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SURFACE TETHERIN IS A NOVEL CELL-SPECIFIC BIOMARKER FOR INTERFERON RESPONSE IN SYSTEMIC LUPUS ERYTHEMATOSUS

Y. El-Sherbiny[*1,2], M. Y. Md Yusof [1,2], E. Hensor[1,2], M. Wittmann[1,2], P. Emery[1,2], E. Vital[1,2]
[1]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, [2]NIHR Leeds Biomedical Research Unit, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom

My abstract has been or will be presented at a scientific meeting during a 12 months period prior to EULAR 2016: Yes
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Background: Type I interferons (IFN-I) have diverse effects on immune cell populations in SLE, Measuring IFN-I response using PBMCs or whole blood interferon-stimulated gene (ISG) expression does not completely explain clinical features of SLE and IFN blocking therapy. Furthermore, the proportions of cell populations in blood altered with disease activity. Bone marrow stromal antigen 2/Tetherin (BST2), is a cell surface protein eminent in viral immunology as interferon-induced viral restricting molecule expressed on most circulating leucocytes.

Objectives: To develop a cell-specific IFN-I assay

Methods: PBMCs were collected from 133 SLE patients and 19 healthy controls. Disease activity was measured using BILAG-2004. PBMCs were analysed by flow cytometry for cell surface BST2 protein on each immune cell subset. Cells were FACS-sorted into naïve and memory B-cells, plasmablasts, CD3+ T-cells, NK-cells and monocytes in 12 SLE patients and 16 healthy controls. Expression of *BST2,* as well as 32 other ISGs, were measured using qPCR and a 33-gene IFN score calculated.

Results: Analysis of sorted cells confirmed that surface BST2 is a valid cell-specific IFN assay. *BST2* expression correlated with BST2 surface protein within each immune subset: naïve B-cells ($r=0.63$, $p=0.009$); memory B-cells ($r=0.78$, $p<0.001$); plasmablasts ($r=0.58$, $p=0.018$); NK cells (0.63, $p=0.008$); T-cells ($r=0.61$, $p=0.012$); monocytes ($r=0.47$, $p=0.064$).

We next used surface BST2 to compare IFN activity of each subset with clinical features in 133 patients. A strong correlation between the PBMC 33-gene IFN score and surface BST2 was found for each cell subset (all $p<0.001$) confirming validity of BST2 as a biomarker.

BST2 was significantly higher in SLE than HC on naïve and memory B-cells ($p=0.004$, $p=0.003$), plasmablasts ($p=0.047$), T cells ($p=0.043$), but not different on monocytes ($p=0.406$).

Association of total BILAG score with BST2 on naïve and memory B-cells (Tau-a = 0.23 and 0.22 respectively) was substantive and approximately twice as strong as monocytes and T-cells (Tau-a = 0.12 and 0.14). A similar pattern was seen for anti-dsDNA titre, with no association with monocyte BST-2 (Tau-a = 0.07) but a substantive association for memory B cell BST-2 (Tau-a = 0.18).

Conclusions: IFN-I response differs in cell subsets. This can be measured in a fast, cost-effective, convenient assay using flow cytometric analysis of surface BST2. Our results show that IFN activity measured on B cells is more clinically relevant than on other cell populations.

Disclosure of Interest: None declared