Title

Distinct interferon scores are separately associated with activity and long term sequelae in SLE

Authors

Katie Dutton, Antonios Psarras, Md Yuzaiful Md Yusof, Paul Emery, Yasser El-Sherbiny, Edward M Vital

Background

Type I interferon (IFN-I) has a crucial role in the pathogenesis and activity of Systemic Lupus Erythematosis (SLE). IFN-I targeted therapies are currently in phase III clinical trials. Early findings suggest that anti-INF-I therapy responses are superior in individuals with high INF-I signature. In established SLE, the level of IFN-I activity can be measured using an interferon gene expression score. We previously described two independent interferon gene expression scores that we called Score A and B. We also previously described a memory B cell flow cytometric marker (Tetherin) that can be used to measure IFN-I response in B cells.

Objective

To describe the clinical phenotype of IFN-high SLE patients and to correlate this with Score A, Score B and Tetherin levels.

Methods

IFN gene expression Scores A and B as well as memory B cell tetherin were measured in 156 consecutive SLE patients attending the Leeds SLE clinic. For this preliminary analysis, we selected 59 patients across a spectrum of levels of IFN assays for detailed retrospective notes review.

Results

Characteristic	**Internal organ involvement**	**Previous cyclophosphamide**	**Cardiovascular Disease**	**Objective flare 3 months before or after test**	**Increased glucocorticoid dose 3 months before or after test****
Number of patients					
Yes (n=)	21	13	5	18	15
IFN Score A median (IQR)					
No	0.02 (0.40)	0.04 (0.82)	0.03 (0.40)	0.024 (0.029)	0.02 (0.19)
Yes	0.04 (1.15)	0.03 (0.45)	1.00 (0.96)	0.39 (1.08)	0.33 (1.39)
P	0.124	0.913	0.024	0.042	0.030
INF Score B median (IQR)					
No	0.12 (0.33)	0.15 (0.42)	0.18 (0.35)	0.17 (0.30)	0.17 (0.30)
Yes	0.28 (0.64)	0.22 (0.48)	0.79 (0.74)	0.34 (0.50)	0.34 (0.50)
P	0.037	0.150	0.019	0.343	0.343
Memory B cell tetherin median (IQR)					

No	1318 (2176)	1537 (2787)	1637 (2879)	647 (830)	682 (1174)
Yes	1714 (2866)	1192 (2602)	664 (1186)	3450 (1965)	3419 (1942)
P	0.740	0.666	0.310	<0.001	<0.001

*numerically there was a stepwise increase in score B comparing 0, 1 and 2 internal organs affected but not statistically significant.

**There were also significant correlations between average dose of prednisolone in over 3 months before and after the sample date and IFN Score A (Rho = 0.402, p=0.014) and memory B cell tetherin (Rho = 0.537, p<0.001)

There was no substantive relationship between interferon assays and number of previous oral immunosuppressants. There was a trend to higher tetherin levels in patients with exposure to 1 or more antimalarials (p=0.068).

Conclusion

High interferon is associated with more severe disease. We observed a stronger relationship between Score A and tetherin with parameters that reflect current disease activity, while long term sequelae were more clearly associated with Score B. Interferon assays may allow clinicians to better stratify SLE patients for therapy and severity prediction.