Making Economic Sense of Cancer Biospecimen Banks

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In the post-genomics era of biomedical science, ever more powerful technologies enable scientists to decipher the complex molecular and genetic underpinnings of cancer and other chronic diseases. However, findings from these studies may not lead to new diagnostics and therapeutics as quickly as researchers had hoped, and the reason may lie with the most important—and most neglected—component of these endeavors: the biospecimen, the piece of tumor tissue excised from a cancer patient that researchers use as the starting point for their work. The vast majority of cancer biospecimens are afterthoughts. Once removed from the body, little attention is given to how the biospecimen is treated and stored, resulting in cancer researchers knowing little about the history of their basic starting material or the patient from which it came.

Recognizing the severity of this problem, the National Cancer Institute (NCI) is leading efforts to develop standard operating principles for harvesting, processing, and storing human tissue samples. Toward this end, the Office of Biorepositories and Biospecimen Research (OBBR) developed the *NCI Best Practices for Biospecimen Resources*, a set of principles that, as adopted, will lead to greater uniformity in the way biospecimens are handled and result in superior documentation of the exact procedures used in a cancer center.¹

The response to *Best Practices* from surgeons, pathologists, and researchers has been highly positive. Yet, despite the near universal agreement that such standards are needed, there is widespread recognition that implementing the principles in *Best Practices* to create a critical mass of platinum-level biospecimens will not happen for free. Although instituting the principles in *Best Practices* comes at a significant cost, the real question is, what is the cost of doing it wrong? How much has it cost us, and how much will it continue to cost if we are forced to repeat experiments or if we get conflicting experimental results because our initial materials are of unknown quality?

To better understand the costs of handling biospecimens according to a strict set of standard operating principles and to further the process of developing an economic model for self-sustaining biorepositories, the OBBR sponsored a 1-day workshop in June 2008 entitled “Economic Considerations for Implementing the *NCI Best Practices for Biospecimen Resources*.” This workshop brought together experts and opinion leaders from industry, academia, government, and patient advocacy communities to discuss experiences and to contribute ideas on how to build and operate platinum-level biorepositories. Discussions were aimed

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at understanding what the value proposition is for institutions procuring high-quality biospecimens and determining if it is possible for a platinum-level biorepository to operate on a cost-recovery, self-sustaining model.

Assessing the Benefits of High-Quality Biospecimens

The workshop made it clear that creating a platinum-level biorepository for cancer biospecimens would have significant benefits for cancer research, cancer patients, and the national economy because biospecimens represent concentrated sources of data and information about cancer. The cancer research community has recently awakened to the fact that research is suffering because of a lack of high-quality biospecimens harvested and stored according to standard protocols. As several speakers noted, the quality of data generated using today’s molecular technologies depends directly on the quality of samples studied.

There is a new appreciation that biospecimens taken directly from the body are living representations of the person from whom the specimens originated, and, like all living tissues, respond to whatever external stimuli they encounter, including prolonged exposure to room temperature or rapid cooling in liquid nitrogen. The problem researchers face is not just how biospecimens are collected, processed, and stored, but also that there is often little documentation of what procedures were used for a given sample. Researchers are left trying to compare results of experiments conducted in different laboratories on biospecimens collected by

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various, often undocumented, methods. The undocumented nature of the starting materials calls into question the generalizability of any findings, and thus, the ultimate value of research dollars spent on such studies.

Workshop comments made it clear that investigators are willing to pay reasonable costs for high-quality biospecimens, with associated tracking data, when such specimens are available. The question then becomes: What is reasonable from the perspective of the user and the biorepositories? Comments from those in the field suggest that academic researchers may pay as much as \$200 per sample, while those in the private sector may pay as much as \$20,000 for mission-critical biospecimens. That researchers are now beginning to place a high value on platinum-level biospecimens suggests that there should be economic models capable of sustaining such high-quality biorepositories, perhaps with some federal support.

According to advocates in attendance, patients also will benefit if they know that the biospecimens they donate are used in the most effective manner possible. Indeed, the development of personalized medicine, with the benefits of more effective and less toxic individualized therapies and lower overall cost, depends on the availability of high-quality biospecimens obtained and processed according to a set of best practices–based standard operating procedures.

Advocacy groups are aware of the issues regarding poor-quality biospecimens, and some have started to establish their own biorepositories. Such efforts, however, may not be cost-effective in the long run because of the small scale at which these biorepositories operate. As a result, such groups are allocating money to biospecimen collection and storage that might be better spent on patient care and research. Patient advocates are also aware of the need to improve the way in which data generated from biospecimens are collected and disseminated across the research community. In short, advocacy groups are well positioned to be an important voice in support of efforts to standardize biospecimen collection procedures and to establish platinum-level biorepositories.

As the U.S. economy transitions from production-based to one that is more information-based, developing platinum-level biorepositories becomes a matter of economic competitiveness. Economist Jeffrey Furman, PhD, assistant professor in the Strategy and Policy Department at Boston University in Boston, Massachusetts, noted that long-term economic growth depends on the ability to draw on a constantly growing body of scientific and technical knowledge. Biorepositories have the power to amplify the impact of scientific discoveries by enabling future generations to build on past discoveries. Dr. Furman also noted that the private incentives for establishing such a knowledge-generating institution are too low, so there is a need for public funding for such institutions.

