EDRN-GLNE Colon Cancer Reference Set

Purpose: The Early Detection Research Network and the Great Lakes-New England Clinical, Epidemiological and Validation Center (GLNE CEVC) announces the availability of serum, plasma and urine samples for the early detection for colon cancer.

Background: Two prospective studies were used to collect samples to make this EDRN reference set. GLNE 001, (Preliminary Clinical Characterization of Serum, Plasma, and Urine Biomarkers for Colorectal Neoplasms) was a prospective, cross-sectional clinical trial to collect serum, plasma, urine, and common data elements on subjects undergoing routine screening colonoscopy or subjects undergoing surgery or endoscopy for colon cancer. GLNE 007 (Evaluation of Stool Based Markers for the Early Detection of Colorectal Cancers and Adenomas) is an on-going prospective, cross-sectional clinical to collect serum, plasma, urine, stool, and common data elements. In both protocols, subjects were undergoing routine colonoscopy (or being seen in surgery clinic for colorectal cancer) when the samples were collected. Samples were collected while the target lesions were still in place in the colon. Subjects were either normal (without adenomas or cancer), with pathologically confirmed adenomas or pathologically confirmed colorectal adenocarcinoma. Exclusion criteria for both protocols included known hepatitis C or HIV, ulcerative colitis, Crohns's Disease or IBD, history of cancer within 3 years, or genetic colon diseases including FAP or HNPCC. Samples were collected from 4 sites around North America.

The reference set consists of replicate aliquots from 50 subjects with colorectal adenocarcinoma, 50 subjects with adenomas confirmed by pathology, and 50 subjects with normal colons after colonoscopy. Normals selected for the reference set did not have polyps of any kind found on colonoscopy.

Common data elements were obtained for all samples (both protocols). These deidentifed data sets include demographics, personal and family cancer history, colon and GI symptoms and history, colonoscopy preparative regimens and timing of sample collection and colonoscopy findings. Information on colon cancer stage, adenoma size and number, and incidental polyps are included in this data set. All samples are blinded by use of an 8-digit barcode number.

Collection SOPs:

Serum was collected in red top tubes (without additive), allowed to clot for a minimum of 30 minutes to a maximum of 60 minutes, then held at 4ºC for 12-26 hours, before centrifugation and freezing at -80 ºC. 300 ul serum aliquots that have never been thawed are available in this reference set. Plasma samples were collected in purple top tubes (EDTA) and held at 4ºC for 12-26 hours before centrifugation and freezing at -80 ºC. 300 ul plasma aliquots that have never been thawed are available in this reference set. SOPs were strictly adhered to by study staff at all sites. Quality and compliance with SOPs was assessed by review of annotation of samples, training of all study staff and

review of procedures and facilities during audit visits. Only samples that were handled within the timeframes specified by the SOPs were included in the reference set.

Urine samples were collected from subjects (not a clean catch), stabilized with 1M EDTA within 10 minutes of collection and aliquoted within 4 hours of collection (held at 4 C until aliquoting). 5 ml aliquots of urine are available in this reference set.

In order to gain access to the samples, a scientific proposal must be submitted to the Specimen Committee.

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.

The Specimen Committee is comprised of:

- PI of study the GLNE and at least one of the co-Investigators
- Chair of the EDRN GI Collaborative and at least one other EDRN PI
- EDRN Biostatistician
- NCI Program Director

Information on applying for these specimens can be found at http://edrn.nci.nih.gov/resources/sample-reference-sets/edrn-pre-validation-reference-set-specimen-sharing-guidelines. An investigator with a promising biomarker should contact the NCI Program Director (301-435-1594) about access to these colon specimens and the process of submitting a proposal.

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: a detailed description of the population (cases and controls), potential confounders, assay methodology, analyses with performance characteristics (sensitivity, specificity), cutoffs.
3. Methods: describe the assay methodology, where it is going to be performed, reproducibility
    - Volume, type (sera, plasma, urine) and number of aliquots (at 300ul or 5 ml-urine)
4. Data Analysis Plan
5. Collaboration
6. Future Plans

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 colorectal cancer from normal and/or adenomas.
- 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 FOBT.
- The assay has been shown to be reproducible with data regarding the inter- and intra-assay variability