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The Integrated Informatics News Source

March 28, 2013

SoftGenetics, Mayo Collaborate on Clinical NGS Data Review and Storage Software

by Uduak Grace Thomas

SOFTGENETICS this week launched Geneticist Assistant Workbench, a tool that provides clinical laboratories with a streamlined way to track, review, store, and interpret the results of next-generation sequencing-based tests in order to identify potentially pathogenic mutations that are associated with conditions such as cancer and hereditary disease.

Geneticist Assistant lets clinical labs build knowledgebases that contain information about variants associated with specific diseases, John Fosnacht, SoftGenetics' vice president, explained to *BioInform*. It lets labs classify these variants as benign, pathogenic, deleterious, or otherwise, and stores this information so that clinicians can reference it each time they run the test, he said.

This "saves tremendous amounts of time" since labs will no longer have to research the effects of each variant every time they test for the disease, he said. They'll only have to focus on classifying any novel variants and incorporating that information into the knowledgebase, he said.

SoftGenetics developed the tool in collaboration with researchers at Mayo Clinic's laboratory medicine, information technology, and health science research departments.

Kevin LeVan, SoftGenetics product manager, told *BioInform*, that his company handled the system's development while Mayo provided insights into what features and interfaces they needed as well as what outside databases should be linked to the Workbench.

Specifically, the Mayo researchers were looking for a clinical decision support tool for an NGS-based 14-gene hereditary colon cancer test they plan to launch in May, Matthew Ferber, Mayo's clinical laboratory director and one of the developers of the Workbench, told *BioInform*.

"The SoftGentics tool does not render decisions or make automated interpretations for clinical diagnostic laboratories like ours," he said. Rather, "it acts as an information consolidator so that laboratory directors can make decisions more quickly."

Ferber said that Mayo selected SoftGenetics as its partner out of a pool of undisclosed companies that responded to a call for applications asking them to develop a tool that would make it easier and faster for clinical researchers to go through variant lists and also to ensure that they are getting the most accurate and useful information.

He explained that at the time Mayo and SoftGenetics began developing Geneticist Assistant, there were no good tools for checking the quality and completeness of sequencing experiments, which was one of his lab's requirements.

"If I were [using Mayo's test for] hereditary colon cancer and I [got] a list of 12 variants from those 14 genes … I'd want to go off in my research world and investigate those 12 alterations." However, he added, that may be "only half the story; what's equally important is what was missed."

For instance, while reviewing the details of the experiment and the results, "I [may] realize that I actually did sequence [only] half of the MSH2 gene," he said. In that case, "it doesn't matter how many variants were returned to me on my result sheet. I've missed one of the most important diagnostic genes for hereditary colorectal cancer."

Mayo had the choice to "either wait and see what other [companies were] going to build, or jump in, learn what the problems are, and begin handcrafting a solution that we

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would need for our practice," he said.

Geneticist Assistant helps researchers get better quality and more complete results by "creating a very dynamic electronic worksheet that really allows you to review the quality of experiments" and connecting researchers to tools and resources they need to classify variants, Mayo's Ferber said.

The software, he said, "is really not focused on decision making" or using "proprietary algorithms for grading pathogenicity;" rather; "it's focused on supporting decisions" by "collating independent nodes of information so that board certified expert[s] can render a decision."

Also, because it archives decisions that pathologists make, other clinicians have access to the same experimental results and information about variants and can apply them to new patients, he said. This way, "you gain consistency among colleagues," Ferber said.

As a first step, Geneticist Assistant reviews sequence data to ensure that it's of good quality and notes genetic regions where sequencing errors occurred or where additional sequencing is needed, Fosnacht explained. It lets users note the problem areas and generate re-sequencing or additional sequencing requests as necessary.

If there are no errors in the files, he said, researchers can then generate reports that include the list of relevant variants along with external data from public literature and scores from prediction tools like PolyPhen. This report is then reviewed by pathology experts who make the final determination about the status of the mutations before they are included in Geneticist Assistant's knowledgebase, he said.

Later on, as more information becomes available, labs can update their knowledgebase to include the most current information about the disease variants they are interested in, he said.

The workbench can accept both BAM and VCF files and it accepts data sequenced on multiple instruments including those from Illumina, Life Technologies' Ion Torrent, and Roche. It also incorporates variant prediction information from programs such as SIFT, PolyPhen2, LRT, and Mutation Taster; as well as conservation scores data from PhyloP and SiPh. It logs all variants that are identified by individual, sample, and disease panel in a MySQL database and annotates the variants with information from resources such as the Catalogue of Somatic Mutations In Cancer database and PubMed.

Ferber said that Mayo will initially use the new workbench for its hereditary colon cancer panel, but that his lab plans to use it for other "focused panel tests" and whole-exome sequencing projects.

SoftGenetics officially launched Geneticist Assistant this week at the American College of Medical Genetics and Genomics' Annual Clinical Genetics meeting held in Phoenix, Ariz.

Fosnacht told *BioInform* that his firm will offer annual licenses for Geneticist Assistant. Licensees, he said, will receive a server which can run on Linux or Windows, and they can purchase as many clients as they would like. Also, they can access the program over the internet, or a local network, or it can be run locally on a single computer, he said.

He declined to disclose how much the licenses will cost or provide details about how revenue from software sales will be split with Mayo Clinic.