CENTER FOR CANCER RESEARCH

Connecting the Cancer Community

Center for Cancer Research: Chinese Interactions

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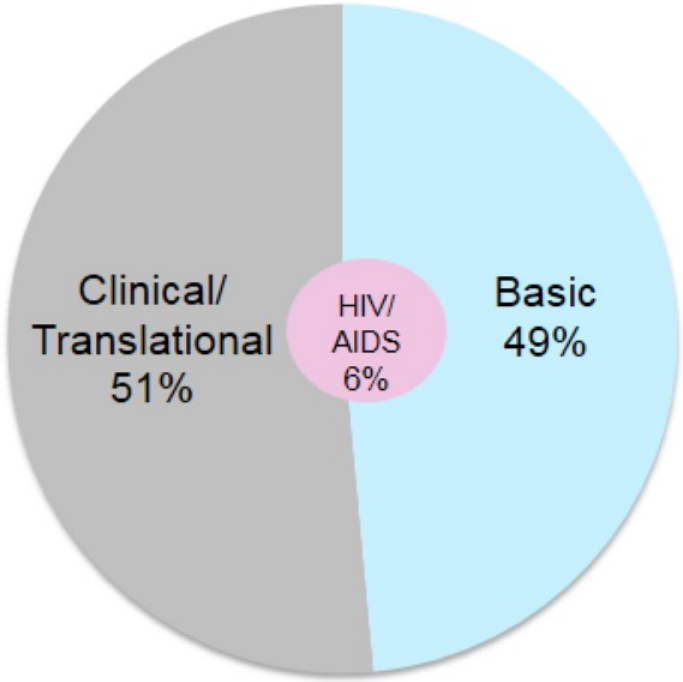
NATIONAL CANCER INSTITUTE

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

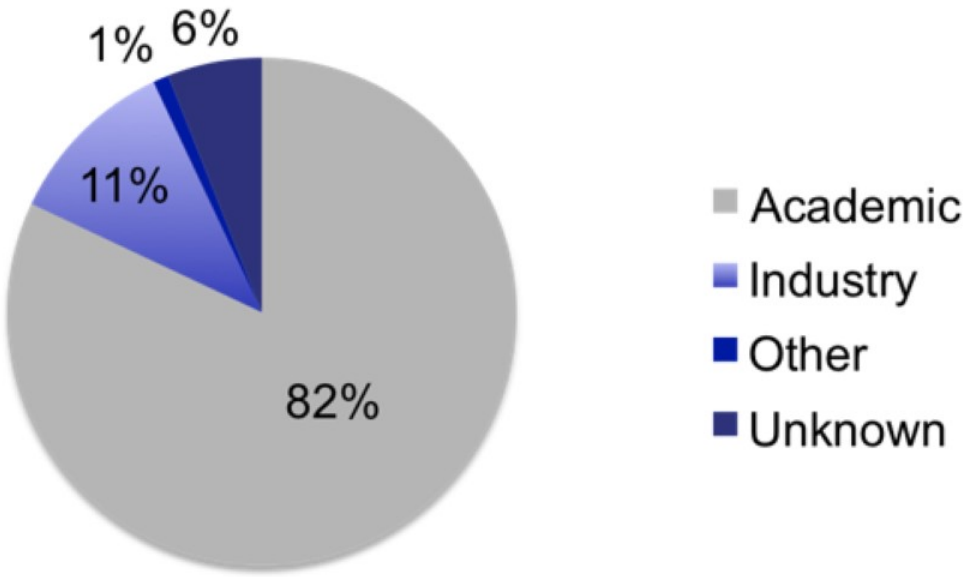
- **Sustained support for high-risk, high-impact research**
- **Highly interactive, interdisciplinary culture for basic and clinical scientists:**
  - generation of new knowledge
  - efficient bench to bedside to bench translation
  - development of new technologies
- **Access to the world's largest 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

- 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”

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Collaborative Studies Between NCI and Fudan University

