



Center for Cancer Research: Chinese Interactions

Lee J. Helman, Scientific Director for Clinical Research

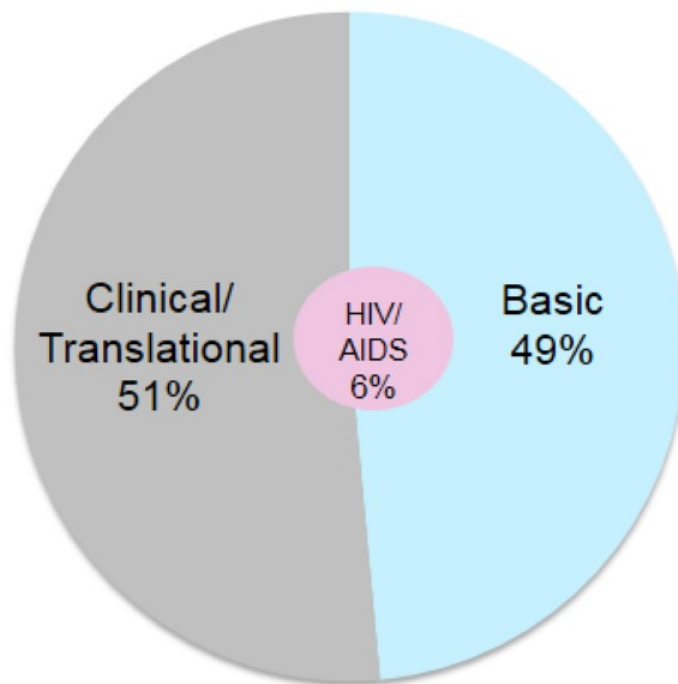
Xin Wei Wang, Laboratory of Human Carcinogenesis

June 2015



CCR Vision

Integrate basic, translational, and clinical research to make cancer preventable, curable, or chronically manageable.





Distinctiveness of NCI's CCR Derives from a Convergence of Multiple Attributes

- **Sustained support for high-risk, high-impact research**
- **Highly interactive, interdisciplinary culture for basic and clinical scientists:**
 - generation of new knowledge
 - efficient bench to bedside to bench translation
 - development of new technologies
- **Access to the world's largest cancer-focused clinical research center**
- **Focus on rare cancers and underserved patient populations**
- **Borderless collaborations that enable joint ventures among cancer research's thought leaders within and outside the NCI**
- **Flexibility to rapidly reallocate resources**
- **Multi-faceted training for the next generation of scientific leaders**



CCR:China Connections

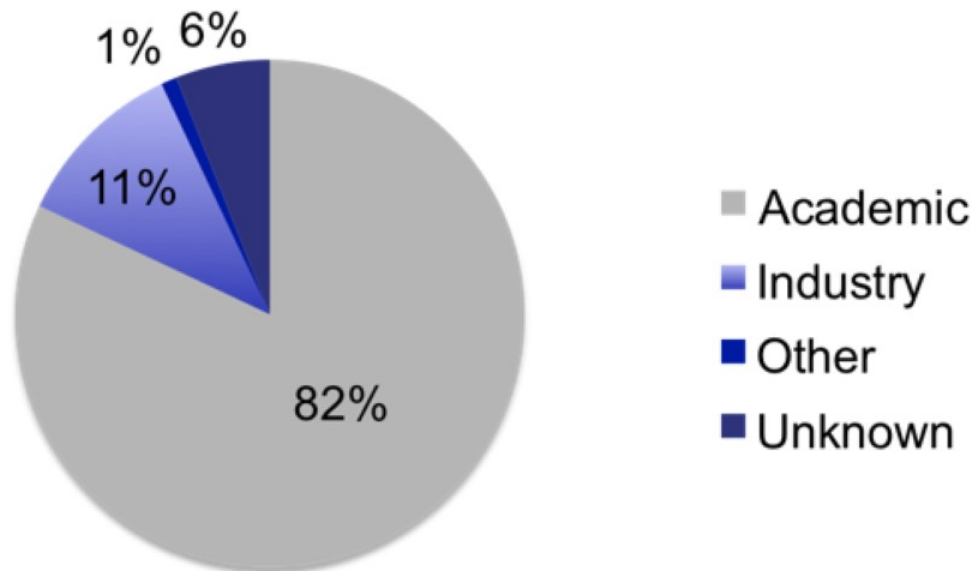
- **Personnel**
- **Collaborations**
- **Via HHS/NIH/NCI**



