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Faster Access to Genomic Information

For James Hadfield, Genomics Core Director at the Cambridge Research Institute, the MiSeq[®] system opens up a whole new range of possibilities.

Supporting Cancer Research UK scientists' genomic experiments at the Cambridge Research Institute (CRI), James Hadfield needs to stay on top of the newest technologies. Starting the Genomics Core Facility at the CRI five years ago, the focus was inevitably on microarrays. Over the past four years though, the lab has focused more and more on next-generation sequencing. It now offers services to more than 500 CRI, MRC Laboratory of Molecular Biology, and University of Cambridge scientists.

Two years ago, James was part of the Technology Working Group for the Stratified Medicines Initiative*, a project between Cancer Research UK and the Technology Strategy Board, which aims to sequence a minimum of nine different cancer mutations in 9,000 cancer patients over the next three to four years. Today, some NHS hospitals are testing the tumors of cancer patients for mutations; however, they only test for a few gene faults at a time and, as testing is not centralized, it is often done on only a few samples at once, rather than on a large scale. The Stratified Medicines Initiative aims to develop tests that can cover many of the known mutations of the most common types of cancers, making genetic testing cheaper, more reliable, and improving commercial availability. During working group discussions it became clear that faster sequencing technologies were going to be required. Hadfield began speaking with Illumina about the possibility for a method for more personalized, targeted sequencing. From these conversations, he was introduced to the MiSeq personal sequencing system.

Not all cancer genes contain these mutational hot spots, making it necessary to resequence whole genes. To this end, Hadfield's lab had previously resequenced TP53 from long-range PCR amplicons. During the 2011 AGBT meeting, it was clear that this project aligned nicely with the MiSeq system, and a proof-of-concept study was performed with Illumina.

We recently had an opportunity to talk to James Hadfield about his experience and thoughts regarding the future of personal genome sequencing.

Q.Why does the MiSeq system provide a good way to approach this study?

James Hadfield (JH): We are looking at different methods to sequence regions of interest in cancer patient genomes that are likely to be relevant for clinical utility and inform treatment to arrive at a more personalized cancer therapy. MiSeq allows the speed of data generation that fits into a clinical treatment context. We'll be able to get results in a matter of hours or days, or certainly within a week or two. It will allow us to get enough data to robustly call mutations in heterogeneous tumors that may be important in relapse. Researchers at CRI would like to pick up those mutations earlier so the appropriate therapy can be prescribed.



James Hadfield runs the Genomics Core Facility at the Cambridge Research Institute. He also moderates SEQanswers.com, writes the CoreGenomics blog, and developed the widely used Google Map of High-throughput Sequencers.

Q.What makes the MiSeq system accessible to a clinical lab?

JH: All clinical labs in the UK, and across the world, have systems in place for taking tumors, extracting DNA, PCR amplifying specific loci, and performing Sanger sequencing. Long-range PCR is one method to capture genomic loci for use on the MiSeq. It's a method that's understood by all clinical labs today. I see long-range PCR, or other PCR and next-generation PCR modalities, along with MiSeq, as being easy enough to run that they can fit into a clinical lab quite seamlessly.

"The speed of turnaround is really the biggest change for us. Being able to get data this fast is quite fantastic."

Q. How does the quality of data from the MiSeq system compare to what you are used to?

JH: The data quality is excellent. It's as good as, if not very slightly better, than the data we've seen off of the Genome Analyzer[™] and HiSeq[®] sequencing instruments.

Q. What is the biggest benefit of the MiSeq system?

JH: The speed of turnaround is really the biggest change for us. Being able to get data this fast is quite fantastic. People want to do some quick experiments, method development, and multiple iterative experiments, which we just haven't been able to do on a sequencer where each run can take 10 to 12 days on booked-up sequencers. An iterative project that requires six sequencing runs with data analysis in between each run can take several months or even a year to complete. With the MiSeq, that may come down to just a few weeks.

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Q. What applications do you expect the MiSeq system to be useful for?

JH: Quite simply, we'll be able to do projects that we may have held off doing in the past such as single-end, long-read sequencing and method development. We'll be able to do iterative experiments on any flavor of run that we choose that fits our experiment, get a result very quickly, get analysis done, and move on to the next step. We'll be able to test methods far more quickly than we ever thought we'd be able to in the past. And I think a really big development is targeted amplicon sequencing methodologies. That's where I really want to do some work as soon as we possibly can.

Q. How is "personal genome sequencing" an enabling technology?

JH: Scientists at CRI would like to understand how they can apply personal sequencing to impact the prescribing decision for cancer patients. However, there is a lot of work to do before this technology gets to patients. There is a potential need for sequencing to be performed in clinically certified labs if the data are to be given back to the patient's physician. There's always a need to come up with faster, better ways to capture DNA. Projects like the Stratified Medicines Initiative with the NHS and Cancer Research UK will start to get some personalized genomic information back to doctors to help treat their patients.

Learn more about the MiSeq system at www.illumina.com/miseq

*http://science.cancerresearchuk.org/research/research-strategy/our-progress/stratified-medicine-programme

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