Oncologists Partner with Watson on Genomics

Genetic sequencing has become increasingly affordable and accessible for cancer patients, but the complexity of processing and analyzing the data—and the time that that takes—means that relatively few patients truly benefit from the effort. That may soon change under a new collaboration between cancer centers and IBM’s Watson, a powerful cognitive computing program capable of reviewing reams of data and pinpointing potential treatment options within minutes.

“With Watson, oncologists can quickly identify the most likely driver alterations that are causing the cancer and which drugs they should be thinking about for that patient,” says Steve Harvey, vice president of IBM Watson Health. “Our system is doing in a few minutes what it would take days or weeks to do manually.”

Participants in the program, which is available to subscribers, upload patients’ sequencing data into the Watson Health Cloud platform, where it is analyzed by Watson Genomic Analytics. The program searches for actionable mutations and reviews the most-current evidence-based guidelines, clinical trials, journal articles, and patient outcomes. It then produces a report for the oncologist, listing potential treatment options alongside supporting evidence.

So far, 14 cancer centers have joined the project and are helping to expand Watson’s capabilities by uploading clinical data and providing feedback on the quality of the results. For example, the University of North Carolina (UNC) Lineberger Comprehensive Cancer Center examines DNA sequencing data. Lineberger is one of 14 cancer centers collaborating with IBM to apply Watson to the analysis of DNA data from patients with cancer.

Watson isn’t as good as people at deciding which mutations are actionable in a tumor, but I think we can fix that within a year by refining the algorithms it uses to analyze information.”

Sharpless then plans to conduct a clinical trial in which oncologists would receive two sets of recommendations for a patient—one from the molecular tumor board and another from Watson. The goal is to determine how often those two lists agree and, if they differ, which one is better at helping clinicians make treatment decisions.

Training Watson to select potentially effective drugs is by far the most challenging aspect of the project, says Sharpless.

“Ingesting the medical literature and keeping abreast of the field is a very powerful advantage of Watson,” he says. “But picking a drug based on that information isn’t easy. Some of the best drugs we have—such as Taxol and platinum—aren’t easily identifiable and what makes patients respond to those agents isn’t always clear.”

Tackling the problem will require training Watson on a very large set of clinically annotated genomic data, which does not currently exist at any single institution, he says. Several large private and public organizations are working toward that goal, including IBM, Flatiron Health, Google Genomics, and the American Society of Clinical Oncology, as well as major health insurers.

Watson doesn’t replace humans, but it is helping clinicians to work more efficiently and to conduct genomic sequencing and analysis on a much larger scale, says Sharpless.

Committee Approves Bill to Boost NIH Funding

A bill aimed at boosting federal funding for biomedical research and streamlining the drug approval process has been introduced into the U.S. House of Representatives after being unanimously approved in committee.

The 21st Century Cures Act would increase annual funding for the NIH by 3%, or $1.5 billion total over the next 3 years, and provide an additional $10 billion spread over 5 years for an Innovation Fund to support promising research initiatives focused on precision medicine. The bill would also boost FDA funding by $550 million spread over 5 years and instruct the agency to expand the scope of the data it uses during the drug approval process.*

“For many years, we have been going through an incredibly exciting time in cancer research, yet the funding has not kept up with the scientific opportunity,” says George Weiner, MD, director of the Holden Comprehensive Cancer Center at the University of Iowa in Iowa City and president of the Association of American Cancer Institutes. “We’re very excited about the bill, and the fact that it was developed in a bipartisan manner is very encouraging.”

The bill would also make deidentified data from NIH-supported clinical trials more available to biomedical researchers. The provision is in line with earlier proposals by the NIH calling for researchers to publish results from early-phase trials and those involving unapproved drugs.

“The scientific community and the public expect data generated with federal funds will be shared to enable further insights to be gained, to help enhance the quality of research, to increase transparency in federal research spending, and to improve the return on investment in research,”

*At press time, the full House of Representatives approved $8.75 billion over 5 years for the NIH and precision medicine. Funding for the FDA did not change.