CCR:China Connections

- Personnel**

- 10% of CCR PIs are of Chinese descent
- Over 150 recent alumni (over the last 5 years) are now working in China





CCR:China Connections

Collaborations

• In 2014, 18 different PIs had active collaborations with 33 Chinese investigators at 28 different institutions

NASOPHARYNGEAL CARCINOMA CHEMOATTRACTANT RECEPTORS
LIVER CANCER
 KIR/HLA ABC TRANSPORTERS
BLADDER CANCER
 PROTEOGLYCAN RECEPTOR
NEUROBLASTOMA
 SCREENING NATURAL COMPOUNDS
ALS BRAIN CANCER
 SMURF PROTEINS
HPV HBV HIV
 TNF-INDUCED NECROSIS WP1 GENE

- 2nd China Medical School
- Beijing Genome Institute
- Beijing University First Hospital
- Beijing University of Technology
- Chang Gung University
- China Academy of Traditional Chinese Medicine
- China Agriculture University
- Chinese Academy of Medical Sciences
- East China Normal University
- Fudan University
- Guanganmen Hospital
- Hong University of Science and Technology
- Institute for Nutritional Sciences
- Institute of Biomedicine and Biotechnology
- Institute of Pathology
- Institute of Virology
- Liver Cancer Institute
- Nanjing Medical University
- National Center of Biomedical Analysis
- Natl. Cancer Centre Duke-NUS
- Ocean University
- Shanghai Institute of Biochemistry and Cell Biology
- Shengjing Hospital of China Medical University
- Shenyang Pharmaceutical University
- State Key University
- Sun Yat-Sen University
- University of Hong Kong
- Zhejiang University



CCR:China Connections

- **Via HHS/NIH/NCI**
 - Participated in or organized symposia in China
 - Co-funded project announcements
 - NIH/Ministry of Science and Technology (MOST)
 - NIH IRP
 - US-China Program for Biomedical Research Cooperation a.k.a “Intramural to China”



Xin Wei Wang, Ph.D.
Deputy Chief
Laboratory of Human
Carcinogenesis

**Collaborative Studies
Between NCI and Fudan
University**

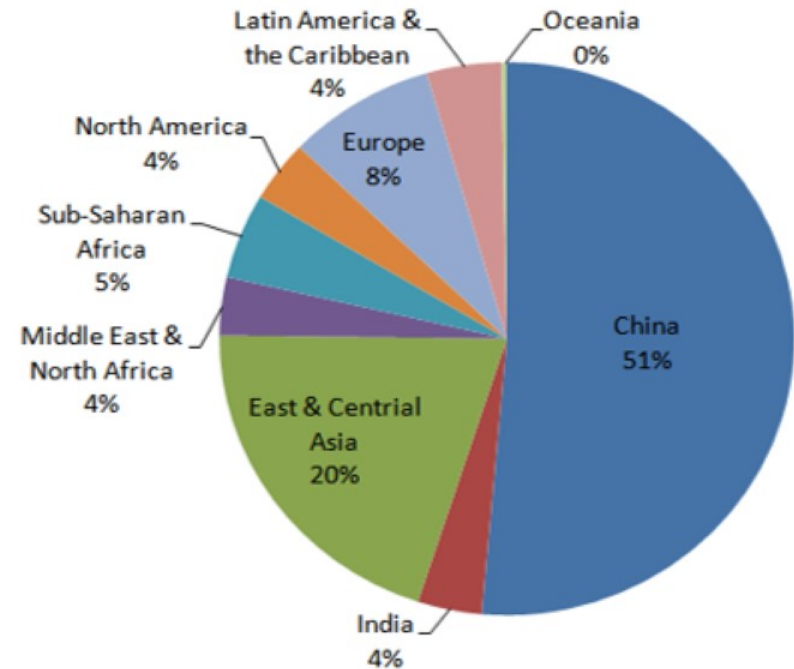
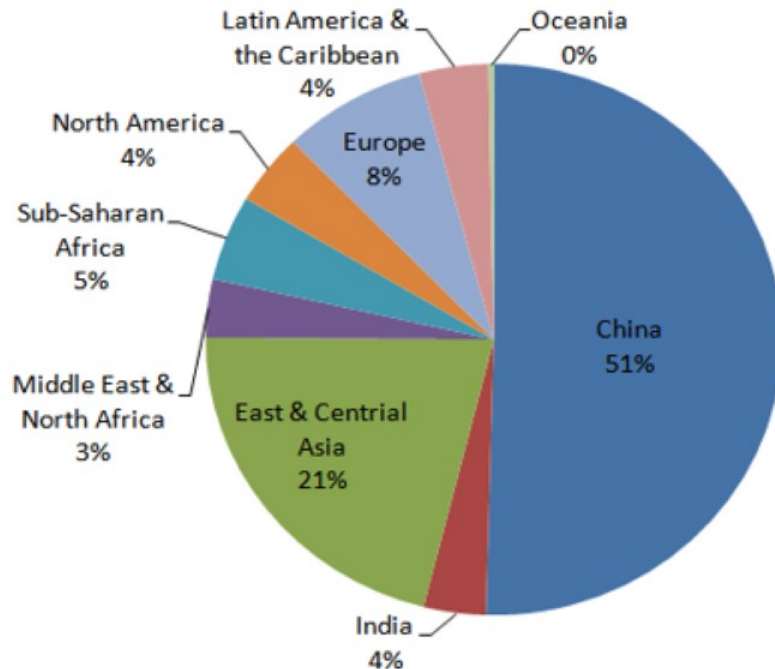
Liver Cancer is the Second Leading Cause of Cancer-related Death Worldwide



