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DEFECTS WITHIN THE MYELOID DERIVED SUPPRESSOR CELLS (MDSCs) COMPARTMENT MAY FACILITATE ABERRANT IMMUNE RESPONSES IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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Background and objectives There is a currently unmet need to define the mechanisms involved in the homeostatic control of the immune response in autoimmune diseases. MDSCs (characterised in mice as CD11b+Gr1+ and in humans as CD14-HLA-DR_{low}CD15+CD33+) represent a heterogeneous population of myeloid precursors of macrophages, dendritic cells and granulocytes with a distinct regulatory role in suppressing

T-cell responses. We sought to delineate the role of these cells both in murine and human lupus.

Materials and methods We used the lupus prone (NZB x NZW) F1 female mice [3 months old, pre-SLE (n=6) and 6-8 months old, SLE mice (n=6)]. C57BL/6 (B6) female mice [3 mo (n=2) or 6 mo (n=6)] were used as controls. B6 mice immunised with myelin peptide in adjuvant (Experimental Autoimmune Encephalomyelitis) were used as a disease control. Cells were isolated from the bone marrow and spleen of the indicated groups and were stained with fluorescent-conjugated antibodies. Cells were stained for the aforementioned markers and for 7AAD. Analysis was performed in humans as well, using samples from SLE patients (n=18), healthy controls (n=20) and multiple sclerosis (MS) patients (n=31) as disease control. The phenotype and enumeration of cell populations were performed by flow cytometry.

Results Compared to healthy B6 mice, splenic MDSCs of pre-SLE F1 animals were decreased both in frequency and absolute numbers (*p=0.012), indicating a defect in the MDSC compartment in F1 lupus mice. MDSCs were significantly expanded in the spleen of F1 diseased animals compared to healthy F1 controls (*p=0.017) albeit at significantly lower levels compared to mice with EAE (**p<0.0001). In humans, subjects with active lupus (n=8) exhibited higher numbers of MDSCs in the peripheral blood compared to inactive patients (n=10) and healthy controls, but at lower levels compared to patients with active MS (n=14). Ongoing experiments using in vivo transfer of murine MDSCs address their potential to halt renal disease progression and the cells/molecules involved.

Conclusions Together these data suggest defective MDSC accumulation and/or expansion in the periphery in lupus which may contribute to the immune deregulation observed in this disease. Identification of the cell subsets and the molecules involved may provide additional therapeutic targets for the restoration of immune tolerance in lupus.