

Concept for RFA:

# Consortium on Translational Research in Early Detection of Liver Cancer

*Jo Ann S. Rinaudo, PhD*

*Sudhir Srivastava, PhD, MPH*

## Purpose

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The purpose of this initiative is to form a liver cancer consortium

- Improve the surveillance of hepatocellular carcinoma (HCC) in high risk populations
- Better stratify patients at risk of developing HCC
- Increase the fraction of HCC detected at an early stage

## Background

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### **Senate Committee on Appropriations in 2015 stated –**

“the Committee encourages NCI to continue to support liver cancer research across its portfolio, including research focused on the development of biomarkers to serve as early detection markers of cancer to offer the prospect of improved outcomes.”

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### **NCI Workshop – *Liver Cancer: A Remerging Disease in the 21<sup>st</sup> Century* (2014) recommendations**

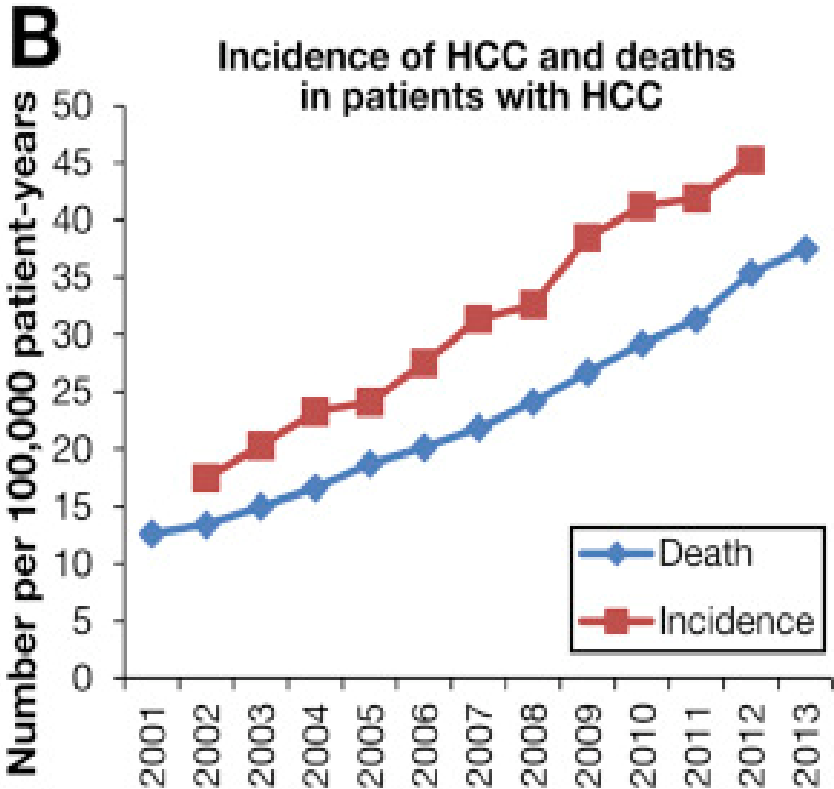
- Patients cohorts (viral and non-viral etiologies of liver disease)
- Liver cancer consortium (study continuum of liver disease: fibrosis – cirrhosis – liver cancer)
- Biorepositories

