ESPN research grant 2018 interim report

Anne Couderc (Idiopathic Nephrotic Syndrome WG)

Anti-UCHL1 IgG in idiopathic nephrotic syndrome

Our study evaluating the link between Ubiquitin C-terminal hydrolase-L1 (UCH-L1) and Idiopathic Nephrotic Syndrome (INS) has produced some interesting results. UCH-L1 is expressed in cultured podocytes but is not detectable in glomeruli examined in renal biopsies from normal people as well as in patients with INS. Previously we identified that some patients with INS presented with anti UCH-L1 autoantibodies in the plasma that were correlated with the level of proteinuria. Moreover, anti UCH-L1 autoantibodies purified from patients with massive proteinuria induced proteinuria in mice.

Here, we studied the expression of UCH-L1 in cultured podocytes, in standard conditions and after activation of the different TLRs expressed in podocytes.

We observed that, in standard conditions of culture, UCH-L1 is mainly expressed in the cytoplasm of an immortalized podocyte cell line. Interestingly, UCH-L1 expression was significantly increased after TLR3 stimulation by Poly(I:C) for 48 hours. In addition, UCH-L1 expression was also addressed at the membrane after TLR3 activation. Interestingly, agonists of TLR3 include virus RNAs such as EBERs (the so called small RNAs associated to EBV infection) suggesting that UCH-L1 belongs to the podocyte response to virus and specially to EBV replication. Consequently, this study opens interesting perspectives about the role of UCH-L1 and anti UCHL1 autoantibodies in INS. Dr Stephanie Bonneric, a fellow in our department, will continue this work during her PhD. We plan to have definitive data during her PhD in the next years.

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