

## Molecular genetic identification of PODXL nonsense mutation in a family with familial renal disease

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### Background

Podoclyxin, a transmembrane protein and a component of the filtration barrier in podocytes is encoded by PODXL. Pathogenic variants in PODXL have recently been described in families with autosomal dominant focal segmental glomerulosclerosis. Here we report a family, originally from Sudan, with variable phenotypes, including end stage renal disease and haematuria and proteinuria with preserved renal function in an autosomal dominant pattern.

### Methods

Clinical, pathological and family history data were combined with whole genome sequencing data in the proband and segregation analysis in other family members.

### Results

The proband had presented at the age of 20 years with haematuria but with preserved renal function. During her first pregnancy significant proteinuria developed prompting a renal biopsy post partum which showed thin basement membrane disease. A second pregnancy was also complicated by significant proteinuria. A family history revealed 4 out of 7 siblings had haematuria and the proband's mother who had developed end stage renal disease at 50 years of age. A maternal uncle also was reported to have end stage renal disease. Genetic testing was performed in the proband and mutations in COL4A3, COL4A4 and COL4A5 were excluded. Whole genome sequencing identified a heterozygous nonsense mutation in PODXL which segregated from her mother. Wider family screening is now taking place.

### Conclusion

In a large family with familial haematuria and end stage renal disease we have identified a pathogenic variant in PODXL as the likely cause. This widens the phenotypic spectrum of disease associated with PODXL mutations, which was recently reported to be associated with FSGS.