NewGene
Next Generation Diagnostics

NewGene Clinical Services

Utilising the latest technologies to deliver molecular diagnostics and genomic services, NewGene is able to offer significant benefits leading to improved clinical delivery:

- **TURNAROUND** - Clinically relevant turnaround times
- **RESPONSE** - Emerging clinical need can be met with rapid development of new tests
- **SAVINGS** - The high throughput capacity of the technology gives rise to savings in both time and cost
- **QUALITY** - An excellent track record in external quality assessment
- **FLEXIBILITY** - NewGene can develop a bespoke service to meet your specific needs.

All results and interpretation are reported by an HCPC registered Clinical Scientist.
NewGene also works closely with the NHS and pharmaceutical companies on the validation of biomarkers and the development of diagnostic tests.

Atypical Haemolytic Uraemic Syndrome

Atypical haemolytic uraemic syndrome (aHUS) is characterised by haemolytic anaemia, thrombocytopenia and acute renal failure. Causative mutations have been identified in the genes that encode the various components and regulators of the alternative complement pathway. These include the complement regulators, factor H (*CFH*), factor I (*CFI*) and membrane cofactor protein (*CD46*), and the complement activators factor B (*CFB*) and complement factor C3 (*C3*). Mutations in these genes are found in 60% of aHUS cases in both the familial and sporadic forms of the disease.

With aHUS, recovery of renal function is uncommon and many patients require long-term dialysis or a kidney transplant.

However, as most complement proteins are produced by the liver, a kidney transplant in patients with a *CFH, CFI, C3* or *CFB* mutation is likely to be lost to recurrent disease.

In contrast, membrane cofactor protein is a transmembrane protein expressed by nearly all cell types with high levels of expression in the kidney, where it functions locally to limit complement activity.

Consequently, in patients who have aHUS secondary to a *CD46* mutation, recurrence is unusual after transplantation of kidneys that express normal membrane cofactor protein. It is important, therefore, to define the etiology of aHUS prior to kidney transplantation.

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Mutation screening in aHUS

Mutation screening of these complement genes by Sanger sequencing was established in the Northern Molecular Genetics Service in Newcastle in 2005. In a collaborative programme NewGene has applied the parallel sequencing capability of next generation sequencing to this clinical setting. The results demonstrate rapid diagnosis enabling timely decision making on appropriate treatment pathways

The test includes the simultaneous analysis of all coding regions and splice sites in five key genes:

- *CFH* (factor H)
- *CD46* (membrane cofactor protein)
- *CFI* (complement factor I)
- *C3* (complement factor C3)
- *CFB* (complement factor B)

Mutations in these genes are found in 60% of aHUS cases. While the disorder membrano-proliferative glomerulonephritis (MPGN II) is frequently related to homozygous Factor H deficiency.

In addition NewGene has developed a single nucleotide polymorphism (SNP) genotyping assay. Combining accurate primer extension chemistry with MALDI-TOF mass spectrometry, this simple Sequenom test targets eight SNPs within three aHUS genes (*C3, CFH and CFI*). The SNP profiles from each patient are subsequently compared to confirm sample identity within each tested batch of patients.

Confirmation of the mutation status of all positive samples for hereditary disorders will be carried out by bi-directional Sanger sequencing.

For more information visit our website:
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