
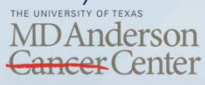



## The Texas Hepatocellular Carcinoma Consortium (Tx HCCC)




DAN L. DUNCAN  
COMPREHENSIVE  
CANCER CENTER




THE UNIVERSITY OF TEXAS  
**MD Anderson**  
Cancer Center  
Making Cancer History<sup>®</sup>



UT MEDICINE  
**CTRC**  
HEALTH SCIENCE CENTER SAN ANTONIO



**UT Southwestern**  
Harold C. Simmons  
Comprehensive Cancer Center



NCI  
Designated  
Comprehensive  
Cancer Center

### The Start of the Texas Hepatocellular Carcinoma Consortium

- Existing investigators with an interest in HCC were at Baylor (Drs El-Serag, Kanwal and Moore) and UT Southwestern (Dr Singal)
- In 2013 Drs Marrero (UTSW), Feng (MDACC) and Beretta (MDACC) came to Texas. All with track record on HCC
- Met at MDACC 2 years ago to plan a consortium dedicated to HCC
- This led to submission of CPRIT MIRA

### Cancer Center Planned Serendipity

- All Centers indicated that HCC was identified in their Catchment Area Analysis as a significant and growing cancer. They were looking for ways to address the issue.
- Dr. El-Serag indicated that his liver collaborations with Mike Lewis, were a direct result of the DLCCC Symposium Presentation.
- Further Collaborations developed out of our Liver Disease Oriented Working Group (DOWG)
- Plus, everyone has a sense of their colleagues doing comparable work around the State.
- All Centers underwrote a planning retreat for the Consortium









### Cancer Prevention and Research Institute of Texas

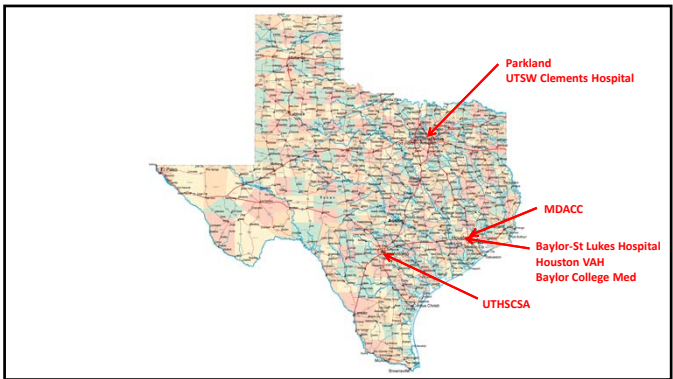
- MIRA – Multi-Institutional Research Award – a mechanism created by CPRIT scientific leadership with input from the University Oversight Committee – to foster collaboration between institutions in Texas.
- \$9.8 Million over 3 years – potential for renewal

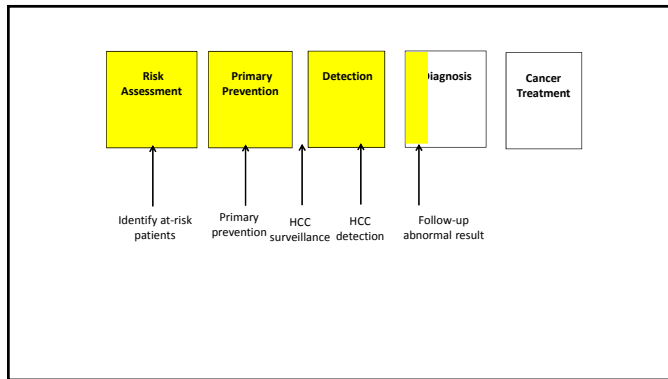
Ultimately this was the spark that lit the tinder the Centers in Texas had gathered.

