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Editorial Open Access

The Synovial Signature and Response to Biologics-A step towards Personalized Medicine in Refractory Rheumatoid Arthritis

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Editorial

Rheumatoid Arthritis is a multi-system autoimmune disease in which symmetrical joint inflammation, hyperplasia of the synovium, and formation of invasive granulation tissue (pannus) stand out as distinctive disease features. The advancing disease process eventually proceeds to joint destruction with deformity and persistent disability [1-3]. Through-out its' history the disease have displayed a complex heterogeneity in both disease course and patient response to therapy. Clinical response depends on disease state and disease characteristics indeed there are different subtypes of RA with different genetic backgrounds that interpret into benign or destructive, seropositive versus seronegative RA.

With the widespread implementation of the biologic strategy, rheumatologists have experienced a victorious shift that has un-doubtfully improved the disease outcome with up to 65-70% of the treated patients achieving either remission or low disease activity. However, with autoimmune diseases one should always expect the unexpected, despite their reported efficacy in refractory rheumatoid arthritis (RA), still a proportion of patients ranging from 20-40% display poor/no response to their first line biologic DMARDs therapy. A part of this variability might be due to drug concentration and pharmacokinetic which is influenced by the characteristics of the patient such as age, gender, renal and liver functions, body mass index (BMI), or smoking status, as well as disease status and disease characteristics. Concomitant use of synthetic DMARDs might additionally affect drug concentrations [4-10].

The rationales behind the primary failure of biologics remain poorly understood with a number of recent researches and trials assigning primary drug failure to a number of factors referred to as predictors of response to biologic therapy.

Amongst these predictors the most recently investigated point in the field was the impact of cytogenetic markers within the synovium to the response to such therapy which can be described as the "synovial signature". Different studies have evaluated the contribution of synovial phenotypes and local cellular aggregates to the in-situ cytokine profile which might presumably affect response to therapy. In one study by Klaasen et al. [10], lymphocytic synovial aggregates favored a good response in RA. In another late trial by Dennis et al. [11], the investigators reported four major phenotypes of RA synovium the lymphoid, the myeloid, the low inflammatory and fibroid phenotypes. Each phenotype displayed a distinctive underlying gene signature, with the study revealing that the synovial myeloid but not the lymphoid favored a good EULAR response with tumor necrosis factor inhibitors. Such findings were also associated with a corresponding distinctive serum cytokine profile with the myeloid type being associated with higher levels of soluble intracellular adhesion ICAM-1which displayed the most robust response to TNF-I , whereas the lymphoid genotype was associated with higher serum C-X-C motif chemokine 13 (CXCL-13) showing a poor response [11,12]. This study highlighted the extreme importance of synovial gene expression and emphasized the hypotheses that synovial phenotypic variations "Synovial Signature" might to a great extent affect serum cytogenetic biomarkers and thereby affecting disease expression and response to therapy [10-12].

The deeper we investigate the better the recognition of such cellular and molecular variants and the more successful we apply the treat to target strategy, a novel approach towards "Personalized Medicine" in refractory disease.

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