BIOGRAPHICAL SKETCH

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NAME: Jian Cao

eRA COMMONS USER NAME (credential, e.g., agency login): JIAN-CAO

POSITION TITLE: Assistant Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
China Pharmaceutical University, Nanjing, China	BS	06/2003	Biological Pharmacy
Chinese Academy of Sciences, Beijing, China	PhD	06/2009	Biochemistry and Molecular Biology
Yale University, New Haven, Connecticut	Postdoctoral	07/2013	Cancer Epigenetics

A. Personal Statement

My general research interest is to identify and target oncogenic epigenetic mechanisms in cancer. Epigenetic mechanisms are commonly hijacked by tumors. Epigenetics-targeting therapies are attractive because (1) epigenetic alterations are reversible, and (2) epigenetic features are regulated by enzymes or chromatin-binding proteins that are largely targetable.

I have a strong background in studying dysregulated KDM5 family histone H3K4 demethylases in cancer (**Contributions to Science 1**, during postdoc training). I also made significant contributions to cancer immunology, especially epigenetic regulation of cancer immunology (**Contributions to Science 2**, during postdoc training and independent career). Since I started my own lab at Rutgers Cancer Institute of New Jersey in 2019, I have published three research articles as a corresponding author (***Genome Res.*** 2019, ***Nat. Commun*** 2020, and ***Biomed. Pharmacother.*** 2023). My current study focuses on the oncogenic function of Hepatitis B virus integrations in *KMT2B* in hepatocellular carcinoma. This study is supported by an NIH R01.

Ongoing projects that I would like to highlight include:

R01 CA272578 (NIH/NCI)
07/15/22-06/30/27
Hepatitis B virus integrations in KMT2B drive hepatocellular carcinoma
Role: PI

Citations:

1. Hui Zheng, Lizhen Wu, Qian Xiao, Xin Meng, Alex Hafiz, Qin Yan, Renquan Lu, **Jian Cao #**. Epigenetically suppressed tumor cell intrinsic STING promotes tumor immune escape. ***Biomed Pharmacother***. 2023 Jan;157:114033. doi: 10.1016/j.biopha.2022.114033. (**# correspondence**) PMC9826630.
2. Yingxia Zheng #, Zheyi Chen, Yichao Han, Li Han, Xin Zou, Bingqian Zhou, Rui Hu, Jie Hao, Shihao Bai, Haibo Xiao, Wei Vivian Li, Alex Bueker, Yanhui Ma, Guohua Xie, Junyao Yang, Shiyu Chen, Hecheng Li #, **Jian Cao #**, and Lisong Shen #. Immune suppressive landscape in the human esophageal squamous cell carcinoma microenvironment. ***Nat Commun.*** 2020 Dec 8;11(1):6268. doi: 10.1038/s41467-020-20019-0. (**# correspondence**) PMC7722722.
3. Xun Chen, Jason Kost, Arvis Sulovari, Nathalie Wong, Winnie S. Liang, **Jian Cao #** and Dawei Li **#**. A virome-wide clonal integration analysis platform for discovering cancer viral etiology. ***Genome Res.*** 2019

May;29(5):819-830. (**# correspondence**) PMC6499315.

4. Lizhen Wu*****, **Jian Cao***, Wesley Cai, Sabine Lang, John Horton, Daniel Jansen, Zongzhi Liu, Jocelyn Chen, Meiling Zhang, Bryan Mott, Katherine Pohida, Ganesha Rai, Stephen Kales, Stephen Kales, Mark Henderson, Xin Hu, Ajit Jadhav, David Maloney, Anton Simeonov, Shu Zhu, Akiko Iwasaki, Matthew Hall, Xiaodong Cheng, Gerald Shadel, and Qin Yan. KDM5 histone demethylases repress immune response via suppression of STING. ***PLoS Biol.*** 2018 Aug 6;16(8). (*** equal contribution**) PMC6095604.
5. **Jian Cao** and Qin Yan. Cancer Epigenetics, Tumor Immunity, and Immunotherapy. Trends Cancer. 2020 Jul;6(7):580-592. doi: 10.1016/j.trecan.2020.02.003. PMC7330177.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2019 - Resident Member, Rutgers Cancer Institute of New Jersey, Rutgers, The State University of New Jersey, New Brunswick, NJ
2019 - Assistant Professor, Department of Medicine, Rutgers-Robert Wood Johnson Medical School, Rutgers, The State University of New Jersey, New Brunswick, NJ
2013 - 19 Associate Research Scientist, Department of Pathology, Yale University, New Haven, CT
2009 - 13 Postdoctoral Associate, Department of Pathology, Yale University, New Haven, CT

Academic and Professional Achievements and Honors

2019 New Investigator Award, Rutgers Cancer Institute of New Jersey
2018 Career Development Award, Melanoma Research Foundation
2018 Team Science Award, Melanoma Research Alliance
2011 Susan G. Komen Scholar-In-Training Award, American Association for Cancer Research
2009 Outstanding Ph.D. Thesis Award, Chinese Academy of Sciences
2009 Presidential Scholarship for Academy Excellence, Chinese Academy of Sciences

