Presentation title: Translating exome and whole genome sequencing to the clinic

Abstract:
Since sequencing the draft human genome in 2001, the number of diseases with known genetic basis has increased >50-fold to over 3000. Despite this remarkable success, >2000 Mendelian disorders remain unsolved, and up to 70% of patients presenting at the clinic with genetic disorders remain undiagnosed. Clinical-grade genome sequencing holds the dual promise of improving diagnostic rates, and empowering genetic research through the discovery of novel disease-associated variants. The long-term research value of performing whole exome and genome sequencing in a diagnostic setting on thousands of individuals will offset the initially higher cost and complexity, than a targeted gene-panel approach.

In late 2012, we established the Kinghorn Centre for Clinical Genomics (KCCG) with the aim of implementing genomic medicine in Sydney. At the heart of the KCCG are 2 Illumina HiSeq 2500 sequencers that are used for rapid turnover exome sequencing, and more recently, one the world's first HiSeq X Ten sequencing suites, with capability of sequencing more than 300 whole human genomes per week. Since we intend to provide NATA-certified, clinical-grade sequencing, much of our work over the past 12 months has been focused on the development of standardised procedures for test procurement in the clinic through to wet-lab processes, bioinformatics and clinical reporting. The bioinformatics workflow includes phenotype capture, read alignment, mutation calling, variant annotation and filtering by inheritance pattern, rarity, predicted functional impact and known disease association.

To date, we have sequenced exomes from >100 patients, from a range of conditions, largely reflecting the undiagnosed caseload at the Sydney Children's Hospital. We will present some early success stories from sequencing these exomes and reflect on the possibilities presented by low-cost whole genome sequencing in the diagnosis of inherited disease.

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