In one case study, Dr. Furman and Scott Stern, PhD, associate professor in the Department of Management and Strategy at the Kellogg School of Management at Northwestern University in

Chicago, Illinois, found that a significantly greater number of scientific publications resulted from studies using American Type Culture Collection materials, a high-quality biorepository, compared with materials obtained from other sources. In addition, these publications were cited more frequently, and such citations appeared over longer periods of time than similar publications using materials from other resources.² The implication of this finding is that knowledge-enhancing institutions are closely associated with the process of knowledge generation and, therefore, economic competitiveness in an information-based economy.

Research by economist Gregory Tasey, PhD, of the National Institute of Standards and Technology in Gaithersburg, Maryland, points to another beneficial effect that would be expected to accrue from the development of platinum-level cancer biorepositories. His work has shown that increased investment in technical infrastructure (“infrastructure”) and associated standards-setting procedures reduce the time for new technologies to generate positive economic returns.³ Improved technical infrastructure is estimated to have a large impact on improving research and development efficiency and thereby can significantly reduce the average cost of new drug development. Although there is an imperative to increase the flow of findings from discovery to clinic, improved research and development efficiency would be expected to have a marked impact on the rate at which new diagnostics and therapeutics would penetrate the nation’s oncology clinics.

Costs Associated with High-Quality Biospecimens

Of course, implementing a set of standard operating procedures for both biospecimen harvesting and data generation will incur incremental costs when compared with today’s *laissez faire* system. Operating a platinum-level biorepository for cancer biospecimens will be labor- and data-intensive, 2 factors that would likely account for the majority of costs associated with such a facility.

Colonel Craig Shriver, MD, director of the U.S. Army’s Clinical Breast Care Project (www.cbcp.info), made this point clear in speaking about the high-quality repository of breast cancer samples his program has operated at Windber Research Institute in Windber, Pennsylvania, since 2000. As of May 1, 2008, this collection of blood, serum, RNA tubes, lymph nodes, and breast tissue exceeded 30,000 samples from more than 3,750 patients. Each of these samples was collected using an established set of standard operating procedures that includes thorough documentation and rapid transfer from the operating room to the processing laboratory. The entire process is designed to maximize biospecimen quality. With 8 years of experience behind the program, Dr. Shriver was able to determine the costs involved in operating the biorepository, which included hiring additional clinical and laboratory staff to handle tissue transfer and processing.

Overall setup costs incurred in creating the biorepository came in at just under \$3.35 million. It cost nearly \$1 million each in clinical and tissue bank setup costs, while creating the bioinformatics system accounted for the remaining expenses, all of which were incurred over the first 2 years of biorepository

operations. Operating costs for the Army's facility associated with clinical tasks have averaged \$395 per patient. Much of this expense arises from personnel costs. Ongoing operational costs associated with tissue receiving, storage, and distribution have averaged \$188 per patient. Bioinformatics costs have averaged \$278 per patient based on 1,000 patients per year, putting the total cost per patient for operating this platinum-level biorepository at \$861 per patient.

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Quality control and bioinformatics are key concerns for industrial users of biospecimens, not surprising given the regulatory requirements that drug and diagnostic companies must address with their products. James Eliason, PhD, scientific advisor at Michigan Neonatal Biotrust in Detroit, Michigan, noted that human tissue use has soared since completion of the Human Genome Project. Increased tissue use has increased demands for high-quality specimens associated with clinical data, well-documented patient consent, and medical histories. Pharmaceutical and diagnostics companies are willing to pay for high-quality materials; yet, corporate customers have become concerned enough about the quality of existing biospecimens that many are now incurring considerable expenses instituting their own quality control efforts.

At the Brigham and Women's Hospital in Boston, Massachusetts, pathologist Lynn Bry, MD, PhD, and information technology consultant Neil Herring, MBA, have developed an interesting approach to biospecimen acquisition and processing that focuses on the more than 15,000 biospecimens collected in the course of clinical care and then disposed of daily from Partners HealthCare System. The Crimson Project (www.crimsonproject.com) is largely a bioinformatics system that takes online requests for specific biospecimens and then queries the live stream of samples received in clinical laboratories and pathology departments for appropriate materials. This prospective model, which developers acknowledge would not be viable for all retrospective biorepositories of the type envisioned for the oncology community, operates on the premise of dedicated collection per known need. More than 90% of the samples processed by Crimson go out to researchers immediately, greatly reducing storage and maintenance costs. Average fully-loaded costs for collection are approximately \$8–15 per blood sample, which Crimson's billing system can charge to investigators, allowing banking sites to recoup costs for services provided. At this rate, within Brigham and Women's Hospital, the system and banks it supports will break even about 4 years into the program.

Conclusion

It's clear from workshop discussions and comments that there is a strong consensus that the development of platinum-level biorepositories is essential to the future of cancer research and clinical oncology. Opinion leaders in the field, as represented by those at this workshop and at other OBRR-sponsored meetings, appear to be fully on board to create support for such facilities. Surgeons and pathologists appear to be eager to participate,

seeing this effort as creating a new mission-critical role for their professions in the post-genomics era.

There are, however, critical issues that need to be resolved. The field needs to better understand the economics of biorepositories and whether federal dollars would be needed and available

to support such facilities, or whether a cost-recovery model can be developed that would sustain these facilities. There are also questions of intellectual property rights that need to be addressed, as well as industry buy-in to any models that require data sharing. Nonetheless, there was strong sentiment that a critical mass in support of developing platinum-level biorepositories for cancer has developed and that momentum is now operating in favor of this effort. **CTS**

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