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Letter to the Editor

LETTER TO THE EDITOR

Kidney immunology: embracing the complexity to advance the field

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Abnormal immunity is involved in the pathophysiology of virtually any renal disease [1] and uremia *per se* has a significant impact on the immune system [2]. Nonetheless, the current understanding of specific immune abnormalities associated with different kidney diseases is quite rudimentary. This is responsible, at least in part, for the absence of specific treatments for most of these conditions.

Steroids, alkylating agents and calcineurin inhibitors have been the main treatments for most glomerular diseases, despite their different immune pathogenesis [3]. This simplistic treatment attitude was initially driven by the limited therapeutic options. However, the availability of biologics has offered numerous novel treatments that have not been integrated in the armamentarium of the nephrologists due to a lack of knowledge of the immune pathogenesis in individual glomerular diseases, including specific immune cells and molecular pathways that should be targeted.

A clear understanding of the pathophysiology of membranous nephropathy allowed testing the hypothesis that rituximab-induced B-cell depletion reduces disease severity by arresting pathogenic autoantibody production [4]. It also resulted in a growing number of trials testing other biologics in this condition, which will likely translate into a further improvement in disease outcomes. Unfortunately, such success stories are uncommon in nephrology.

How can we do better? Immunology is not a major component of the nephrologists' curriculum and kidney diseases do not represent a key interest for immunologists. A strong commitment by the nephrology community is required to strengthen the immunological background of future generations of nephrologists through education and *ad hoc* funding opportunities.

In-depth human immunology research is essential to better understand kidney disease mechanisms, which will allow us to classify nephrological diseases based on pathophysiological principles instead of descriptive histological features. Immune nephrology (or 'kidney immunology') should become a key specialty of nephrology aimed at understanding the role of immunity in the pathophysiology of kidney diseases and at defining optimal immune modulating treatment strategies (Figure 1).

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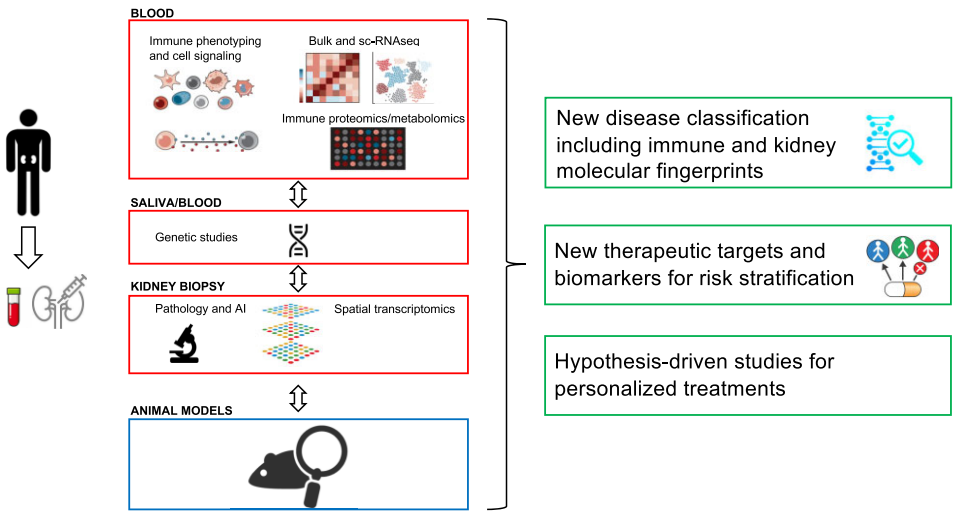

FIGURE 1: In-depth characterization of the human immune response in kidney disease. Human samples can be used for extensive profiling of immune, genetic and kidney abnormalities. The hypotheses generated from human studies can be tested in animal models and then in human mechanistic studies. Ultimately, these studies have the potential to identify new treatment targets and biomarkers that will improve the outcomes of affected individuals.

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CONFLICT OF INTEREST STATEMENT

None declared.

REFERENCES

1. Tecklenborg J, Clayton D, Siebert S *et al*. The role of the immune system in kidney disease. *Clin Exp Immunol* 2018; 192: 142–150
2. Betjes MGH. Uremia-associated immunological aging and severity of COVID-19 infection. *Front Med (Lausanne)* 2021; 8: 675573
3. Ponticelli C, Locatelli F. Glucocorticoids in the treatment of glomerular diseases: pitfalls and pearls. *Clin J Am Soc Nephrol* 2018; 13: 815–822
4. Faul C, Donnelly M, Merscher-Gomez S *et al*. The actin cytoskeleton of kidney podocytes is a direct target of the antiproteinuric effect of cyclosporine A. *Nat Med* 2008; 14: 931–938