Cancer Center Chosen for Groundbreaking Study

Late last year, the National Institutes of Health chose Yale Cancer Center (YCC) and two other research institutions from among 150 applicants to conduct an extensive groundbreaking study on cancer genomics and experimental drugs. The program, overseen by the National Cancer Institute (NCI), is called MATCH (Molecular Analysis for Therapy Choice).

The study has two phases. First, cancer tissue from about 3,000 patients across the country will be molecularly analyzed to detect their genetic mutations. Yale’s Tumor Profiling Laboratory will be heavily involved in this phase, along with the other two institutions chosen, Massachusetts General Hospital and MD Anderson Cancer Center, as well as the NCI diagnostic testing facility in Frederick, Maryland. All are known for expertise in genomic analysis and Ion Torrent next-generation sequencing.

This phase is expected to take about two years.

In the second phase, 1,000 patients will be matched with clinical trials designed to test new therapies against the patients’ specific mutations. The NCI has persuaded about 20 pharmaceutical companies to donate the new drugs, which are ready for clinical trials. The trials will range across cancers and mutational types. Since many of the mutational subsets will be small, it’s unlikely that a single cancer center could enroll enough patients to conduct a credible trial, so a patient’s participation in a given trial will not be limited by geography. For instance, a lung cancer patient in Chicago with a particular mutation may get linked to a trial being run at Yale, clinicians in Chicago will administer the therapy according to the guidelines of the Yale trial and report the results to Yale clinicians.

Almost all of this is unprecedented in cancer research and medicine. MATCH reflects the NCI’s growing commitment, in terms of both funding and focus, to genomics and translational research. All clinical trials sponsored by the NCI, for example, must now include collection of tissue and genomic analysis.

Yale Cancer Center is at the forefront of genomics and translational research, which certainly factored into the NCI’s decision to choose it for this prestigious but complex study. “We probably were selected because we’ve pushed the sequencing technology as far as anybody in the country,” said Jeffrey L. Sklar, MD, PhD, Director of the Molecular Tumor Profiling Laboratory, of Molecular and Genomic Pathology, and of the Molecular Diagnostics Program.

The NCI and the participating research centers are determining standard operating procedures, and also deciding which genes to analyze. About 200 have been selected, and these will be sequenced to reveal mutations.

To minimize sequencing errors, the NCI will push software manufacturers for constant improvement. As part of the MATCH study, Dr. Sklar’s lab will have access to these evolving technologies.

Dr. Sklar says it’s still unclear what kinds of mutations the NCI wants to match with clinical trials. A growing number of drugs are aimed at specific mutations, and preliminary trials have shown that some of the drugs can be effective. That’s one possible category for matches.

Dr. Sklar believes that the NCI is also interested in trials on “cross-tumor mutations.” Research has made clear that the same mutations often appear in different kinds of cancers. In lung cancer, for instance, a mutation in the EGFR gene is well known and is often targeted with erlotinib (Tarceva). If that same mutation appears in a pancreatic cancer, would that cancer respond to the lung-cancer drug? Or what about a mutation suspected of activating a protein or a pathway? If a known inhibitor exists, would it work on that mutation in a number of cancers? The MATCH study might begin to answer such questions.

“Before being selected for MATCH, Dr. Sklar’s small lab—three pathologists, two technicians, and an informaticist—was already working at capacity to satisfy Yale’s in-house needs for sequencing. The new study will add a huge workload. To handle it, Dr. Sklar bought more equipment and added two technicians, another informaticist, and a case coordinator.

“The new equipment will more than double our potential throughput,” he said. He expects the MATCH study to claim 25 to 35 percent of the lab’s new capacity. Once the study’s first phase is over, Yale researchers will benefit from this expansion.

Dr. Sklar sees other benefits to participating in the study as well. To minimize sequencing errors, the NCI will push software manufacturers for constant improvement. As part of the MATCH study, Dr. Sklar’s lab will have access to these evolving technologies. The same will be true for advanced technologies in tissue preparation. And when the clinical phase starts, Yale will almost certainly host several trials.

“So patients who come here potentially could have access to these new drugs, which a nonparticipating center won’t have,” Dr. Sklar said. “We’ll learn early on what’s effective and not effective.”

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