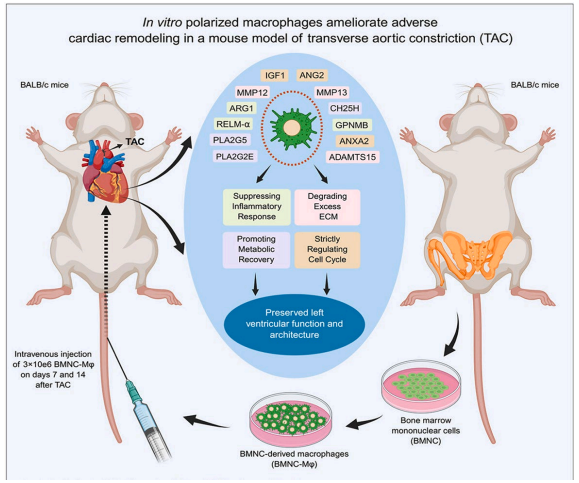
ヒューマン・オルガノイド生命医科学と情報・数理科学の融合研究

大阪大学ヒューマン・メタバース疾患研究拠点
申請代表：渡場 康弘

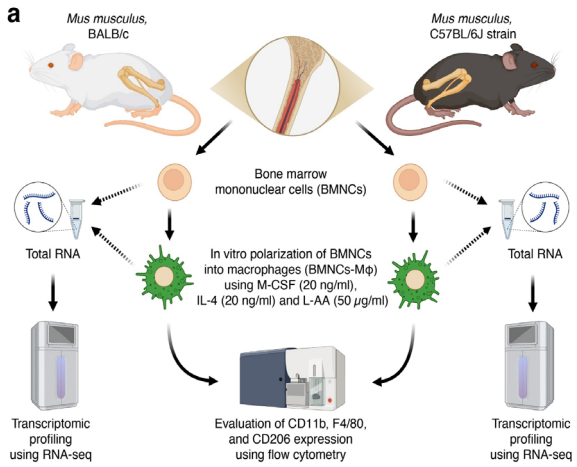
Usage Report

1. ***In vitro* polarized macrophages ameliorate adverse cardiac remodeling in a mouse model of transverse aortic constriction**. Imad ABUGESSAISA, collaboration with Miyagawa's team PRIMe

Research objective: Evaluate the efficacy of bone marrow mononuclear cell (BMNC)-derived macrophages (BMNC-Mφ) in treating a mouse model of transverse aortic constriction (TAC). **Overview of the research**: In *in vitro* experiments, BMNC were polarized into BMNC-Mφ. We then performed transcriptomic analysis to confirm BMNC-Mφ marker genes compared to BMNC. BMNC-Mφ phenotypes were further validated by flow cytometry and RT-qPCR. **Results and figures:** [**1**] Transcriptomic profiling showed a close similarity between *in vitro* polarized BMNC-Mφ and resident cardiac macrophages.[**2**] BMNC-Mφ preserved LVEF, LVFS, and LVIDs, promoted angiogenesis, and reduced fibrosis area compared to the control group. [**3**] Pathways enriched in BMNC-Mφ, particularly those related to oxidative metabolism, were preserved in BMNC-Mϕ−treated LVs. [4] BMNC-Mφ ameliorated adverse cardiac remodelingvia metabolic recovery, immunosuppression, regulation of cell cycle and ECM.



In vitro polarized macrophages ameliorate adverse cardiac remodeling in a mouse model of transverse aortic constriction. Workflow



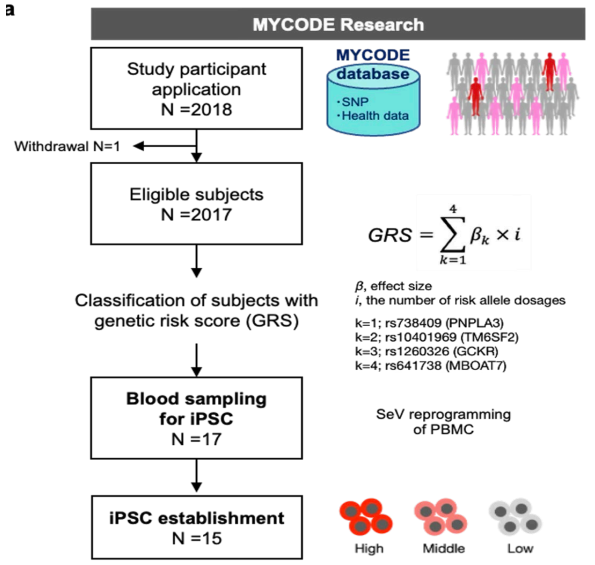
Transcriptomic profiling of C57BL/6J and BALB/c mouse-derived bone marrow mononuclear cells and in vitro polarized macrophages. Workflow

