Bone marrow mesenchymal stromal cells (BM-MSCs) are multipotent stem cells that can differentiate into chondrocytes, osteoblasts and adipocytes. SLE has been implicated as a stem cell disorder with impaired immunomodulatory function of SLE BM-MSCs and improvement of lupus nephritis with healthy MSC transplantation has been suggested. However, the exact differentiation defects of SLE BM-MSCs have not been addressed, nor and potential interventions studied. Our previous work indicates upregulation of IFN beta specific genes in human SLE bone marrow derived MSCs compared to normal bone marrow MSC. Here we set out to investigate the differentiation defects of SLE BM-MSCs and potential intervention approaches.

We compared 6 age paired BM aspirates from healthy controls and SLE patients. BM-MSCs from SLE patients and healthy controls were isolated and cultured. The MSC surface markers are positive for CD73, CD90 and CD105, but negative for CD34 and CD45 in both healthy and SLE BM-MSCs after culture. No difference was observed in the surface markers between SLE and healthy BM-MSCs. However, SLE MSCs display significantly reduced osteoblastogenesis markers, such as ALP (6 fold, p<0.05), RUNX2 (8 fold, p<0.05), OCN (4 fold, p<0.05) and BSP (4 fold, p<0.05). The osteoblast induction and ALP staining analysis for osteoblastogenesis also suggested a reduced differentiation with the SLE BM-MSCs. In contrast to the downregulation of osteoblast markers, the expression of IFN beta is increased 5 fold (p<0.05) in SLE BM-MSCs. When BM-MSCs from healthy controls were treated with IFN beta for 6 hours, reduced ALP (12 fold, p<0.05), RUNX2 (11 fold, p<0.05), OCN (8 fold, p<0.05) and BSP (7 fold, p<0.05) were observed, suggesting that IFN beta plays an important role in inhibiting SLE BM-MSC differentiation into osteoblasts. Conversely, when IFN beta neutralising antibody was applied to SLE BM-MSCs, the osteoblastogenesis markers were significantly enhanced.

IFN-I signature is an important feature of SLE. Our present work suggests that SLE BM-MSCs produce IFN beta, mediating a decrease in osteoblastogenesis capacity. The successful rescue of the SLE BM-MSCs osteoblastogenesis defect with an IFN beta neutralising antibody highlights IFN as a new potential therapeutic target for SLE treatment.