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Enhanced expression of AXL correlates with PLA2R in membranous nephropathy

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Objectives : Phospholipase A2 receptor （PLA2R）is the most frequently targeted auto-antigen in membranous nephropathy (MN), which accounts for approximately 70-80% primary MN. However, the precise mechanisms remain to be elucidated.The microarray data from the NEPTUNE study has revealed that AXL was among the top (1%) up-regulated genes in the glomeruli of patients with MN compared with other nephrotic syndrome.
Methods : To investigate the role of AXL played in glomerular injury of patients with MN, we performed RNAscope in situ hybridization, immunofluorescence and immunogold analyses and found that AXL was expressed in podocytes.
Results : Furthermore, the ELISA and immunohistochemical analyses revealed that the expression level of AXL was heightened and correlated with poor clinical features in serum and renal biopsy specimens from patients with MN. Notably, upon the stimulation with GAS6, the ligand of AXL, the level of PLA2R was upregulated in cultured human podocyte in vitro due to delayed degradation while the knockout of AXL reversed the effect. At last but not the least, CoIP and BLI experiments demonstrated that AXL interacted with PLA2R.
Conclusions : In conclusion, the present study shows that AXL is implicated in PLA2R overexpression in the pathogenesis of membranous nephropathy .