Steward BW & Wild CP, World Cancer Report 2014
www.who.int

Incidence: 782,000 new cases

Mortality: 746,000 deaths

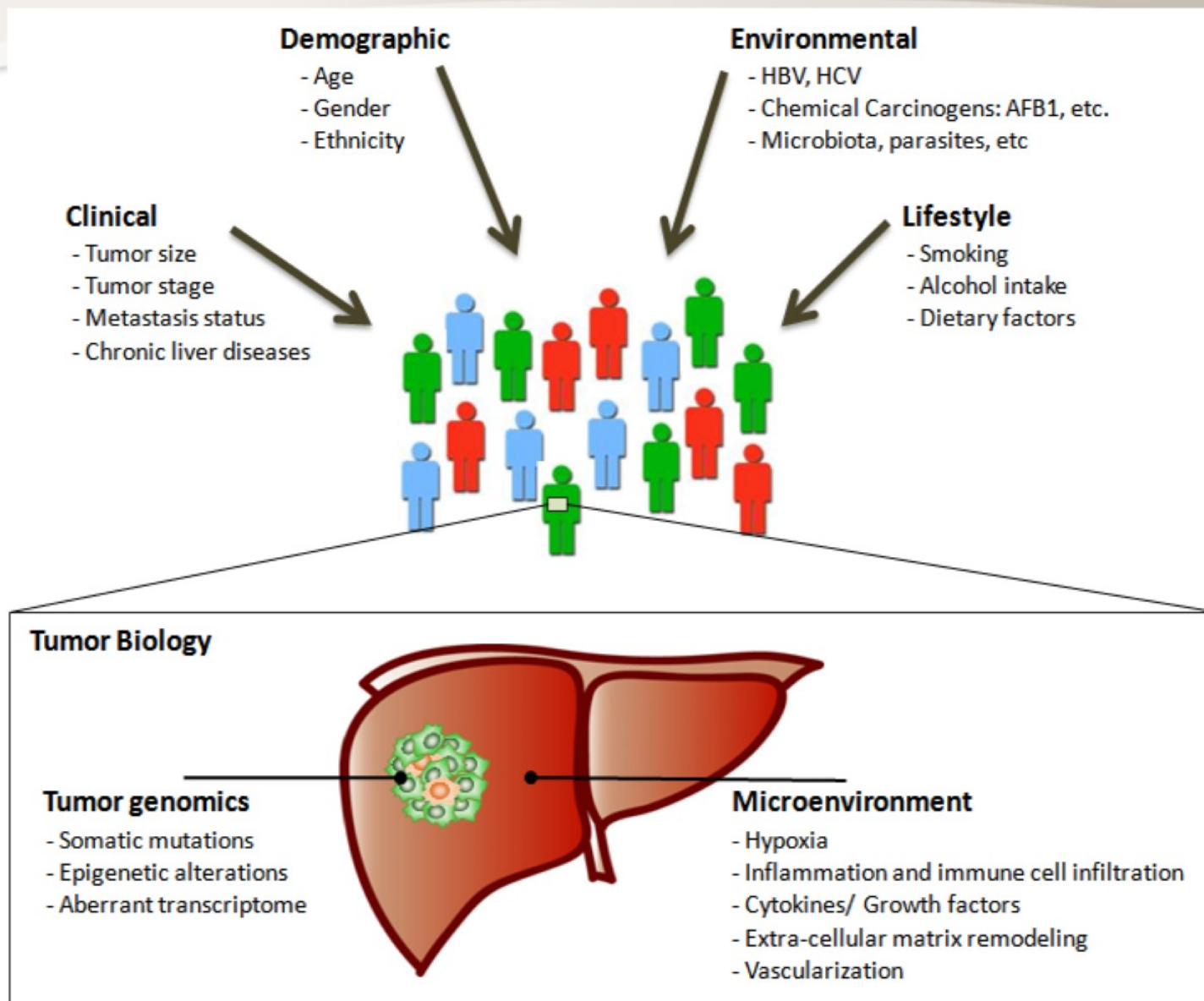


A liver cancer patient dies every 42 seconds

The Etiology and Features of Liver Cancer Heterogeneity



Sonya Parpart



Collaborative Studies Between NCI and Fudan University (1999-present)



- 1999: Established a formal collaboration between the Liver Carcinogenesis Research Group of the National Cancer Institute and the Liver Cancer Institute (LCI) of Fudan University (Dr. Zhao-You Tang)
- 2009: Jointly established a Personalized Liver Cancer Care and Research Center (PLCCRC) to perform genomic and genetic screens of liver