### The Texas Hepatocellular Carcinoma Consortium (THCCC)

Principal Investigators

 <small>ADMINISTRATIVE CORE</small> <b>Hashem B. El-Serag, MD, MPH</b> <small>Baylor College of Medicine</small>	 <small>COHORTS &amp; SAMPLES CORE (CSC)</small> <b>Jorge Marrero, M.D.</b> <small>UT Southwestern</small>	 <small>STATISTICAL COORDINATING CORE (SCC)</small> <b>Ziding Feng, PhD</b> <small>MD Anderson Cancer Center</small>
 <small>PROJECT 1</small> <b>Faitha Kanwal, MD, MSHS</b> <small>Baylor College of Medicine</small>	 <small>PROJECT 2</small> <b>Hashem B. El-Serag, MD, MPH</b> <small>Baylor College of Medicine</small>	 <small>PROJECT 3</small> <b>David Moore, PhD</b> <small>Baylor College of Medicine</small>
 <small>PROJECT 4</small> <b>Laura Beretta, PhD</b> <small>MD Anderson Cancer Center</small>	 <small>PROJECT 5</small> <b>Amir Singal, MD</b> <small>UT Southwestern</small>	





### Overview of THCCC

Our overarching goal is to reduce the burden and mortality of HCC in Texas.

- multidisciplinary group of investigators with vast experience and expertise in HCC research.
- researchers from UT Southwestern Medical Center and Parkland Health and Hospital System in Dallas, Baylor College of Medicine and MD Anderson in Houston, and UT San Antonio
- inclusion of sites all across Texas will enrich the diversity and representativeness of our patients, ensuring a racially and ethnically diverse cohort with a wide range of socioeconomic status.
- critical gaps and needs in the HCC prevention process and appropriate ways to address them

### Project 1: Risk Factors of Hepatocellular Carcinoma in Non-Alcoholic Fatty Liver Disease

(PI: Fasiha Kanwal)

**Aim 1:** To examine the risk of HCC in NAFLD patients. We will estimate the overall, as well as the age and race/ethnicity sub-group incidence rates for HCC in NAFLD patients, and compare it to the incidence in 2 control cohorts.

**Aim 2:** To identify predictors of HCC in NAFLD. We will assess the role of demographic (e.g., age, race) and metabolic traits (e.g., diabetes, obesity, dyslipidemia, hypertension diagnoses and biomarkers like hemoglobin A1c) in the development of HCC in NAFLD patients.

**Aim 3:** To determine the chemopreventive effect of common treatments in NAFLD including metformin, statins, angiotensin converting enzymes inhibitors and angiotensin receptor blockers and the risk of HCC among patients with NAFLD.

### Project 2: Metabolic Syndrome and HCC Risk Stratification in Patients with Cirrhosis

(PI: Hashem El-Serag)

**Aim 1:** Examine the Association between Metabolic Syndrome and HCC Risk in Cirrhosis.

**Aim 2:** Develop and optimize an index for predicting the risk of progression from cirrhosis to HCC using a set of candidate factors derived from the literature, Aim 1 or uncovered by other THCCC projects.

**Aim 3:** Examine the Association between Metabolic Syndrome and HCC Risk in Cirrhosis.

### Project 3: Circadian Disruption and Bile Acids as HCC Risk Factors

(PI: David Moore)

**Aim 1:** Test the ability of the CAR inverse agonist androstanol to prevent tumorigenesis in wild type mice in response to chronically elevated bile acids and jet lag.

**Aim 2:** Test the ability of human specific CAR activators to promote hepatocarcinogenesis in humanized mice.

**Aim 3:** Determine whether elevated serum bile acids or circadian disruption increase risk of human HCC.

### Project 4: Novel Biomarkers For Hepatocellular Carcinoma

(PI: Laura Beretta)

**Aim 1:** To evaluate the ability of novel HCC biomarkers to distinguish between patients with cirrhosis but no HCC and patients with cirrhosis and HCC in a surveillance setting

**Aim 2:** To evaluate the performance of AFP, AFP-L3, DCP, OPN and selected panel from Aim 1 in detecting HCC during surveillance: A Phase-3 Validation Study

**Aim 3:** Genomic classification of the incident HCC tumors and association between novel biomarkers, somatic mutations and HCC subtypes: An Exploratory Study

