Whole Genome Analysis

100,000 Genomes Project Cancer Programme

Preliminary analysis of somatic small non-synonymous variants v1.1

Participant information

Participant name	D.O.B	Gender	NHS number	Laboratory sample ID	GeL participant ID	GMC	Sample date	Date analysis issued
XX								

Tumour information

Tumour type	Tumour subtype	ICD10 code	Sample type	Reported tumour content	Tumour sample cross-contamination
Colorectal	adenocarcinoma	N/A	FF	Medium 40-60%	PASS

Domain 1 variants

Variants in a virtual panel of potentially actionable genes*. Actionable genes are defined as genes in which small variants (SNVs and indels <50bp) have reported therapeutic, prognostic or clinical trial associations**, as defined by the GenomOncology Knowledge Management System. Where known, the “variant-level actionability” category and applicable tumour type are indicated. For other variants in these genes, their impact on gene function has not yet been characterised and therefore their actionability status is unclear. This means:
(i) local evaluation will be required for listed variants which are not yet characterised (i.e. “variant-level actionability” is denoted N/A)
(ii) even if well characterised as actionable for some tumour types, the listed variants may not be actionable in the participant’s specific tumour type
*Current potentially actionable genes for solid tumours: 77 genes, listed at Actionable genes in solid tumour v1.1 document
**Links are provided to clinical trials within the United Kingdom which are both actively recruiting participants or closed to recruitment.

Gene	Gene-level actionability	GRCh38 coordinates ref/alt allele	Transcript	cDNA and protein change	Predicted consequences	Population germline allele frequency (1KG)	VAF	Alt allele/ total read depth	COSMIC ID	Variant-level actionability	Gene mode of action
ALK	Therapeutic (NSC lung ca); Trial (NSC lung ca); Trial (NSC lung ca); Trial (NSC lung ca); Trial (NSC lung ca); Trial (solid neoplasm); Trial (solid neoplasm); Trial (solid neoplasm)	2:29220810 G>A	ENST00000389048	c.3541C>T p.(Arg1181Cys)	missense_variant	N/A	0.15	20/130	N/A	Trial (NSC lung ca); Trial (NSC lung ca); Trial (NSC lung ca); Trial (NSC lung ca); Trial (NSC lung ca); Trial (solid neoplasm); Trial (solid neoplasm); Trial (solid neoplasm)	oncogene
KRAS	Therapeutic (colorectal ca); Therapeutic (NSC lung ca); Trial (colorectal ca); Trial (colorectal ca); Trial (NSC lung ca); Trial (NSC lung ca); Trial (NSC lung ca); Trial (NSC lung ca); Trial (solid neoplasm); Trial (solid neoplasm); Trial (solid neoplasm); Trial (solid neoplasm); Trial (glioma); Trial (MPNST); Trial (melanoma); Trial (neuroblastoma); Trial (rhabdoid tu); Trial (rhabdomyosarcoma); Trial (schwannoma); Trial (sarcoma-ST)	12:25225628 C>T	ENST00000256078	c.436G>A p.(Ala146Thr)	missense_variant	N/A	0.3	35/118	COSM19404 COSM1165198	Therapeutic (colorectal ca); Therapeutic (NSC lung ca); Trial (colorectal ca); Trial (NSC lung ca); Trial (colorectal ca); Trial (glioma); Trial (MPNST); Trial (melanoma); Trial (neuroblastoma); Trial (NSC lung ca); Trial (rhabdoid tu); Trial (rhabdomyosarcoma); Trial (schwannoma); Trial (sarcoma-ST); Trial (solid neoplasm); Trial (solid neoplasm); Trial (solid neoplasm)	oncogene
TP53	Trial (ovarian ca)	17:7673796 C>A	ENST00000269305	c.824G>T p.(Cys275Phe)	missense_variant	N/A	0.49	40/82	COSM10701 COSM99932 COSM3723938 COSM1637959	Trial (ovarian ca)	oncogene, tumour suppressor

Domain 2 variants

Variants in a virtual panel of cancer-related genes***. Cancer-related genes are defined as genes in which any variants have been causally implicated in cancer, as defined by the Cancer Gene Census (Wellcome Trust Sanger Institute)
***Current cancer-related genes: 590 genes, listed at Cancer census genes v1.1 document

