Surgeon leadership enables development of a colorectal cancer biorepository

Vassiliki L. Tsikitis, M.D., Kim C. Lu, M.D.*, Miriam Douthit, M.A., Daniel O. Herzig, M.D.

Department of Surgery, Oregon Health and Science University, 3181 SW Sam Jackson Park Rd, Mailcode L223A, Portland, OR 97239, USA

KEYWORDS: Colon cancer; Rectal cancer; Biorepository; Tissue bank; Registry

Abstract

BACKGROUND: We hypothesized that surgeons can improve the collection of all necessary elements (tissue and clinical data) needed to build a complete, robust research biorepository.

METHODS: All colorectal cancer patients treated at a university medical center and its affiliates were eligible for inclusion. Data were collected from an 18-page personal and family health questionnaire, a prospectively maintained clinical database, and molecular testing. Tissues included serum, plasma and peripheral blood mononuclear cells, and tumor and normal tissue. We compared 2 groups: the surgeon-referred group and the other clinician-referred group. The primary outcome was the complete collection of data (ie, preoperative/staging clinical data, blood samples, and tissue collection). Statistical analysis was performed using the Student t test.

RESULTS: Since 2006, 452 patients were approached, and 430 (95%) have been enrolled. Of these, 124 were referred by their surgeon, and 306 were consented in a clinic or over the telephone. Of patients referred by their surgeon, tumor tissue, blood samples, and preoperative/staging clinical data were obtained in 119 patients; conversely, in patients referred by oncologists or other clinicians, only 133 patients had complete data (96% vs 43.5%, P < .05). A total of 257 tissue samples were obtained from all patients. Additional testing has been performed on 228 specimens including immunohistochemistry, microsatellite testing, and genotype mutational analysis.

CONCLUSIONS: Surgeon-directed enrollment in a biorepository improves the ability to collect blood and tissue samples. Surgeons should take a leadership role in the development of tumor biorepositories.

© 2013 Elsevier Inc. All rights reserved.

The advancement of translational research depends on the quality collection of human tissues with accompanying complete clinical annotation. A biorepository with defined research goals and established standard operative procedures forwards science with the potential not only to improve existing treatments but also to further develop new drug targets and molecular biomarkers. Surgeons play a key role in the establishment of a successful biobank. Without extensive collaborative support from operating rooms and surgeons, a biorepository cannot be developed. Pathologists are traditionally overseers of biorepositories. They have expertise in processing and storing human tissue. Oncologists have extensive access to patients with tumors but have a limited ability to collect tissue.

In this article, we show that a surgeon-directed biorepository improves the collection of all necessary elements needed to build a complete, robust research resource. In 2005, the Oregon Health and Science University Division

The authors declare no conflicts of interest.

* Corresponding author. Tel.: +1-503-494-4373; fax: +1-503-494-8884.
E-mail address: luk@ohsu.edu

Manuscript received November 16, 2012; revised manuscript January 22, 2013

0002-9610/$ - see front matter © 2013 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.amjsurg.2013.01.020
of Gastrointestinal and General Surgery and the Knight Cancer Institute funded the development of the Oregon Colorectal Cancer Registry (OCCR, IRB3082). The registry includes both clinical and demographic information linked to blood and tissue collected during the treatment process since 2006. The registry was established to provide a resource for researchers examining the genetic and molecular basis of colorectal cancer.

Methods

Registry linked with biorepository

All colorectal cancer patients treated at a university medical center and its affiliates were eligible for inclusion in the biorepository. With the assistance from the registry coordinator, surgeons and/or medical oncologists obtained informed consent during the first clinic visit or afterward over the telephone. All participating patients signed an institutional review board–approved genetic consent form and medical release authorization.

The biorepository acts as a bank for all biologic materials (eg, blood and tissues) and is linked to a registry database that contains demographic and oncologic outcomes of the patients whose tissues are banked. Data are collected from an 18-page preoperative personal and family health questionnaire completed by the patient, a prospectively maintained clinical database that can include oncologic outcomes, and molecular testing results. Specimen collection for the biorepository includes serum, plasma and peripheral blood mononuclear cells, and tumor and normal tissue maintained as snap frozen samples, cryovials, and paraffin blocks. Qualified pathology personnel are responsible for the fixation and preservation of the tissue to ensure quality research tissue can be retrieved when needed (eg, for RNA analysis). Part of the tissue is stored in the optimal cutting temperature with the goal to be available for frozen sections. The rest is fixed in formalin. Paraffin archival specimens are always available for macrodissection and microdissection techniques. These paraffin tissues were used in our genomic studies as shown in the Results section of this article. The histologic evaluation of the tissue stored is performed in the pathology department; the tissue stored usually contains at least 80% tumor load to guarantee high-quality research tissue later on for genetic studies.

Patient consent, institutional review board maintenance, and data gathering are completed by the registry coordinator. The software system used links the tissue stored with a patient’s demographic and diagnostic data, which are part of the registry. The registry is approved to collect data in 4 main areas of interest including (1) preoperative data points, such as comorbidities, family history, dietary habits, medication exposure, preoperative staging, diagnostic testing, laboratory values, and American Society of Anesthesiologists score; (2) operative data points, such as operation performed, approach, length of surgery, complications, and blood loss; (3) surgical pathology data points, such as stage, node ratios, tumor size, lymphatic invasion, and differentiation; and (4) postoperative data points, such as complications, a return to the operating room, length of stay, and discharge destination.

