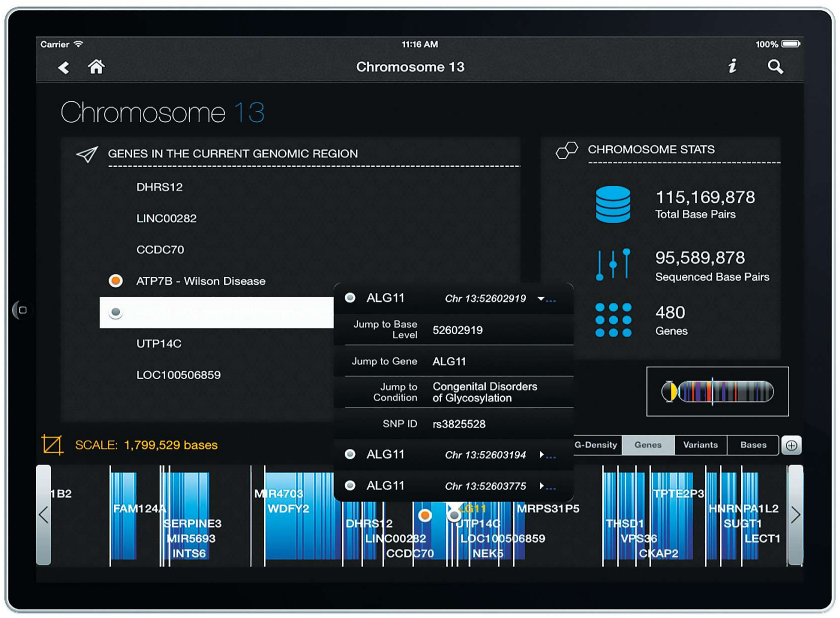
GEN Genetic Engineering & Biotechnology News
December 2014
www.GENengnews.com
TOOLS TECHNOLOGIES TECHNIQUES

Genomic Singularity Is Near



Physicians and patients can visualize genomic data with the Illumina MyGenome App, an iPad-compatible educational tool. The app's graphically accessible format can help users tour chromosomal landscapes and explore associations between genes and biological traits and common conditions, including conditions identified as potentially significant in their clinical reports.

Kate Marusina, Ph.D.

The explosive growth of DNA-based diagnostics empowers us to take a closer look at our own health and to demand answers from healthcare providers to questions that have never been asked before.

Even if we do not fully understand the clinical relevance of most of the genetic changes, the information that has been validated is significant enough to change the status quo of medical care.

It is only natural that mobile devices are tapped for their unprecedented power and flexibility to deliver physiological data and lab results when and where it is needed most. As the maturing world of mobile devices meshes with the rapidly emerging word of genomics and biosensors, medicine could literally be found at our fingertips. This powerful combination not only gives more tools to treat the existing conditions but could also shift medicine into a true preventative mode.

Some visionaries hypothesize that mobile data will eventually lead to the demise of brick-and-mortar hospitals. One such visionary, geneticist and cardiologist Eric Topol, M.D., advocates the widened use of wearable, wirelessly networked biosensors to advance personalized medicine. In his popular book, "The Creative Destruction of Medicine," Dr. Topol even anticipates that digital tools could empower a consumer-led democratization of medical care.

The data for each individual will be networked to produce a comprehensive picture of disease biology while maintaining the full ability to characterize a particular individual's unique

see page 38

Immunoassays Expand Range of Applications

Richard A. Stein, M.D., Ph.D.

Immunoassays have been at the forefront of biotechnological innovation, driving advances in both the lab and the clinic, sparking scientific insights and guiding diagnostic and therapeutic decisions.

As such, immunoassays represent a technological vanguard, one that possesses the potential, like any vanguard, to mobilize the common run.

To realize this potential, researchers and developers are working to broaden the appeal and applicability of immunoassays. They are improving immunoassay sensitivity and specificity, adding multiplexing capabilities, decreasing costs, and devising platforms that are not only highly capable and readily available, but also portable. These advancements promise to markedly expand the population of end-users benefiting from rapid, inexpensive, and accurate testing. Such testing, extended to resource-constrained settings, may signifi-

see page 22

IntelliCyt's iQue Screener is a high-throughput instrument that incorporates flow cytometry. The instrument can sample suspended immune cells and other objects, and it can generate multiplexed data—up to six measurements per object. In antibody screening campaigns, iQue Screener can present antigens on cells and maintain the antigens' native conformations.

