Mucopolysaccharidosis type 3 (MPS3) (Sanfilippo syndrome)

Introduction
Mucopolysaccharidosis type 3 (MPS3 / Sanfilippo syndrome MIM #252900) is an autosomal recessive lysosomal storage disorder caused by impaired degradation of heparan sulfate (found in the urine of affected patients). The syndrome is characterised by severe central nervous system degeneration, but only mild somatic disease (moderately severe claw hand and visceromegaly, little or no corneal clouding or skeletal change). Onset of clinical features usually occurs between 2 and 6 years; severe neurologic degeneration occurs in most patients between 6 and 10 years of age leading to a vegetative state, and death occurs typically during the second or third decade of life (primarily from aspiration pneumonia). Type A is reported to be the most severe of the 4 subtypes of Sanfilippo syndrome with earlier onset and rapid progression of symptoms and shorter survival (typically during the teens).

Affected patients have a characteristic pattern of urine metabolites and a deficiency in one of the enzymes involved in heparan sulphate degradation; biochemical enzyme analysis utilises these features to confirm a clinical diagnosis.

Testing is currently available for types A and B which are due to deficiencies of the enzymes N-sulfoglucosamine sulfohydrolase (SGSH) and alpha-N-acetylglucosaminidase (NAGLU), respectively. There have been several recurrent mutations identified in both the SGSH and NAGLU genes although these are generally population specific.

Referrals

- Clinically affected patients should have their diagnosis confirmed by biochemical analysis (including disease subtype e.g. A); this should be arranged either locally or with the Enzyme Unit, Great Ormond Street Hospital. Such patients may then be referred for mutation analysis. If the necessary patient samples are unavailable genetic testing can be undertaken in the parents of the affected child.

- Carrier testing can be offered to the adult relatives of affected patients once a disease causing mutation has been identified.

Prenatal testing
Prenatal testing is available for families in whom mutations have been identified or in whom appropriate family studies have been undertaken. This service is also offered by biochemical analysis. Please contact the laboratory to discuss.

Service offered

- Mutation screening: Direct sequencing of all coding exons and intron-exon boundaries.
- Detection of known mutations in relatives of patients with confirmed MPS3A or MPS3B mutations by direct sequencing.

Target reporting time
8 weeks for routine mutation screen in index case. 2 weeks for carrier testing using mutation specific tests. For urgent samples please contact the laboratory.

Contact details for Biochemistry/ Enzyme Unit:
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