



Response to: 'Circulating interferon- α measured with a highly sensitive assay as a biomarker for juvenile inflammatory myositis activity.' by Melki et al

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Response to: ‘Circulating interferon- α measured with a highly sensitive assay as a biomarker for juvenile inflammatory myositis activity.’ by Melki *et al*

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We thank Dr. Melki and colleagues for their interest in our work on IFN α assessment in SLE. In their correspondence, they show that IFN α protein measurement by digital ELISA is also correlated with disease activity in other IFN- dependent autoimmune diseases, and in this case, juvenile IIMs.

Since IFNs (especially IFN α) are involved in the pathogenesis of several autoimmune diseases such as SLE, myositis, Sjögren’s syndrome, and systemic sclerosis (1), monitoring their presence in the circulation of patients might help physicians to better evaluate disease activity and/or predict future flares. However, until recently, clinicians lacked a robust and standardized method for the measurement of IFNs in serum because IFN concentrations are usually very low and often not detectable with the use of classic immunoassays. Tools for indirect measurement of IFN α activity through an IFN gene expression score have a very low availability. These scores are not only notoriously difficult to standardize but are also less sensitive to change than direct measurement of IFN α . The advent of the ultrasensitive Simoa digital ELISA technology now makes it possible to reliably measure very low concentrations of IFN α (2). The studies by Melki *et al* and ourselves show that direct measurement of IFN α might improve monitoring of clinical activity in myositis and SLE, respectively.

Of note, the area under the ROC curve value of 0.81 for IFN α concentration as a discriminator between active versus inactive juvenile IIM determined by Melki and colleagues is similar to the value of 0.83 that we had previously reported in SLE. In Melki and colleagues’ study, the optimal cutoff threshold of IFN α concentration permitting the ability to distinguish active from inactive juvenile IIM was 42 fg/ml,

which is not only substantially lower than the value observed in our study (266 fg/ml) as being optimal to distinguish active from inactive SLE, but also lower than the value (136 fg/ml) calculated as the threshold below which IFN α values are within the range of those in healthy controls. The discrepancy between the 2 studies might be explained by the different types of antibodies used in the digital IFN α ELISAs, the different types of disease studied, as well as by age and demographic differences between the patient populations. It is therefore clear that the implementation of the digital IFN α ELISA to meet clinical grade standards still requires further investigation. Moreover, the determination of the specific roles of type I IFNs versus type II and type III IFNs in the pathogenesis of various autoimmune diseases will be facilitated by the use of this highly sensitive digital ELISA technology that enables the measurement of cytokines at physiologic concentrations.

The prognostic value of elevated levels of IFNs in the prediction of a disease flare also remains to be studied. It is therefore important that this technology be developed for the measurement of other types of IFNs, particularly the IFN β and IFN λ subtypes. In conclusion, the translation of digital ELISA technology into the clinical laboratory setting will enhance the potential for routine measurement of IFN α in the monitoring of several “nonmonogenic” interferonopathies.

1. Muskardin TL, Niewold TB. Type I interferon in rheumatic diseases. *Nat Rev Rheumatol* 2018;14:214–28
2. Rodero MP, Decalf J, Bondet V, Hunt D, Rice GI, Werneke S, et al. Detection of interferon α protein reveals differential levels and cellular sources in disease. *J Exp Med* 2017;214:1547–55)