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

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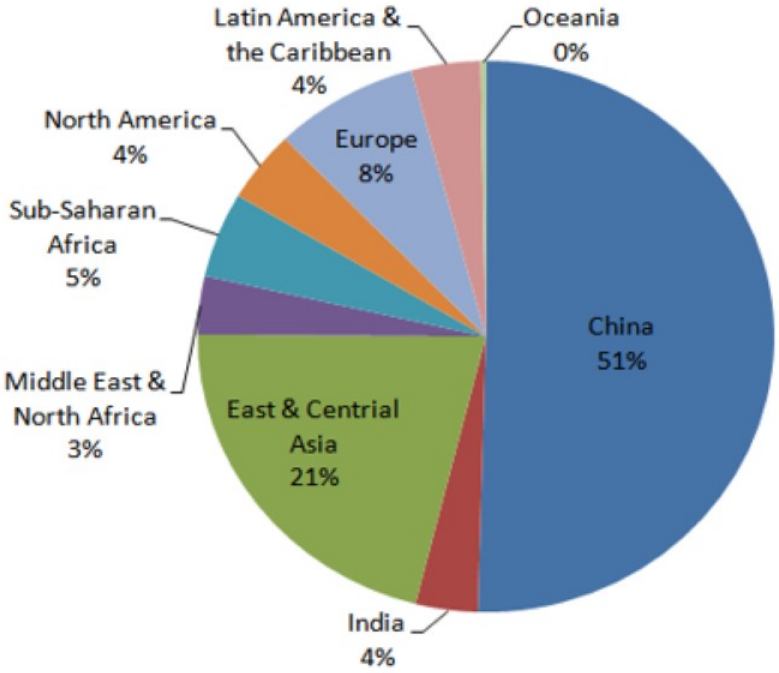
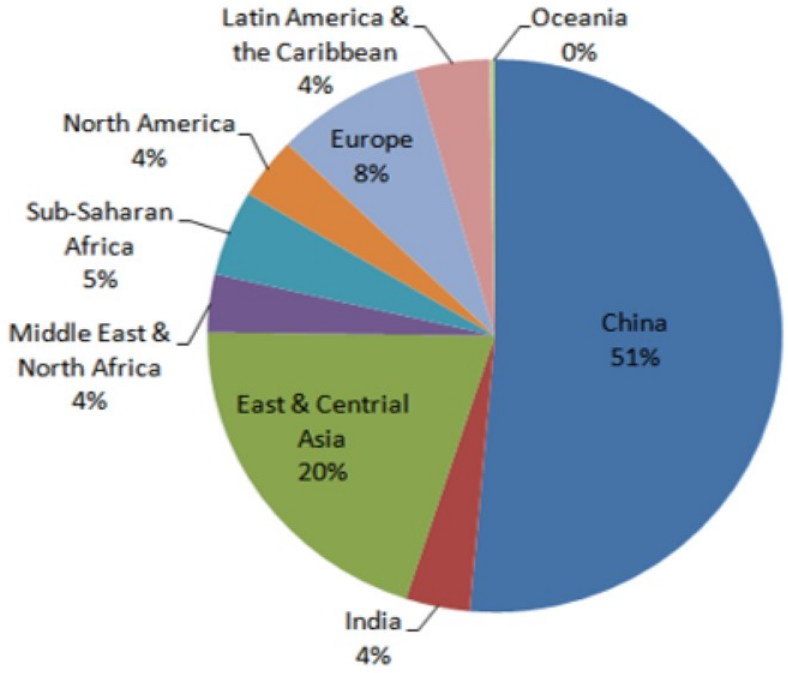
Steward BW & Wild CP, World Cancer Report 2014
www.who.int