## Background

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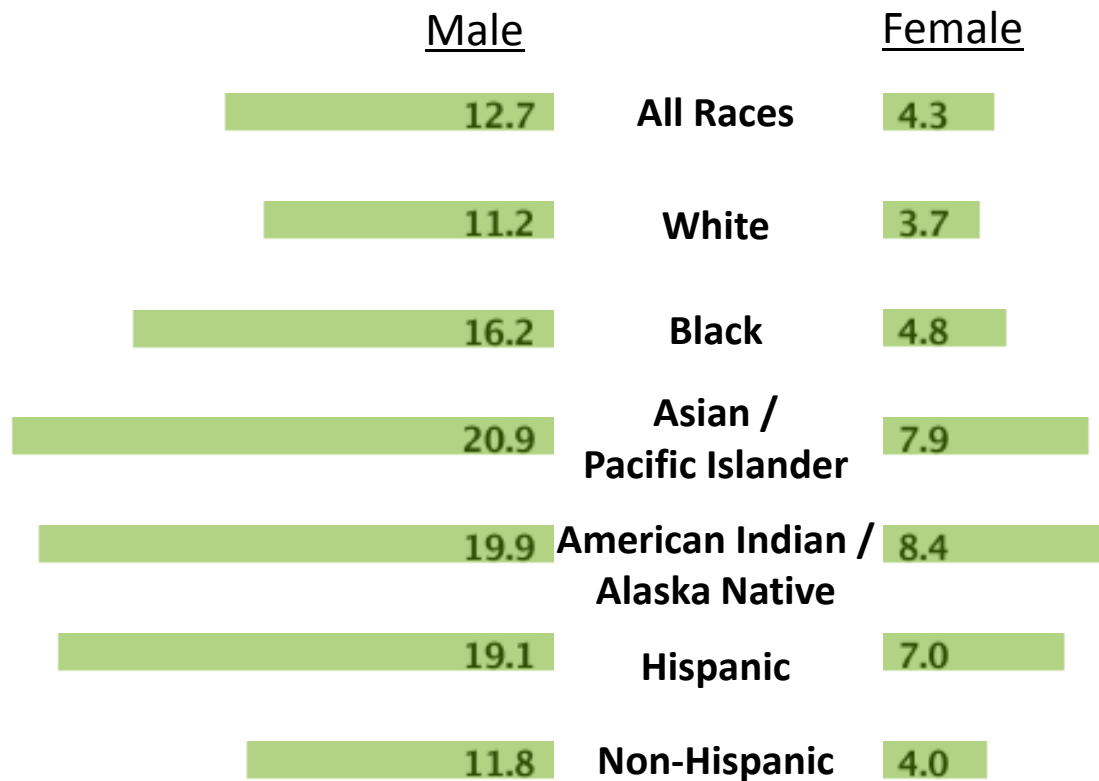
- Hepatocellular carcinoma (HCC) is second most common cause of cancer death worldwide.
- In the U.S. in 2016, 39,230 newly diagnosed cases of HCC and 27,170 deaths.
- U.S. death rates for liver cancer increased (Annual Report to the Nation on the Status of Cancer)
  - Liver cancer is 3X higher in men than women
  - Racial/ethnic health disparities (e.g. incidence higher in African Americans and Hispanics)
- Patients with advanced liver cancer have a 5-year survival of <5%.

# HCC Incidence and Mortality Rates (2001 – 2013)



# Liver and Intrahepatic Bile Duct Cancer

Number of New Cases per 100,000 Persons by Race/Ethnicity & Sex



## Rationale for Surveillance & Early Detection of HCC

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- Advanced stage HCC diagnosis has a median survival of less than one year.
- Early stage detection with resection/transplantation can achieve a 5-year survival of 70%.
- Surveillance/early diagnosis offers potential for curative interventions.

# HCC Etiologies

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- **Viral**

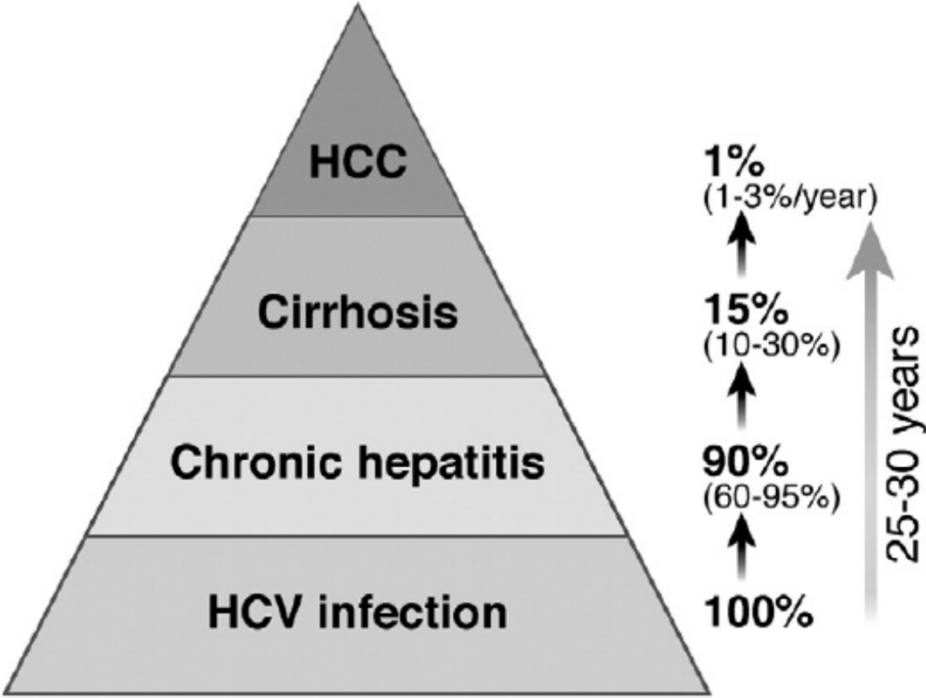
- HBV (~ 20%)
- HCV (~50-60%)