Genomic Singularity

Continued from page 1

genotype. But for now, genetic data is just beginning to find its way to mobile interfaces, we are still some years away from the fully portable genomic representations needed for the advent of "digital medicine."

Digital Pedigrees, Genetic Risks

Genetic counselors provide risk assessment, education, and emotional support to the individuals and families at risk because of genetic predisposition. Genetic counselors interpret the results of genetic testing and have training and expertise to communicate diagnostic testing results, especially when the results are not immediately applicable or straightforward. To accomplish these tasks, genetic counselors often make use of medical pedigrees. A medical pedigree is a graphical representation of a family's health history.

With the rapid increase of genetic testing and wider availability of whole genome sequencing, medical pedigrees have expanded to capture families' genetic mutations. Pedigrees now capture positive results for mutations that may potentially render the individual susceptible to cancer, cardiovascular disease, diabetes and other diseases.

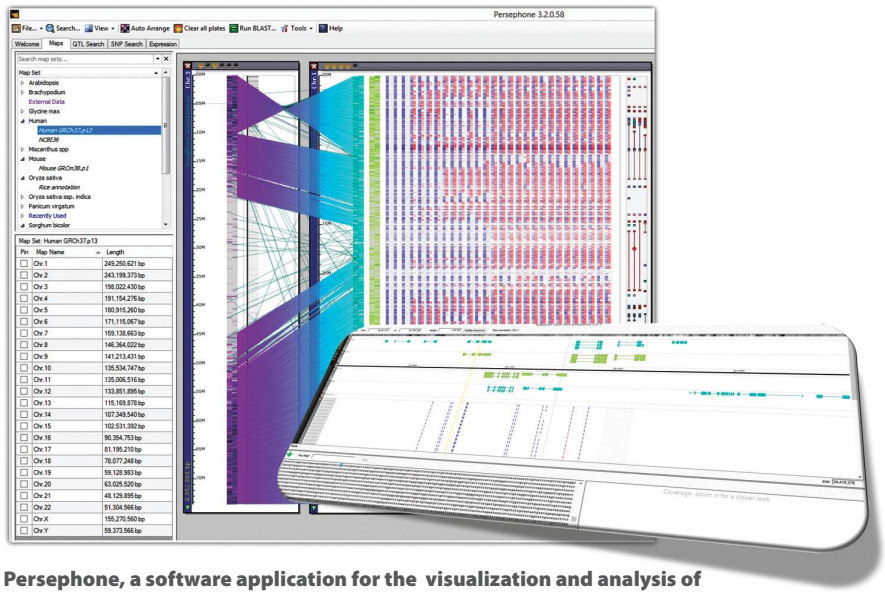
"The pedigree's utility lies in its ability to depict complex relationships at a glance, so that disease patterns, risks, and biological relationships are immediately apparent," says Jeffrey Miller, lead analyst and programmer at the Center for Biomedical Informatics (CBMi) at The Children's Hospital of Philadelphia. "Pedigree nomenclature is now fairly standardized. However, to the present day, valuable pedigree information is captured on paper by hand."

CBMi developed Proband, an app for taking family history pedigrees on an iPad. Available at the iTunes store, Proband carries the motto "Pedigrees Made Simple" and promises to enable pedigree capture at the point of interview, easing the transition from paper to screen. The mobility of the application ensures that a genetic counselor can continue facing the patient while holding an iPad, just as he or she would a paper notepad. The app can capture any level of detail, including confirmed diagnosis.

Users have commented on ease of tracing the diagnosis up the family tree. Creating pedigrees in the electronic format provides obvious benefits of data recovery, interchangeability, security, and uniformity.

Miller asserts that in the future, Proband will be able to incorporate test results and other personal health information stored in electronic health records. "Querying pedigrees based on scientific and medical questions is another near-term goal," he adds.

