Background
The efficacy of immune checkpoint inhibition in triple negative breast cancer (TNBC) is only modest for a small subset of patients. Recent multi-omics studies of the tumour microenvironment (TME) have elucidated the heterogeneity of stromal cells and suggested that stromal subsets may play an important role in regulating anti-tumour immunity.

In this study, we explored how stromal cells contribute to the immunosuppressive TME and how we can potentially target these to improve immune responses in TNBC.

Method
1. Isolate and expand primary stromal cells ex vivo
   - Primary untreated TNBC breast tumours and normal breast samples were collected and dissociated into single cell suspensions using protocol in our previous studies.
   - Single cell RNA sequencing (scRNAseq) of cultured stromal cells to characterise these.

2. Stromal-immune coculture
   - Day 1: Primary stromal cells were seeded into a 96-well
   - Day 2: PBMCs were stained with CFSE dye and stimulated with conjugated anti-CD3/28 beads. Stimulated PBMCs were added to cultured stromal cells and left for 4 days
   - Day 6: co-cultured PBMCs were harvested and analysed using flow cytometry and scRNAseq

3. Therapeutically targeting stromal cells
   - High throughput drug screen to identify novel stromal targeting drug candidates
   - Addition of drug candidates to stromal-immune cocultures to assess effect on stromal cell-induced immunosuppression

Results
1. Characteristics of ex vivo primary stromal cells
   - Stromal heterogeneity preserved upon early passages of TNBC stromal cells
   - Distinct shift in gene expression and composition of stromal cells upon extensive cell culture

2. Functional assessment of stromal-immune interactions
   - TNBC stromal cells suppress both CD4 and CD8 proliferation in vitro

3. High throughput drug screen to identify novel stromal targeting drug candidates
   - Treatment with talabostat led to no effect on stromal cell viability but shifted cells from aSMA+ to aSMA-phenotypes
   - Talabostat treatment reversed stromal cell-induced suppression on CD4 and CD8 T cell proliferation in vitro

Conclusion
Talabostat reverses stromal-induced T cell suppression and is a potential stromal-targeting therapeutic strategy to eliciting more effective immune response in TNBC.

Reference

Acknowledgements
Contact detail: Dr Julia Chen | j.chen@garvan.org.au
This presentation must not be used or distributed. Any re-use is the responsibility of the author/presenter. Contact them for permission to reprint and/or distribute.