KCCG NEWS

An update from the Kinghorn Centre for Clinical genomics

KINGHORN CENTRE FOR CLINICAL GENOMICS

GARVAN INSTITUTE OF MEDICAL RESEARCH

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Updates

Welcome to our third bimonthly newsletter. KCCG has been particularly busy over recent months developing local and global relationships through meetings, conferences and courses. An important aspect of our work is to engage with different communities and stakeholders in genomic medicine: this engagement is vital to realising the potential of clinical genomics in Australia. We've provided a snapshot of some of our efforts here. We hope you enjoy the update.

Partnership with Genomics England

The Garvan Institute of Medical Research has signed a memorandum of understanding with Genomics England, the organisation established by the UK's Department of Health to deliver the world-first 100,000 Genomes Project. The two organisations will share resources and expertise to advance genomic medicine in Australia and the UK. Under the terms of the agreement, Garvan and Genomics England will work together to make genomic information more accessible, meaningful and usable, particularly by developing better ways to capture clinical information and integrate it with genomic data. The two institutions will collaborate to develop next-generation genomics databases and to establish clear ethical and legal frameworks around the use of genomic information.

Sydney Genomics Collaborative Update

On 7 December, KCCG hosted a Scientific Symposium on the NSW Health-funded Sydney Genomics Collaborative. This one-day event brought together more than 80 clinicians, researchers and stakeholders in the NSW genomics community to learn about the Collaborative's programs and its progress since 2014; discuss current health-focussed research projects using whole human genome sequencing; and connect members of the research and clinical community to establish or enhance strategic collaborations.

The day included updates from the 2014/15 NSW Genomic Collaborative grants awardees seeking to better understand treatment response in melanoma and the genetic basis of schizophrenia, mitochondrial disease, and congenital heart disease in babies.

The Hon. Jillian Skinner, NSW Minister for Health, launching the inaugural Sydney Genomics Collaborative Scientific Symposium on 7 December.

KCCG Production News

KCCG has an ongoing commitment to improving its processes and the introduction of Illumina's new v2.5 chemistry has improved our standard average sequencing depth from 31.6 times (v2.0) to 35.5 times coverage. We are also seeing greater average data yield (129.5 Gbp of data per lane of sequence) and higher quality metrics (Q30 > 82.5%). This translates into more high quality data per dollar for the users of our whole genome sequencing services.

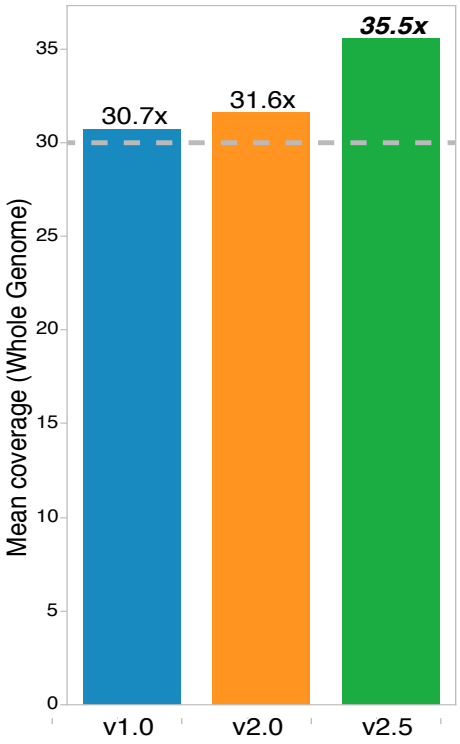

Figure 1. KCCG introduces new WGS Chemistry on the HiSeq X Sequencing Platform.

The KCCG is pleased to announce that we can now offer sequencing of non-human genomes. We have recently demonstrated that under standard conditions, the HiSeq X is capable of sequencing the mouse genome at an average depth of greater than 40 times, yielding more than 140 Gbp of high quality (Q30 > 86%) data per lane of sequence.

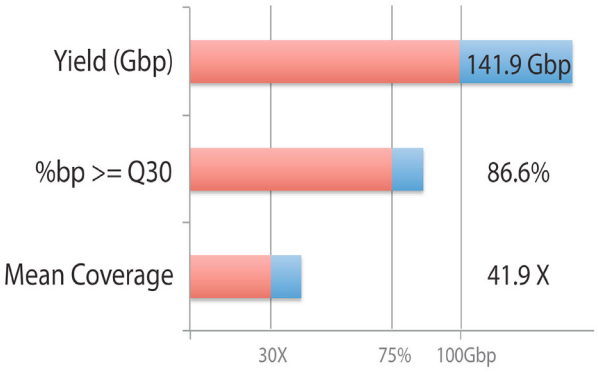

Figure 2. HiSeq X sequencing performance of mouse genomes.