In its current release, Proband can be annotated with ICD-10 diagnosis codes and the Human Phenotype Ontology. Despite Proband's apparent simplicity, development of the app was challenging. It passed through multiple iterations and took almost two years. Miller's team worked closely with genetic counselors to create an interface that captures complex relationships.



Persephone, a software application for the visualization and analysis of genomic data, was developed by Ceres to facilitate the investigation of large datasets. This screenshot depicts a cross-species comparison that encompasses a whole chromosome. Note that multiple samples show thousands of variants each and that it is possible to extrapolate trait-related regions from one species onto another that has a high degree of synteny. "Zooming" a selected region makes it easier to evaluate several annotation methods and segregate variants from each sample at the single nucleotide level. Also, the magnitude of variant importance may be assessed.

Plant Genomics, Human Diagnostics

The need to compare whole genomes evolved much earlier in plant science than in human genetics. Accordingly, plant science preceded human genetics in the development of visualization software, which may one day allow clinicians the ability to compare a patient's genetic test on a tablet in the same way a doctor might read results of an MRI or blood panel.

Persephone, a novel genome visualization software developed by Ceres, enables easy switching between reference samples. The software rapidly zooms in from the chromosomal level down to a single nucleotide. On top of this data, users can layer additional relevant annotations. The effect is similar to a geobrower zooming from the whole Earth to the level of an individual street and even a house.

Managing data overload for various sets of users is key. There are only so many pixels on a screen. While a researcher wants access to all possible data, clinicians generally prefer a simplified view, such as a view of SNPs

News MOLECULAR DIAGNOSTICS

> Roche Plans $467M Diagnostics Manufacturing Facility in China

Roche will establish a CHF 450 million (about $467.2 million) diagnostic manufacturing facility at China's Suzhou Industrial Park, the pharma giant's eighth worldwide and first in the Asia-Pacific region.

The facility—set to become fully operational by 2018—will focus on producing immunochemistry and clinical chemistry tests and will grow its workforce to more than 600 people "over the next several years," Roche said.

> Myriad, AbbVie Sign Expanded Agreement for Tumor BRACAnalysis CDx™

Myriad Genetics signed an expanded agreement allowing AbbVie to use Tumor BRACAnalysis CDx ™ as a companion diagnostic in support of AbbVie's novel poly (ADP-ribose) polymerase or PARP inhibitor, veliparib. The collaboration builds upon Myriad's previous agreements with AbbVie under which the company is providing BRACAnalysis CDx testing to support several of AbbVie's ongoing Phase III clinical studies of veliparib, including neo-adjuvant and metastatic breast cancer.

Myriad's Tumor BRACAnalysis CDx is a companion diagnostic test for identifying both germline (hereditary) and somatic (tumor) cancer-causing mutations in the BRCA1 and BRCA2 genes. According to Myriad, Tumor BRACAnalysis CDx has undergone significant analytic validation and has been shown to identify up to 50% more patients with cancer-causing BRCA 1/2 mutations compared to germline testing alone.

> PDI Acquires RedPath Integrated Pathology

PDI acquired all of the outstanding shares of RedPath Integrated Pathology, expanding the oncology diagnostic product portfolio for its subsidiary Interpace Diagnostics.

As part of the transaction, PDI obtains all RedPath Integrated Pathology assets including the PathfinderTG® platform, which PDI said uses clinical algorithms to stratify patients according to risk of cancer by assessing panels of DNA abnormalities in patients who have lesions (cysts or solid masses) with potential for cancer. Also included in the deal are the PathfinderTG Pancreas, a diagnostic test reimbursed by Medicare to determine risk of cancer in pancreatic lesions, and any additional PathfinderTG applications in late-stage development with ongoing clinical studies.

> Accelerate Collaborates with CDC for Early Detection of Biothreat Agents

Accelerate Diagnostics entered into a research collaboration with the Rapid Antimicrobial Susceptibility Testing Laboratory at the U.S. Centers for Disease Control and Prevention (CDC) to develop tests for the rapid analysis of antibiotic-resistant biothreat agents based on Accelerate's high-speed identification and antibiotic susceptibility testing platform.

