Reviewer’s report

Title: transcriptomic analysis reveals new aspects of the chronic kidney disease-related immune dysfunction

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Reviewer: Dominique Guerrot

Reviewer’s report:

The manuscript by Zaza and colleagues describes differences between the immune transcriptomic profile of stage 3 & 4 CKD patients and chronic hemodialysis patients.

The subject is clearly of interest, since CKD is increasingly recognized as a major cause of CV disease, while the mechanisms linking decreased GFR and inflammation on the one hand, and inflammation and CKD-associated CVD on the other hand are poorly understood.

This manuscript presents an interesting, original and hypothesis-generating work. By combining transcriptomic Affymetrix screening with secondary confirmation with mRNA and protein analyses, the authors provide convincing data which open new insights in this clinically relevant field.

I have several comments, as follow:

MAJOR REVISIONS:

- The absence of a control population is a major negative point, which decreases the value of the paper. For example, differences in the expression selected mRNA between HD and CKD patients may either reflect the indirect consequences of reduced clearance of “uremic toxins” in HD patients (especially middle size molecules), or consequences of the bioincompatibility due to the technique itself. Comparison with normal GFR patients would be helpful, even if I acknowledge the difficulty to select the control population due to potential biases related to comorbidities. In addition, it would be interesting to compare the magnitude of the differences between HD and CKD patients with the difference between these 2 populations and control patients.

- Since the focus is on the differences between CKD and RRT patients in this study, there is clearly a lack of details regarding the modalities and quality indicators of the extrarenal suppleance therapy. This should be added in the Methods paragraph and discussed. Specifically, at least the following data should be provided: Hemodialysis or pre- post- mid- mixed- hemodiafiltration technique, Kt/V, and Substituted volume (if HDF)

- The vascular access is a major source of inflammation in HD patients. Consequently, since inflammation and comparison between HD and non-HD is the heart of the subject, this information must be provided and adequately discussed: native AV fistula ? goretex ? central catheter ?
MINOR REVISIONS:

- What do the authors mean by non-immune mediated glomerulonephritis? If diabetes and cancer are excluded, etiologies of glomerular disease excluding immunological involvement are relatively rare (Alport, TBM, secondary FSGS,…). Could the authors please provide the diagnoses for these 7 patients?
- The stage of CKD patients or the mean GFR should be provided in the abstract.
- Limitations related to the choice of the genes studied (to which extent does this Affymetrix array provide a valuable overview of inflammation? What is excluded?) should be briefly discussed, for the clinicians who are not necessarily familiar with this technique. In addition limits related to the small size of the population should be emphasized.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:
No competing interest