Background: STING (stimulator of interferon genes) is a cytosolic protein that is found in endoplasmic reticulum (ER) membrane, mitochondria and mitochondrial-associated membranes. Although it is well established that STING plays an important role in innate immune responses, its potential involvement in rheumatic disease processes remains to be clarified (1).

Objectives: The aims of this study were to evaluate the levels of STING and its relationship with local inflammation in the synovial fluid (SF) of patients with psoriatic arthritis (PsA), rheumatoid arthritis (RA), gout, calcium pyrophosphate (CPP) crystal-induced arthritis (CPP-IA), osteoarthritis (OA) and OA with CPP crystals (OA+CPP).

Methods: SF was collected from the knees of 60 untreated patients: 10 with PsA, 10 with RA, 10 with gout, 10 with OA+CPP, 10 with OA and 10 with OA+CPP. SF was examined under optical light microscopy. White cell count (WBC) and the polymorphonuclear cell (PMN) percentage were determined in SF according to standard procedures. SF IL-6, IL-1β, and intra- and extra-cellular STING levels were assayed by ELISA.

Results: The levels of WBC were higher in SFs from gouty patients (27.7±20.56 10³/mm³), while OA and CPP+OA patients showed the lowest WBC count (0.3±0.3 10³/mm³), 0.3±0.28 10³/mm³). SFs from inflammatory arthritis contained elevated percentages of PMN (85.5±10.86%, CPP-IA: 84±13.31%, RA: 80.3±8.14%, PsA: 42.6±35.97%). Extracellular STING was determined in OA (440±143.31 pg/ml), OA+CPP (225±205.06 pg/ml) and CPP-IA (475±7.07 pg/ml) SF, while was not detectable in RA, PsA and gout. Intracellular STING levels were similar and the highest in SFs from gout (96.4±35.44 pg/ml) and RA (90.6±23.13 pg/ml), while remained under detection limit only in SFs from PsA. SF concentration of IL-6 was lower in OA (354.8±377.56 pg/ml) and OA+CPP (389.56±104.14 pg/ml) as compared with inflammatory arthropathies (PsA: 3807±1448.86 pg/ml; RA: 17542±2334.87 pg/ml; gout: 19356±84.56 pg/ml; CPP-IA: 20389.56±104.14 pg/ml). The patients with gout and RA had the highest levels of IL-8 (2159.54±347.09 pg/ml; 2039.6±97.74 pg/ml) and IL-1β (35.93±20.46 pg/ml; 44.36±23.16 pg/ml), while OA showed the lowest concentrations (IL-8: 23.21±11.32 pg/ml; IL-1β: 0.47±0.13 pg/ml). In the total group of patients, we found a negative correlation between extracellular STING and IL-6 (r=−0.53; p=0.004) and IL-1β (r=−0.47; p=0.012). There was a positive correlation between intracellular STING and IL-8 (r=0.54; p=0.017), IL-1β (r=0.77; p<0.001) and IL-6 (r=0.69; p=0.009).

Conclusion: This study is the first to define the presence of STING in SF of different arthritides. The highly variable levels of extracellular STING in OA, OA+CPP and CPP-IA SF may be due to the activation of factors that reduce its interaction with the ER. The effect of downregulating factors in PsA might explain the low concentration of intracellular STING in these patients.

References:

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