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Editorial: Molecular markers in rheumatic diseases and their comorbidities

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Editorial on the Research Topic

[Molecular markers in rheumatic diseases and their comorbidities](#)

Biomarker research in the field of rheumatic diseases is an emerging topic due to its relevance in the evaluation of preclinical stages, clinical outcomes, and prognosis (1). In this regard, the Research Topic “Molecular Markers in Rheumatic Diseases and Their Comorbidities” presents a collection of interesting articles.

Systemic autoimmune rheumatic diseases (SARD) are a group of pathologies characterized by an inflammatory condition that involves overactivated or suppressed genes, DNA functional changes, HLA class I and II associations, and a bulk of autoantibodies against nuclear and cytoplasmic components (2, 3). It is well-known that other chronic inflammatory conditions may trigger or enhance the inflammatory state of SARD. Examples of some of these comorbidities are vascular aging, increased arterial stiffness, metabolic syndrome, etc. (4–8). This constitutes a real challenge to clinicians because, in addition to managing SARD, they have to offer adequate control of comorbidities in a multidisciplinary setting with the aim of improving the quality of life of their patients (9). Liang et al. showed elevated levels of human epididymis protein 4 (HE₄), a protein expressed in several tissues and used as a biomarker in ovarian cancer (10), in patients with rheumatoid arthritis (RA) compared to healthy subjects; those who were positive for HE₄ had a higher prevalence of interstitial lung disease (ILD); these data are the first to identify a correlation between HE₄ levels and ILD.

In recent years, vitamin D deficiency has been associated with pleiotropic dysfunction or health issues such as suicidal ideation, bone turnover, etc. (11). In this Research Topic, Diao et al. carried out a systematic review and meta-analysis of vitamin D deficiency between ankylosing spondylitis (AS) patients and healthy controls, proposing a possible protective role of vitamin D in AS.

The achievement of remission is one of the clinical outcomes of the management of patients with rheumatic diseases. Su et al. studied a possible biomarker for clinical remission in adult-onset Still's disease (AOSD) through the measurement of cysteine-rich angiogenic inducer 61 (Cyr61) levels (12). They identified elevated levels of Cyr61 in asymptomatic AOSD patients and showed an inverse correlation of Cyr61 with proinflammatory IL-1 β , IL-6, and IL-17. Therefore, the authors highlighted the involvement of Cyr61 in tissue repair.

Some biomarkers can be detected in serum 9–10 years before the clinical onset of the disease, for example as antinuclear antibodies (13) or anti-citrullinated peptide antibodies (14). Another example discussed in this Research Topic is an inhibitor of apoptosis: survivin. Erlandsson et al. suggested that survivin shows a strong clinical association with arthralgias in preclinical RA.

MicroRNAs (miRNAs) have been associated with a myriad of inflammatory rheumatic diseases and their comorbidities, which include cardiovascular diseases (15). In the extensive research by Li et al., 42 up-regulated and 45 down-regulated miRNAs were found in AS compared with controls. Finally, García-Ortiz et al. studied the Xq28 risk haplotype in the Mexican population associated with susceptibility to childhood-onset systemic lupus erythematosus.