Gene	GRCh38 coordinates ref/alt allele	Transcript	cDNA and protein change	Predicted consequences	Population germline allele frequency (1KG)	VAF	Alt allele/total read depth	COSMIC ID	Gene mode of action
APC	5:112839499 TGCAA>T	ENST00000508376	c.3906_3909delGCAA p.(Leu1302>fs)	frameshift_variant	N/A	0.13	14/110	N/A	tumour suppressor
CREBBP	16:3758051 T>TA	ENST00000262367	c.3370-4dupT	splice_region_variant	N/A	0.2	12/61	N/A	oncogene, tumour suppressor
FAT1	4:186620732 C>T	ENST00000441802	c.5854G>A p.(Val1952Ile)	missense_variant	N/A	0.28	28/99	COSM1054196 COSM1054194	tumour suppressor
FIP1L1	4:53453080 CAG>C	ENST00000337488	c.1459_1460delAG p.(Arg483>fs)	frameshift_variant	N/A	0.11	9/83	COSM249696 COSM4435275	N/A
IDH2	15:90088607 T>C	ENST00000330062	c.514A>G p.(Arg172Gly)	missense_variant	N/A	0.24	27/112	COSM33731	oncogene

Domain 3 variants

Small variants in genes not included in domains 1 & 2. These are not included in this document but are accessible via the Supplementary Analysis.

Sequencing quality information

See online Technical Information v1.1.main document and/or LabKey QC portal for details and expected ranges of QC metrics

Sample type	Mapped reads, %	Chimeric DNA fragments, %	Insert size median, bp	Genome-wide coverage mean, x	Unevenness of local genome coverage, x	COSMIC content with low coverage (<30x), %	Total somatic SNVs	Total somatic indels	Total somatic SVs
Germline	95.38	0.40	482.8	29.3	6.65	N/A	N/A	N/A	N/A
Tumour	95.68	0.37	447.4	84.6	13.45	1.15	31152	21184	262

Additional information

- **The pathways for sample processing and data analysis are not yet accredited end-to-end for diagnostic use. Accordingly, any result intended for use in informing clinical management should be confirmed using a test accredited for clinical use.**
- **Sensitivity: the depth of WGS used in this analysis will detect 99% of SNVs with an allele frequency of ≥0.3, 95% of SNVs with an allele frequency of ≥0.1 and 60% of indels with an allele frequency of ≥0.4 (estimate is based upon admixtures analysis of a highly accurate catalog of variants produced in the "platinum genomes" project). Consequently, variants with allelic frequencies below this level, or in areas of low coverage may not be detected. False negative results cannot be excluded.**
- Somatic calls are filtered according to the quality and quantity of reads. Full details of the filters used in this analysis can be found in the Technical Information v1.1.main.
- Variants present in the germline are subtracted to produce a list of somatic variants. Accordingly, variants detected in both the germline and the tumour will not be listed in this analysis.

- In this analysis MNVs (multiple nucleotide variants) are reported as multiple consecutive SNVs and therefore the protein change may require correction.
- Only variants with specific consequences (transcript ablation, splice acceptor variant, splice donor variant, stop gained, frameshift variant, stop lost, initiator codon variant, transcript amplification, inframe insertion, inframe deletion, missense variant, splice region variant, incomplete terminal codon variant) in canonical transcripts are reported. The complete list of canonical transcripts can be accessed at List of canonical transcripts v1.1.
- A variant may have multiple entries in COSMIC database due to the use of different reference sequences. In these cases links to all COSMIC entries are provided.
- Structural variants (SVs) and copy number variants (CNVs) are not included in this analysis. These variants types are included in the Supplementary Analysis.
- For a full description of the methods used to produce these results and for further information regarding QC metrics please refer to the Technical Information v1.1.main. All related documentation is available at Genomics England Website.
- 'N/A' indicates that information is not available or not applicable.

Genomics England
Queen Mary University of London
Dawson Hall
Charterhouse Square
London
EC1M 6BQ

Sequencing Laboratory
Illumina Laboratory Services United Kingdom - Hinxton
The Ogilvie Building, Wellcome Trust Genome Campus
Hinxton Nr Saffron Walden
Essex
CB10 1DR