Abstract: 155P

Integrative transcriptomic and proteomic analysis show circulating osteoprogenitors to have a mixed immune and mesenchymal progenitor function in humans

Jack Feehan[1-3], Macsue Jaques[3], Dmitri Kondrikov[4], Nir Eynon[3], Tissa Wijeratne[2,3], Vasso Apostolopoulos[2,3], Jeffrey M. Gimble[5], William D. Hill[4], Gustavo Duque[1-3]*

[1] *Department of Medicine - Western Health, The University of Melbourne, Melbourne, Australia*
[2] *The Australian Institute for Musculoskeletal Science (AIMSS), Western Health, Victoria University and The University of Melbourne, Melbourne, Australia*
[3] *Institute for Health and Sport, Victoria University, Melbourne, Australia*
[4] *Department of Pathology and Laboratory Medicine, The Medical University of South Carolina, Charleston, SC, USA*
[5] *Center for Stem Cell Research and Regenerative Medicine, Tulane University School of Medicine, New Orleans, LA, USA.*
[6] *Department of Veterans Affairs, Ralph H Johnson VA Medical Center, Charleston, SC, USA*

Background: Circulating osteoprogenitor (COP) are a cell population in the peripheral circulation that possess functional and phenotypical characteristics of multipotent stromal cells (MSCs). While there is functional overlap, it is not known how COP cells are related to bone marrow (BM)-derived MSCs (BM-MSCs) and other better characterized stromal progenitor populations such as adipose-derived stromal cells (ASCs). This study compares COP cells to BM-MSCs and ASCs through detailed integrative transcriptomic and proteomic analyses.

Methods: Primary COP, ASC, and BM-MSCs (n=16 each) were isolated and expanded in culture, before undergoing RNA and protein extraction. RNA underwent transcriptome sequencing, while protein was analyzed via label free mass spectrometry. The transcriptome and proteome of the cells underwent analysis for differentially expressed genes (DEGs) and protein expression and pathway analysis, as well as integrative multiomics characterization using the Limma-Voom, and Mixomics R packages.

Results: The contrast analyses reveled 7,669 DEGs between adipose and marrow, 14,477 DEGs between adipose and COP, and 14,408 DEGs between marrow and COP. Protein analyses revealed 1,520 proteins DE between adipose and marrow cells, 2,087 proteins differentially expressed between adipose and COP cells, and 2,074 proteins DE between marrow and COP cells. The most differentially expressed genes and proteins were associated with immune system functionality, including HLA-DRA, CYBB and ITGAX. Pathway analysis supported these findings, with COP cells having enrichment for innate and adaptive immune cells functions. Despite the significant differential regulation between the cell types, there was no difference in genes from the stem cell differentiation and proliferation gene ontologies, with all cell types broadly having similar expression.

Discussion: COP cells have a distinct gene and protein expression pattern to BM-MSCs and ASCs, with a significantly stronger immune footprint, likely owing to their hematopoietic lineage. However, they also have a similar pattern of expression BM-MSCs and ASCs, in genes and proteins in progenitor cell differentiation and proliferation pathways. This study shows COP cells to be a unique but functionally similar population to BM-MSCs and ASCs, sharing their proliferation and differentiation capacity, but with a strong immune phenotype, with potential for translational regenerative medicine strategies.