PHSA Laboratories

Children's & Women's Health Centre of British Columbia

Release of Primary Data Policy

Division of Genome Diagnostics

The Division of Genome Diagnostics at BC Children's and BC Women's Hospitals (C&W) provides clinical genetic testing for the province of BC. Genetic data is intended for use in conjunction with a clinical presentation and other markers of disease status and progression for the management of patients with genetic disorders. With the introduction of increasingly more complex genomic techniques into the clinical setting, comes the associated increase in the amount of primary data generated, and an increase in technology-specific artifact. The C&W Division of Genome Diagnostics policy on release of primary genetic data is based on patient centered care, ensuring appropriate clinical interpretation of complex data, and maintenance of patient privacy and confidentiality.

1. Primary data are assessed, validated, interpreted, and reported by the Laboratory Geneticist.

2. Primary data are not released outside of the Division, except in the following circumstances:
    a. De-identified data may be shared with Laboratory Professionals, certified in the relevant subspecialty, for the purposes of quality assurance and/or consultation.
    b. De-identified data may be shared with Vendors for the purposes of quality assurance, such as technology trouble-shooting.
    c. Primary data may be released to Research Investigators following agreement and approval by the Clinical Research Ethics Board and the Department of Pathology & Laboratory Medicine.

Assay Specific Details:

1. Chromosome Microarray Analysis (CMA)

The Cytogenetic Laboratory provides single nucleotide polymorphism (SNP) chromosome microarray analysis for the diagnosis of a variety of indications. This technique identifies copy number variants (CNV) and regions of homozygosity (ROH) within the genome. The data analysis algorithm and associated parameters depends on the indication for testing. The interpretation of CMA data is based on the clinical information available at the time of analysis.

Reported data:

- All CNVs above the established clinical thresholds are interpreted as benign, pathogenic or of unclear clinical significance (VUS) in accordance with American College of Medical Genetics (ACMG) guidelines[1]. Clinically relevant CNV gene content is included in the report and is also available through publicly available genome browsers. CNVs below the established thresholds are reported only if classified as likely pathogenic or pathogenic.

- All ROHs above the established clinical threshold are reported with interpretation regarding their significance, including the possibility of uniparental disomy (UPD) and/or the likelihood of an autosomal recessive disorder in the patient [2, 3, 4, 5]. Clinically relevant ROH gene content is available through publicly available genome browsers, or is provided to the referring physician, upon request.

Primary data available to Clinicians practicing in the area of Medical Genetics:

- Excel files containing genomic coordinates for ROHs observed below the clinical thresholds but above background.

Primary data available to Research Investigators, under a BCCH REB approved research protocol:

- Excel files containing genomic coordinates for CNVs observed below the clinical thresholds but above background

Primary data, not released:

- Microarray hybridization data files (i.e. the CEL files, CNCHP or CYCHP files)

2. Massively parallel (next-generation) sequencing

Approaches to next-generation sequencing (NGS) in the clinical setting currently range from single gene testing, targeted panels, and whole exome sequencing; with the future potential of clinically available whole genome sequencing and copy number variant assessment. The interpretation of sequence data is based on the clinical information available at the time of analysis.

Reported data:

- Following quality assessment, mapping, filtering, annotation, and validation, sequence variants and/or CNVs meeting clinical parameters and/or thresholds are included in the final report. Reported variants are classified as pathogenic, likely pathogenic, and variants of uncertain clinical significance (VUS) in accordance with ACMG guidelines[1].

Primary data including filtered and unfiltered variant call files (vcf) will not be released to Clinicians.

Primary data available to Research Investigators, under a BCCH REB approved research protocol:

- fastq, bam and/or vcf files will be considered for release on a study-by-study basis to research investigators who:
    - have REB approval that specifically allows access to NGS data
    - possess the necessary tools and skills to appropriately assess data quality
    - have given consideration to the risks of incidental findings
- The process and fees for release of data will be coordinated by the Research Study Coordinator according to established departmental processes[6].

Primary data, not released:

- output data file (vendor specific)

References:

1. **American College of Medical Genetics standards and guidelines for interpretation and reporting of postnatal constitutional copy number variants.** PMID: 21681106

2. Papenhausen P, Schwartz S, Risheg H, Keitges E, Gadi I, Burnside RD, Jaswaney V, Pappas J, Pasion R, Friedman K, Tepperberg J.: UPD detection using homozygosity profiling with a SNP genotyping microarray. Am J Med Genet A. 2011 Apr;155A(4):757-68.

3. Tucker T, Schlade-Bartusiak K, Eydoux P, Nelson TN, Brown L.: Uniparental disomy: can SNP array data be used for diagnosis? Genet Med. 2012;14:753-756.

4. Rehder CW, David KL, Hirsch B, Toriello HV, Wilson CM, Kearney HM.: American College of Medical Genetics and Genomics: standards and guidelines for documenting suspected consanguinity as an incidental finding of genomic testing. Genet Med. 2013 Feb;15(2):150-2.

5. Hamamy H, Antonarakis SE, Cavalli-Sforza LL, Temtamy S, Romeo G, Kate LP, Bennett RL, Shaw A, Megarbane A, van Duijn C, Bathija H, Fokstuen S, Engel E, Zlotogora J, Dermitzakis E, Bottani A, Dahoun S, Morris MA, Arsenault S, Aglan MS, Ajaz M, Alkalamchi A, Alnaqeb D, Alwasiyah MK, Anwer N, Awwad R, Bonnefin M, Corry P, Gwanmesia L, Karbani GA, Mostafavi M, Pippucci T, Ranza-Boscardin E, Reversade B, Sharif SM, Teeuw ME, Bittles AH.: Consanguineous marriages, pearls and perils: Geneva International Consanguinity Workshop Report. Genet Med. 2011 Sep;13(9):841-7.

6. Laboratory Research Guidelines, Department of Pathology and Laboratory Medicine, Children's and Women's Health Centre of British Columbia. See https://bcchr.ca/research-support/clinical-research-support/laboratory-services