N SLE PATIENTS IN SUSTAINED LOW DISEASE ACTIVITY, NOVEL INTERFERON ASSAYS PREDICT FLARES AND GLUCOCORTICOID REQUIREMENTS

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Background: Objectives of therapy in SLE are to maintain low disease activity and minimise glucocorticoid exposure. Disease activity is unpredictable with periods of low disease activity followed by flares. Once disease is controlled, there is an unmet need for predictors of sustained remission or flares to decide when glucocorticoids can be safely tapered. Type 1 interferon (IFN-I) activity is associated with disease activity in SLE. We recently validated two novel assays for IFN-I. First, a 2-score gene expression system that is continuous and accounts for modularity of the IFN transcriptome. Second, the flow cytometric biomarker tetherin that allows measurement of IFN status in individual cell subsets, with memory B cell tetherin (tetherin) correlating best with disease activity.

Objectives: To determine whether IFN assays can predict flare and glucocorticoid requirements in patients with lupus

Methods: Retrospective notes review was done in 165 consecutive patients with SLE who submitted IFN biomarker samples between 2011 - 2015. The reviewer was blinded to biomarker status.

For the interferon scores, RNA was extracted from PBMCs and a custom Taqman array was used to measure expression of 30 interferon stimulated genes normalised to *PP1A* and then calculate IFN Score A (12 genes predominantly responsive to IFN-alpha) and IFN Score B (14 genes also responsive to other IFN subtypes and inflammatory mediators). For tetherin, PBMCs were analysed fresh with conventional surface staining. MFI of CD317 (tetherin) was measured on CD19+CD27+CD38- lymphocytes.

We performed two analyses: (1) In patients in sustained low disease activity (defined as no BILAG A or B in the six months prior to IFN biomarker sampling), prediction of new disease activity in the following six months (defined as new BILAG A or B). (2) The association between IFN biomarkers and change in mean monthly glucocorticoid dose following biomarker sampling (defined as same or increased vs. decreased or no glucocorticoid prescription). Since tetherin is measured on B-cells we excluded patients who were B cell depleted after rituximab. IFN biomarkers were compared between groups using Mann-Whitney U Tests.

Results: Of 165 patients, 92 were in sustained low disease activity prior to biomarker sampling. Of these, new BILAG A/B activity occurred within 6 months of sampling in 16 (17%). New BILAG A/B activity was associated with higher levels of IFN Score A (p=0.027,n=83), IFN Score B (p=0.097, n=83) and tetherin (p=0.026, n=92).

Of 143 patients with complete data, glucocorticoid doses were increased or maintained after sampling in 45 and decreased or not prescribed in 98. Increased/maintained glucocorticoids were associated with higher IFN Score A (p=0.003, n=113), IFN Score B (p=0.013, n=113) and tetherin (p=0.043, n=84).

After adjustment for age, gender, pre and post-sampling glucocorticoid dose, substantive associations with flare remained for IFN Score A (OR=1.44/unit, 95% CI 0.998–2.082, p=0.051) and tetherin (OR=3.135/1000 units, 95% CI 1.179-8.335, p=0.022).

Conclusions: SLE patients in low disease activity with high IFN Score A, Score B and tetherin levels have an increased risk of disease activity and/or glucocorticoid exposure in the months that follow biomarker testing. There is a potential role for use of these IFN assays as predictive biomarkers in SLE in the future.