- **Non-Viral**

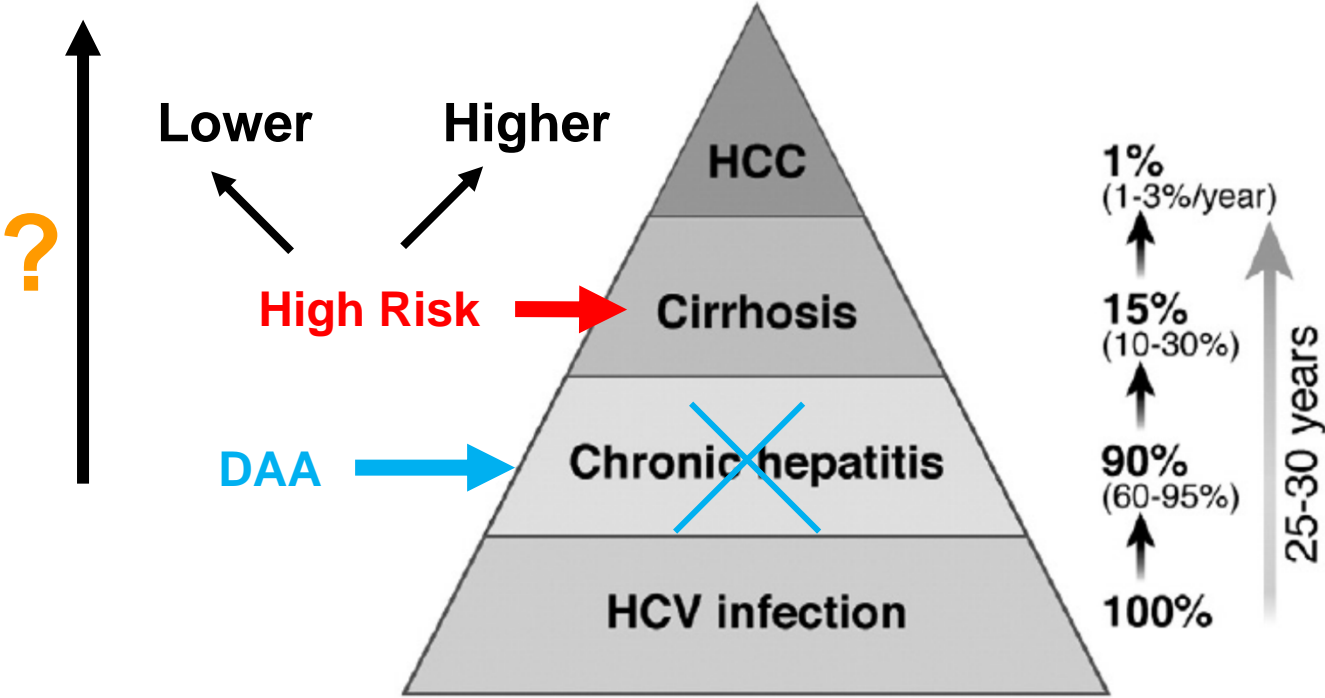
- Obesity / NAFLD / NASH (~4-13%)
- Alcoholic Liver Disease (~5%)