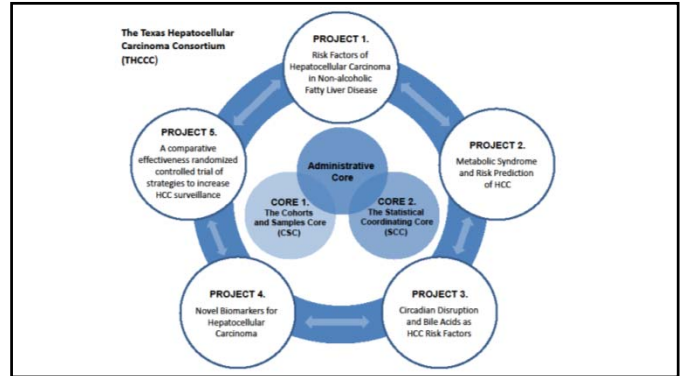
**Project 5: A Comparative Effectiveness Randomized Controlled Trial of Strategies to Increase HCC Surveillance Timeline**

(PI: Amit Singal)

Aim 1: Compare the clinical effectiveness of the intervention strategies to increase completion of the HCC surveillance process

Aim 2: Compare patient-reported satisfaction and acceptability of the HCC surveillance strategies

Aim 3: Evaluate whether intervention effects are moderated by patient sex, race/ethnicity, socioeconomic status, health care utilization, and documented vs. unrecognized cirrhosis



**Administrative Involvement**

- Essentially Nada
- We did furnish funds for planning retreat
- Our Center does not manage all member grants – so no grants administration responsibility.

**How it fits in the DLCCC**

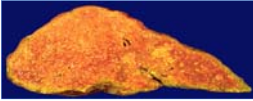
- Dr. El-Serag – PI – is the Leader of our CPPS program.
- Grant counted in CPPS count in DT-2
- Members involved
  - Donna White, PhD Research Member CPPS
  - Jennifer Kramer, PhD Associate Member CPPS
  - Li Jiao, PhD Research Member CPPS & CE
  - Dimitry Bissig Associate Member CCGT & CE
  - David Moore, PhD Research Member NR & CE
  - Fasiha Kanwal, MD, MSHS Clinical Member of CPPS
  - Michael Scheurer Research Member CPPS
- Population Science Biorepository of DLCCC acts as the biorepository for the THCCC ( Managed by DLCCC ) M. Scheurer Director.

**Core Grant Threads**

- HCC identified in Catchment Area Analysis
  - “hepatocellular carcinoma (HCC) (5<sup>th</sup> most common in Hispanic and Black males),”
  - “**Hepatocellular Surveillance:** HCC and its risk factors HCV and NAFLD disproportionately affect Hispanic residents of our catchment area. Texas Latinos have the highest age adjusted incidence rates of HCC in the nation.” **CPPS Scientific Accomplishments**
  - “**Multi Center Texas HCC Research.** In an initiative focused on the catchment area CPPS Members (El-Serag, Kanwal) are working with investigators in the NR Program (Moore), MDACC (L Berretta, Z Fang), and UT Southwestern (Marrero, Singal) to develop a multi-investigator grant application as well as a trans-Texas HCC network. This research is supported by the Population Sciences Biorepository.” **CPPS Future Directions**

**Site Visit**

- Worked into CPPS Presentation
- You only have 10 minutes – we used 12 slides, this was one.



Incidence Rates for Liver & Bile Duct, 2007-2011  
Hispanic (Male all races and ages)



**Risk Factors**

- Genetic epidemiology of HCV-related HCC (VA Merit El-Serag)
- Constitutive Androstane Receptors (CAR) in HCC (Moore (NR), El-Serag, White)

**Outcomes**

- Effectiveness of HCC surveillance (El-Serag)
- Effectiveness of Tenofovir in reducing HCC in patients with HBV (Kanwal)
- Guideline-based treatment of HCC (R01 NCI, Davila)

**Collaborations**

- Texas Hepatocellular Carcinoma Consortium (THCCC)
- First Annual HCC Symposium