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INCOMPLETE AND SYSTEMIC LUPUS ERYTHEMATOSUS REVEAL A DIFFERENT PATTERN OF INTERFERON-STIMULATED GENES UP-REGULATION

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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) play a central role in the pathogenesis systemic lupus erythematosus (SLE). IFN-I activity has been used as a biomarker by measuring interferon-stimulated gene (ISG) transcripts in the peripheral blood of SLE patients, but its relationship with clinical features still remains unclear. Incomplete lupus erythematosus (ILE) describes individuals with new onset of features suggestive of SLE, but do not fulfil diagnostic criteria. Up to 20% of these patients eventually progress to SLE.
Objectives: To investigate ISG expression in patients with ILE and explore possible qualitative differences between established and early stages of SLE.
Methods: A meta-analysis of known ISGs indicated 33 genes of importance[1]. The expression of 33 ISGs was measured using qPCR in PBMCs from individuals with SLE (n=54), ILE (n=27), and healthy controls (HC; n=14). SLE was defined using 2012 ACR/SLICC criteria. ILE was defined as ANA +ve, 1-2 clinical ACR/SLICC criteria, and symptom duration <12 months. Factor analysis (FA) was used to reduce expression data to a limited set of factors, which were compared between patient groups using ANCOVA test.
Results: FA on SLE patients indicated two factor scores explaining 80% of the data variance. The majority of variability was explained by Factor F1; however, Factor F2 appeared more relevant to the presence of fully established SLE. F1 and F2 were significantly different between patient groups; p=0.005 and p=0.044 respectively. F1 was similarly high in both SLE [SLE:HC=4.22 (1.80, 9.88), p=0.001] and ILE [ILE:HC=2.96 (1.20, 7.32), p=0.019]. In contrast, F2 was increased only in SLE [SLE:HC=1.38 (0.95, 2.00), p=0.086] but not in ILE [ILE:HC=1.02 (0.69, 1.51), p=0.917]; a significant difference was observed between SLE and ILE patients [SLE:ILE=1.35 (1.04, 1.77), p=0.026].In total, 16 and 14 genes loaded onto F1 and F2 respectively. Most of the genes were involved in IFN signalling pathways. Genes related to apoptosis and ubiquitination were present in both F1 and F2. Additionally, F1 loaded genes were mainly associated with antiviral immunity, complement regulation, and Th2 responses; genes loaded onto F2 were associated with regulation of IFN-I, dsDNA binding, chemotaxis, and Th1 responses.
Conclusions: IFN-I activity is present in ILE. However, the majority of measured ISG expression (F1) cannot distinguish ILE and SLE. F1 represents genes that distinguish healthy individuals, but show little variation at different stages of disease development. We define a subset of ISGs (F2), the expression of which is only increased in patients with confirmed clinical SLE. ISG expression is not unidimensional: qualitative differences in expression of distinct ISGs can contribute to clinical progression after disease initiation.
References: [1] Chiche L et al, A&R 2014
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