cancer patients to identify new diagnostic biomarkers for molecular re-staging and treatment stratification
- 2009: Launched a multi-center RCT to assess the use of biomarker-guided adjuvant therapy in HCC patients
- Multiple collaborations with other LCI investigators including 3 formal Collaboration Agreements: Dr. Lun-Xiu Qin (Prof. of Surgery), Dr. Jia Fan (Director of Zhongshan Hospital), Dr. Qin-Hai Ye (Prof. of Surgery), Dr. Hui-Chuan Sun (Prof. of Surgery), Dr. Jian Zhou (Prof. of Surgery)
- Hosted and mentored 6 Visiting Fellows; including 5 MD/PhD students



Timeline and Milestones

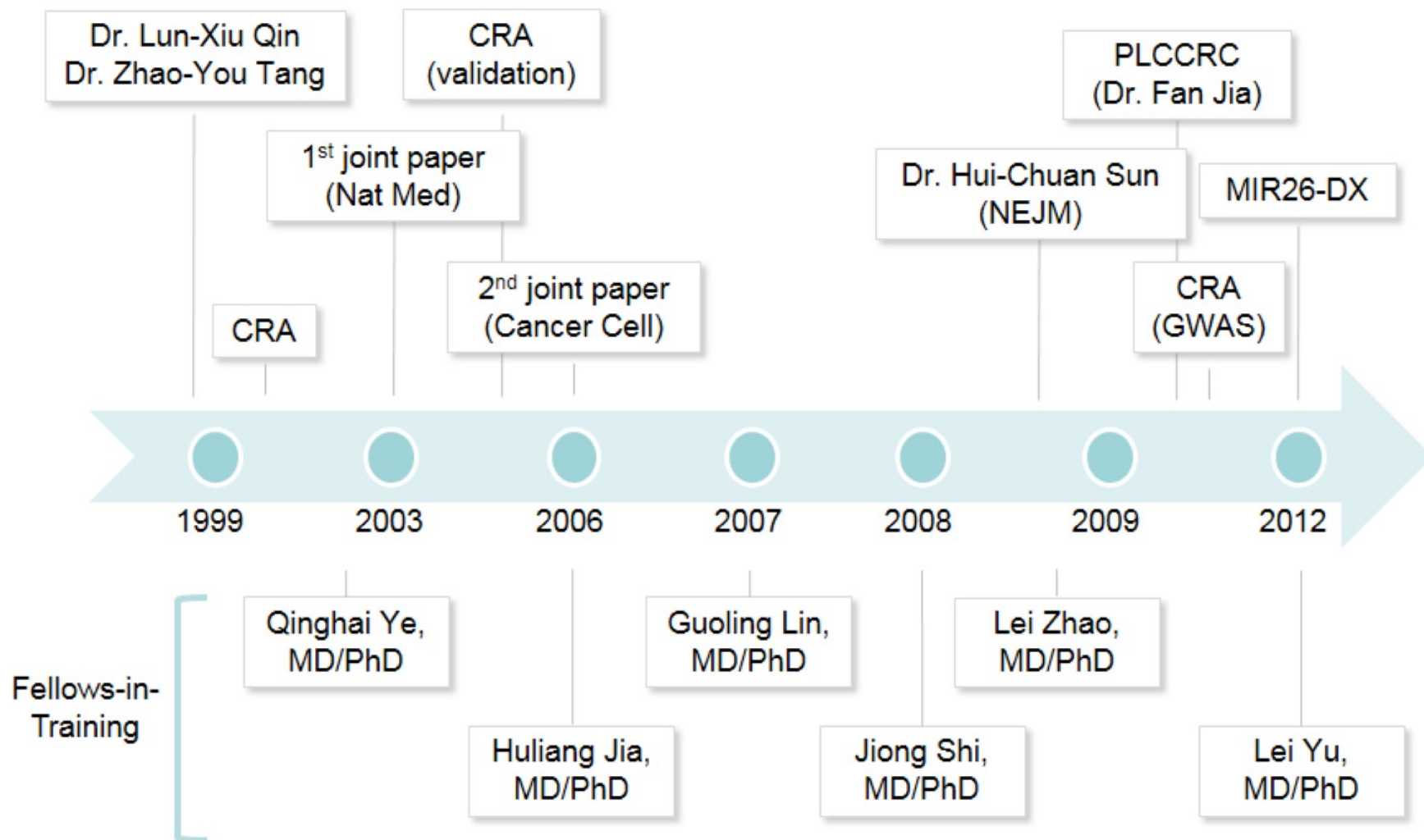
(Collaboration between NCI and Fudan University)



