COMPLEMENT ACTIVATION IN PODOCYTOPATHIES:

A PILOT STUDY TO DETERMINE ITS PATHOGENIC ROLE

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Disclosure of conflicts of interest:

I have nothing to disclose

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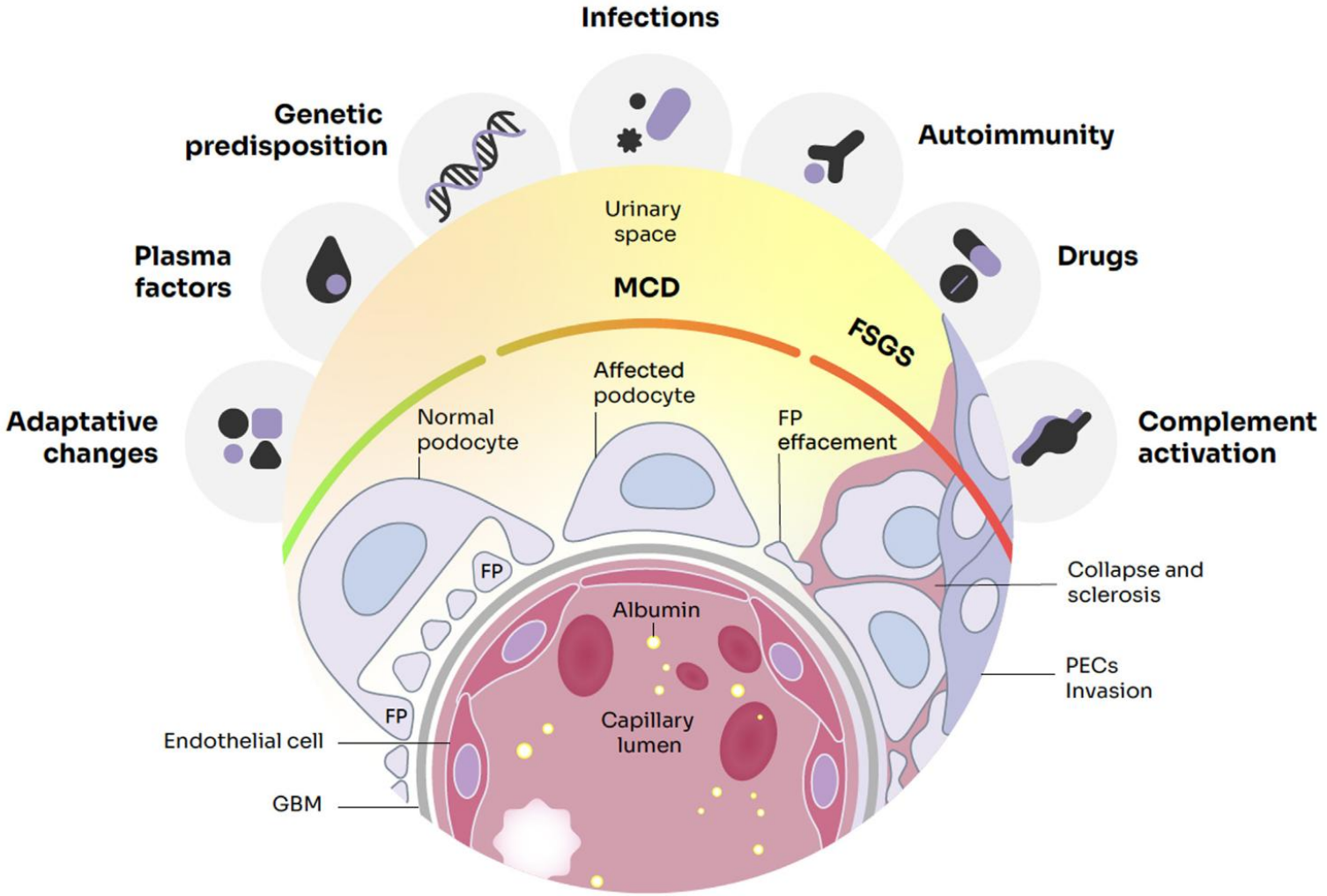
BACKGROUND

Potential pathogenetic mechanism related to podocyte damage



Kidney Int Rep. 2024 Jan 29;9(3):520-522.

