PacBio Continues Push into Human Sequencing, Sees New Market in HiSeq X Ten Customers

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Premium

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NEW YORK (GenomeWeb) – Pacific Biosciences said last week that it received a record of 16 instrument orders in the third quarter from customers in a broad range of markets, including microbiology, ag-bio, HLA, and human sequencing.

Notably, the company has received orders from two firms that have invested in Illumina's HiSeq X Ten for large-scale human population sequencing that want to use the PacBio RS II system to resolve structural variations, complex regions like the major histocompatibility complex, and create better assemblies, CEO Mike Hunkapiller said during a conference call discussing the firm's third quarter results.

Also during the call, management touted the company's progress in the infectious disease market and noted that for the first time the technology has been used to *de novo* sequence a cancer genome in collaboration with Genentech.

In addition, last week the company launched its latest chemistry and software package, which increase average read lengths to between 10,000 and 15,000 bases. The chemistry and software improvements have "enabled us to expand our business into larger scale projects, including a growing number of human sequencing projects," Hunkapiller said during the call.

The firm's progress in these areas and record bookings led the company to increase its full-year 2014 revenue guidance, now predicting that its revenues will increase 100 percent compared to 2013. For more details on PacBio's third quarter financial results, see this *GenomeWeb Daily News* story.

Korean sequencing firm Macrogen and J. Craig Venter's startup Human Longevity — which were among the first customers to purchase a HiSeq X Ten system — also each placed orders for two RS II instruments this quarter.

Hunkapiller said that such purchases may be "the beginnings of a bit of a trend," and represent a "new component [of customers] relative to what we've seen in the past." He added that while Macrogen and Human Longevity were the only two customers to make public their RS II purchases, "we have seen interest from other sites" with HiSeq X Ten systems and "it's something that we're actively following."

Additionally, in collaboration with Genentech, researchers have used PacBio technology to *de novo* sequence two lung cancer cell lines. Jonas Korlach, PacBio's chief scientific officer, presented

details of the sequencing at last week's American Society of Human Genetics meeting in San Diego. He told *In Sequence* that the results would be published in an upcoming publication.

The researchers sequenced to 50x coverage and assembled the genome of a lung cancer cell line in around 12,000 contigs with an N50 of just over 1 mb. The largest contig was over 26 mb, Korlach said in a presentation at the conference. Previously, the genome had been assembled with short read sequencing technology and had an N50 of .018 mb and the longest contig was .28 mb, he said. Korlach said the Genentech researchers were particularly interested in using SMRT sequencing to study methylation and its relationship to drug sensitivity and resistance.

As previously reported by *Clinical Sequencing News*, the Icahn Institute for Genomics and Multiscale Biology at Mt. Sinai has purchased a PacBio system that it plans to install in a new clinical next-generation sequencing laboratory for HLA haplotyping, targeting structural variants in cancer, and running diagnostic assays for conditions that involve long tandem repeats like Fragile X syndrome.

Even as PacBio continues to push into these newer markets, Hunkapiller said that the company is still doing well in its key area of microbial sequencing. This quarter, the US Centers for Disease Control and Prevention ordered two PacBio RS II systems, bringing its total to three.

"The CDC has become one of our largest customers and is a key user for us in the infectious disease area," he said.

Hunkapiller cited a National Institutes of Health study led by Julie Segre, which used the PacBio RS II system to retrospectively analyze a 2011 outbreak of antibiotic resistant Enterobacteriaceae at an NIH hospital as being key to driving attention to the use of the technology in the microbiology arena.

Since then, a number of other studies have been published using PacBio technology to study pathogens. For instance, researchers from the University of Leicester took advantage of the ability of SMRT sequencing to directly measure epigenetic events and found six biological phases of the *Streptococcus pneumoniae* bacteria that were each characterized by a different methylation pattern related to the virulence of the organism. That study waspublished in *Nature Communications*.

Hunkapiller also said during the call that the development project with Roche was going well, noting that the firm hit its first milestone, which resulted in a $10 million payment from Roche, earlier than anticipated. He did not provide details on a timeline, but said that the company is focused on creating a "diagnostic compatible device for [Roche] to sell in the [*in vitro* diagnostic] marketplace."

Aside from focusing on the development project with Roche, Hunkapiller said one aspect of its current RS II platform the company will focus on is improving the front end of the workflow, such as using the SMRT cell capacity more efficiently, "which is a bigger issue for bigger projects like human" genome sequencing.

Improvements in that area will also lead to longer read lengths and increased throughput, he said.