【Grant-in-Aid for Scientific Research (S)】

Broad Section I

Title of Project： **Establishment of an integrated locomotive science including dynamics of bone-articular cells and regulation by immune system**

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Research Project Number：19H05654　Researcher Number：50282661
Keyword：Integrated Locomotive Science, Locomotive Disease, Single-cell Analysis

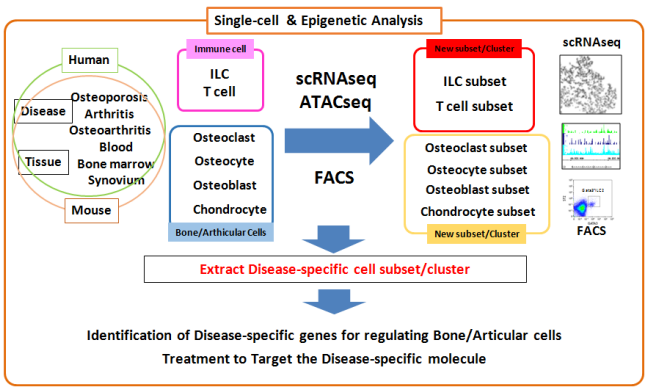
【Purpose and Background of the Research】

Locomotion is an essential activity to maintain homeostasis of the body. Representative locomotive diseases such as osteoarthritis (OA), osteoporosis and rheumatoid arthritis severely restrict patient's activities of daily living and thus lead to social problems. The difficulty in overcoming those diseases is caused by the diversity and the heterogeneity of the cellular complex associated with bone and articular cartilage. The purpose of this project is to analyze the underlying mechanism of bone and cartilage homeostasis. Using technology for molecular and cellular analysis, transgenic mouse analysis, we elucidate the mechanisms for maintaining the locomotive homeostasis, especially focusing on the regulation by immune system such as innate lymphoid cells (ILC).

【Research Methods】

We collect synovium, bone marrow, and articular cartilage from naïve mouse and OA model mouse, and we analyze comprehensively the proportion and the transition of synovial fibroblast, macrophage, other immune cells such as ILC, osteoblast, osteoclast, osteocyte, and chondrocyte, by using immunohistochemistry assay and mouse genetic modification technology. Furthermore, we perform single-cell RNA sequences (scRNAseq) to analyze the heterogeneity of those cells and the subsets related to each cell type.

Figure. Integrated Locomotive Science.



We investigate the difference and the overlap between mouse and human about the phenomenon which were observed in those specific mice with OA.

【Expected Research Achievements and Scientific Significance】

This project focuses on the elucidation of heterogeneity of the cells associated with bone and cartilage by understanding the molecular changing in a single cell.From these insights, we could unveil the mechanisms for the locomotive system. Understanding of the mechanism by investigating the effect of immune cells such as ILC, it will be expected that those insights would discover the regulation of the diseases and lead to establishing treatment by targeting molecules associated.

【Publications Relevant to the Project】

・Komatsu N, Okamoto K, Sawa S, Nakashima T, Oh-hora M, Kodama T, Tanaka S, Bluestone JA, Takayanagi H., Pathogenic conversion of Foxp3+ T cells into TH17 cells in autoimmune arthritis, ***Nat Med***. 2014 Jan;20(1):62-8.
・Kobayashi H, Chang SH, Mori D, Itoh S, Hirata M, Hosaka Y, Taniguchi Y, Okada K, Mori Y, Yano F, Chung UI, Akiyama H, Kawaguchi H, Tanaka S, Saito T., Biphasic regulation of chondrocytes by Rela through induction of anti-apoptotic and catabolic target genes, ***Nat Commun***. 2016 Nov 10;7:13336.
・Omata Y, Frech M, Primbs T, Lucas S, Andreev D, Scholtysek C, Sarter K, Kindermann M, Yeremenko N, Baeten DL, Andreas N, Kamradt T, Bozec A, Ramming A, Krönke G, Wirtz S, Schett G, Zaiss MM.,Group 2 Innate Lymphoid Cells Attenuate Inflammatory Arthritis and Protect from Bone Destruction in Mice, ***Cell Rep***. 2018 Jul 3;24(1):169-180.

【Term of Project】 FY2019-2023
【Budget Allocation】 154,300 Thousand Yen
【Homepage Address and Other Contact Information】
http://www.u-tokyo-ortho.jp/