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Soluble ST2 is an early marker for hypertensive nephrosclerosis signatured in glomerular mesangial cell

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Objectives : Hypertensive nephrosclerosis (HN) holds significant clinical importance; nevertheless, the absence of a diagnostic marker for HN remains a challenge. Here, we explored the relationship between sST2 and early HN, with a specific emphasis on their interaction in glomerular mesangial cells.
Methods : This is a retrospective, human-derived material research conducted in participants who received kidney biopsy for suspected glomerular disease between 2019 and 2022. Serum sST2 levels of healthy control (HC), HN, and lupus nephritis (LN) groups were measured using an ELISA. The association between the level of serum sST2 and kidney function, stratified by quartiles of serum creatinine (SCr) and urine protein/creatinine ratio (uPCR), and the degree of mesangial proliferation was evaluated. In in vitro study, an intraglomerular hypertensive status was simulated using a pressurizing device, exerting a pressure of 3mmHg on primary cultured human mesangial cells (hPMC).
Results : Of total, 51 participants (HC, 9; HN, 15; LN, 27) were included. Serum sST2 levels were significantly higher in both HN and LN groups than the HC group (Figure 1). Even in the lowest quartile (Q1) of SCr and uPCR in HN, sST2 level was significantly higher than that of HC (Figure 2). Both HN and LN groups with mesangial proliferation had significantly higher serum sST2 levels than HC. When stimulated in a pressurizing device, hPMCs exhibited increased inflammation, apoptosis, and necrosis; these processes were markedly reduced after treatment with an sST2 blocking antibody.
Conclusions : sST2 may serve as a mesangial cell-specific diagnostic marker for early HN, particularly preceding changes in SCr or proteinuria. Furthermore, the inhibition of sST2 holds potential as a therapeutic agent for HN.

Figure 1.png

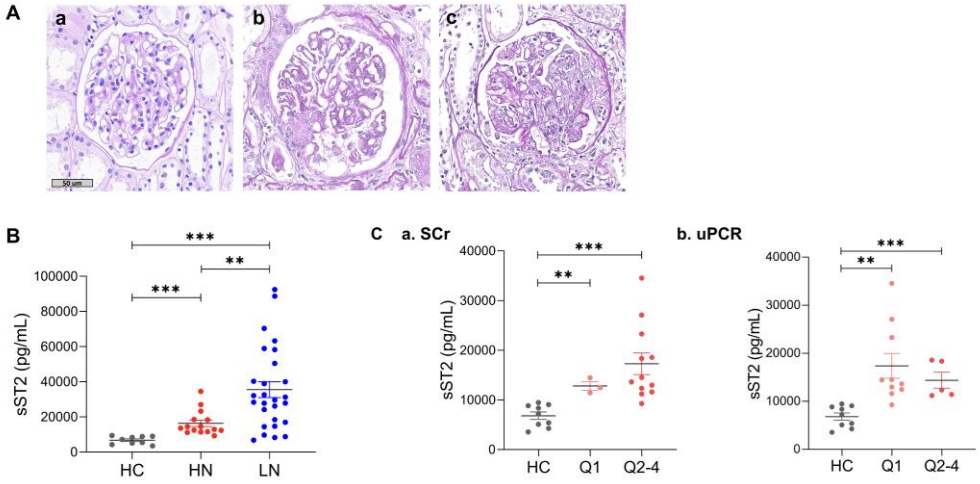
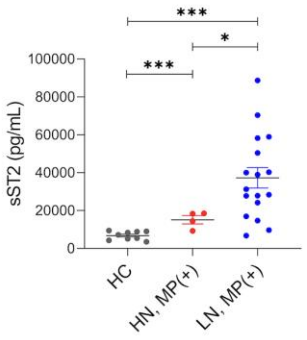


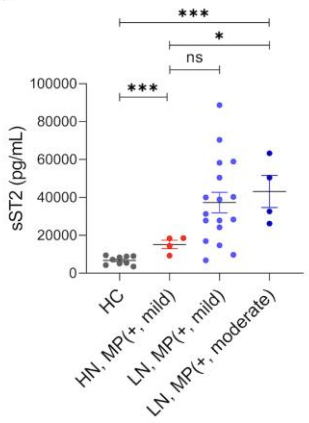
Figure 1.png

A. Mesangial proliferative HN and LN with sST2

a.

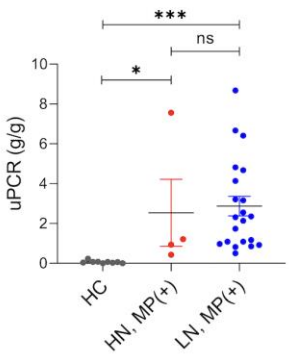


b.



B. Mesangial proliferative HN and LN with uPCR

a.



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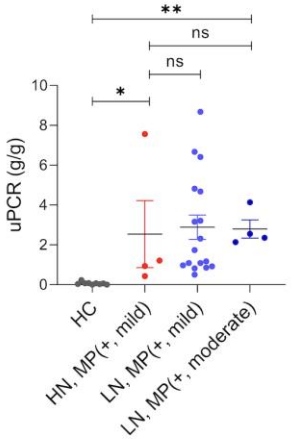
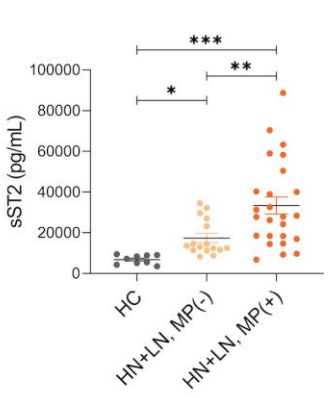


C. Mesangial proliferation in pooled HN and LN

a.



b.