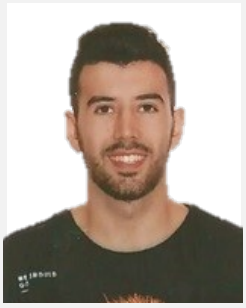
ImmunoTools *special* Award 2021



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Biomarkers in urine for the non-invasive diagnostic of renal pathology in systemic autoimmune diseases

Nephritis is the most frequent severe manifestation in Systemic Autoimmune Diseases (SADs). Suspicion of SAD-associated nephritis is based on the detection of abnormalities in urinalysis (proteinuria, hematuria), and the diagnosis is confirmed by renal biopsy. However, the invasiveness of this diagnostic technique makes it unsuitable for the early detection of renal pathology or to monitor the response to treatment. Currently, the monitoring of renal inflammatory activity is carried out using serum and urinary analytical parameters that are neither very specific nor able to differentiate renal activity from chronicity [1]. Therefore, the need to establish new non-invasive biomarkers capable of discriminating the renal activity of the pathology and its severity, predicting renal flares and monitoring response to treatment and disease progression are clearly necessary.

Unlike other sources of information, such as serum or tissue, urine collection is not an invasive procedure and can be easily self-collected, allowing for repeated sampling. In addition, urinary biomarkers seem to be more promising than serum markers because they are derived from inflamed renal tissues. Therefore, urine could be considered an ideal source for finding potential biomarkers in the study of nephritis associated with SADs [2].

The common histological finding in patients with renal pathology associated with SADs is the deposition in the kidney of autoantigen-autoantibody immune-complexes, which mediate tissue damage. B lymphocytes and plasmacytoid dendritic cells (pDCs) are considered to be the central immune effectors in the generation and maintenance of the symptoms because of their role in the production of autoantibodies and type I IFN. Additionally, it is been revealed that T cells can drive inflammation and antibody production, thus contributing to the development of the pathology [3].

The working hypothesis of this project is based on the fact that typical pathologies of SAD-associated nephritis are due to the characteristics of the local immune response, and these should be reflected in immunological parameters in urine. Infiltrating immune populations and different soluble mediators, such as pro-inflammatory cytokines, should be reflected in the composition of patients' urine. Therefore, the monitoring of these characteristics in urine can be very useful as a non-invasive method in the follow-up of patients with SAD-associated nephritis under treatment.

Our aim is to find non-invasive urinary biomarkers of nephritis in SADs patients, and for this purpose we will use two different techniques and the reagents provided by ImmunoTools. On the one hand, we will use flow cytometry to characterize infiltrating-lymphoid cells in the urine, specifically T and B cells. On the other hand, we will assess the levels of IL-6 in urine of these patients by ELISA. There are evidences that serum levels of IL-6 could have value as diagnostic biomarkers in lupus nephritis [4].

The ImmunoTools award will provide us with the opportunity to approach the role of the renal infiltrate in the generation of the pathogenic immune response in the renal microenvironment in SADs. Likewise, we expect that the data resulting from our analysis will allow us to improve the estimation of each patient's risk of renal pathology, as well as their response to treatment.

References:

1. Mok, C.C. and C. Mohan, Urinary Biomarkers in Lupus Nephritis: Are We There Yet? Arthritis Rheumatol, 2021. 73(2): p. 194-196
2. Morell M, Pérez-Cózar F, Marañón C. Immune-Related Urine Biomarkers for the Diagnosis of Lupus Nephritis. Int J Mol Sci. 2021. 22(13):7143
3. Shi, G., et al., Systemic Autoimmune Diseases 2014. J Immunol Res, 2015. 2015: p. 183591
4. Abdel Galil SM, Ezzeldin N, El-Boshy ME. The role of serum IL-17 and IL-6 as biomarkers of disease activity and predictors of remission in patients with lupus nephritis. Cytokine. 2015. 76(2):280-287

ImmunoTools *special* AWARD for **Francisco Pérez Cózar** includes 10 reagents

FITC - conjugated anti-human CD3, IgG

PE - conjugated anti-human CD19

PerCP - conjugated anti-human CD4

APC - conjugated anti-human CD8, CD20

human ELISA-set (for one 96 plate): IL-6

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