ImmunoTools *special* Award 2014

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Translational immunomodulation using adipose-derived stromal cells

Mesenchymal stem cells isolated from adipose tissue, designated adipose-derived stromal cells (ASCs), possess extraordinary regenerative capacities (*Zuk 2013*). In addition to this, ASCs have strong immunosuppressive qualities, directly by cell-cell contact as well as through soluble molecules (*Gebler et al. 2012*). Part of this intriguing feature is that ASCs inhibit maturation of antigen-presenting cells, namely dendritic cells (DCs), and immune cells of the blood (*Melief et al. 2013*).

ASCs are highly responsive to a plethora of inflammatory factors and actively reduce immune responses. Upon stimulation with pro-inflammatory molecules, ASCs respond by inhibiting production of inflammatory cytokines and stimulate production of anti-inflammatory cytokines; thus, ASCs emerge as a strong potential candidate for treating conditions such as Crohn's disease or Graft versus Host disease *(Gimble et al. 2012*).

In order to elucidate how ASCs promote immunosuppression, two cell-based models have been designed. For a broadly-based assessment of the effects of ASCs on a range of immune cells, ASCs are co-cultured with Peripheral Blood Mononuclear Cells (PBMCs). By investigating subsets of cells, this model provides detailed insights to specific cell types. To shed light on how ASCs affect the maturation of antigen-presenting cells, ASCs are co-cultured with purified populations of DCs. These models form a backbone to document the immunomodulatory effects and serve as a platform to build upon. To investigate the properties of ASCs in a pathophysiological setting, we wish to introduce secreted factors, mainly cytokines, to the DC and PBMC co-culture models in order to better predict how cells respond to such conditions.

To characterise the immunosuppressive effect of ASCs by flow cytometry, we plan to use specific antibodies for maturation of DCs (CD11c-APC, CD40-FITC, CD80-FITC, CD86-FITC, and HLA-DR-FITC) and for co-culture experimentation of ASCs with

PBMCs (CD45-PerCP, CD54-FITC, and Il-6 PE). To mimic pathophysiologic conditions, the cells will be exposed to cytokines (rh IFN-γ, rh TNF-α, rp TNF-α, rh IL-12, rh IL-17A, rh IL-17F, rh IL-1β /IL-1F2, rh IL-6, and rh IL-22). As part of the analysis, we will measure the production of cytokines by ELISA (IL-4, IL-6, IL-8, TNF-α). An ImmunoTools Award would be a significant contribution to this study, and would permit extended research on the fascinating subject of the immunomodulatory capabilities of ASCs.

Gebler, A., Zabel, O. & Seliger, B., 2012. The immunomodulatory capacity of mesenchymal stem cells. *Trends in molecular medicine*, 18(2), pp.128–34. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22118960 [Accessed February 20, 2014].

Gimble, J.M., Bunnell, B.A. & Guilak, F., 2012. Human adipose-derived cells: an update on the transition to clinical translation. *Regenerative medicine*, 7(2), pp.225–35. Available at: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3321837&tool=pmcentrez&rendertype=abstract [Accessed May 14, 2014].

Melief, S.M. et al., 2013. Adipose tissue-derived multipotent stromal cells have a higher immunomodulatory capacity than their bone marrow-derived counterparts. *Stem cells translational medicine*, 2, pp.455–63. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23694810.

Zuk, P., 2013. Adipose-Derived Stem Cells in Tissue Regeneration: A Review. *ISRN Stem Cells*, 2013, pp.1–35. Available at: http://www.hindawi.com/isrn/stem.cells/2013/713959/.