Accelerate Diagnostics said it is developing a fully integrated, easy-to-use platform that provides high-speed identification and antibiotic susceptibility testing of pathogens, working directly from patient samples. The platform can enable laboratories to provide critical microbiology results in hours instead of days.

> PositiveID Inks Agreement With U.S. Special Operations Command

PositiveID signed a U.S. Special Operations Command Cooperative Research and Development Agreement with the Special Operations Research, Development, and Acquisition Center, Science and Technology Directorate (USSOCOM SORDAC-ST), to further develop the company's real-time PCR pathogen detection system, Firefly Dx, for use across the USSOCOM mission space.

PositiveID's Firefly Dx is a point-of-need, handheld system designed to deliver molecular diagnostic results using real-time PCR chemistry. It is being developed to meet the growing need in military and healthcare markets for more rapid and accurate point-of-need diagnostics. Firefly Dx is designed to derive results from a sample in less than 20 minutes, at the point of need, compared to two to four hours for a laboratory-based device, the company said. ■

from a particular assay.

"We envision a time when genomics will transition from discovery to diagnostics," says Timothy Swaller, vice president of genomic technologies at Ceres. "Persephone's diagnostic view will focus only on informative mutations attributable to a particular trait or disease. A future mobile application would bring this essential information to a patient's bedside for a physician's assessment or to an experimental field for a plant breeder to select new hybrids."

Swaller notes that Persephone can align millions of markers for hundreds of samples, and call every variant based on a public or internal reference. "The only limitation is how much information we can compress to fit onto a screen," he explains. To develop these capabilities, Ceres programmers had to create multiple proprietary data compression, storage, and retrieval methods.

"The current release of Persephone is ideally suited for exploratory research," asserts Swaller. "The speed with which our software zooms to selected regions radically improves the ability to manage massive datasets generated by DNA sequencing and genetic testing."

In house, for example, Persephone was used to identify a compilation of genes responsible for a certain quantitative trait in sorghum samples. Whole genomes of hundreds of plants were rapidly aligned and visualized at the macro level. Once the chromosomal region was identified visually, Persephone zoomed in on a cluster of five genes and then on mutations in a few of those genes that disrupted the amino acid translation. Swaller points out that Persephone reduced the search for mutations from weeks to days.

Unified Programming Interface

"Our applications aim to provide high-definition, relatively comprehensive snapshots of the patient status at any given point of time," says Gil Alterovitz, Ph.D., director of the Biomedical Cybernetics Laboratory at Harvard Medical School. "Snapshots taken over a period of time help patients maintain their health and interact with physicians regarding their care.

"Each data source has a different system for how its data is formatted, transmitted, and utilized. Getting all the essential data in one place will radically transform the future of medicine."

Developed as an initiative under a larger $15 million grant from the Office of the National Coordinator for Health Information Technology, a project named Substitutable Medical Apps and Reusable Technology (SMART) Genomics aims to create a unified application programming interface (API). Such an interface would enable programmers to create apps that could work with data from multiple sources, such as electronic health records, sequencers, and genetic lab results without needing to be adapted to each one.

"The SMART Genomics API (http://smart-platforms.org) can be compared to a language translator that enables people speaking in all different languages to understand each other," continues Dr. Alterovitz. Three apps developed on SMART Genomics platform to date are Genomics Advisor, Diabetes (DB) Bear EMR, and Genomics Precision Medicine.

Genomics Advisor integrates clinical and genomic information in a single user-friendly interface. Users simply log in individually to reach the data sources that they have been cleared to access. The data sources may include Electronic Health Records (EHRs) and personal genomics information obtained via commercial services such as **23andMe**. As the log ins progress, more and more information populates the Genomics Advisor app, providing consumers with risk profiles for various diseases, related co-morbidities, and gene-drug interaction information.

The DB Bear EMR app incorporates Genomics Advisor as a module and adds an ability to integrate EHR, genetic, and glucose meter device data to provide live feed to treating physicians. The app incorporates interactive features, such as bear avatars linked to physical toy bears, and screens that engage pediatric patients and help kids to comply with diabetes treatment regiment.

See Genomic Singularity on page 40