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Adipogenic differentiation of MSC alters their immunomodulatory properties in a tissue-specific manner

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Chronic inflammation is associated with formation of ectopic fat deposits that might represent damage-induced aberrant mesenchymal stem cell (MSC) differentiation. Such deposits are associated with increased levels of inflammatory infiltrate and poor prognosis. Here we tested the hypothesis that differentiation from MSC to adipocytes in inflamed tissue might contribute to chronicity through loss of immunomodulatory function. We assessed the effects of adipogenic differentiation of MSC from bone marrow or adipose tissue- on their capacity to regulate neutrophil recruitment by endothelial cells and compared the differentiated cells to primary adipocytes from adipose tissue. Bone marrow derived MSC were immunosuppressive, inhibiting neutrophil recruitment to TNF α -treated EC, but MSC-derived adipocytes were no longer able to suppress neutrophil adhesion. Changes in IL-6 and TGF β 1 signaling appeared critical for the loss of the immunosuppressive phenotype. In contrast, native stromal cells, adipocytes derived from them and mature adipocytes from adipose tissue were all immuno-protective. Thus disruption of normal tissue stroma homeostasis, as occurs in chronic inflammatory diseases, might drive 'abnormal' adipogenesis which adversely influences the behavior of MSC and contributes to pathogenic recruitment of leukocytes. Interestingly, stromal cells programmed in native fat tissue retain an immuno-protective phenotype.

Biography

Helen McGettrick completed her PhD in 2006 and followed 3 Post-doctoral research positions at University of Birmingham (UK). She was appointed as a University Fellow in Inflammation Biology in 2011, and a year later, she successfully won a five year Arthritis Research UK Career Development Fellowship. She was recently awarded the prestigious "Garrod Prize" by the British Society for Rheumatology in 2016. She is an Honorary Lecturer at the University of Glasgow and Newcastle University (UK). She has more than 30 published articles with \approx 760 citations, has filed 3 patents and received funding from Wellcome Trust, Pfizer and British Heart Foundation.

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