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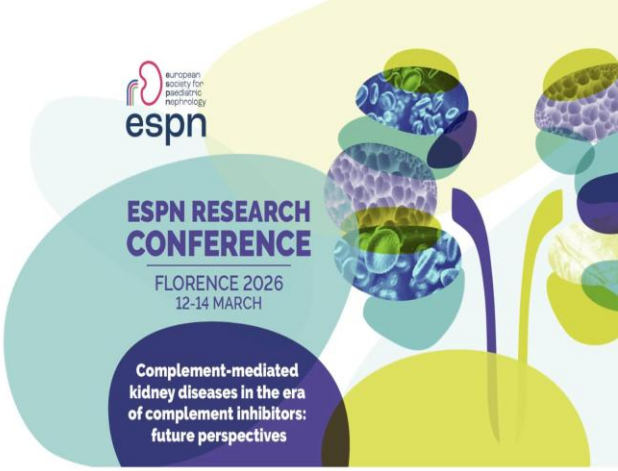
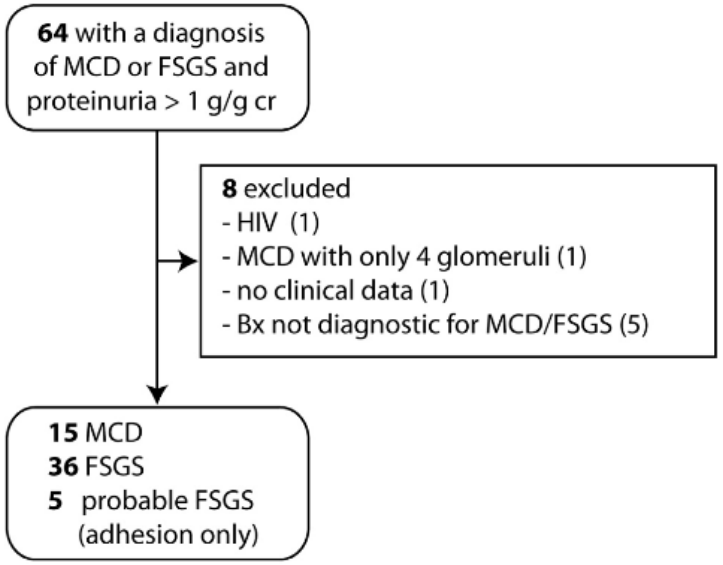
CLINICAL RESEARCH

A Prospective Study on Complement Activation Distinguishes Focal Segmental Glomerulosclerosis from Minimal Change Disease

Alexandra Cambier[1], Natacha Patey[2], Virginie Royal[3], François Gougeon[4], Dominique S. Genest[5], Soumeya Brachemi[6], Guillaume Bollée[6], Clémence Merlen[7], Arnaud Bonnefoy[7], Anne-Laure Lapeyraque[1] and Stéphan Troyanov[5,8]





- Cambier et al compared urinary fragments of terminal pathway activation, sC5b9, and C5a expressed as creatinine ratios, between MCD and FSGS.
- They included patients with proteinuria >1 g/g creatinine.

Kidney Int Rep. 2023 Dec 29;9(3):661-670.

