**Hereditary Mixed Polyposis Syndrome**

**HMPS1 OMIM 601228, 603054 (GREM1); HMPS2 OMIM 610069, 601299 (BMPR1A)**

**INTRODUCTION**

Hereditary mixed polyposis syndrome is characterised by polyps of multiple and mixed morphologies and an increased risk of colorectal carcinoma. Polyp types include: juvenile polyps, Peutz-Jeghers polyps, serrated polyps and adenomas. Inheritance is autosomal dominant. Altered expression of two genes is reported in association with HMPS. These are GREM1 (HMPS1) and BMPR1A (HMPS2).

HMPS1 is caused by a ~40kb duplication of the region from exon 2 of SCG5 (upstream of GREM1) to just upstream of the CpG island of GREM1. The duplication has so far only been identified on a specific haplotype and in HMPS patients of Ashkenazi heritage, (Jaeger et al, Nature Genetics, 44(6), June 2012).

HMPS2 is caused by loss of function variants in the BMPR1A gene, irrespective of ethnic origin (O’Riordan et al, Colorectal Disease, 12, 570-573, Cao et al, J. Med. Genet, 2006, 43, e130).

**TESTING AND REFERRALS**

**Diagnostic:**
- Clinically affected patients.
- UK referrals must be made through Clinical Genetics departments.

**Pre-symptomatic test for Familial Mutation:**
- Individuals at risk of developing HMPS. Clinically unaffected relatives of individuals in whom a HMPS causing pathogenic mutation has been identified.
- Referrals from Clinical Genetics only.
- Requests for pre-symptomatic testing should either be discussed with the laboratory in advance or be accompanied by details regarding the known pathogenic mutation in the family.

**Prenatal:**
- Prenatal testing is not usually requested.
- Prenatal requests would only be accepted from Clinical Genetics and must be discussed with the laboratory and arranged in advance.

**STRATEGY & TECHNICAL INFORMATION**

- Mutation screening in diagnostic referrals is undertaken as follows; 
  - BMPR1A: fluorescent sequencing analysis of exons 1-11 and dosage analysis by multiplex ligation-dependant probe amplification (MLPA) for large scale deletions/duplications
  - GREM1 duplication: PCR and fragment analysis across the GREM1 duplication breakpoint.
- When a pathogenic mutation has been identified in an individual, subsequent testing of family members (presymptomatic or diagnostic confirmation) involves testing for the familial mutation only.

**TARGET REPORTING TIMES**

- Diagnostic test (BMPR1A): 40 working days
- Diagnostic test (GREM1): 10 working days

N.B. Details are correct for the date of printing only – last updated 09/08/2012

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**Sample Requirements:**

5-10ml venous blood in plastic EDTA bottles (>2ml from neonates)

A completed DNA request card should accompany all samples.

Consent for testing is assumed to have been obtained by the referring consultant.

**Contact Details:**

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http://www.ouh.nhs.uk/geneticslab

**Useful links:**

http://www.ukgtn.org/  
http://www.eddnal.com/  
http://www.geneclinics.org/

Online Mendelian Inheritance in Man