Whole Genome Analysis from 100,000 Genomes Project Cancer Programme

Release notes for version 1.1 (composite WGA):

- WGAs are currently being returned from the Initiation Implementation Phase of the Cancer Main Programme on participants with solid tumours for whom paired fresh frozen and germline samples were submitted and passed quality assurance checks.

- It is envisaged that the initial review of these WGAs will be carried out within the GMC accredited Molecular Pathology/Genetics Laboratory therefore these analyses will be returned to GMC nominated individuals in these laboratories.

- WGAs are currently identified via two IDs; the Genomics England Participant ID and the Lab Sample ID for the fresh frozen tumour sample in line with NHS working practice. Provision of additional identifiers is under evaluation.

- The WGA is released as a paired set of formats:
    - a ***preliminary analysis*** containing small variants in Domain 1 (77 genes containing variants annotated as potentially actionable by Genome Oncology) and Domain 2 (590 genes listed in the Cancer Gene Census).
    - a ***supplementary analysis*** containing the content of the preliminary analysis **and** additional small variants (occurring outside Domains 1 & 2), copy number variants (CNVs), structural variants (SVs) and pan-genome analyses of mutational burden, signatures and regions of hypermutability.

- Further division of the SVs and CNVs into Domains 1, 2 and 3 is under development.

- Quality metrics are provided as part of these WGAs and are also via the GMC Labkey portal. Additional quality metrics are under development, including high resolution coverage metrics relating to clinically important bases and genes, to better assess the likelihood of false negative findings.

- Variants called in 'clinically actionable' genes are annotated against GenomeOncology (the database underlying https://www.mycancergenome.org/), and clinical trials with active sites within the UK with eligibility for solid tumours are listed (via https://clinicaltrials.gov/ , both trials open and closed to recruitment). Further refinements of curation of UK clinical trial annotations with the GenomeOncology development team are under development.

- Provision of a visualization tool by which GMCs can evaluate the read-level support of called variants is under development to better enable assessment of the likelihood of false positive/negative findings. Variants were not filtered out based on low count/frequency in the current version of the pipeline, to allow for the detection of low level variants. This may be reviewed in subsequent versions of the pipeline. Provision of an estimate on the expected false positive rates across a range of variant allele frequencies for the average coverage observed in these samples is under development.

- Delivery of pertinent germline findings (known pathogenic or likely pathogenic variants in cancer susceptibility genes relevant to that tumour type) is under development and will be included in subsequent releases of the cancer WGA

Feedback is cordially invited and should be forwarded to cancerscience@genomicsengland.co.uk