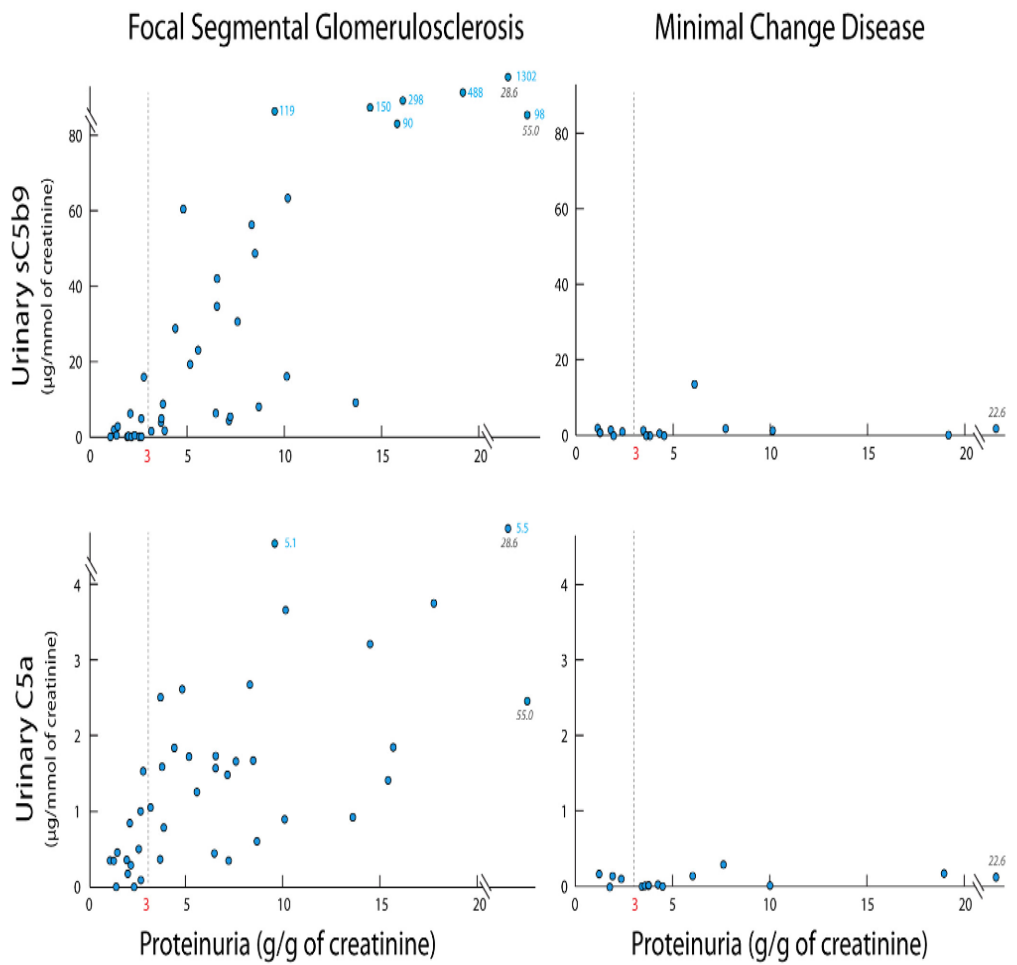


Figure 2. Urinary sC5b9 and C5a creatinine ratios compared to proteinuria in focal segmental glomerulosclerosis and minimal change disease. FSGS, focal segmental glomerulosclerosis; MCD, minimal change disease. Proteinuria was associated with urinary sC5b9 ($\rho = 0.85$; $P < 0.001$) and C5a ($\rho = 0.71$; $P < 0.001$) in FSGS, but not in MCD ($P > 0.05$).

- Patients with FSGS presented urinary sC5b9 levels of 8.7 (1.7–52.3) mg/mmol of creatinine, which was much higher than 0.8 (0.0–1.5) mg/mmol of creatinine in MCD;
- Patients with FSGS also showed significantly higher urinary levels of C5a (1.26 mg/mmol of creatinine) than patients with MCD (0.06 mg/ mmol of creatinine.

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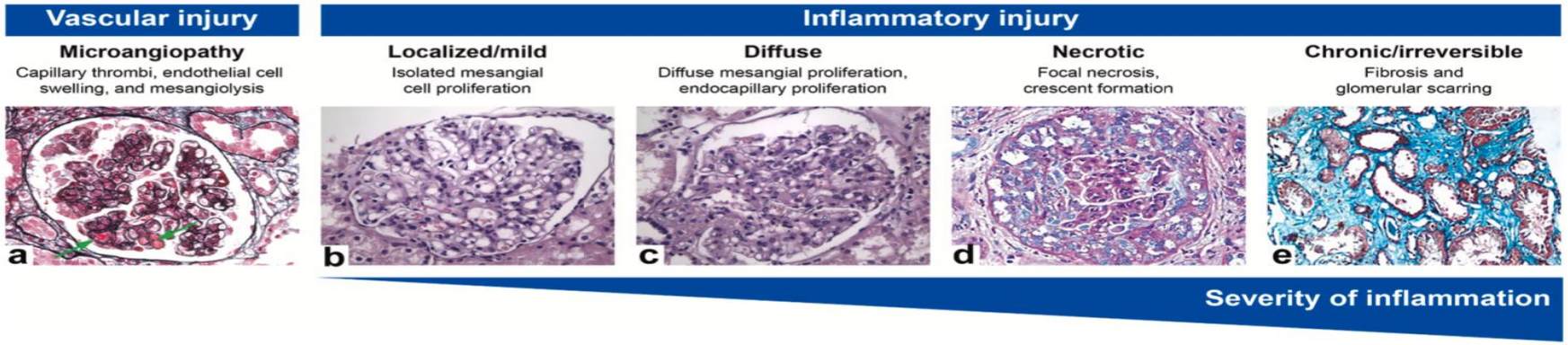
Complement and Podocytopathies: Do We Have a New Biomarker?