— Norma Jeane Devine
Revving Up the Immune Therapy Business

As checkpoint inhibitors and other cancer immune therapies continue to advance in the clinic, giant pharmaceutical companies and nascent biotechs are positioning themselves to make the most of these agents.

Merck and Bristol-Myers Squibb both have FDA-approved checkpoint inhibitors—pembrolizumab (Keytruda) and nivolumab (Opdivo), respectively—and are pushing to expand their approved uses. For example, nivolumab was approved in March to treat advanced squamous non–small-cell lung cancer. Novartis has gained ground on competitors by buying GlaxoSmithKline’s cancer portfolio, investing in Aduro Biotech (Berkeley, CA), and hiring a leader in the field, Glenn Dranoff, MD, PhD, this past spring from Dana-Farber Cancer Institute in Boston, MA, to head their efforts.

These companies are also developing first-line therapies, as well as reexamining their portfolios to find other drugs—some already FDA-approved, others not—that might prove effective in combination with checkpoint inhibitors. Research presented at major conferences this year supported the idea that patients will see greater benefits if checkpoint inhibitors are given together or in combination with targeted therapies, chemotherapies, or cancer vaccines. Companies are testing many combinations to determine which are most effective against which types of cancer.

“The trend toward consolidation in cancer—where a single pharma company can offer a suite of agents covering a range of cancers and combinations—is definitely real,” says Bruce Booth, a partner in Atlas Venture, a Cambridge, MA–based venture capital firm specializing in life sciences and technology.

Dranoff agrees, saying it makes sense to have a wide range of therapies in-house that can be tested in combination. He notes that Novartis now has programs in checkpoint inhibitors, cancer vaccines, and CAR T cells, in addition to treatments such as imatinib (Gleevec) that are directed at specific genetic defects.

“I think there’s enormous potential for coupling,” Dranoff says. “That’s going to be a theme of the work we’ll be doing.”

Large companies are also buying and partnering with start-ups to augment their pipelines, says Booth, referring to a flurry of recent sales, including AbbVie’s $21 billion purchase of Pharmacyclics (Sunnyvale, CA) to acquire the hematologic oncology drug ibrutinib (Imbruvica). In June, Celgene and Juno Therapeutics of Seattle, WA, announced a 10-year collaboration to develop CAR T-cell therapies, a deal that will net Juno about $1 billion.

In addition, Novartis has invested $2.50 million in Aduro Biotech, an immune therapy company developing small molecules to activate the STING pathway, which may detect tumor cells and trigger an aggressive antitumor response.

Meanwhile, young biotechs, such as Jounce Therapeutics of Cambridge, MA, are advancing the science on other immune modulators. However, these biotechs have to be more selective, says Jounce CEO Richard Murray, PhD. They cannot cast a wide net, testing many compounds, like large pharmaceutical companies can.

“Biotech probably has to really start pushing the boundaries of where some of these new pieces of biology and therapeutic paradigms might emerge,” says Murray, whose company is pursuing T cell–directed therapy, as well as therapies aimed at macrophages and other cell types that may initiate or improve the immune system’s antitumor response.

“A balancing approach between the more established space and the new frontier ... makes sense,” he says.

Gene “Switch” Stops Colon Cancer in Mice

Reactivating a tumor suppressor gene that is mutated in the majority of human colorectal cancers led to rapid tumor regression and restoration of normal cell function in mice, according to findings from a recent study that may help spur development of targeted treatments (Cell 2015;161:1539–52).

Researchers used RNAi to generate transgenic mice in which they could alternately silence and restore expression of the tumor suppressor gene adenomatous polyposis coli (APC) by administering or withdrawing doxycycline. As expected, they found that APC suppression produced tumors in the small intestine and colon triggered by deregulation of the Wnt signaling pathway, which controls cell proliferation and survival. Within 2 weeks of APC restoration, the tumors completely regressed, and there were no signs of relapse over a 6-month follow-up period, even in tumors containing p53 or KRAS mutations.

“We’ve known that the APC gene is important to drive the initial events of
Committee Approves Bill to Boost NIH Funding


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