Oxford Molecular Genetics Laboratory

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Next Generation Sequencing Cancer Panel (Hereditary Cancer Solutions)

The oxford Medical Genetics Laboratory offers sequence and copy number analysis of a number of hereditary cancer genes using our next generation sequencing (NGS) panel.
Diagnostic samples undergoing NGS are processed for the full panel of 38 genes but analysis and interpretation is restricted to genes of clinical importance based on patient/family phenotype. Data reveal and analysis of additional clinically relevant genes is available, if required. Please see commonly requested panels below - in special cases, combinations of the panels listed can be analysed and patient specific 'custom' panels can be put together.
Single, syndromic associated genes are also analysed using this methodology

Panel	Genes
Bowel cancer/polyp >10 polyps/FH CRC	***APC, BMPR1A, EPCAM*, GREM1*, MLH1, MSH2, MSH6, MUTYH, NTHL1, PMS2, POLD1, POLE, PTEN, SMAD4, STK11***
Lynch-like MSI high	***EPCAM*, MLH1, MSH2, MSH6, MUTYH, PMS2, POLD1, POLE***
Breast cancer	***BRCA1, BRCA2, CHEK2* c.1100del, *PALB2, PTEN, STK11, TP53***
Ovarian cancer	***BRCA1, BRCA2, BRIP1, EPCAM*, MLH1, MSH2, MSH6, RAD51C, RAD51D***
Breast-ovarian cancer	***BRCA1, BRCA2, BRIP1, CHEK2* c.1100del, *EPCAM*, MLH1, MSH2, MSH6, PALB2, PTEN, RAD51C, RAD51D, STK11, TP53***
Breast-gynaecological cancer	***BRCA1, BRCA2, BRIP1, CHEK2* c.1100del, *EPCAM*, MLH1, MSH2, MSH6, MUTYH, PALB2, POLD1, POLE, PTEN, RAD51C, RAD51D, STK11, TP53***
Breast-bowel cancer	***APC, BMPR1A, BRCA1, BRCA2, CHEK2* c.1100del, *EPCAM*, GREM1*, MLH1, MSH2, MSH6, MUTYH, NTHL1, PALB2, PMS2, POLD1, POLE, PTEN, SMAD4, STK11, TP53***
Paraganglioma/phaeochromocytoma	***FH, MAX, RET, SDHA#, SDHAF2, SDHB, SDHC, SDHD, TMEM127, VHL***
Prostate cancer	***BRCA1, BRCA2, CDH1, CHEK2* c.1100del, *TP53***
Pancreatic cancer	***CDKN2A, BRCA2, EPCAM*, MLH1, MSH2, MSH6, PALB2***

ROI: *POLD1* (exons 8-13), *POLE* (exons 9-14), *PTEN* (includes promoter), *CDK4* (exon 2), *RET* (exons 10&11).
*Analysis of *EPCAM* and *GREM1* is for copy number changes only.
#Sequence analysis of *SDHA* is undertaken by Sanger Sequencing. Copy number analysis is not undertaken.
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REFERRAL PROCEDURE

- Diagnostic referrals are accepted from clinical genetics only. For NHSE referrals please refer to eligibility criteria: https://www.england.nhs.uk/wp-content/uploads/2018/08/rare-and-inherited-disease-eligibility-criteria-march-19.pdf
- If a pathogenic/likely pathogenic is found using NGS, family testing can be undertaken using Sanger sequencing or MLPA.
- Clinical information and details of relevant family history should be provided with all referrals.
- Further information about the cancer panels can be obtained from the laboratory (oxford.cancergenetics@nhs.net)

STRATEGY AND TECHNICAL INFORMATION

- Sequence and dosage analysis is undertaken by Next Generation Sequencing using the Custom Hereditary Cancer Solution (HCS) by Sophia Genetics along with the Sophia DDM analytical platform. Data is generated for 38 cancer susceptibility genes with analysis restricted to the relevant panel. Data reveal and analysis of additional clinically relevant genes is available, if required.
- Regions of interest (ROI) are minimally defined as coding exons +/- 10bp and covered to 100% at >50x reads. Analytical sensitivity for single nucleotide substitutions is estimated to be >99%; analytical sensitivity for small insertions/deletions may be slightly lower.
- Putative pathogenic variants detected by NGS are confirmed by Sanger sequencing or Multiplex Ligation-dependent Probe Amplification (MLPA), as appropriate.

TARGET REPORTING TIMES (National Target)

Diagnostic screen <10 genes:	42 calendar days
Diagnostic screen ≥10 genes:	84 calendar days
Predictive testing for known familial variant:	14 calendar days
Diagnostic testing for known familial variant:	42 calendar days

NB This information is only valid on the day of printing – last updated 23/10/2019