Abstract:
Translational medicine integrates biomedical research with clinical and diagnostic strategies to improve health. A resourceful tool of translational medicine in the field of oncology is tumor tissue biobanking. Tumor tissue biobanking is used for biomedical research for the discovery of diagnostic and prognostic biomarkers that could provide insight into disease treatment and prevention. The presented case demonstrates that tumor tissue biobanking serves as a valuable resource for identifying diagnostic and prognostic biomarkers of colorectal cancer from a series of colorectal adenocarcinoma tissue specimens. In these tissue specimens, mutated oncogenic BRAF and microsatellite instability were associated with a poor clinical features and patient prognosis.

Background:
Tumor tissue biobanking (TTB) plays a major role in translational medicine by serving as a resource for biomedical research that aids clinicians in patient diagnosis and the development of therapeutic strategies. So TTB can be accomplished by TTB through the discovery of diagnostic cancer-predictive biomarkers or novel biomarkers that are characteristic of a particular mutational and pathological status within a tumor tissue sample. This is derived from a spectrum of archived TTB samples that are associated with a set of data, which constitutes immunohistochemical, proteomic, microarray expression, sequencing, and genotyping analysis. As anticipated, this process relies on histotechnology for providing the service of processing, preservation, and histological analysis of TTB samples. The process of identifying and characterizing a diagnostic biomarker from tumor tissue for TTB is depicted in the schematic below. This process entails the acquisition of tumor and control tissue samples, which can be allocated from TTB, the discovery of a diagnostic novel biomarker within the tumor tissue sample using biotechnological approaches, and validation of the biomarker using repetitively testing existing within tumor tissue samples. The study of these TTB samples will ultimately allow the clinician to perform surveillance of early stages of the disease and choose a particular therapy that will prevent the development of malignant cancer and have the best outcome for the patient (1-3). The broad implication of this process is etiological insight into pathogenesis of cancer and disease prevention.

TTB can help in understanding the pathogenesis and progression of colorectal cancer. This disease entails a series of mutations in tumor suppressive genes, such as p53, or oncogenes such as KRAS or BRAF, that promote genomic instability and tumorigenesis. It is important that a clinician may use this mutational status to strategize an effective therapy (3-5).

Methodology:
Frozen TTB specimens that were colorectal adenocarcinomas collected between the years 2000 and 2009 were analyzed for mutations in the BRAF oncogene from a study population of 475 patients. BRAF mutations were detected using DNA sequencing and polymerase chain reaction. Genetic instability was an upstream event of a BRAF mutation, was determined using microsatellite instability testing. Statistical analysis entail a Fisher exact and X2 tests (5).

Results:

Table 1. Categorization of patient tumors by BRAF mutation (Analysis population: 475). Twelve percent of the study population have BRAF mutation with a higher trend in females and older individuals. BRAF mutations were prominent within the proximal colon, associated with a moderate differentiation status and higher microsatellite instability.

Figure 1. Survival Kaplan-Meier curve comparison of patients containing BRAF wild-type or mutant status (TTB samples) (Analysis population: 322). The patients containing BRAF-expressing colorectal adenocarcinomas (RED) contained a statistically significant (p = 0.018) decrease in percent overall survival. Analysis based upon a 120 month interval with a median follow-up analysis of 60 months.

Discussion:
Insight into the clinical effects and patient prognosis were determined based upon TTB of colorectal adenocarcinoma tissue samples that contained the biomarkers BRAF and microsatellite instability. Results of these studies demonstrate that TTB colorectal adenocarcinoma tissue samples that contained mutated BRAF were more prominent in older individuals and females, exhibiting high microsatellite instability, arise particularly in the proximal colon, and reduce overall survival. Since colorectal cancer may be resistant to chemotherapy and diminish patient prognosis, this information is absolutely essential in the development of therapeutic strategies to eliminate mutated BRAF-expressing colorectal tumors in order to improve survival and prognosis of the patient. In other words, conventional 5-fluorouracil or EGFR-based therapies may not be effective in treating BRAF-expressing colorectal tumors and require a more specific therapy. This study recognizes the need for specific and personalized therapies based on the characterization of a tumor tissue sample. TTB is advantageous for this approach by the onset or change in levels of biomarkers that are crucial in diagnostic and prognostic determinations (1-2).

This study provides an example of how TTB is essential in translational medicine by identifying diagnostic and prognostic biomarkers, which can be further investigated as therapeutic targets, from TTB samples. In the presented case, these biomarkers identified from TTB colorectal adenocarcinoma samples were mutated BRAF and microsatellite instability. This study captures the essence of TTB by the characterization of biomarkers that advance our understanding of the pathogenesis of a disease, such as colorectal cancer. TTB permits the study of colorectal adenocarcinoma tissue samples using the biotechnological applications of DNA purification, polymerase chain reaction, DNA sequencing, and microsatellite instability testing. As shown in the schematic below, tumorigenesis drives the cellular transformation of normal cells into early and symptomatic cancer. The development of this process is attributed by the onset or change in levels of biomarkers that are crucial in diagnostic and prognostic determinations (1-2).

Conclusion:
This study demonstrates that a series of biotechnological approaches can be used to characterize and identify diagnostic and prognostic biomarkers, which can be further investigated as therapeutic targets, from TTB samples. In the presented case, these biomarkers identified from TTB colorectal adenocarcinoma samples were mutated BRAF and microsatellite instability. This study captures the essence of TTB by the characterization of biomarkers that advance our understanding of the pathogenesis of a disease, such as colorectal cancer. TTB permits the study of colorectal adenocarcinoma tissue samples using the biotechnological applications of DNA purification, polymerase chain reaction, DNA sequencing, and microsatellite instability testing. As shown in the schematic below, tumorigenesis drives the cellular transformation of normal cells into early and symptomatic cancer. The development of this process is attributed by the onset or change in levels of biomarkers that are crucial in diagnostic and prognostic determinations (1-2).

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