Conclusion: Increased Tim-3 expression on neutrophils may be a novel indicator to assess disease activity and severity in AS, which may serve as a negative feedback mechanism preventing potential tissue damage caused by excessive inflammatory responses in AS patients.

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POS0370

TYPE I INTERFERON PATHWAY ASSAYS IN PATIENTS WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES - SYSTEMATIC LITERATURE REVIEW (SLR) AND DEVELOPMENT OF CONSENSUS TERMINOLOGY FROM A EULAR TASKFORCE

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Background: The interferon (IFN) pathway is a complex system with multiple proteins and diverse downstream effects on gene and protein expression. IFNs have been implicated in multiple RMDs. Despite significant potential, IFN assays have not progressed into clinical practice.

Objectives: To perform a SLR on IFN assays in RMDs and propose a consensus terminology.

Methods: OvidMedline, Embase and Web of Science were searched for reports of IFN and RMDs up to October 2019. Information about the properties of assays measuring type I IFN and measures of truth were extracted and summarised. Terminology was agreed through an interactive consensus process with reference to the existing evidence.

Results: 10037 abstracts were identified. 275 fulfilled eligibility criteria, and were used for data extraction. Some used more than one technique to measure IFN-I pathway activation. Hence, 275 papers generated data on 393 methods. There was great heterogeneity in the methods used and presentation of results. IFN-I pathway activation was measured using: qPCR (n=121), immunoassays (n=101), microarray (n=69), reporter cell assay (n=38), DNA methylation (n=14), flow cytometry (n=14), cytopathic effect assay (n=11), RNA sequencing (n=9), Plaque

reduction assay (n=8), Nanostring (n=5), bisulphite sequencing (n=3). All papers fulfilled Face Validity. Due to lack of gold standard for IFN-I pathway activation, evidence of criterion validity was variable. Concurrent validity was presented for n=150 assays. The terminology used to describe aspects of type I IFN pathway activation was not consistent, so a consensus terminology for IFN research (Table 1) was proposed by the taskforce.

Table 1. Consensus terminology

Term	Abbreviation	Definition
Interferon	IFN	Proteins with anti-viral activity; IFNs are mediators of an anti-viral response. They belong to the Type I, Type II and Type III IFN families.
Type I interferon	IFN-I	The IFNs alpha, beta, omega, kappa, epsilon, secreted by any nucleated cell, and binding to the IFNAR, which is expressed on any nucleated cell.
Type II interferon	IFN-II	IFN gamma, mostly secreted by T cells, binding to the IFNGR, which is expressed on most leucocytes.
Type III interferon	IFN-III	IFN lambda, which are structurally more similar to IL-10 but share downstream signalling and gene expression with IFN-I.
Interferon-stimulated genes	ISGs	Genes whose expression is known to be upregulated by any kind of IFN. Individual ISGs may not exclusively represent Type I IFN pathway activation.
Type I Interferon pathway activation		Any evidence for function of the components of the Type I IFN pathway. This includes: secretion of a Type I IFN protein, binding to the IFNAR, initiation of JAK/STAT signalling pathways, expression of IFN-stimulated genes, expression of IFN-stimulated proteins.
Type I interferon pathway assay		An assay measuring one or more components of the Type I IFN pathway at a molecular or functional level.
Interferon stimulated gene expression signature		A qualitative description of coordinated expression of a set of ISGs that is indicative of Type I IFN pathway activation.
Interferon stimulated gene expression score		A quantitative variable derived from expression of a defined set of ISGs that is indicative of Type I IFN pathway activation.
Interferon stimulated protein score		A variable derived from expression of a defined set of soluble biomarkers known to be upregulated by IFN, although not specific for Type I IFN.
Interferonopathy		Monogenic diseases in which there is constitutive Type I IFN pathway activation with a causal role in pathology. The clinical picture may resemble rheumatic musculoskeletal diseases. However, most diseases with IFN pathway activation are not Interferonopathies.

Conclusion: Diverse methods have been reported as IFN assays and these differ in what elements of type IFN-I pathway activation they measure. The taskforce consensus terminology on type I IFN reporting should be considered for research and clinical applications.

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