References

- Califf RM. Biomarker definitions and their applications. *Exp Biol Med.* (2018) 243:213–21. doi: 10.1177/1535370217750088
- Moutsopoulos HM. Autoimmune rheumatic diseases: one or many diseases? *J Transl Autoimmun.* (2021) 4:100129. doi: 10.1016/j.jtauto.2021.100129
- Szekanecz Z, McInnes IB, Schett G, Szamosi S, Benko S, Szucs, et al. Autoinflammation and autoimmunity across rheumatic and musculoskeletal diseases. *Nat Rev Rheumatol.* (2021) 17:585–95. doi: 10.1038/s41584-021-00652-9
- Kwiat VR, Reis G, Valera IC, Parvatiyar K, Parvatiyar MS. Autoimmunity as a sequela to obesity and systemic inflammation. *Front Physiol.* (2022) 13:887702. doi: 10.3389/fphys.2022.887702
- Vazquez-Del Mercado M, Perez-Vazquez FJ, Gomez-Banuelos E, Chavarria-Avila E, Llamas-Garcia A, Arrona-Rios KI, et al. Subclinical parameters of arterial stiffness and arteriosclerosis correlate with QRISK3 in systemic lupus erythematosus. *PLoS One.* (2018) 13:e0207520. doi: 10.1371/journal.pone.0207520
- Perez-Vazquez F, Back M, Chavarria-Avila E, Gomez-Banuelos E, Ramos-Becerra CG, Pizano-Martinez O, et al. Enalapril influence on arterial stiffness in rheumatoid arthritis women: a randomized clinical trial. *Front Med.* (2019) 6:341. doi: 10.3389/fmed.2019.00341
- Gomez-Banuelos E, Navarro-Hernandez RE, Corona-Meraz F, Madrigal-Ruiz PM, Martin-Marquez BT, Pizano-Martinez OE, et al. Serum leptin and serum leptin/serum leptin receptor ratio imbalance in obese rheumatoid arthritis patients positive for anti-cyclic citrullinated peptide antibodies. *Arthritis Res Ther.* (2015) 17:335. doi: 10.1186/s13075-015-0850-8
- Vazquez-Del Mercado M, Gomez-Banuelos E, Chavarria-Avila E, Cardona-Munoz E, Ramos-Becerra C, Alanis-Sanchez A, et al. Disease duration of rheumatoid arthritis is a predictor of vascular stiffness: a cross-sectional study in patients without known cardiovascular comorbidities: a STROBE-compliant article. *Medicine.* (2017) 96:e7862. doi: 10.1097/MD.00000000000007862
- Dougados M, Soubrier M, Antunez A, Balint P, Balsa A, Buch MH, et al. Prevalence of comorbidities in rheumatoid arthritis and evaluation of their monitoring: results of an international, cross-sectional study (COMORA). *Ann Rheum Dis.* (2014) 73:62–8. doi: 10.1136/annrheumdis-2013-204223
- Sun ML, Yang ZY, Wu QJ, Li YZ, Li XY, Liu FH, et al. The Role of human epididymis protein 4 in the diagnosis and prognosis of diseases: an umbrella review of systematic reviews and meta-analyses of observational studies. *Front Med.* (2022) 9:842002. doi: 10.3389/fmed.2022.842002
- Calderon Espinoza I, Chavarria-Avila E, Pizano-Martinez O, Martinez-Garcia EA, Armendariz-Borunda J, Marquez-Aguirre AL, et al. Suicide risk in rheumatoid arthritis patients is associated with suboptimal vitamin D levels. *J Clin Rheumatol.* (2022) 28:137–42. doi: 10.1097/RHU.0000000000001823
- Lin J, Li N, Chen H, Liu C, Yang B, Ou, et al. Serum Cyr61 is associated with clinical disease activity and inflammation in patients with systemic lupus erythematosus. *Medicine.* (2015) 94:e834. doi: 10.1097/MD.0000000000000834
- Arbuckle MR, McClain MT, Rubertone MV, Scofield RH, Dennis GJ, James JA, et al. Development of autoantibodies before the clinical onset of systemic lupus erythematosus. *N Engl J Med.* (2003) 349:1526–33. doi: 10.1056/NEJMoa021933
- Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, Bingham CO 3rd, et al. 2010 Rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. *Arthritis Rheum.* (2010) 62:2569–81. doi: 10.1002/art.27584
- Tanase DM, Gosav EM, Petrov D, Teodorescu DS, Buliga-Finis ON, Ouatu A, et al. MicroRNAs (miRNAs) in cardiovascular complications of rheumatoid arthritis (RA): what is new? *Int J Mol Sci.* (2022) 23:5254. doi: 10.3390/ijms23095254

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Conflict of interest

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