original tumor samples; in fact, the scientists found changes that could potentially guide anticancer drug choices. They identified amplification of 2 known oncogenes, including *ERBB2,* which is targeted by trastuzumab (Herceptin; Genentech), in a colon cancer patient.

Velculescu says larger clinical trials will be needed to determine the best applications of this approach. The team has started looking at patients with early-stage tumors to see how useful the technique will be in that setting. They believe this effort may be more challenging than it has been with advanced tumors because a smaller amount of circulating DNA may be produced by cancers at an early stage. The researchers are also working with tumor types other than breast and colorectal and have found chromosomal changes in circulating DNA in every type of cancer they've looked at so far. ■

Harnessing the Crowd

Following an approach that's already widespread in such fields as astronomy and aviation, cancer scientists recently showcased results from a pair of open-source computational research challenges that drew input from investigators worldwide. The results were presented at the seventh annual DREAM (Dialogue for Reverse Engineering Assessments and Methods) conference in San Francisco, CA, in November.

Open-source, or crowdsourcing, challenges aim to solve specific research problems by exploiting the collective wisdom and resources of the scientific community.

The first challenge, sponsored by the National Cancer Institute (NCI), tasked researchers with developing a computational model for ranking the response of breast cancer and lymphoma cell lines to drug treatment. A total of 51 research teams participated, with the winners hailing from Aalto University in Helsinki, Finland, and the University of Texas Southwestern Medical Center in Dallas.

In a second challenge, still ongoing and sponsored by Sage Bionetworks, in Seattle, WA, 354 research teams are developing models for predicting breast cancer survival based on clinical and genomic data.

Dan Gallahan, PhD, deputy director of the NCI's Division of Cancer Biology, says crowdsourcing augments traditional research, which tends to be more open ended and constrained by publication priorities. "What we get from these challenges are solutions to specific scientific problems," he says. "Ideally, as scientists refine these models, we'll be able to use algorithms for prescribing specific drugs or drug combinations based on a patient's molecular profile." NCI incentivized scientists with a guarantee that the winning model would be published in *Nature Biotechnology*.

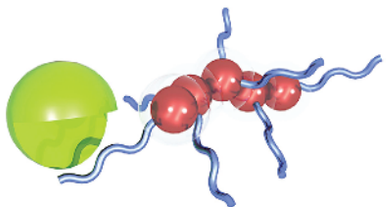
The winners of the Sage challenge have been promised a publication in *Science Translational Medicine* about their computational model. Sage Bionetworks has been ranking models with an accuracy score that appears on a public leaderboard. This method allows teams to compare how their efforts stack up. Additionally, because the scores link back to a model's publicly available underlying code, scientists can combine analytical approaches and build off each other's work, explains Thea Norman, PhD, Sage's director of strategic development.

"We had one person with a strong clinical background borrow code from someone with a background in machine learning, and the model from that collaboration scored highest on the leaderboard," Norman says. ■

Synthetic Biomarkers Identify Early Cancer

Using protease-susceptible peptides that result in breakdown products that can be measured in urine, researchers at Massachusetts Institute of Technology (MIT) in Cambridge, MA, believe they have created a way to detect cancer much earlier than is possible with current technologies that depend on blood tests, biopsies, or imaging.

Many types of cancer and a variety of other diseases, such as atherosclerosis, could be found with this new detection method, says Gabriel Kwong, PhD, a researcher in the laboratory of Sangeeta Bhatia, MD, PhD, at MIT and lead author of an article describing the technique in mouse models of colorectal cancer and liver fibrosis (Nature Biotechnol 2012;31:63–70).



Justin H. Lo

In this diagram, iron oxide "nanoworms" (brown) are coated with peptides (blue) that are cleaved by enzymes (green) found at the disease site. Accumulating in the urine, the peptides can be detected with mass spectrometry.

Early on, cancer and many other conditions produce abnormal protease activity that is not easily detectable by current means. Kwong and colleagues suggest, though, that peptides susceptible to the cleaving power of those proteases will yield fragments shed into the urine that can serve as indicators of nascent disease. Without "interrogating" cells in this way, notes Kwong, "you are really depending on what the disease cells give you."

Kwong and his colleagues winnowed about 50 candidate peptides down to 10 by testing their response to recombinant versions of proteases commonly expressed by diseased cells. They used strings of iron oxide nanoparticles, or "nanoworms," to ferry the sacrificial peptides to the diseased tissue in mice.

However, because the peptides can be sliced and diced in any number of ways, Kwong attached D isomer–rich derivatives of glutamate-fibrinopeptide B to the peptides so they cleave in a regular way. This allowed them to be measured with mass spectrometry and interpreted as signals of disease-associated protease activity. He also developed a coding system for classifying those peptide fragments into the 10 easily identifiable types.

In the colorectal cancer model, Kwong and his team tested the synthetically generated peptide fragments against carcinoembryonic antigen (CEA), a blood biomarker of colorectal cancer. Tumors that produced measurable amounts of the synthetic biomarkers were 60% smaller than those that produced measurable amounts of CEA. ■

For more news on cancer research, visit *Cancer Discovery* online at http://CDnews.aacrjournals.org.

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