EDRN Pancreatic Cancer Reference Set

I. Introduction

Pancreatic cancer is the 4th most common cause of cancer death in the United States. It was estimated in the United States that in the year 2010, 43,140 cases of pancreatic cancer would be diagnosed and 36,800 patients would die of this disease. This dismal survival rate is largely due to our failure to diagnosis a cancer at an early stage when the option of curative resection is still possible. This is in large part related to the late presentation of symptoms, our inability to identify a pre-malignant precursor lesion for the majority of cancers and high likelihood of metastases even when the tumor is as small as 1 to 2 cm in size.

The current biomarker for pancreatic cancer is CA 19-9. Increased levels of CA 19-9 are strongly associated with pancreatic cancer. It is elevated in 70-80% of pancreatic cancer patients, but it is also elevated in about 20% of patients with benign conditions of the pancreas. Therefore is not good enough for diagnosing pancreatic cancer. New biomarkers for the early diagnosis of pancreatic cancer must perform better than CA 19-9, both in sensitivity and specificity. There is an urgent need for novel markers that can lead to the early diagnosis of pancreatic cancer. The purpose of this pancreatic reference set is for the validation of promising biomarkers for the early detection of pancreatic cancer.

II. Source of Samples

Overview of the Resource

The reference set is comprised of serum/plasma samples consented and samples collected prospectively. The reference set contains samples from subjects with pancreatic cancer (n=100), chronic pancreatitis (n=63), acute benign biliary obstruction (n=31), and healthy controls (n=61).

Use of Specimens

The reference set is divided into three reference sets. Each set contains CA19-9 matched samples.

- 33-34 pancreatic cancer (19-20 early [Stage IA, IB, and IIA] and 14 late [Stage IIB])
- 20-21 healthy controls
- 21 chronic pancreatitis
- 10-11 benign - biliary obstruction

In order to gain access to the samples, a scientific proposal must be submitted to the specimen committee.

III. Specimen Committee

This Committee will evaluate proposals for access to these specimens and make recommendations to the Executive Committee (EC) of the EDRN on the release of these samples. Final approval for the use of the samples is determined by NCI staff.

The Specimen Committee is comprised of:

- PI of study the EDRN validation study or one of the co-Investigators
- EDRN GI Collaborative group investigator

- EDRN Biostatistician
- NCI Program Director

An investigator with a promising biomarker should contact the NCI Program Director overseeing access to these pancreatic cancer specimens about the process of submitting a proposal. The EDRN website has the forms for requesting access to any EDRN reference sets (http://edrn.nci.nih.gov/resources/sample-reference-sets).
The proposal should include:

1. Introduction
   - Clinical Relationship of investigator
   - Background and Significance (discussion of the disease and of the marker(s) to be studied)

2. Preliminary Data
The preliminary data on the biomarker(s) performance should include a detailed description of the population (cases and controls), potential confounders (etiology of pancreatic disease,), assay methodology, analyses with performance characteristics (sensitivity, specificity), cutoffs, complimentary to CA19-9.

3. Methods
Describe the assay methodology and reproducibility, volume of sample needed, and type of sample needed (sera or plasma).

IV. Criteria for Approval

The criteria the Committee will use to approve the use of samples will be:
- A pilot trial has been performed in which the novel tumor marker, or a marker panel, distinguishes pancreatic cancer from controls.
- The true positive fraction and the false positive fraction are known through the use of ROC curves and the performance is either comparable or better than CA19-9 (standard biomarker for pancreatic cancer), or complementary to CA19-9.
- The assay has been shown to be reproducible with data regarding the inter- and intra-assay variability.

Upon approval, the investigator would first gain access to one randomly picked set among the three for pre-validation. The EDRN pancreatic reference set is sent blinded to the investigator. The investigator performs the assay and the data are sent back to the EDRN Data Management and Coordination Center (DMCC) for analysis and determination of the performance of the biomarker(s). This ensures there is no bias in the analysis. Upon successful performance of the biomarker(s) in the pre-validation set, investigator could have access to the other two reference sets. Note that the investigator will always remain blinded to the samples, until such time as the reference set is exhausted, then the samples can be unblinded.