Points to consider when using interferon assays

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Interferons are type of protein called a cytokine. They have important roles in the immune system. Interferons are split into three distinct families—Type I, Type II, and Type III. Due to their role in

autoimmunity, Type I interferons are a therapeutic target that have been investigated in many RMDs and are also a possible biomarker that can be measured to help support diagnosis, prognosis, prediction of response to therapy, and patient stratification.

Activation of the Type I interferon pathway can be measured at different levels and using different readouts. Despite this, assays to detect this have not moved into clinical practice, and there is uncertainty about their use. A key barrier to their uptake has been the diversity of approaches, ranging from simply measuring interferon levels to assessing gene expression and cell-based functional assays. In addition, there is a lack of standardization which hampers clinicians and scientists who may wish to compare different sets of results.

Since these molecules are involved in a number of RMDs, EULAR—the European Alliance of Associations for Rheumatology—has created a new document to help identify and define clinical applications for these assays in specific settings, as well as to promote consistency and harmonization in how they are used.

The new EULAR points-to-consider were developed by a multidisciplinary task force. The group included rheumatologists, immunologists, translational scientists, and a patient partner. The project was completed in line with EULAR standardized operating procedures.

The paper, published in the *Annals of the Rheumatic Diseases*, is the first systematic approach to evaluate the use of these assays in clinical research and practice in rheumatology. The work includes two overarching principles. These acknowledge that the interferon pathway is a complex system with multiple subtypes and diverse downstream effects on gene and protein expression.

They also emphasize that although Type I interferon pathway activation

is a common hallmark in many RMDs, the available assays require further validation for most clinical uses. The points to consider include 11 statements on terminology, reporting practices, and clinical applications.

Implementing Type I interferon pathway assays has the potential to improve clinical management in rheumatology and other specialties. EULAR believes that these points to consider create a framework for the future implementation of these and other biomarkers.

More information: Javier Rodríguez-Carrio et al, 2022 EULAR points to consider for the measurement, reporting and application of IFN-I pathway activation assays in clinical research and practice, *Annals of the Rheumatic Diseases* (2023). DOI: 10.1136/ard-2022-223628

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