Initiation

Development

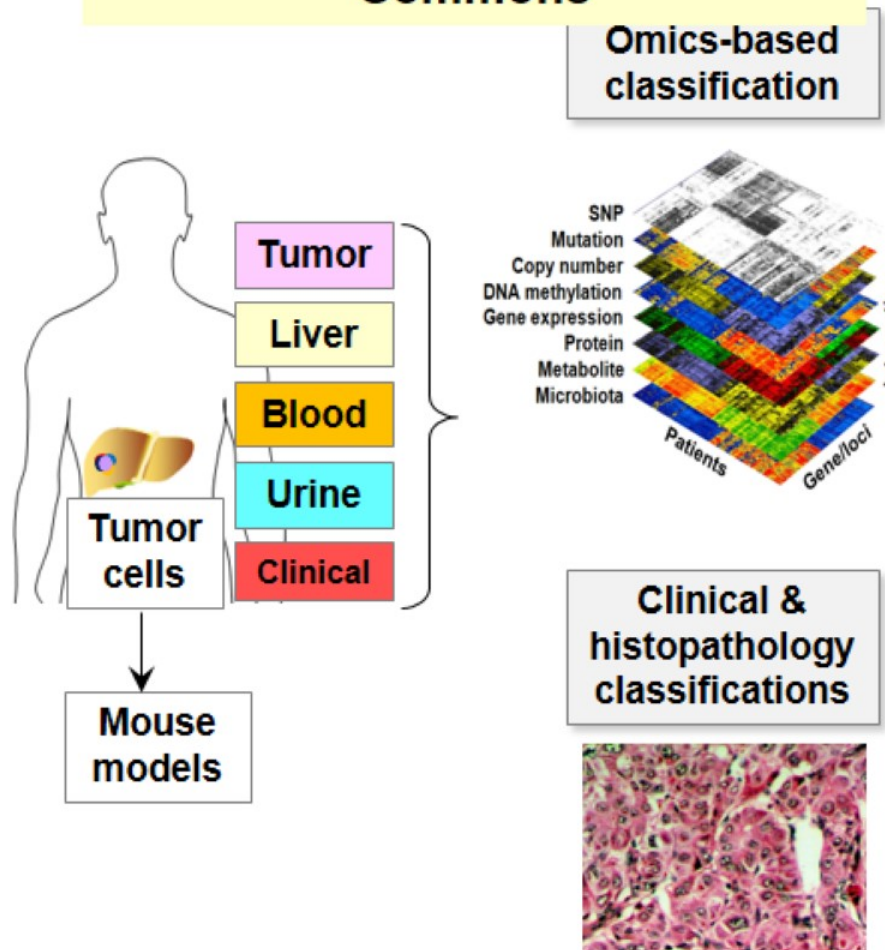
Growth



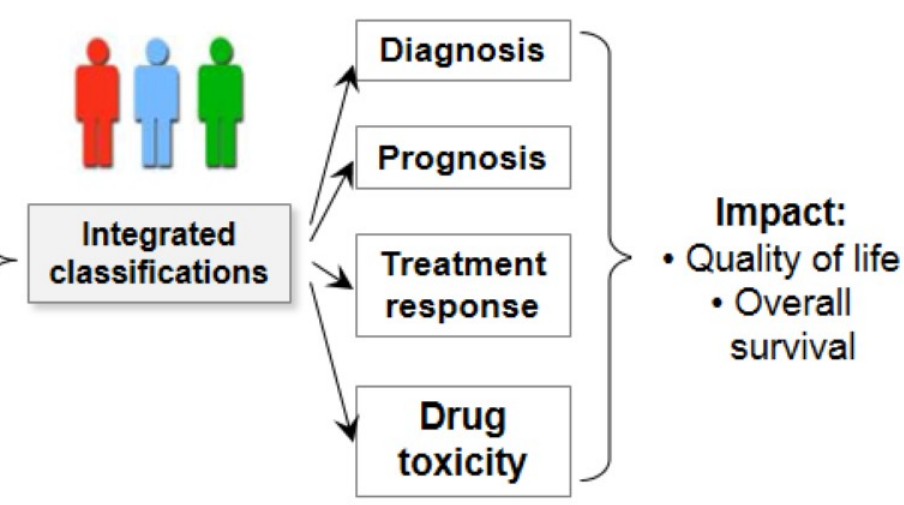
A Systems Biology Strategy to Improve Outcome for Liver Cancer Patients



Biobank & Information Commons



Biomarker-guided Interventions





Major Accomplishments

- **A molecular signature predictive of HCC metastasis and relapse in early stage tumors** (*Ye et al, Nat Med 2003; Roessler et al, Cancer Res 2010*)
 - Established proof of concept that the ability to metastasize may be an inherent quality of the primary tumor; a HeproDX test by GoPath Laboratories
- **A unique immune response signature of the liver microenvironment is predictive of HCC metastasis** (*Budhu et al, Cancer Cell 2006*)
 - Solidified the contribution of the tumor stroma to HCC progression
- **A gender-related HCC biomarker (miR-26) predicts response to interferon therapy** (*Ji et al, N Engl J Med 2009*)
 - Identified a clinically relevant predictive HCC biomarker; developed a miRNA-26 companion diagnostic test used in concert with a multi-center RCT (NCT01681446)
- **Integrated genomics of HCC** (*Roessler et al, Gastroenterology 2012; Oishi et al, Hepatology 2013; Budhu et al, Gastroenterology 2013*)
 - Molecular and bioinformatics strategies to define HCC subtypes and driver genes (potential optimal druggable targets)

Collaborative Studies Between NCI and Fudan University (1999-2015)



- **>20 joint Peer-reviewed publications**
 - Cancer Cell (1)
