PODOCYTE-ASSOCIATED MESSENGER RNA PROFILES IN LUPUS NEPHRITIS: DOES SEVERITY OF THE HISTOLOGICAL LESIONS HAVE AN EFFECT ON THE INTENSITY OF PODOCYTE INJURY?

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Introduction and Aims: Glomerular deposition of immune complexes and inflammation induce podocyte injury in lupus nephritis (LN). This study hypothesized that the severity of the histological lesions of LN affects podocyte-associated mRNAs profiles in kidney tissue and urine.

Methods: Thirty-three patients with LN were grouped according to the presence of mild mesangial (classes I and II) or moderate-to-severe immune complex deposition, proliferation and/or inflammation (classes III, IV and V) in kidney biopsy. Tissue and urine mRNA of nephrin, podocin, podocalyxin, α-actinin-4, transient receptor potential cation channel 6, and of growth factors VEGF-A and TGF-β1 and the transcription factor FOXP3 were measured using real time PCR. These mRNAs were correlated with histological severity of LN, extent of glomerular immune deposits, and tissue infiltrating cells.

Results: Podocyte-associated mRNAs were inhibited in renal tissue of patients with LN irrespective of histological class when compared to controls. However, significantly higher expression of podocyte mRNAs in urine, including those of growth factors and FOXP3, were found in patients with moderate-to-severe nephritis, mostly in class III and IV proliferative forms (Figure 1). The number of invading CD8⁺ T cells, B cells and macrophages correlated positively with urine podocyte mRNAs. The number of CD8⁺ T cells was greater in class III-IV-V patients. Although the number of CD68⁺ cells was greater in class III-IV-V patients, this result did not reach statistical significance compared with class I-II (Figure 2). Urine podocyte mRNAs also correlated with proteinuria levels.

Conclusions: Inhibition of podocyte-associated mRNAs in kidney tissue suggests that podocyte injury occurs regardless of class severity of LN. The higher excretion of podocyte mRNAs in urine, mostly in patients with moderate-to-severe lesions, may reflect more intense structural glomerular damage with detachment of podocytes to urine.