However, linking it to FSGS is a stretch, since the majority of progression of kidney disease in patients of African descent. This is not the case for segmental glomerulosclerosis (FSGS). The lack of recognition that FSGS is a lesion associated with hypertension, vascular damage and aging—thus a pathogenic process different from primary FSGS. Without proper patient selection, genomics, proteomics, metabolomics, ROC curves, c-statistics and other sophisticated approaches are likely to produce conflicting results.

Secondly, novel biomarkers will only be useful to the clinician if they can outperform traditional ones, e.g. proteinuria. This is particularly true for patients with minimal change disease, FSGS and MN where remission of proteinuria equals excellent long-term outcome. Similarly for LN, markers such as MCP-1 have yet to prove superior to the combined use of traditional markers.

Genetic biomarkers are too insensitive to be useful in clinical practice. Preliminary data from our cohort with end-stage MN undergoing transplantation suggest that the simultaneous presence of the HLA-DQWA1 risk allele in the recipient and donor
kidney is not enough to induce recurrent disease—more than genetic risk is needed. The study of Sadowski et al., reporting that a single gene causes steroid-resistant nephrotic syndrome in 30% of children and young adults, owns its success to the fact that patients had an excellent ‘marker’ for a genetic disease: a positive family history. However, mutations in adult patients without family history are extremely rare and screening is not recommended.

We agree with Doctors Mariani and Kretzler regarding the ‘paucity of robust data from RTC to support treatment recommendations’ in glomerular diseases. However, this is in great part due to the lack of interest from the funding agencies in conducting translational research. Instead, significant funding is invested in sophisticated research far away from the bedside, thus delaying clinician access to therapeutic approaches that could help patients today.

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Moderator’s view: Biomarkers in glomerular diseases—translated into patient care or lost in translation?

Pierre Ronco1,2,3

1Sorbonne Universités, UPMC Univ Paris 06, UMR_S 1155, Paris F-75005, France, 2INSERM, UMR_S 1155, Batiment Recherche, Hôpital Tenon, 4 rue de la Chine, Paris F-75020, France and 3Department of Nephrology and Dialysis, AP-HP, Hôpital Tenon, Paris F-75020, France

Correspondence and offprint requests to: Pierre Ronco; E-mail: pierreronco@yahoo.fr

A biomarker is defined as ‘A characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacologic responses to therapeutic intervention’ [1]. Characteristics of an ideal biomarker are indicated in Table 1 [2, 3]. In the field of renal function and renal diseases, urinary protein excretion, urinary sediment, serum creatinine and estimated glomerular filtration rate (eGFR) are commonly used parameters that fulfill the definition of a biomarker. However, they lack both specificity and sensitivity. For instance, persistence of low-grade proteinuria in membranous nephropathy or systemic lupus erythematosus (SLE) may result from still active disease or scar lesions that imply a different therapeutic strategy. Measurement of total proteinuria does not tell us about its composition, and the respective part of glomerular proteinuria made of albumin and high-molecular weight (HMW) proteins (in the case of severe alteration of the glomerular filter) and of tubular proteinuria, made of low-molecular weight proteins, which is an ominous prognostic factor in most glomerular diseases [4–6]. Serum creatinine levels start to rise only when a substantial part, >50%, of the nephrons have been destroyed. eGFR is more sensitive than creatinine but yet, lags far behind renal lesions.

Therefore, there is an urgent need for more sensitive and specific biomarkers of glomerular diseases with the aim of detecting early onset, predicting outcome, monitoring disease activity and adapting therapies. Such biomarkers are eagerly awaited in randomized clinical trials where it is no longer possible to rely on hard end points such as remission of nephrotic syndrome in chronic glomerulopathies or end-stage renal disease (ESRD), which calls for surrogate, reliable biomarkers. For instance, in patients with membranous nephropathy, a proteinuria end point at 12 months may be too soon to evaluate the true effect of treatment as mentioned by Fervenza and De Vriese [7], and some authors argue that this end point should not be earlier than 18 months from the start of treatment, that is 2 years from the diagnosis as an average [8].

In the past decade, a growing number of publications have been devoted to novel biomarkers of glomerular diseases. These biomarkers are the fruits of the substantial advances that have occurred in the understanding of the pathomechanisms of immune-mediated glomerulonephritis. But what has really been achieved that can be translated in practical terms for the pathologists, the clinicians and more importantly for the patients? Where do the advances modify diagnostic tests and classification of diseases leading to a new ontology? What