During follow-up, the registry database will be updated with information regarding clinical and pathologic recurrence, subsequent imaging studies, and the overall outcome. To test our hypothesis, the patient cohort was divided into a surgeon-referred group and an other clinician–referred group. The groups were analyzed with the primary outcome variable as a complete collection of data (ie, preoperative/staging clinical data, blood samples, and tissue collection). Statistical analysis was performed using the Student t test.

Results

Molecular analysis linked to clinical outcomes

Since inception of the program in 2006, 452 patients were approached to join the registry, and 430 (95%) patients have been enrolled. Of these, 124 patients were referred by their surgeon and consented at the time of surgery, and 306 patients were consented in a clinical setting or over the telephone. Of the patients referred by their surgeon, tumor tissue, blood samples, and preoperative/staging clinical data were obtained in 119 patients; conversely, in patients referred by oncologists or other clinicians, the combination of tumor tissue, blood samples, and preoperative/staging clinical data were obtained in 133 patients (96% vs 43.5%, \( P < .05 \)). The difference was because of incomplete tumor tissue and blood samples when patients were consented postoperatively. The initial institution may not have obtained or may have discarded excess tissue before a patient’s consent to join the registry. In all, a total of 257 patient tissue samples were obtained. In addition to a more successful accrual of patient tissue by the surgical team, molecular testing was undertaken on 228 of those specimens under the supervision of the same surgical team.

Comments

Biorepositories provide a critical link between clinical circumstances and research needs. In order for translational research to be successful, 2-way interaction between clinical and laboratory scientists is essential.\(^5\)\(^6\) Tissue analysis or clinical data alone are not sufficient to provide insight into novel methods of detection or treatment of colorectal cancer. Although biobanking has occurred in some form for decades, modern tissue collection and storage for molecular and genetic analysis is an emerging science.\(^5\)\(^6\) Small tissue banks created at university medical centers have unique advantages and challenges.\(^7\) In particular,
although there are fewer specimens in a single-center biorepository, the quality of the associated clinical information, tissue availability, and flexibility to adapt to specific institutional needs may be superior to a multicenter or national central biorepository. In addition, a single-center biorepository can incorporate the needs of the researchers and the questions to be addressed in the development of the biorepository.  

We reported our effort to develop a single-center biorepository for the purpose of providing clinical information and tissue samples to perform studies on the molecular and genetic basis of colorectal cancer. Surgeons represent the initial interface with the majority of colorectal cancer patients. Because most curative-intent treatment includes resection in the early stages of care, surgeons play a critical role in identifying eligible patients to participate in a registry, in obtaining more complete preoperative/intraoperative clinical information, and in prospectively collecting enough tissue and blood for future studies. Our report indicates that a surgeon-led effort provides better results for establishing more robust, complete biorepository.

**Conclusion**

Biorepositories are key research resources that combine the traditional function of a tissue bank with clinicopathologic data, genomic data, and patients’ clinical outcomes. Tissue banking and the construction of a patient registry are essential elements of developing personalized cancer treatment. Here, we show that surgeon-directed enrollment in a biorepository improves the ability to collect blood and tissue samples in conjunction with demographic and clinicopathologic data. Surgeons should take a leadership role in developing institutional tumor biorepositories.

**References**


**Discussion**

Alessandro Fichera, M.D. (Seattle, WA): Dr. Lu and the Oregon Health & Sciences University (OHSU) group are to be congratulated for their efforts in creating a large colorectal cancer biorepository. As we move toward more personalized approaches to treatment we will be making decisions based on genetic fingerprint, not just in cancer but also in inflammatory bowel disease and other diseases of the gastrointestinal tract. Investigators involved with creating a biorepository or simply with collecting tissue samples for clinical study know that there are several critically important issues associated with such an endeavor including confidentiality, patient safety, safety of the data, and potential implication with insurability of patients and their siblings. Traditionally, surgeons have been considered poor managers for such an initiative, often rightfully so, and typically it has been up to pathology or medical oncology to manage and organize biorepositories. In colon and rectal cancer, a large component of the overall treatment is surgery, and as surgeons we have access to patients early in their treatment, tissue and other biosamples at surgery, and finally follow-up data in the postoperative period. The OHSU colorectal group has clearly showed us that it is not only possible to organize and manage a biorepository but also with proper education it is possible to achieve very high accrual rates. Having been involved with tissue sample collection on a large-scale, I am very impressed by the results of the OHSU group. I do have a few questions. A major issue with starting and maintaining collection of tissue and other biological samples is funding. How was your biorepository funded, supported, and maintained? Why did you decide to limit data and sample collection to colorectal cancer and to exclude inflammatory bowel disease, another important field in which genetic predisposition is important and outcome seems to be related to the genetic background of the patients? Have you seen an increase in the accrual rate overtime with increased awareness of the importance of personalized medicine? Perioperative data and genetic analysis are extremely important, but they become less meaningful without follow-up data. How successful are you in obtaining long-term information? What is your secret to get 96% of your patients to sign the consent and provide data and tumor and blood samples?