2. **Transcriptomic profiling of C57BL/6J and BALB/c mouse-derived bone marrow mononuclear cells and in vitro polarized macrophages.** Imad ABUGESSAISA, collaboration with Miyagawa's team PRIMe

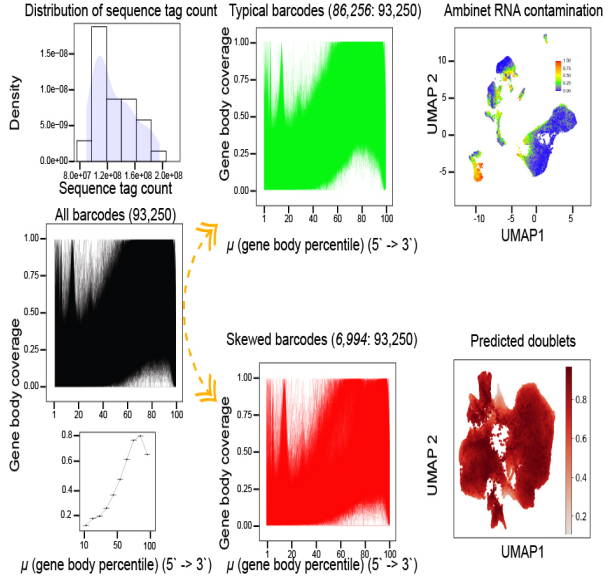
Research objective: Generation and validation of a dataset consisting of transcriptomic profiles derived from bone marrow mononuclear cells (BMNCs) of C57BL/6J and BALB/c mouse and in vitro polarized macrophages (BMNCs-Mφ).**Overview of the research**: Bone marrow mononuclear cells (BMNCs) were isolated from C57BL/6J and BALB/c mice and polarized in vitro into macrophages (BMNC-Mφ) using M-csf, Il-4, and L-ascorbic acid (L-AA). Next, the anti-inflammatory phenotype of macrophages was confirmed by flow cytometry (FC) with evaluation of macrophage surface marker expression, such as CD11b, F4/80, and CD206. Total RNA was then extracted from BMNCs and BMNCs-Mφ (the former serving as controls) and sequenced. **Results and figures:** We polarized BMNCs into BMNCs-Mφ and performed RNA sequencing on 12 biological replicates (three in each subgroup: BALB/c-BMNCs, BALB/c-BMNCs-Mφ, C57BL/6J-BMNCs, and C57BL/6J-BMNCs-Mφ).
Computing system(s) used: SQUID (including the frontend nodes)

3. **Human liver organoid (HLO) for Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD).** Imad ABUGESSAISA, collaboration with Takeba's team PRIMe

Research objective: The study focused on the diversity of apparent healthy, but pre-symptomatic MASLD as well as the molecular mechanism driving the pathogenesis of the disease. **Overview of the research**: [1]15 different donor iPSC-derived-liver organoids developed in the same dish. [2] Delineate the MASLD-related gene signatures of HLO between donors in single cell space. [3] Perturbations (Cilofexor (a FXR agonist), AALAT), [4] 0 HLO organoids/donor x 15 donors = 150 HLO, [5] Chromium Next GEM Single Cell 3' Reagent Kits v3.1, [6] ~ 93K scRNA-seq for 150 HLO **Results and figures:** on going. **Computing system(s) used:** SQUID (including the frontend nodes).



Human liver organoid (HLO) for Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD). *Workflow*



Human liver organoid (HLO) for Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD). *Primary analysis of scRNA-seq*

Research and development of image analysis methods for phenotype of retinal organoids
(網膜オルガノイド表現型データの画像解析法の開発)

- Atsushi Watanabe (Graduate School of Medicine), Ryota Koto(CoMIT), Satoko Takemoto(PRIMe), Takashi Michikawa(PRIMe), Hideo Yokota(PRIMe), and Koji Nishida (Graduate School of Medicine and PRIMe)
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- 研究概要
  - Using microscope images of retinal organoids, we conducts quantitative analysis of the cells by image processing and machine learning technologies. Specifically, we are developing methods for extracting individual cells from the images, and for evaluating morphological features and condition of the cells. This contributes to understanding of mechanism of development.
  - Our project is using ONION for sharing data and analysis results (678 files, about 4GB).
  - 西田研究室で培養された網膜オルガノイドの顕微鏡画像をもとに，横田研では画像処理技術および機械学習を活用した細胞形態及び動態の定量解析を行っている．具体的には，画像内から網膜オルガノイド内に存在する特定の細胞を自動的に抽出し、その数を正確に計測する手法を開発している．これにより，細胞の構造的特徴や発達状態を定量的に把握することが可能となり，網膜オルガノイドの状態評価や発生メカニズムの理解に貢献することを目指す．
  - 本プロジェクトでは，西田研，横田研の２拠点間での顕微鏡画像や解析結果の共有を目的としてONIONを使用した．現在のデータ量(678ファイル，約4GB).