Profile: Dr Mark Cowley, Team Leader - Translational Genomics

Dr Mark Cowley leads KCCG's Translational Genomics team, which develops and applies computational tools to maximise the diagnostic potential of the genome for the clinic.

Mark's team was originally responsible for building the computational pipeline for the Illumina HiSeq X system: 'The size of whole genome datasets forced us to re-engineer our analysis pipelines, and switch to larger-scale computing hardware, including the cloud. We also developed tools and algorithms to simplify the process of integrating and interpreting genomic information, and help us focus on the genes that are known to be important in a particular disease' he said. 'This makes it much easier to diagnose diseases that have been described before.'

The search for a variant responsible for a patient's condition or pathology is a major diagnostic challenge in clinical genomics. As a bioinformatician (computational biologist), Mark's toolkit comprises large-scale computing, algorithms, databases and big data. Very big data: the initial sequencing output runs to millions of rows. He applies this toolkit to a puzzle – often a patient puzzle – distilling the data to something relatively small and easy to interpret. Too many candidate variants diminishes the opportunity for achieving a genetic diagnosis. Special software developed in-house, along with numerous other techniques, old and new, help the genomic analysts narrow the list of candidates.

Now, Mark is focused on trying to make use of much more of the genomic data generated by whole genome sequencing to help diagnose those cases where the causative variant isn't easily found. Postdoctoral researchers within his team are developing tools to detect different types of variants in the genome, such as cases where large parts of the genome are completely duplicated or rearranged. 'There's lots of work to be done yet to completely

characterise the genome,' says Mark, 'part of our R&D work is to keep filling those gaps.' Mark wants to continue to develop tools and techniques that will further explain the genome, and bring them into the clinical pipeline. 'Hopefully that'll keep us at the forefront of clinical genomics, keep improving patient care and getting diagnostic rates up and up and up.'

Until now, the genomic view of disease has centred very much on coding DNA, but recently we have started to go further, looking at the regulatory sites. As more whole genomes are sequenced, we will be able to bring strands of information together and see if there are mutations altering the activity of particular genes. We'll also hopefully provide new tools to treat them.

Mark sees that the increasing mass of data clinical genomics is generating will be a crucial driver of genomic research. 'If we do it right', Mark says, 'we've got real potential to improve long-term patient outcomes, not just through applying the technology today, but learning more in the future. This will happen through collaboration, and mining data from large, interconnected databases. From a treatment perspective, he argues, it is vital to take a multidisciplinary approach, and collaborate with researchers and clinicians who have a deep understanding of the disease.

Courses and workshops

October and December were big months for education. We ran our first cancer education session for clinicians and researchers in October (see last newsletter) and Dr Mark Cowley, Professor Leslie Burnett and Dr Tony Roscioli also presented at the two-day *Genomics for Genetic Counsellors (G4GC)* course. G4GC was supported by the Royal Prince Alfred Hospital, the Sydney Children's Hospital Network, the Centre for Genetics Education and KCCG education.

In December, members of the Translational Genomics team provided a variant calling workshop with DNAnexus at *BioInfoSummer*, a key NSW bioinformatics training event.

Finally, more than 20 genetic and medical specialists took part in our first week-long intensive *Clinical Genomic Data Analysis* course. This course was convened by Dr Tony Roscioli and enabled participants to obtain hands-on experience in examining clinical genomic data to better understand the processes that underpin data analysis and genomic reporting.

Participants in our first Clinical Genomic Data Analysis course.

KCCG presentations

Kirsten Boggs, KCCG's first postgraduate student, presented her research findings at the *University of Sydney Master of Genetic Counselling Capstone* presentations last month. Kirsten's project explored Australian stakeholder views on the impact of genomics on the practice of genetic counselling.

KCCG was well represented at the *Australasian Genomic Technologies Association* conference in October, when five Translational Genomics team members presented research.

KCCG team leaders also presented in October/November at: the *Sax Institute 45 and Up Collaborators' Meeting* and the *Big Data and Health Analytics* conference in Sydney; the *Medical Software Industry Association* conference in Melbourne; the *American Society of Human Genetics* in Baltimore, USA, and the *NextGen Genomics, Biology, Bioinformatics and Technologies (NGBT)* Conference in Hyderabad, India. See Talks and Conferences for more detail.

Connect with us online

For current information, visit our website at http://www.garvan.org.au/kccg, follow us on Twitter @kinghorngenomes or email us at kccgenquiries@garvan.org.au.

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