S5A – Biomarker & indices

CIRCULATING TYPE I, II AND III INTERFERONS (IFNS) ASSOCIATE WITH IFN-Scores, BUT DEFINE DISTINCT SUBSETS OF ACTIVE SLE

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Background Serum induced IFN gene expression (IFN-score) is considered a golden standard to assess IFN activity in SLE. So far, IFN-scores have not been compared to serum levels of type I, II and III IFNs.

Aim To investigate how IFN-scores and SLE manifestations relate to serum levels of IFNs type I (alphas), II (gamma) and III (lambda 1).

Methods 461 SLE patients and 322 controls were included. IFN-score was measured by WISH cell assay. INF-alphas and IFN-lambda1 were measured by ELISA. IFN-gamma was measured by MSD 30-plex assay.

Results SLE patients had higher IFN-scores and higher levels of IFN-alphas, IFN-gamma and IFN-lambda1 (p<0.001). IFN-scores correlated with levels of IFN-gamma and IFN-alpha (rho=0.39, and rho=0.25, p<0.0001). Further, patients were grouped according to high levels (>3 rd quartile) of each IFN/IFN-score. The group with high IFN-scores had higher disease activity (SLAM, SLEDAI): weight loss (41%), fatigue (33%), fever (39%), rash (44%), lymphadenopathy (45%), arthritis (40%), nephritis (55%) (p<0.01). Interestingly, incidence of neuropsychiatric SLE, antiphospholipid (aPL) antibodies (abs), and also damage score was lower (p<0.05).

The characteristics of IFN-gamma high group included higher disease activity (SLAM, SLEDAI), and specifically: active nephritis (52%), lymphadenopathy (40%), arthritis (42%), lymphopenia (37%), anaemia (35%) and positivity for Sm (41%), SmRNP (36%) and RNP68 (45%), Ro52 (35%) and Ro60 (33%) (p<0.03).

The common features of IFN-alpha high group included younger age, shorter disease duration, active rash (34%), lymphadenopathy (43%), Ro52 (38%) and La (43%) (p=0.01). Presence of aPL abs and previous vascular events were lower and renal affection was uncommon (p<0.01).

In general, high IFN-scores reflected SLE manifestations that could be further stratified by high IFN-gamma levels and to a lesser extent by high IFN-alpha. High IFN-lambda1 did not define any phenotype of active SLE, except presence of anti-nucleosome abs.

Conclusion We demonstrate that high IFN-score associate more strongly with type II rather than type I IFNs. Importantly, major manifestations of SLE: active nephritis and arthritis, and also anti-Sm/SmRNP antibodies associate with IFN-gamma; while rash associate with IFN-alpha.

Our findings are of major importance while tailoring clinical trials with anti-IFN therapies and demonstrate that importance of IFN-gamma has so far been underscored.