



GeneGo Lands SBIR to Create ‘Off the Shelf’ Systems Bio Package for Oncology Research

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By Vivien Marx

Powered by a \$200,000 Phase I Small Business Innovation Research grant from the National Cancer Institute, GeneGo is continuing its push to develop disease-specific versions of its pathway analysis software suite. The company is using the SBIR award to develop a software package called MetaMiner (Oncology) that will integrate experimental “omics” data with functional analysis tools for cancer research.

GeneGo is collaborating with the Dana-Farber Cancer Institute and the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University on the platform, which will include a database of cancer-specific information that GeneGo has been annotating for more than three years, as well as a range of analytical tools for network and interactome analyses.

“We are not using patient data to build this software,” Yuri Nikolsky, CEO of GeneGo, told *BioInform*. “We will populate it with a lot of public data, from databases and publications,” he said, adding that the company has already imported many of these datasets. “Most importantly it’s about data analysis.”

The project marks the company’s second effort to modify its MetaCore and MetaDrug systems biology tools for a particular disease area. Last fall, GeneGo embarked upon its first such project, a collaboration with the Cystic Fibrosis Foundation to develop a product called MetaMiner (CF) [[BioInform 09-14-07](#)]. GeneGo released the commercial version of MetaMiner (CF) in March [[BioInform 03-28-08](#)].

Nikolsky said that the company’s goal of refining its generic pathway tools for research in particular diseases mirrors the evolution of the broader systems biology field.

“Systems biology has moved into disease areas, so I think the stage of the development of genetic tools is more or less over — they represent human biology, medicinal chemistry, biology of model organisms quite well already in a general sense,” he said. “Now you need to specialize in disease areas, pathology areas, and toxicity.”

According to the SBIR grant abstract, GeneGo plans to develop a module for clustering omics samples of the same type, such as microarray expression profiles, in “large cancer patient cohorts based on functional descriptors.” The company expects this module to help select clinically distinct sub-populations “with unique combination of functional biomarkers and pathway-linked drug targets.”

MetaMiner (Oncology) will also use GeneGo’s network-analysis algorithms to integrate the associations between different types of omics data for the same patient — including data from DNA sequencing, genome-wide methylation, SNP and gene copy number assays, gene expression, proteomics, and metabolomics.

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“This method is already successfully applied in personalized and translational medicine,” GeneGo said in the grant abstract. “Here, we propose to implement it at the level of the off-the-shelf product.”

Kornelia Polyak, associate professor at Dana-Farber and consultant on the grant, explained to *BioInform* in an e-mail that the collaboration is an expansion of an existing, multiple year, “very productive” relationship she has had with the company.

Polyak will help with software development and testing, and GeneGo will design the algorithms for the project, she said.

She confirmed that the MetaMiner database will not include patient clinical data. Instead, she said, the partners will analyze omics data, from, for example, de-identified breast tumors “to find patterns specific for cell types — stem cells and differentiated cells — and [in]

pathways that are disturbed in breast cancer.”

The team’s approach is to define cancer pathways well, she said. “That means having a lot of high-quality input data, since a program can only be as good as the input is.”

Nikolsky said GeneGo expects MetaMiner (Oncology) to be of interest to a variety of oncology professionals, including clinicians, researchers, investigators, and also pharmaceutical companies working with a diverse set of omics data. “Everything can be analyzed in one environment,” he said.

Clustering to Know Why

Currently, the standard way to classify patient sub-populations is by applying different types of statistical analysis such as supervised and unsupervised clustering to identify gene expression signatures. However, Nikolsky said, “the signatures don’t really make functional sense,” because researchers don’t perform pathway and network analysis on these genes until after the signature has been established.

As a result, he said, an experiment may identify a set of genes that are descriptive about metastasis in breast cancer but do not link into pathways and networks. “This is something we don’t want to do,” he said.

He explained that there are more than 1,000 genes statistically associated with cancer, but the genetic mechanisms and the role these genes play in the disease are unknown. Nikolsky believes that it is possible to link these two realms by pulling together information about these genes and the pathways and networks in which they reside. That would enable network analysis with descriptors that have functional meaning.

“One big advantage of function-based pathways [is that] you really have something that is up-regulated or down-regulated in cancer; that is how you can obtain potential therapeutic targets as well,” Nikolsky said, adding that the technology GeneGo is developing through the NCI grant could deliver valuable information for both therapeutics and theranostics. “You can pinpoint functional units [that] are important and involved in certain types of cancer,” he said.

Another important component of MetaMiner (Oncology) is annotation, which will help to shape disease-specific maps and pathways with information about genes and compounds. “Basically we need to understand everything that has been published on the disease and put it in the pathway maps,” Nikolsky said.

While the project is an expansion of GeneGo’s previous effort to develop MetaMiner (CF), Nikolsky noted that MetaMiner (Oncology) is a much more ambitious task.

“Cystic fibrosis is a Mendelian [single gene] disease, it is much easier than cancer,” he said. “Now we are expanding that experience and moving it into a much larger disease area.”

Built to Mine

MetaMiner (Oncology) is being built on top of GeneGo’s existing MetaCore/MetaDrug platform and will encompass the company’s curated database of structured cancer domain knowledge, including gene-disease associations, cancer-specific pathways, and anti-cancer compounds.

According to Julie Bryant, GeneGo’s vice president of business development, GeneGo is planning to launch MetaMiner Oncology commercially as a series of modules with the first one slated to be released sometime between the summer to fall of next year.

According to the SBIR grant abstract, the tools to be developed will include enrichment analysis procedures for eight functional ontologies and a toolkit for network and interactome analyses.

GeneGo said that MetaMiner will be integrated with products from other vendors, including “omics hardware,” third-party bioinformatics software, workflow software packages, translational medicine platforms, and public domain resources such as the NCI’s cancer Biomedical Informatics Grid.

The project will initially develop methods to cluster omics samples in a database, which includes not only working on algorithmic tools but also visualization, Nikolsky explained. Subsequently, in a second phase, GeneGo’s algorithms will be put to work on the data to link gene signatures, pathways, and disease.

Nikolsky said that GeneGo has been involved in cancer research for approximately three years and that it recently wrapped up a \$1 million Phase II SBIR project to discover breast cancer biomarkers in a collaboration with the Mayo Clinic that NCI awarded the firm in 2006 [[BioInform 10-06-06](#)].

He said that some pharmaceutical companies and foundations in cancer research have indicated interest in the new MetaMiner project, but did not provide further details.

GeneGo is not alone in applying pathway analysis tools to oncology research. In response to an e-mail from *BioInform*, a spokesperson for Ingenuity explained that the company’s Ingenuity Pathways Analysis platform “already supports the cancer use case” and can handle a range of data types, including gene expression, SNPs, genotyping, proteomics, and metabolomics.