Clinical Next-Gen Sequencing Will Usher in Changes for Vendors, Execs Say at Burrill Conference

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By Tony Fong

NEW YORK (GenomeWeb News) – As next-generation sequencing makes its way into the clinic, platform vendors will need to change their operations to accommodate the shift, company executives said this week at the Burrill Personalized Medicine Meeting held in Burlingame, Calif.

Those changes include new emphases on different geographies, as well as disease areas, and new approaches to handling the data.

Once a tool exclusively used by researchers, NGS technology is increasingly being used for clinical applications, and that change presents new challenges for vendors operating in the space.

During a panel discussion held on Tuesday, Complete Genomics CEO Cliff Reid said, for example, that the firm has to date largely focused on the US and European market. But the sequencing space is seeing "the first utility of clinical sequencing," and as a result, moving forward, his firm will need to turn its attention to Asia, where much of the interest in sequencing, as well as government funding, is in targeted use of the technology to tackle human diseases.

Illumina CEO Jay Flatley echoed that view, saying that currently about 55 percent of the company's business is domestic, and 45 percent international. Those percentages will gradually weigh more heavily toward its international business, he said, with stronger adoption of clinical sequencing, especially as the technology increasingly is gaining the attention of the cancer research community.

He added that the technology has applications in other disease areas, noting that Illumina is targeting trisomy 21 testing and will have "a number of exciting" launches that target that space. The firm already has inked supply deals to provide Verinata Health and Sequenom with its HiSeq instruments for use in developing and commercializing their T21 tests.

But while the panel and others at the meeting presented clinical sequencing as an inevitability, it is several years away from becoming widespread, though there have been instances where NGS technology has already made a clinical impact. In one widely reported case, NGS was used to diagnose the genetic mutation XIAP in a young boy in Wisconsin named Nicholas Volker. He was subsequently treated with a cord blood transplant, which in all probability saved his life.

In a separate presentation, Life Technologies Chairman and CEO Greg Lucier also cited the use of the Ion Torrent Personal Genome Machine benchtop instrument to identify the strain of *E. coli* responsible for an outbreak in Europe during the summer.

During the two-day meeting, presenters and audience participants said that for all the promise of NGS technology and other forms of genomic medicine, the technology will need acceptance from the physician community. While emphasis has been placed on incorporating genetics and new genomic technologies into medical school curriculums and training doctors about the technologies, others pointed to the pathology field as an entry point now for NGS in the medical field.

Creating a curriculum around genomics in medical school and then creating a specialty around it will likely take decades, Complete Genomics' Reid said. Meanwhile, pathologists "are embracing it … and are absolutely thrilled" about the potential of the technology, he said.

Still, even he acknowledged the limits of NGS. When asked if he had had his genome sequenced, he said he hadn't and added that the clinical utility of having his genome sequenced is limited right now.

Hugh Martin, CEO of Pacific Biosciences, also said that he has not had his genome sequenced. But one of the main research focuses of his firm is cancer, in which he has a personal interest, as he was diagnosed with multiple myeloma in 2009.

Cost, Informatics Factor in Clinical Future

As the technology improves and the speed of data generation increases, the price of sequencing has plummeted and continues to fall. One consequence of this is that cancer-related sequencing can now be done on a large scale, Flatley said. He added that at some point, the price will reach the point when every tumor could be sequenced.

Complete Genomics has dropped its price of sequencing a whole human genome — the only service the firm offers — from about $20,000 to about $4,000 in the last few years, but Reid said that the rate of the price decreases will start decelerating, especially in the clinical space. Research-grade sequencing prices will continue being trimmed, but soon clinical-grade sequencing prices will reach a "comfortable" price of a "few thousand" dollars, he said.

The industry, though, still does not have a solution for the bioinformatics bottleneck, and while a small number of firms such as Omicia, Station X, and Personalis offer genomic interpretation services, Reid said that there is essentially no industry comprised of such businesses.

In his keynote presentation on Monday, Ralph Snyderman, former dean of the Duke University School of Medicine as well as founder and chairman of personalized medicine tools firm Proventys, said that the ability to sequence the genome has "far exceeded" the ability to validate the results or understand its clinical meaning.

Longer term, as sequencing moves into the clinical realm, Flatley said that another issue is how to store the genomic data in such a way that electronic medical records will be interoperable with each other. While some are pushing for the development of standards on the informatics and storage side, Reid also cautioned that doing so too early could have unseen hazards.

The technology is developing at such a rapid pace, he said, that any standards being created may be unable to keep up with the technological changes and be limiting.

Another consequence of the movement of NGS into the clinic is the increasing role that regulators will need to play — and on that front, the consensus is that the US Food and Drug Administration is lagging badly in getting its arms around the technology and developing regulations around it.

Flatley called for a "seismic change" in the way that FDA regulates genomic information. Regulation of a whole genome or exome, he said, cannot be done in the same manner that a four-gene test is regulated.