






ORIGINAL RESEARCH

Association between type I interferon pathway activation and clinical outcomes in rheumatic and musculoskeletal diseases: a systematic literature review informing EULAR points to consider

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ABSTRACT

Background Type I interferons (IFN-I) contribute to a broad range of rheumatic and musculoskeletal diseases (RMDs). Compelling evidence suggests that the measurement of IFN-I pathway activation may have clinical value. Although several IFN-I pathway assays have been proposed, the exact clinical applications are unclear. We summarise the evidence on the potential clinical utility of assays measuring IFN-I pathway activation.

Methods A systematic literature review was conducted across three databases to evaluate the use of IFN-I assays in diagnosis and monitor disease activity, prognosis, response to treatment and responsiveness to change in several RMDs.

Results Of 365 screened, 276 studies were selected that reported the use of assays reflecting IFN-I pathway activation for disease diagnosis (n=188), assessment of disease activity (n=122), prognosis (n=20), response to treatment (n=23) and assay responsiveness (n=59). Immunoassays, quantitative PCR (qPCR) and microarrays were reported most frequently, while systemic lupus erythematosus (SLE), rheumatoid arthritis, myositis, systemic sclerosis and primary Sjögren's syndrome were the most studied RMDs. The literature demonstrated significant heterogeneity in techniques, analytical conditions, risk of bias and application in diseases. Inadequate study designs and technical heterogeneity were the main limitations. IFN-I pathway activation was associated with disease activity and flare occurrence in SLE, but their incremental value was uncertain. IFN-I pathway activation may predict response to IFN-I targeting therapies and may predict response to different treatments.

Conclusions Evidence indicates potential clinical value of assays measuring IFN-I pathway activation in several RMDs, but assay harmonisation and clinical validation are urged. This review informs the EULAR points to consider

WHAT IS ALREADY KNOWN ON THIS TOPIC

→ The type I interferon (IFN-I) activation pathway has been related to a number of rheumatic and musculoskeletal diseases (RMDs), but the optimal assays for detection and clinical applications are unclear.

WHAT THIS STUDY ADDS

- This systematic review revealed significant heterogeneity in IFN-I evidence in RMDs in terms of clinical applications (diagnosis, measurement of disease activity, prognosis, prediction of response and assay responsiveness) that may account for the lack of transition of IFN-I assays into clinical practice.
- Immunoassays, quantitative PCR and microarrays were reported most frequently, while systemic lupus erythematosus (SLE), rheumatoid arthritis, myositis, systemic sclerosis and primary Sjögren's syndrome were the most studied RMDs.
- IFN-I pathway activation was associated with disease activity and flare occurrence in SLE, although in most contexts the added value to existing instruments in clinical care needs to be determined.
- IFN-I assays can predict response to IFN-I targeting drugs and may also predict response to other classes of therapies.

for the measurement and reporting of IFN-I pathway assays.

INTRODUCTION

Type I interferons (IFN-I) are cytokines with well-known antiviral and immunomodulatory activities, involved in both innate and adaptive

Rheumatic And Musculoskeletal Diseases Eular

**Fabiola Atzeni, Ignacio Francesco
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