1) The FSGS population was significantly older, and many patients already had advanced chronic kidney disease compared to patients with MCD;

2) The FSGS population had higher histological chronicity findings compared to patients with MCD;

3) Do terminal complement components in the urine reflect the activity of FSGS lesions or are they just reflective of the severity and chronicity of kidney injury? The degree of urinary complement fragments may be influenced by impairment of kidney function, level of proteinuria, and metabolic acidosis.



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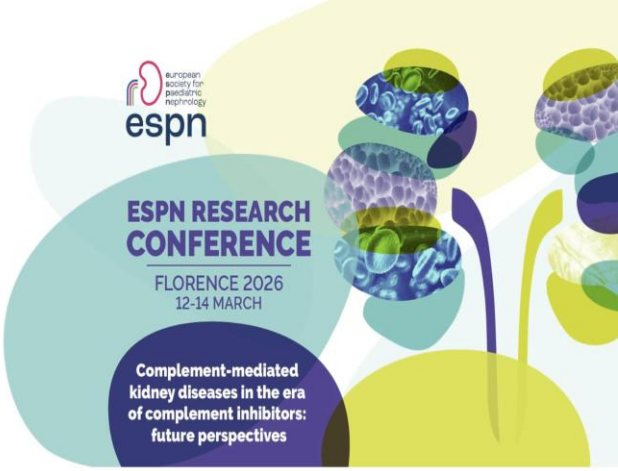
PURPOSE



- To evaluate urinary and plasma sC5b9 levels in pediatric patients with SSNS and SRNS (genetic and non-genetic) with preserved renal function, compared with patients with non–immune-mediated chronic kidney failure;

- To assess the potential role of urinary sC5b9 as a biomarker for prognosis and personalized therapy.

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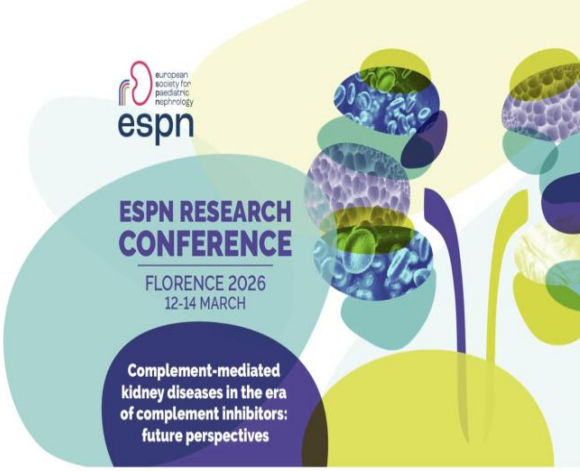
METHODS