 - Cancer Res (2)
 - Hepatology (4)
 - Gastroenterology (3)
 - Nat Med (1)
 - N Eng J Med (1)
 - J Hepatology (1)

- **Inventions:** 7 U.S. and/or international patents/applications

- **Awards**
 - Two NSFC grants to Fudan University
 - 2008 Natural Sciences Award (1st place), MOE



Challenges & Unanswered Questions

- **Better define tumor molecular subtypes:** the liver cancer genome is highly complex; each tumor type contains hundreds of somatic alterations along with alterations of complex liver milieu; a need to consolidate molecular signatures and integrate data from multiple 'omics' platforms to define key cancer drivers
- **Translate research findings to the clinic:** the presence of considerable genomic alterations constitutes a bottleneck to effectively rank, triage and evaluate key cancer drivers as druggable targets; a need to develop precision models that incorporate both genomic changes in tumor cells and the appropriate liver milieu; clinically relevant biomarkers of therapeutic response needed; immune therapy
- **The role of less-studied risk factors:** dietary factors, lifestyle factors, liver fluke, etc.
- **Health disparities and global health:** understudied populations and comparisons
- **Group/Collaborative efforts:** Bench/Clinical/Multi-Institutional collaborations; NCI-Sponsored liver consortium and well-defined epidemiology/population studies
- **Lack of funding/resources for liver-related research and biobanks/repositories**