Athanasiou et al.: CFHR5 and isolated C3 glomerulopathy

SUPPLEMENTARY MATERIAL

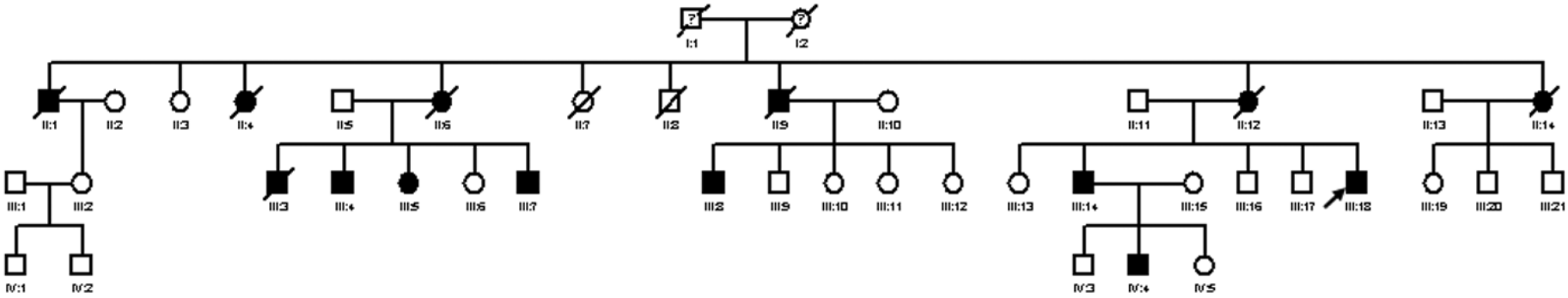
DESCRIPTION OF TWO FAMILIES

Family CY5388 (Supplementary Figure 1A): The proband was first seen in late 1988, at age 36, with a long history of episodes of recurrent macroscopic hematuria, continuous microscopic hematuria, mildly elevated serum creatinine at 1.5 mg%, hypertension and proteinuria at 1.2g/day. A renal biopsy was performed in June 1990. There were six glomeruli and one was sclerosed. The remaining showed mesangial hypercellularity with increased matrix. Immunofluorescence and EM were not available. No definitive diagnosis could be made. The patient lost renal function gradually and he received a renal transplant in 1995. Fifteen years later the patient remains well with a functioning kidney graft. It gradually became evident that there was a strong family history, with his mother also showing microscopic hematuria but no renal impairment. One maternal aunt an uncle and a cousin eventually reached hemodialysis. The cousin who had continuous microscopic hematuria and repeated episodes of macroscopic hematuria died suddenly from an acute myocardial infarct at age 50. In 2009, when a molecular genetic analysis for CFHR5 was performed this family was found to have the same mutation. At this time 9 family members have been screened and 6 mutation carriers were identified.

F**amily CY5399 (Supplementary Figure 1B):** The proband was referred to the Dept of Nephrology in Sept 1998 at age 12, with continuous microscopic hematuria and intermittent episodes of macroscopic hematuria beginning at age 6 and continuing almost

annually, with every feverish URTI. She was considered to have IgA nephropathy and because of the young age, the absence of proteinuria and the normal kidney function, no biopsy was attempted. At age 21, in 2007, she presented with another episode of synpharyngitic macroscopic hematuria and continues to have microscopic hematuria currently. In Sept 2009, her younger brother, aged 19, while serving in National Guard, developed a pyrexial tonsillitis with gross, macroscopic hematuria at the same time. This settled with antibiotics. Renal US studies were normal. The initial impression of familial IgA nephropathy was abandoned when molecular studies for the CFHR5 nephropathy, that had just being recognised, proved positive. The father, aged 48 also carries the *CFHR5* mutation. He was found to have microhematuria that he was not aware. He has no proteinuria and like his two children he maintains normal kidney function. In view of the molecular diagnosis, characteristic clinical features and preserved renal function no renal biopsies have been performed.

Supplementary Figure 1A



Supplementary Figure 1B