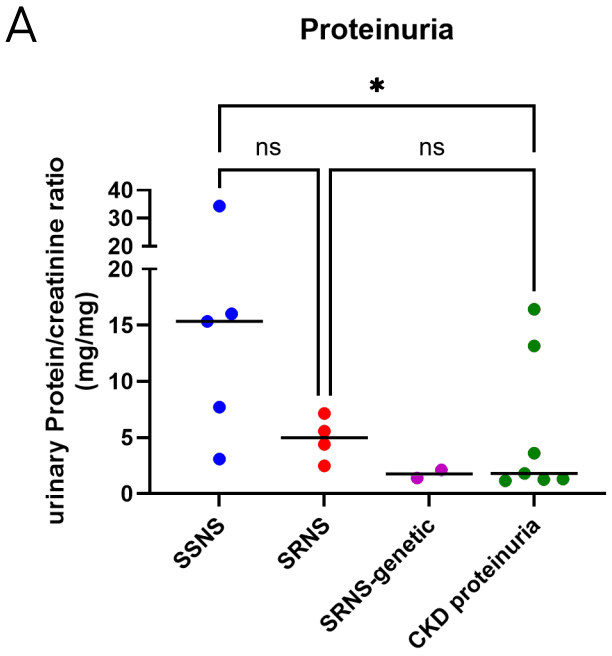


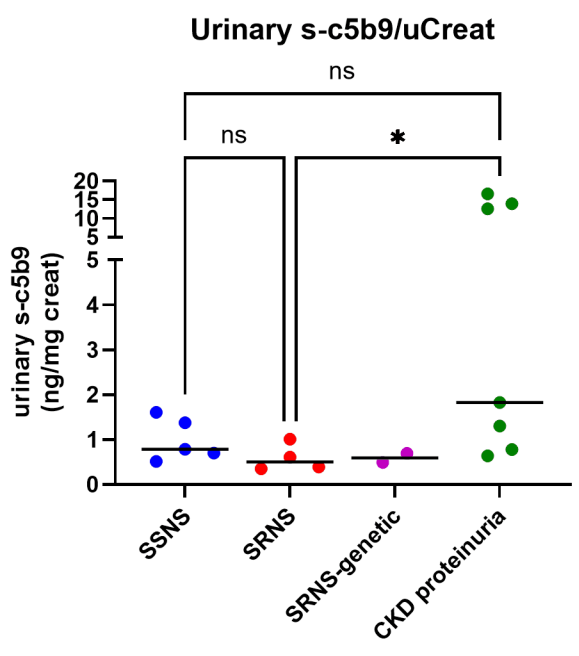
We conducted a prospective observational pilot study in pediatric patients followed at Bambino Gesù Children's Hospital.

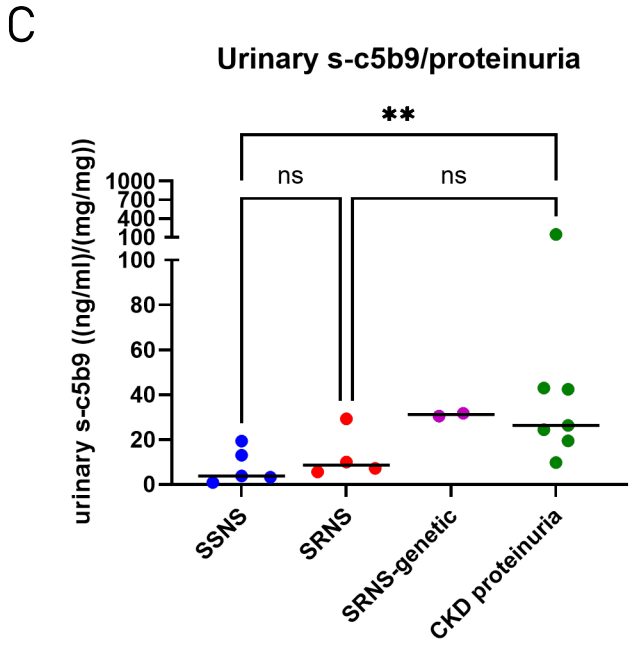
Patient selection

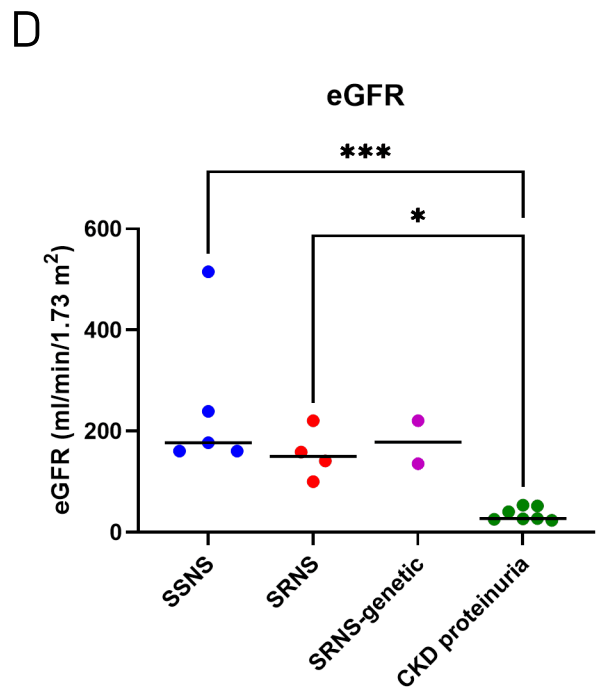
18 children with active proteinuria (uPCR >1 mg/mg) were enrolled

