Understanding Sex-Specific Differences in Cardiac Remodelling associated with Cardiovascular Disease

Malathi S.I. Dona[1,2], Fumihiko Takeuchi[1,3], Alexander R. Pinto[1,2,3], Michael Inouye[1,4]

1. Baker Heart and Diabetes Institute, Melbourne, Australia
2. La Trobe University, Melbourne, Australia
3. University of Melbourne, Australia
4. University of Cambridge, Cambridge, UK

Cardiovascular disease remains the leading cause of death worldwide. Sex-specific differences in cardiovascular disease (CVD) prevalence, progression, and outcomes are well-documented but poorly understood. Left ventricular (LV) remodelling is a defining characteristic of CVD, closely linked to its progression and adverse outcomes. Current diagnostic and therapeutic approaches often fail to address sex-specific differences in cardiac conditions, potentially leading to suboptimal treatments.

Recent single-cell omics studies from our lab and others have uncovered key drivers of LV remodelling in both mouse models and human across various contexts. However, sex-specific differences remain underexplored in many of these studies due to methodological and data limitations, leaving a critical gap in the translational relevance of current findings. This project aims to address these gaps by integrating large-scale population-level data with high-resolution single-cell omics datasets to gain deeper insights into the mechanisms, progression and outcomes of LV remodelling in CVD. The UK Biobank is a large-scale cohort with rich health, lifestyle, genetics, and imaging data from participants across the UK. The information derived from 42,000 UK Biobank participants who underwent cardiac magnetic resonance (CMR) imaging offers a unique opportunity to study sex-specific differences in LV remodelling. Analysis of UK Biobank CMR imaging-derived data, together with clinical and genetic information, can provide valuable insights into **sex-specific clinical and genetic risk factors** associated with LV remodelling in CVD. By integrating these population-level genetic findings with single-cell omics data, this research aims to identify **sex-specific cellular and molecular drivers** of LV remodelling in CVD. This could lead to the identification of novel **sex-specific therapeutic targets** guiding the development of personalised and more effective strategies for the prevention and treatment of CVD.