Mount Sinai Team Launches Workflow Management Software for Genetic Testing, Dx Laboratories

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NEW YORK (GenomeWeb) – The Clinical Genome Informatics group and genetic testing laboratory at the Icahn School of Medicine at Mount Sinai have developed a data management platform called ClinLabGeneticist that is designed to facilitate whole exome sequencing-based testing in clinical genetic laboratory settings.

Specifically, the developers explained in a Genome Medicine paper published yesterday, the software automates data and process management associated with assessing variants for genetic testing and disease diagnosis. The platform provides a complete workflow for testing-associated tasks including tools for uploading variant lists, distributing work assignments, reviewing and evaluating variants, selecting variants for validation, generating reports, and communicating between lab personnel. It also boasts a central database where all the genetic testing data, notes and comments, variant validation data, and final clinical reports are stored and archived.

The system includes a comprehensive repository of variants that draws on data from more than 10 publicly available repositories of disease- and non-disease-related variant information such as dbSNP, 1000 Genomes, the Scripps Wellderly dataset, and ClinVar, to annotate variants in samples and asses pathogenicity. It also pulls in data from internal sources such as the Mount Sinai biobank and an internally curated disease variant database. Also available in the repository is data on the functional effects of variants and pre-computed variant annotations from tools such as SIFT, PolyPhen, and Mutation Assessor.

ClinLabGeneticist is disease-agnostic and can be used to explore variants associated with various rare genetic disorders although it could also work, with some adjustments, for germline cancer assessments, Rong Chen, director of clinical genome informatics at the Icahn Institute and one of the developers of the system, told GenomeWeb.

So far, the software has been used to evaluate more than 17,000 variants in 245 genes associated with 53 diseases, according to the researchers. They provide three case studies in the paper that help demonstrate the efficacy of the system for analyzing de novo, recessive, compound heterozygous, and secondary variants in samples from individuals with various inherited diseases and disorders.

According to its developers, ClinLabGeneticist helps researchers in clinical labs bridge the gap between actual clinical practice and testing guidelines from agencies such as the American College of Medical Genetics, College of American Pathologists, and Clinical and Laboratory Standards Institute. With many clinical testing laboratories switching recently from panel-based tests to next-generation sequencing technologies, many researchers

working in these contexts find existing products designed to work with NGS data hard to use, preferring to generate and distribute variants using more familiar albeit tedious Excel spreadsheets, Chen said.

However, as the number of clinical samples sequenced grows and the amount of data generated from these tests multiplies, labs need tools that help them scale up to meet the growing demand and reduce the time to results. That's precisely what ClinLabGeneticist is designed to do and why its creators have opted to make the source code publicly available so academic labs can run the same code used in Mount Sinai for free, Chen said — commercial laboratories would need to contact Mount Sinai to obtain a software license if they want to use the tool.

ClinLabGeneticist differs from existing solutions such as GeneInsight that support genetic testing by clinical laboratories but are primarily designed for variant data storage and classification as well as report generation. It also differs from commercial offerings such as Geneticist Assistant and ANNOVAR, which are sold by SoftGenetics and Tute Genomics, respectively, and were initially developed primarily for research use and as such do not sufficiently address the needs of clinical laboratories. For example, these tools often don't provide distinct access points to their systems that accommodate the needs of the different players — administrators, directors, and report reviewers for instance— that are part of the clinical testing process, Chen said.

ClinLabGeneticist, on the other hand, offers separate dashboards for administrators and reviewers with unique features that support each user's tasks. The dashboard for administrators gives them oversight over the variant assessment process, enabling them to accomplish tasks such as uploading variant data from patient samples, generating master tables with annotations added in, selecting relevant annotation databases for each variants, and distributing variants for review. They can also merge results, set up reviewer group meetings, resolve discrepancies in variant interpretations, and select variants for validation by Sanger sequencing. They also have the ability to push assessments to laboratory directors for final decisions on clinical reports.

Reviewer's dashboards, on the other hand, allow them to view variants assigned to them, provide interpretations based on the literature, and discuss them with other reviewers assigned the same variant. They also have access to visualization tools within the system, and genes and variants are linked to relevant published literature, the researchers wrote.

Other unique features in the system include the ability to interpret variants at both the gene and variant level, in contrast to other tools that might only support variant-level evaluation. It also manages the complexities associated with assigning variants for review and collating response from multiple reviewers more efficiently than current methods can.

The researchers are now working on a new version of the software that will be able to incorporate clinical information into its workflow, according to the paper. They are also keeping an eye on developments in the analysis of copy number variation and structural variation and plan to enable the system to support those variants when clearer assessment guidelines become available, they wrote.