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CD80 and suPAR in patients with Minimal Change Disease and Focal Segmental Glomerulosclerosis: Diagnostic and Pathogenic Significance: response

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Dr Davin challenges our recent study [1] proposing the utility of using serum suPAR and urinary CD80 level to distinguish idiopathic focal segmental glomerulosclerosis (FSGS) from minimal change disease (MCD). The basis of his argument relates to his supposition that CD80 is likely involved in FSGS, since urinary CD80 is elevated in our study compared to normal controls, and also because of a recent study by Yu et al. that showed the presence of CD80 in glomeruli in some subjects with post-transplant FSGS [2]. The observation that these latter patients had a resolution of proteinuria with CTLA4-Ig [2] which is a ligand for CD80 that blocks CD80 associated T cell activation, was also taken as evidence. Davin also suggests that the higher urinary CD80 levels in MCD may reflect passage of soluble CD80 in the urine as a consequence of activation of the immune system during MCD flares.

We agree that FSGS may be associated with glomerular staining CD80 [2] and with mildly elevated urinary CD80 excretion [1]. However, the increase in urinary CD80 is marked in MCD resulting in minimal overlap between the two groups. Indeed, in our study, 23 of 26 FSGS patients had their urinary CD80 values fall within 2 SD of normal values whereas only 3 of 20 MCD patients in relapse fall in the same group. Furthermore, there was also a separation in suPAR levels. Similarly, Segarra et al found that a serum suPAR level of >3531 pg/ml had a 99% ability to separate MCD and FSGS [3].

Dr. Davin suggests that higher CD 80 urinary levels in MCD than in FSGS might result from CD80 released by T cell during viral infections that usually trigger relapses in MCD. This suggestion is not supported by our early work that demonstrated that serum CD80 levels during relapse in MCD is not different than the one observed in MCD patients during remission and in normal controls [4].

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Potential conflict of interest: Jochen Reiser is an inventor on pending or issued patents around novel therapies in proteinuric kidney disease. He stands to gain royalties from their future commercialization.

The role of CD80 in podocyte diseases is still under active investigation and far from being definitive. There may also be additional differences in the role of CD80 in MCD and FSGS. For example, while CD80 may be present in glomeruli in FSGS, our recent experience suggests that the administration of CTLA-4 Ig is not able to reverse the proteinuria (Alachkar et al Letter to Editor NEJM, March 27, 2014). Indeed, the study by Yu et al [2], included the use of plasma exchange which could also provide a reason for the beneficial response. In contrast, we have found that the administration of CTLA-4 Ig to two patients with MCD resulted in a transient but marked suppression of urinary CD80 excretion and urinary protein excretion (Garin et al, unpublished). In addition, the urinary excretion of CD80 in MCD is due to cell membrane-associated CD80 and not soluble CD80.

We and others have found only a few FSGS patients showing CD80 glomerular staining with mild increase in urinary CD80 excretion. Most of our patients did not show CD80 glomerular staining and they have normal urinary CD80 excretion. In Yu et al study [2], we were surprised to see no data on urinary CD80 excretion even in those patients who had positive CD80 staining in glomerulus.

We do realize that more studies are needed on the sensitivity and specificity of serum suPAR and urinary CD80 in glomerular disease. In addition, studies on urinary suPAR may become increasingly valuable. Recently we did identify a patient with elevations in both who had a podocin-mutation associated FSGS. Thus, more studies are needed. However, our study and the study by Segarra do suggest that serum suPAR and urinary CD80 are in general excellent markers for identifying idiopathic FSGS and MCD, respectively.

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