Access to EDRN Hepatocellular Carcinoma Samples

I. Introduction

The incidence of Hepatocellular Carcinoma (HCC) has been increasing in the United States, and survival continues to be grim with 1- and 3-year survival rates of 29% and 8%. Cirrhosis is the most important risk factor for patients to develop HCC, and is the group of patients that is targeted for screening. Hepatitis C is the most common etiology of cirrhosis in the U.S., but in a case series of patients with HCC we found that fatty liver disease is emerging as an important cause of cirrhosis and HCC. Most patients are diagnosed at an advanced stage when curative surgical intervention (liver transplantation or surgical resection) cannot be performed. This is mostly related to poor performance of the currently used tumor marker, alpha-fetoprotein (AFP). There is an urgent need for novel markers that can lead to the early diagnosis of HCC.

II. Source of Samples

An NCI funded EDRN phase 2 validation study for the early diagnosis of HCC has been completed. A total of 424 cirrhotic controls, 422 cases of which 208 are early stage were enrolled. Serum was collected and stored for each patient, and plasma and genomic DNA were also collected and stored for the majority of the patients. This is largest collection of early stage HCC and is an extremely valuable resource for future validation studies. Aliquots of these collected specimens will be available to investigators with promising biomarkers. There will be 2 sample sets:

a) Reference Set: 50 early stage cases and 50 cirrhotic controls
b) Validation Set: 214 advance cases, 158 are early stage, and 374 cirrhotic controls

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 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

An investigator with a promising biomarker should contact the NCI Program Director (301-435-1594) overseeing access to these HCC specimens about 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 (etiology of liver disease, liver function), assay methodology, analyses with performance characteristics (sensitivity, specificity), cutoffs, complimentary to AFP
3. Methods: describe the assay methodology, where it is going to be performed, reproducibility
   - Volume, type (sera, plasma, DNA) and number of specimens
4. Data Analysis Plan
5. Collaboration
6. Future Plans

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 HCC from cirrhosis without HCC (control group), particularly for early stage HCC.
- 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 alpha-fetoprotein (standard biomarker for HCC), or complementary to alpha-fetoprotein.
- The assay has been shown to be reproducible with data regarding the inter- and intra-assay variability