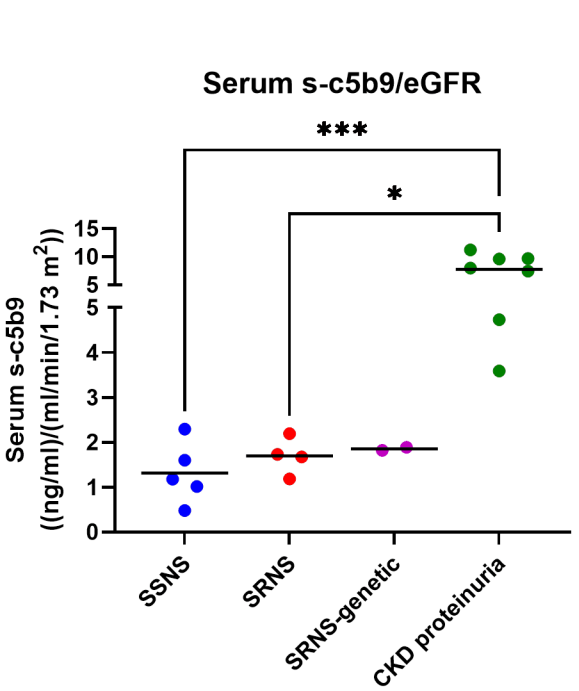
- SSNS (n=5)
- non-genetic SRNS (n=4)
- genetic SRNS (n=2)
- non–immune-mediated CKD (n=7) (eGFR <75 ml/min/1.73 m²)

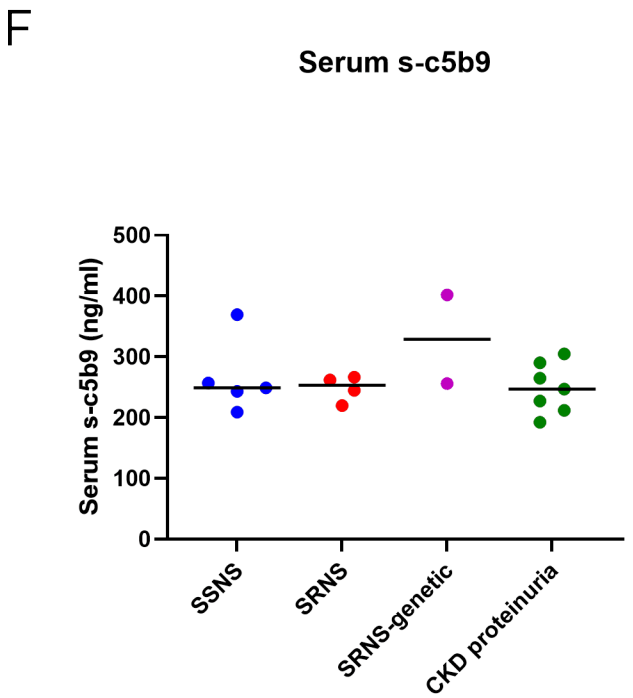












RESULTS

Correlation
Urinary s-c5b9 vs eGFR
r= -0.60, p<0.01

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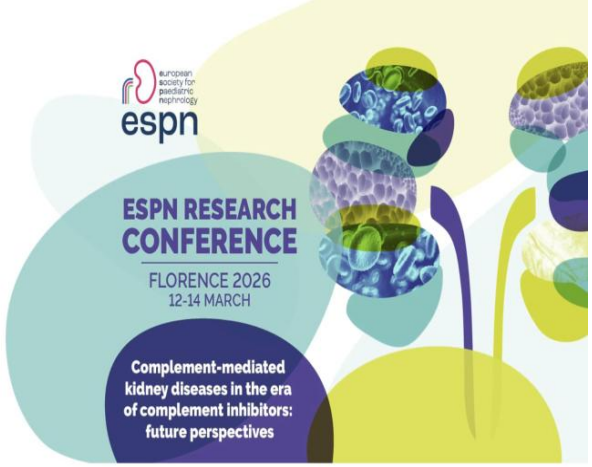
CONCLUSIONS



- Urinary and plasma sC5b9 levels were similar in SSNS and SRNS (genetic and non-genetic) when renal function was preserved;
- CKD patients showed significantly higher urinary and plasma sC5b9, even after normalization, compared with SSNS and SRNS;
- Urinary sC5b9 correlated inversely with eGFR, but not with proteinuria, across the whole cohort;
- Increased sC5b9 appears to be secondary to reduced kidney function, rather than a primary pathogenic mechanism in SSNS or SRNS;
- These results need confirmation in larger studies and more disease types.

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