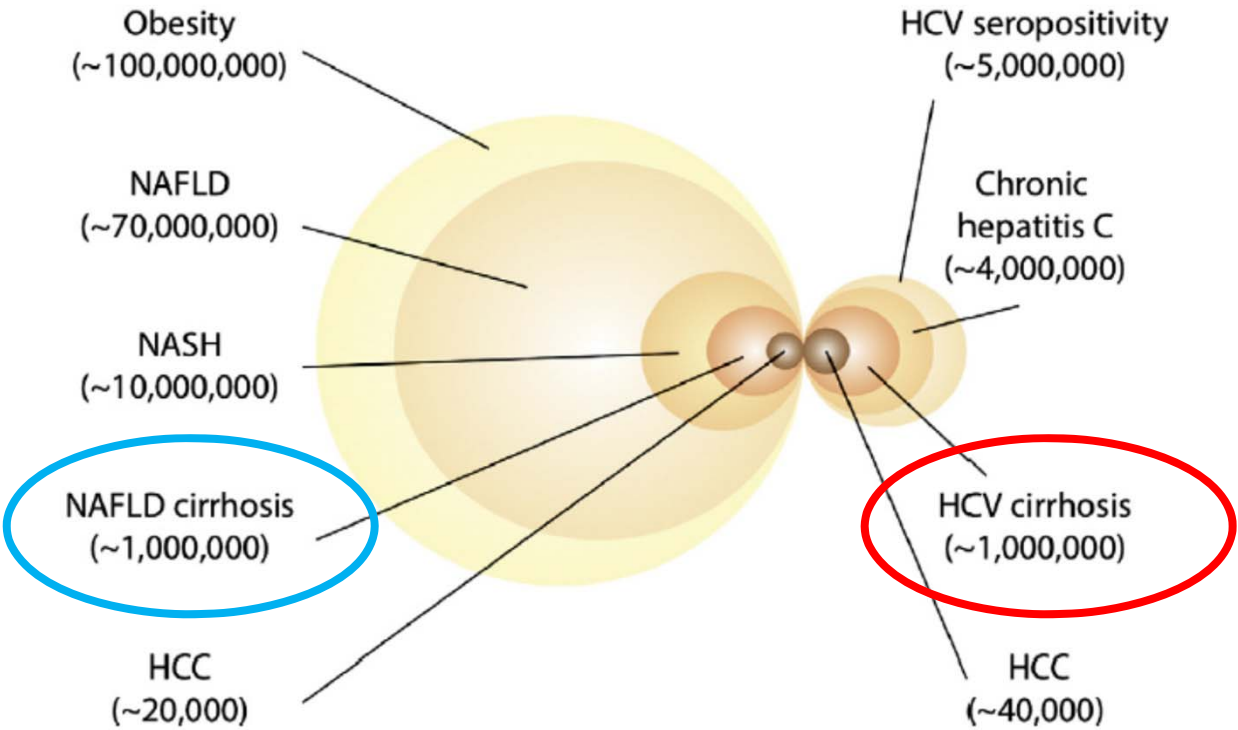
# HCV Progression to HCC



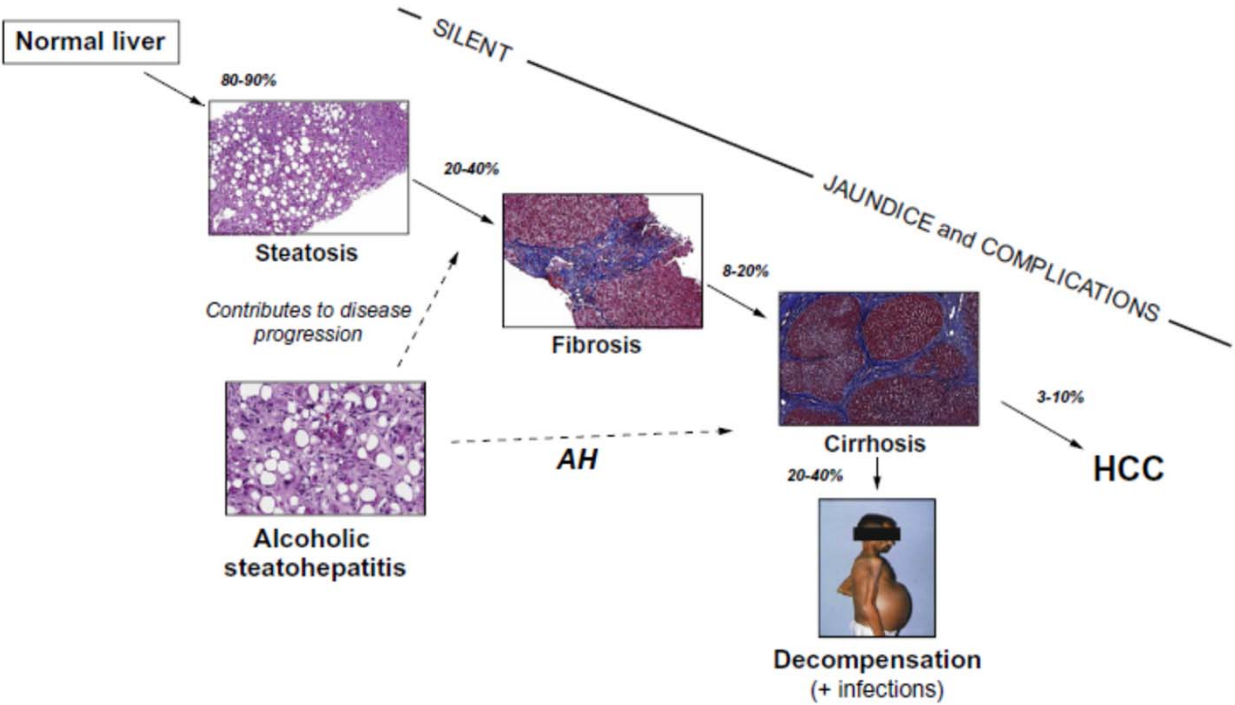
# HCV Progression to HCC



# HCC Burden Associated with NAFLD and HCV Infection



# Alcoholic Liver Disease and HCC



# AASLD Guidelines – HCC Surveillance

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- Patients with cirrhosis from any etiology.
- Alpha-fetoprotein (AFP) lacks adequate sensitivity and specificity for effective surveillance (and for diagnosis).
- Surveillance is based on ultrasound with a recommended screening interval of 6 months.
- Diagnosis of HCC based on imaging techniques and/or biopsy.

# Challenges

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- Patients with cirrhosis represent a large pool of patients that require surveillance.
- Risk of progression to HCC in clinically asymptomatic patients with early stage cirrhosis is unknown.
- Identification of cirrhotic patients at higher risk for HCC.

# Translational Liver Cancer (TLC) Consortium

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- Consortium of liver cancer investigators
- Establish patient cohorts to better define the natural history and progression of liver disease to HCC
- Establish biorepositories from different etiologies (viral, non-viral) and patients with different ethnicities
- Improve effectiveness of surveillance

## Research Objectives

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- Establish cohorts of patients at high risk for liver cancer, i.e. cirrhosis (HBV, HCV, NAFLD, NASH, ALD)
- Stratify patients with cirrhosis to identify those at highest risk for progression to HCC
- Identify biomarkers for HCC arising from different etiologies (viral and non-viral)
