CFHR5 Nephropathy

Contact details

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Samples required

- 5ml venous blood in plastic EDTA bottles (>1ml from neonates)
- A completed DNA request card should accompany all samples

Patient details

To facilitate accurate testing and reporting please provide patient demographic details (full name, date of birth, address and ethnic origin), details of any relevant family history and full contact details for the referring clinician

Introduction

Affected individuals display persistent microscopic haematuria with episodes of macroscopic haematuria associated with intercurrent infections (commonly of the respiratory tract). Renal biopsy demonstrates C3 glomerulonephritis (C3GN, a type of mesangiocapillary glomerulonephritis (MCGN)). 80% men and 20% affected women develop renal failure by the 8th decade of life. The incidence of *CFHR5* nephropathy in the Cypriot population is estimated at 1/1000 to 1/8000; prevalence in the UK Caucasian population is low (<1:100,000) since C3GN is a very rare diagnosis. This autosomal dominant condition is caused by a mutation in the Complement Factor H-Related gene 5 (*CFHR5*; MIM: *608593). The gene is homologous to *Complement Factor H* and *Complement Factor-H Related genes 1-4* which lie at neighbouring loci. *CFHR5* consists of 10 exons which code for 9 homologous short consensus repeat domains, each of which has two internal disulphide bridges. The protein product of *CFHR5* has the ability to co-localise with (and regulate activation of) complement C3 in the kidney.

The most common *CFHR5* gene mutation is a duplication of exons 2 and 3 (c.59-1808_430+3242dup) described in the Cypriot population. Only one other mutation has been published, a frameshift in exon 4 identified in one non-Cypriot C3GN patient.

Referrals

Referrals are accepted from Consultant Clinical Geneticists and Consultant Nephrologists in the following patients:

Cypriot origin with unexplained haematuria or renal disease.

Patients of any ethnicity may be referred if C3GN or MCGN is present.

At risk family members where the familial mutation is known.

Service offered

Detection of exon 2-3 duplication: A single PCR reaction incorporates primers that amplify both a 298bp fragment of the wild type sequence and a 222bp fragment unique to the duplication.

Detection of other mutations: PCR amplification of all 10 exons of *CFHR5* followed by Sanger sequence analysis.

Target reporting time

2 weeks for duplication analysis. 8 weeks for full sequencing analysis of *CFHR5*. Please contact the laboratory for urgent cases.