BIOCENTURY
Innovations
FROM IDEA TO IND

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EMERGING COMPANY PROFILE

SNP IT ALL TOGETHER

By Karen Tkach, Staff Writer

Genomewide association studies can link SNPs to specific disease phenotypes, but the narrow scope of individual SNP studies limits their power of prediction for targeting the associated genes. Genomics plc is developing a computational platform that integrates disparate sets of genomic and phenotypic data to predict the good and bad outcomes of a compound's on-target effects.

The company has "the largest database of its kind that links genetic variation with health and other phenotypic outcomes," said co-founder and director Peter Donnelly. "Most groups in the academic context doing disease studies take individuals with a particular disease and measure them genetically, and compare them with healthy individuals and look for differences. We're in the position where we know the relationship between genetic variation and many different things." Donnelly is also director of the Wellcome Trust Centre for Human Genetics and a professor of statistical science at the University of Oxford.

He said Genomics has amassed public and "semi-public" data from about 2.7 million individuals, including SNPs and phenotypes.

The company establishes genotypes by gathering measurements of about 500,000 SNPs from individuals' genomes, then using genotype imputation — an established statistical method developed by Donnelly and his Oxford colleagues — to predict over six million additional SNPs based on genetic linkage.

In parallel, the company compiles multiple types of phenotypic information associated with SNPs, ranging from binary disease diagnoses to large sets of biomarkers.

Genomics analyzes the amassed information with a computational platform developed in-house to "exploit that multiplicity of measurements" and aid drug development in at least three ways, Donnelly said.

First, the platform can help validate disease targets. For example, the failure of GlaxoSmithKline plc's PLA2G7 inhibitor darapladib in a 2014 Phase III trial for acute coronary syndrome could have been predicted by the platform. In a post-hoc analysis, Genomics found SNPs associated with low PLA2G7 levels did not protect individuals from heart disease, which suggested inhibiting the target would have little effect.

Second, he said, Genomics' platform can identify new opportunities for compounds that fail in one indication by whether other diseases could benefit from inhibiting the gene.

Third, the platform can de-risk targets by identifying safety issues. "You might find that if you have lower levels of gene X you get less heart disease, but if you also get more prostate cancer, the genetics is then pointing to a safety effect."

Genomics has entered research collaborations with four pharmas on projects that include target selection, indication selection and compound repositioning, and has partnered with Oxford and Oxford University Hospitals NHS Foundation Trust to develop tools for a pilot phase of the 100,000 Genomes Project in the U.K. Internally, the company is developing more tools for integrating genomic, phenotype and other "-omics" data sets "to extract the most useful and relevant information" for drug discovery.

GENOMICS PLC, Oxford, U.K.
Technology: Computational genomic analyses for target validation and drug repositioning
Disease focus: Genomics
Clinical status: NA
Founded: 2014 by Peter Donnelly, Gil McVean, Chris Spencer and Gerton Lunter
University collaborators: University of Oxford, Oxford University Hospitals NHS Foundation Trust
Corporate partners: Biogen Inc., Eisai Co. Ltd., Merck & Co. Inc., Vertex Pharmaceuticals Inc.
Number of employees: 40
Funds raised: £11 million ($15.3 million)
Investors: IP Group plc, Invesco Perpetual, Lansdowne Partners Ltd., Woodford Investment Management LLP
CEO: John Colenutt
Patents: Undisclosed

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At least one other company, Global Genomics Group LLC (G3), validates therapeutic targets by analyzing genomic and phenotypic information. But whereas G3 has collected data using its own protocols to build a proprietary pan-omics database of 7,500 individuals, Genomics' methods allow it to integrate and analyze data for over two million individuals from studies that used differing protocols.

COMPANIES AND INSTITUTIONS MENTIONED

Genomics plc, Oxford, U.K.

Global Genomics Group LLC (G3), Richmond, Va.
GlaxoSmithKline plc (LSE:GSK; NYSE:GSK), London, U.K.
Oxford University Hospitals NHS Foundation Trust, Oxford, U.K.
University of Oxford, Oxford, U.K.
Wellcome Trust Centre for Human Genetics, Oxford, U.K.

TARGETS

PLA2G7 (PAFAH; Lp-PLA2) - Lipoprotein-associated phospholipase A2

REFERENCES

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