INTRODUCTION

MAP is an autosomal recessive polyposis predisposition; clinical presentation may be similar to that of attenuated or classical FAP. It is caused by biallelic mutations in the MUTYH gene, which is involved in base excision repair of DNA mismatches during DNA replication.

Two pathogenic variants together account for approximately 73% of MUTYH mutations in the Caucasian population1; these are c.536A>G; p.Tyr179Cys (p.Y165C) in exon 7 and c.1187G>A; p.Gly396Asp (p.G382D) in exon 13. As inheritance of the condition is recessive, approximately 53% of affected Caucasian individuals are homozygous or compound heterozygous for these two variants and ~40% carry one of the variants in addition to a rare mutation. ~7% MAP patients have neither of these two mutations.

There is also a founder mutation in the Indian population – c.1438G>T; p.Glu480X (p.E466X4).

1: Cheadle and Sampson, 2007, MUTYH-associated polyposis–From defect in base excision repair to clinical genetics testing, DNA Repair, 6:274-9

TESTING

Diagnostic: Clinically affected patients
Presymptomatic: Relatives of individuals in whom MUTYH pathogenic mutations have been identified who are at risk of developing MAP (for example siblings)
Carrier: Clinically unaffected individuals at risk of being carriers of MUTYH mutations, for example relatives of known mutation carriers or affected individuals. Spouses of mutation carriers may also need carrier testing.
Prenatal: Prenatal testing is not usually requested.

REFERRALS

- All UK diagnostic & presymptomatic/predictive referrals should be referred through Clinical Genetics departments.
- Requests for presymptomatic/predictive testing should either be discussed with the laboratory in advance or be accompanied by details regarding the pathogenic variant known to be in the family.
- Prenatal requests are only accepted from Clinical Genetics and must be discussed with the laboratory in advance of sample receipt.

STRATEGY & TECHNICAL INFORMATION

- We routinely test only for the two common Caucasian mutations (p.Tyr179Cys & p.Gly396Asp) and, if requested, the common Indian/Asian mutation (p.Glu480X). We do not offer an in-house screen of the remainder of the gene for rare mutations.
- When a pathogenic variant has been identified in an individual, subsequent testing of family members (presymptomatic or diagnostic confirmation) involves testing for the familial variant only.

TARGET REPORTING TIMES

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Reporting Time</th>
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<tbody>
<tr>
<td>Diagnostic test</td>
<td>10 working days</td>
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<tr>
<td>Presymptomatic/Familial Mutation test</td>
<td>10 working days</td>
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N.B. Details are correct for the date of printing only - last updated 11/06/2015