senescent BM-MSCs.				

発表内容の要旨 (課程博士)
Abstract of Presented Research (For the Doctoral Course)

学 籍 番 号 Student ID No.	ID # G 2415	入 学 年 Entrance Year	2024 年 Year
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専 攻 分 野 Major Field	病態解析		
主 指 導 教 員 Chief Academic Advisor	栗原祐史		
発 表 会 区 分 Type of Meeting	中間発表会 ・ 大学院研究科発表会 ・ 松本歯科大学学会 Midterm Meeting / Graduate school research meeting presentation / The Matsumoto Dental University Society		
演題名 / Title of Presentation			
Effects of bioabsorbable materials in combination with spontaneous spheroids transplantation on bone repair microenvironment (生体吸収性材料と自発的スフェロイドの併用により骨修復微小環境に及ぼす影響)			
発表要旨 / Abstract			
Introduction Poly-L-lactic acid (PLLA) exhibits favorable biocompatibility and biodegradability and can eliminate the need for long-term retention and secondary removal surgery associated with metallic fixation devices. It has therefore been widely used for craniomaxillofacial bone fixation. However, PLLA undergoes relatively slow degradation, and degradation-associated alterations in the local microenvironment may induce persistent inflammation and foreign body reactions, thereby compromising bone repair. Spontaneous spheroids have the potential to modulate the local microenvironment and promote tissue regeneration by enhancing cell–cell interactions, extracellular matrix (ECM) formation, and paracrine signaling. This study aimed to evaluate the osteogenic properties of osteogenic cell-derived spontaneous spheroids within a PLLA degradation-associated microenvironment and to investigate their effects on the local immune microenvironment and bone regeneration following PLLA implantation. Materials and Methods In vitro, MC3T3-E1 cells were used to establish two-dimensional monolayer and spontaneous spheroid culture systems, and lactate treatment was employed to simulate the PLLA degradation-associated microenvironment. Four experimental groups were established: monolayer culture (Mon), osteogenic induction (Mon-OD), lactate combined with osteogenic induction (LA-OD), and lactate combined with osteogenic induction followed by spontaneous spheroid formation (LA-OD-Sph). Cell viability was assessed using the CCK-8 assay. Osteogenic differentiation and mineralization were evaluated by alkaline phosphatase (ALP) and Alizarin Red S (ARS) staining, respectively, and the expression of osteogenesis-related molecules was examined by quantitative real-time PCR (qRT-PCR) and Western blotting. In addition, single-cell RNA sequencing (scRNA-seq) was performed on two-dimensional monolayer cells and spontaneous spheroids to compare cellular states and transcriptional characteristics between the two culture conditions. In vivo, a calvarial defect model was established in C57BL/6J mice. The animals were assigned to four groups: defect-only (Control), PLLA implantation (PLLA), PLLA combined with monolayer cells (PLLA+Mon), and PLLA combined with spontaneous spheroids (PLLA+Sph). Evaluations were performed at 1, 3, and 6 months postoperatively. Micro-computed tomography (micro-CT) was used to assess bone regeneration and bone microarchitecture. Hematoxylin and eosin (H&E) and Masson’s trichrome staining were performed to evaluate bone repair and foreign body reactions. Immunohistochemistry/immunofluorescence and			

qRT-PCR were used to assess inflammatory and reparative markers, including CD68, CD86, CD206, IL-10, TNF- α , TGF- β , and HO-1. Scanning electron microscopy coupled with energy-dispersive X-ray spectroscopy (SEM/EDS) was used to characterize PLLA surface degradation and dynamic changes at the material–tissue interface.

Results

In vitro experiments demonstrated that 10 mM lactate did not induce significant cytotoxicity. Compared with two-dimensional culture, spontaneous spheroids exhibited enhanced osteogenic differentiation and mineralization potential. Under the lactate-associated microenvironment, the LA-OD-Sph group showed markedly increased expression of osteogenic and maturation-associated genes, including SP7, RUNX2, SPP1, and HO-1, suggesting that spontaneous spheroids may predominantly promote osteoblastic maturation, matrix formation, and mineralization. scRNA-seq further revealed distinct cellular state compositions and transcriptional profiles between two-dimensional monolayer cultures and spontaneous spheroids, indicating that spontaneous spheroid formation induces functional cell-state remodeling.

In vivo, the PLLA+Sph group exhibited more pronounced bone regeneration during the intermediate and late postoperative stages. PLLA implantation alone was associated with fibrous capsule formation and foreign body giant cell reactions, whereas these responses were attenuated following the application of spontaneous spheroids. At the intermediate stage, the PLLA group showed increased expression of pro-inflammatory markers, including CD86 and TNF- α , whereas the PLLA+Sph group exhibited increased expression of repair-associated markers, including CD206, TGF- β , and HO-1. These findings suggest that spontaneous spheroids may facilitate a shift in the local immune microenvironment from a persistent inflammatory state toward a tissue-reparative state. SEM/EDS analysis further demonstrated time-dependent changes in the PLLA surface and material–tissue interface, with prominent ECM-like deposition observed in the PLLA+Sph group during the early and intermediate stages.

Conclusion

Spontaneous spheroids enhance the osteogenic maturation and mineralization potential of MC3T3-E1 cells within a PLLA degradation-associated microenvironment and attenuate PLLA implantation-associated inflammation and foreign body reactions in vivo, thereby promoting the establishment of a reparative local microenvironment and enhancing bone regeneration. These findings suggest that spontaneous spheroids may improve the biological performance of resorbable PLLA implants through the coordinated enhancement of osteogenic potential and modulation of the immune microenvironment at the material–tissue interface, providing experimental evidence for a potential strategy to mitigate foreign body reactions associated with resorbable fixation materials and promote bone regeneration.