Background and aims Vß2 T cells have predominantly been investigated in tumour immuno-surveillance and the host defense against viral invasion. The precise role of Vß2 T cells in the pathogenesis of SLE remains elusive.

Methods We measured the proportion of peripheral Vß2 T cells as well as the status and chemokine receptor expression profiles in SLE patients and healthy control (HC). In addition, Vß2 T cell infiltration in the kidneys of patients with lupus nephritis was examined.

Results The percentage of peripheral Vß2 T cells in new-onset SLE was decreased, and negatively correlated with the SLE Disease Activity Index score and the severity of proteinuria. These cells had a decreased apoptosis but an increased proliferation, and they showed increased accumulation in SLE kidneys. Moreover, IL-21 production and CD40L, CCR4, CCR7, CCR8, CXCR1 and CX3CR1 expression in Vß2 T cells from SLE patients was significantly higher than from HC (p<0.05), and these factors were down-regulated in association with the repopulation of peripheral Vß2 T cells in patients who were in remission (p<0.05). In addition, anti-TCR Vß2 antibodies activation significantly upregulated these chemokine receptors on Vß2 T cells from HC, and this effect was blocked by inhibitors of PLC-γ1, MAPK/Erk, and PI3K signalling pathways.

Conclusions The distribution and function status of Vß2 T cells from SLE patients are abnormal, and these aberrations may contribute to disease pathogenesis.

Depletion of plasmacytoid dendritic cells with JNJ-56022473 minimises induction of an interferon gene signature in response to TLR9 and SLE immune complex stimulation

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Background and aims Glucocorticoid-induced Leucine Zipper (GILZ) is a GC-inducible gene with multiple immune-regulatory functions, and GILZ deficiency in mice results in the development of a lupus-like phenotype. In Systemic Lupus Erythematosus (SLE), plasmacytoid dendritic cells (pDCs) are major producers of Type 1 interferons (IFNα) in response to nucleic acid-containing immune complexes. GILZ inhibits activation of B cells, T cells and other myeloid cells and we studied whether GILZ regulates interferon secretion by pDC.

Methods We conducted a study of GILZ expression in human peripheral blood mononuclear cells in vitro and in vivo study in GILZ KO mouse model to analyse the regulatory function of GILZ.

Results Our data suggests that loss of GILZ up-regulates type 1 IFN production by pDC in response to TLR7 and TLR9 stimulation. Basal GILZ expression was lower in pDCs than in other myeloid cell types and the relative deficiency of GILZ expression in pDC may predispose these cells to rapid activation and interferon production in SLE. Moreover, GILZ appears to be rapidly downregulated by type 1 interferons and in SLE patients, the level of GILZ, normalised by prednisolone dose, negatively correlated with SLEDAI. Thus, down-regulation of GILZ by type I interferon may allow heightened interferon release by pDC, and this mechanism potentially leads to amplification of inflammation and cyclical disease flare-ups in lupus patients.

Conclusions Restoration of GILZ may be a potential therapeutic strategy that could reduce the GC dependence in SLE, a strategy that is appealing since GILZ has thus far not recapitulated any of the metabolic effects of GC.