- Changes in the viral genome associated with increased risk of HCC (e.g. HCV genome)



## Rationale for Cooperative Agreement Award

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- A consortium of centers will aide in the recruitment of sufficient patients, in the collection of biospecimens, and will help ensure the sharing of these resources. No single site has resources to achieve these goals.
- Investigators gaining access to larger biospecimen resource and more diversified specimens (blood, biopsies, imaging).
- Analysis of the performance of a larger set of biomarker(s) in combination with various imaging modalities.
- Collaborations with other consortia and programs can bring additional resources to the Translation Liver Consortium (e.g. NCI – HCCEC, NIDDK – NASH CR, NIAAA – TREAT, and HCV-TARGET)

**The cooperative agreement mechanism will allow NCI program staff to guide and support the research to facilitate meeting the goal to improve the early detection of liver cancer.**

## U01 / U24 Awards

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- Funding: \$5M / year
- Anticipated Number of Awards: 6-8  
1 Coordinating Center (U24)
- Length of Award in Years: 5

## Reviewers Comments

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### *Program thanks the reviewers for their helpful comments:*

- Applicants will be required to include minorities in the cohorts
- Does not duplicate any existing NIH program but complement and leverage existing NCI and NIH programs
- Does not support development of new imaging methods
- Specific and quantitative evaluation criteria for the initiative were developed

# Thank you.



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