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Topic area: Basic and translational research

Topic: 8. SLE, Sjögren's and APS - etiology, pathogenesis and animal models

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TYPE I INTERFERON ACTIVITY IS ASSOCIATED WITH MUCOCUTANEOUS BUT NOT MUSCULOSKELETAL DISEASE ACTIVITY IN SYSTEMIC LUPUS ERYTHEMATOSUS

A. A. A. Mohamed*^{1,2}, Y. El-Sherbiny², E. M. A. Hensor², M. Y. Md Yusof², S. H. Goma¹, E. A. Abda¹, F. M. Abd-Allah¹, P. Emery², E. M. Vital²

¹Rheumatology and Rehabilitation, Assiut University, Assiut, Egypt, ²Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds University, Leeds, United Kingdom

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Background: SLE is clinically and immunologically heterogeneous(1). Type I interferons (IFN-I) are pathogenic but expression of IFN-I stimulated genes varies. Many existing reports on clinical phenotype and IFN-I were limited by using categorical measures of IFN-I and disease activity scores that were not organ-specific. IFN-I targeted therapies are in development (2,3).

Objectives: To define the clinical phenotype of IFN-I mediated SLE.

Methods: 108 SLE patients and 20 age and sex matched healthy controls were studied. Activity was measured using BILAG-2004. PBMCs were collected for gene expression analysis using TaqMan. Relative expression of 7 interferon stimulated genes was In-transformed, normalized to healthy control and summed to derive a 7-gene IFN-I score.

Results: The most common activity was mucocutaneous and musculoskeletal, which were analysed in detail (Table 1). The relationship between activity and IFN-I score differed between these domains. Overall, IFN-I scores were higher in active mucocutaneous disease. Scores were more variable for BILAG B: this was explained by subtype of BILAG B disease. IFN-I score was increased in subacute and discoid forms (25.3(16.8-32.9), n=7) compared to acute forms (18.4(4.9-31), n=15). Score was also higher in patients with anti-Ro60. In contrast, there was no relationship between musculoskeletal disease activity and IFN-I score.

Numbers of patients with renal, haematological and neuropsychiatric activity were limited but there was a trend to higher IFN-I scores with disease activity.

BILAG Domain Score (n)	IFN Score Median (IQR)	P value vs. D+E	P Value vs. E
Mucocutaneous			
A (6)	27.2 (26.3-31.5)	0.027	0.005
B (22)	20.5 (9.1-32)	0.255	0.181
C (18)	30.7 (11.7-38.2)	0.025	0.042
D (46)	19.3 (3.7-28.1)	NA	0.469
E (16)	14 (4.2-22.6)	NA	NA
D+E (62)	17.6 (3.7-27.6)	NA	NA
Musculoskeletal			
A (6)	24.9 (5-31)	0.846	0.662
B (15)	19.8 (6.5-28.4)	0.652	0.925
C (37)	17.2 (3.5-30.7)	0.445	0.965
D (42)	24.2 (6.2-31.8)	NA	0.746
E (8)	19.4 (10.8-26.3)	NA	NA
D+E (50)	23.5(6.2-31.4)	NA	NA

Conclusions: We identify a relationship between clinical presentation of SLE and IFN-I. High IFN-I activity is linked to anti-Ro60 and non-acute forms of skin disease. We previously reported a worse response to rituximab in this subgroup, whilst response in musculoskeletal disease was consistently good. Measurement of B cell and interferon biomarkers may therefore be important in the selection of the most appropriate targeted therapy for SLE.

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Disclosure of Interest: None declared