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Topic: **Detecting structural variation from whole genome sequence data: application to neurodevelopmental disorders**

Abstract:

Variation within the human genome can take many forms, the most common of which include single nucleotide variation (SNV), short insertions/deletions (indels), and large-scale copy number variation (insertions, deletions; CNV). Rarer structural variations (SV) can include translocations, translocational insertions, inversions, and complex events (such as translocations with deletions or duplications at the breakpoints). There are robust and established methods for detecting CNV from genome-wide microarray data, and for detecting SNV and indels from sequence data. However, detection of CNV and in particular, SV, from whole genome sequence (WGS) data are not yet optimal, particularly for complex events. Here, we will discuss recent work at The Centre for Applied Genomics (TCAG; www.tcag.ca), in particular centred around our recent publication of optimized CNV methods. We will also highlight newer work using anomalous paired-end and split read methods to resolve breakpoints, and touch on the utility of deep learning methods to refine CNV boundaries. These methods form part of TCAG's integrated pipeline for analysis of WGS data from a number of neurodevelopmental disorder projects, most notably the MSSNG project that is examining the genomes of 10,000 subjects from families with autism spectrum disorder.

Reference:

- Trost B, Walker S, Wang Z, Thiruvahindrapuram B, MacDonald JR, Sung WWL, Pereira SL, Whitney J, Chan AJS, Pellecchia G, Reuter MS, Lok S, Yuen RKC, Marshall CR, Merico D, Scherer SW (2018).
- A Comprehensive Workflow for Read Depth-Based Identification of Copy-Number Variation from Whole-Genome Sequence Data. Am J Hum Genet. 102(1):142-155. doi: 10.1016/j.ajhg.2017.12.007. PMID: 29304372 Article available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5777982/.

Bio:

Dr. Wintle's scientific interests lie in the application of genomic technologies to the understanding of individual genetic variability, with a specific focus on the neuromotor condition, Cerebral Palsy. He serves as both Associate Scientific Director of the CP-NET Cerebral Palsy Integrated Discovery Program within Ontario, Canada, and as a founding

member of the Governance Council of the International Cerebral Palsy Genomics Consortium (ICPGC). His most recent work has focused on the discovery of large-scale, highly-penetrant rare variation in children with CP, and the delineation of the extent to which genetic and genomic changes contribute to this disorder.

Dr. Wintle holds a PhD in Molecular and Medical Genetics from the University of Toronto, during which he characterized the human immunoglobulin heavy chain gene cluster, as part of international efforts supporting chromosome 14 mapping for the Human Genome Project. He completed his postdoctoral training at the Centre for Addiction and Mental Health in Toronto, studying the molecular neurobiology of dopamine signalling in the model organism, the nematode C. elegans. Following this, he worked in two related biotechnology startup companies, in a variety of R&D and Operations roles, mainly focused on the complex genetics of autoimmune and inflammatory disorders. Since 2006, he has been with The Centre for Applied Genomics (TCAG), a genome centre located within the Research Institute of The Hospital for Sick Children in Toronto, Canada, where he serves as Assistant Director and a member of its Scientific Management. TCAG is a Genomics Technology Platform of Genome Canada, and a founding member of Canada's Genomics Enterprise, a nationally-funded, pan-Canadian genome sequencing network, and is affiliated with the University of Toronto. A major focus of work at TCAG is in developing approaches to identify and interpret structural variation within whole genome sequence (WGS) data. Dr. Wintle has also acted as a consultant to a wide variety of private- and public-sector biotechnology, market research, and healthcare organizations.