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

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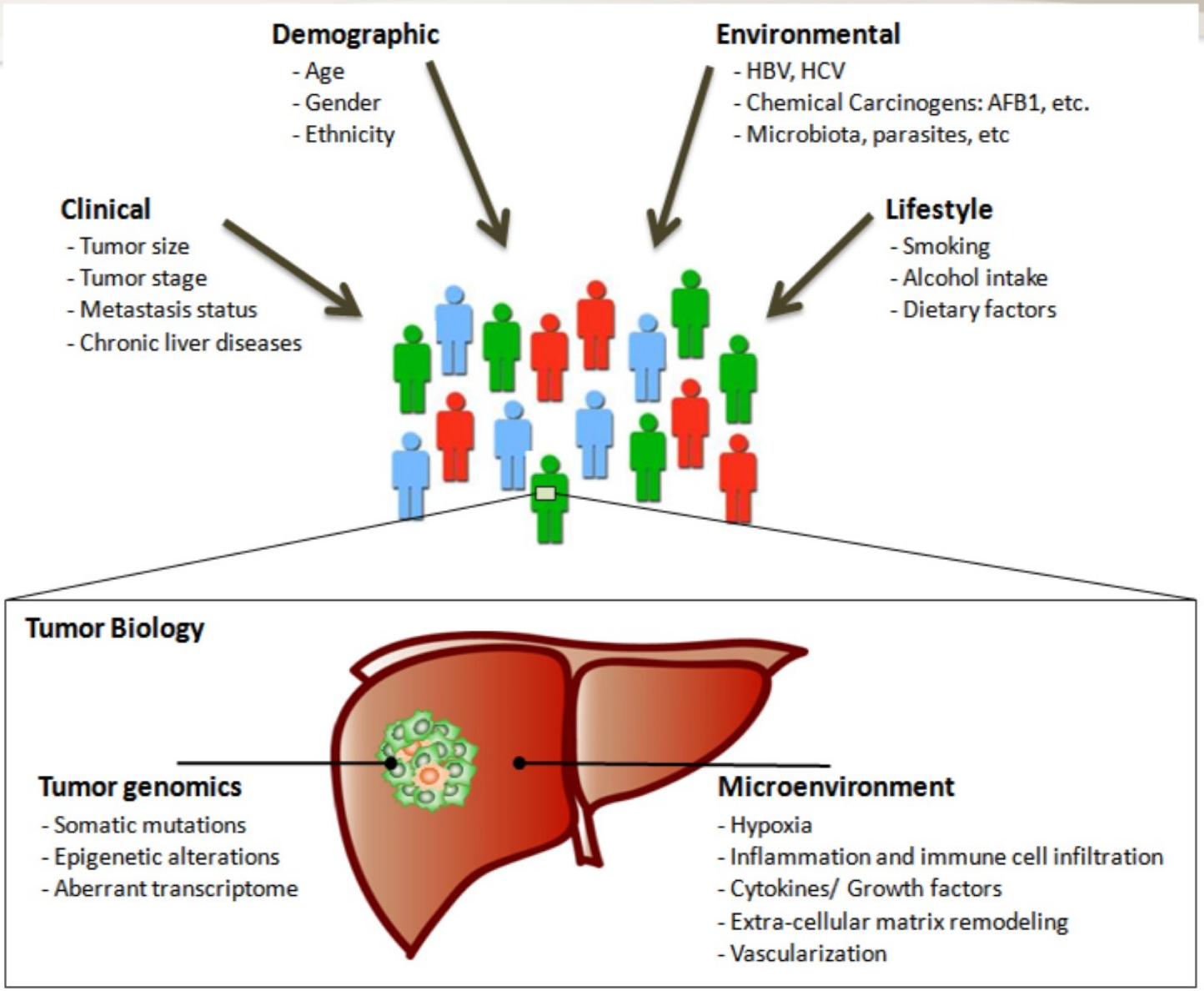
Sonya Parpart



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)

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Initiation

Development

Growth

- 1999: Dr. Lun-Xiu Qin, Dr. Zhao-You Tang
- 1999: CRA
- 2003: 1st joint paper (Nat Med)
- 2003: Qinghai Ye, MD/PhD
- 2006: CRA (validation)
- 2006: 2nd joint paper (Cancer Cell)
- 2006: Huliang Jia, MD/PhD
- 2007: Guoling Lin, MD/PhD
- 2008: Dr. Hui-Chuan Sun (NEJM)
- 2008: Jiong Shi, MD/PhD
- 2009: PLCCRC (Dr. Fan Jia)
- 2009: CRA (GWAS)
- 2009: Lei Zhao, MD/PhD
- 2012: MIR26-DX
- 2012: Lei Yu, MD/PhD

Fellows-in-Training

A Systems Biology Strategy to Improve Outcome for Liver Cancer Patients

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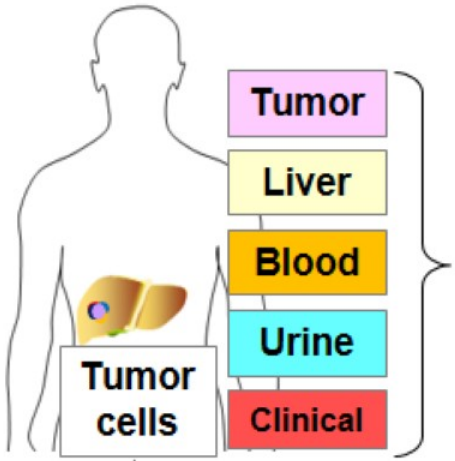
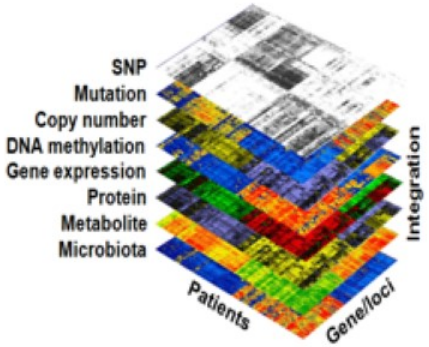
Biobank & Information Commons



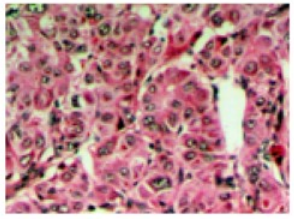
Mouse models

Biomarker-guided Interventions

Omics-based classification



Clinical & histopathology classifications



Integrated classifications

- Diagnosis
- Prognosis
- Treatment response
- Drug toxicity

Impact:
- Quality of life
- Overall survival

Wang XW and Thorgeirsson SS. Hepatic Oncology 2014

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**