Oxford Molecular Genetics Laboratory

Genetics Laboratories, Churchill Hospital, Old Road, Headington, Oxford, OX3 7LE
www.ouh.nhs.uk/geneticslab

Next Generation Sequencing Cancer Panel

The Oxford Medical Genetics Laboratory offers analysis of a number of hereditary cancer genes using our next generation sequencing (NGS) panel. Although most genes are also offered by the laboratory in isolation, the panel is often the primary testing route for patients.
Although diagnostic samples undergoing NGS are processed for the full panel of 80 genes, analysis and interpretation is restricted to genes of clinical importance based on patient/family phenotype. This approach means that if further cancers develop later in life, unmasking and reanalysis of further genes from the panel can be undertaken. This methodology does not provide 100% coverage of all genes. As a laboratory we use Sanger sequencing to ensure full coverage for a number of the highly penetrant genes and for analysis of some technically demanding genes. These are highlighted in bold in the table below. Coverage for each gene is stated on the clinical report.
In special cases, combinations of the panels listed can be analysed and patient specific 'custom' panels can be put together.

Panel	Genes	MLPA
Bowel cancer/polyp >10 polyps/FH CRC	***APC***, ***BMPR1A***, ***MLH1***, ***MSH2***, ***MSH6***, *MUTYH, NTHL1,* ***POLD1***, ***POLE***, ***PTEN***, ***SMAD4***, *STK11*	*APC, GREM1, MLH1, MSH2, MSH6, EPCAM*
Lynch-like MSI high	***MLH1***, ***MSH2***, ***MSH6***, *MUTYH,* ***PMS2***, ***POLD1***, ***POLE***	*MLH1, MSH2, MSH6, PMS2, EPCAM*
Breast	*ATM,* ***BRCA1***, ***BRCA2***, *CHEK2, PALB2,* ***PTEN***, *STK11,* ***TP53***	*BRCA1, BRCA2*
Ovarian	***BRCA1***, ***BRCA2***, *BRIP1,* ***MLH1***, ***MSH2***, ***MSH6***, *RAD51C, RAD51D*	*BRCA1, BRCA2, MLH1, MSH2, MSH6*
Breast-ovarian	*ATM,* ***BRCA1***, ***BRCA2***, *BRIP1, CHEK2,* ***MLH1***, ***MSH2***, ***MSH6***, *PALB2,* ***PTEN***, *RAD51C, RAD51D, STK11,* ***TP53***	*BRCA1, BRCA2, MLH1, MSH2, MSH6*
Breast-uterine-ovarian	*ATM,* ***BRCA1***, ***BRCA2***, *BRIP1, CHEK2,* ***MLH1***, ***MSH2***, ***MSH6***, *MUTYH, PALB2,* ***POLD1***, ***POLE***, ***PTEN***, *RAD51C, RAD51D, STK11,* ***TP53***	*BRCA1, BRCA2* (further MLPA based on family history)
Breast-bowel	***APC***, *ATM,* ***BMPR1A***, ***BRCA1***, ***BRCA2***, *CHEK2,* ***MLH1***, ***MSH2***, ***MSH6***, *MUTYH, NTHL1, PALB2,* ***POLD1***, ***POLE***, ***PTEN***, ***SMAD4***, *STK11,* ***TP53***	*BRCA1, BRCA2* (further MLPA based on family history)
Melanoma	*ACD, BAP1,* ***BRCA2***, ***CDK4***, ***CDKN2A***, *POT1, TERF2IP, TERT promoter*	*BRCA2, CDKN2A, CDK4*
Renal	*BAP1, FH, FLCN, MET,* ***SDHA***, ***SDHAF2***, ***SDHB***, ***SDHC***, ***SDHD***, ***TP53***, ***VHL***	*SDHAF2, SDHB, SDHC, SDHD, VHL*
Prostate	***BRCA1***, ***BRCA2***, *CDH1, CHEK2,* ***TP53***	*BRCA1, BRCA2*
Pancreatic	***CDKN2A***, ***BRCA2***, ***MLH1***, ***MSH2***, ***MSH6***, *PALB2, STK11*	*BRCA2*

*ROI: *POLD1* (exons 8-13), *POLE* (exons 9-14), *MET* (exons 16-19), *PTEN* (includes promoter), CDK4 (exon 2)

REFERRAL PROCEDURE

Diagnostic referrals are accepted for individuals affected by and with a strong family history of cancer.

- Referrals accepted from Clinical Genetics only.
- 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

Gene target enrichment is undertaken using Agilent's HaloPlex Target Enrichment System and libraries are sequenced on an Illumina MiSeq Desktop Sequencer. Sequence data are analysed using a custom-designed bioinformatic pipeline. Where possible, genes of higher interest are covered to 100% either by >30 reads or by Sanger sequencing (see table above). Putative pathogenic variants are confirmed by Sanger sequencing. MLPA is used to detect deletions and duplications in genes as indicated. Variants considered highly likely to be pathogenic, likely to be pathogenic or of uncertain pathogenicity are reported, this is considered in the context of the patient's phenotype and clinical relevance.
Next Generation Sequencing (NGS) Analytical sensitivity for single nucleotide substitutions is estimated to be >99% (95%CI=98.5-100) for bases covered to a minimum depth of 30x. Analytical sensitivity for small insertions / deletions may be lower.
Sanger Sequencing - Analytical sensitivity for single nucleotide substitutions and small insertions/deletions is estimated to be >99%.

- Family tests involve targeted analysis by Sanger sequencing of the relevant exon (see disease specific information sheets).

Please see the current price list and target reporting times on the Oxford Genetics laboratory - Molecular genetics front page

NB This information is only valid on the day of printing – last updated 18/10/2017