C. Contributions to Science

1. I have made significant contributions to the field of histone H3K4 demethylases in cancer. I showed that loss of histone demethylase KDM5A/RBP2 inhibits tumor initiation and development in two mouse cancer models. By combining bioinformatics and experimental approaches, I have shown that KDM5A is critical for breast cancer progression and metastasis. These studies highlight KDM5A as an attractive drug target for anti-cancer therapies. I also contributed in identifying small molecule inhibitors of KDM5A for translational research.

a. **Jian Cao**, Zongzhi Liu, William K.C. Cheung, Minghui Zhao, Sophia Y. Chen, Siew Wee Chan, Carmen J. Booth, Don X. Nguyen, Qin Yan. Histone demethylase RBP2 is critical for breast cancer progression and metastasis. ***Cell Reports*** 2014 Mar; 6(5):868-877. PMC4014129.
b. Lizhen Wu*, **Jian Cao***, Wesley Cai, Sabine Lang, John Horton, Daniel Jansen, Zongzhi Liu, Jocelyn Chen, Meiling Zhang, Bryan Mott, Katherine Pohida, Ganesha Rai, Stephen Kales, Stephen Kales, Mark Henderson, Xin Hu, Ajit Jadhav, David Maloney, Anton Simeonov, Shu Zhu, Akiko Iwasaki, Matthew Hall, Xiaodong Cheng, Gerald Shadel, and Qin Yan. KDM5 histone demethylases repress immune response via suppression of STING. PLoS Biol. 2018 Aug 6;16(8). (*** equal contribution**) PMC6095604
c. Wenchu Lin*, **Jian Cao***, Jiayun Liu, Michael L. Beshiri, Yuko Fujiwara, Joshua Francis, Andrew D. Cherniack, Christoph Geisen, Lauren P. Blair, Mike R. Zou, Xiaohua Shen, Dan Kawamori, Zongzhi Liu, Chiara Grisanzio, Hideo Watanabe, Yoji Andrew Minamishima, Qing Zhang, Rohit N. Kulkarni, Sabina Signoretti, Scott J. Rodig, Roderick T. Bronson, Stuart H. Orkin, David P. Tuck, Elizaveta V. Benevolenskaya, Matthew Meyerson, William G. Kaelin, Jr., and Qin Yan. Loss of the retinoblastoma binding protein 2 (RBP2) histone demethylase suppresses tumorigenesis in mice lacking Rb1 or Men1. ***Proc Nat Acad of Sci USA*** 2011 Aug; 108:13379-86. (*** equal contribution**) PMC3158206.
d. Joyce Sayegh, **Jian Cao**, Mike Ran Zou, Alfonso Morales, Lauren P. Blair, Michael Norcia, Denton Hoyer, Alan J. Tackett, Jane S. Merkel, and Qin Yan. Identification of small molecule inhibitors of Jumonji AT-Rich Interactive Domain 1B (JARID1B) histone demethylase by a sensitive high-throughput screen. ***J Biol Chem*** 2013 Mar; 288(13):9408-17. PMC3611010.

2. I have made significant contributions to cancer immunology. My research centers on targeting epigenetic regulations in cancer cells to boost cancer immunity. I found that the silenced STING pathway, a key pathway of innate immunity, can be reactivated in breast cancer cells by suppressing KDM5 demethylases. I found activation of the STING pathway led to a robust interferon response, which blocked viral infection and was associated with increased tumor-infiltrated lymphocytes and better patient survival in multiple cancer types. I also obtained a detailed immune cell atlas of esophageal squamous cell carcinoma at single-cell resolution. I found that various immunosuppressive mechanisms, including exhausted T and NK cells, regulatory T cells (Tregs), alternatively activated macrophages and tolerogenic dendritic cells are dominant in the tumor microenvironment.

a. Hui Zheng, Lizhen Wu, Qian Xiao, Xin Meng, Alex Hafiz, Qin Yan, Renquan Lu, **Jian Cao #**. Epigenetically suppressed tumor cell intrinsic STING promotes tumor immune escape. ***Biomed Pharmacother***. 2023 Jan;157:114033. doi: 10.1016/j.biopha.2022.114033. (**# correspondence**) PMC9826630.
b. Yingxia Zheng **#**, Zheyi Chen, Yichao Han, Li Han, Xin Zou, Bingqian Zhou, Rui Hu, Jie Hao, Shihao Bai, Haibo Xiao, Wei Vivian Li, Alex Bueker, Yanhui Ma, Guohua Xie, Junyao Yang, Shiyu Chen, Hecheng Li **#**, **Jian Cao #**, and Lisong Shen **#**. Immune suppressive landscape in the human esophageal squamous cell carcinoma microenvironment. ***Nat Commun.*** 2020 Dec 8;11(1):6268. doi: 10.1038/s41467-020-20019-0. (**# correspondence**) PMC7722722.
c. **Jian Cao** and Qin Yan. Cancer Epigenetics, Tumor Immunity, and Immunotherapy. Trends Cancer. 2020 Jul;6(7):580-592. doi: 10.1016/j.trecan.2020.02.003. PMC7330177.
d. Lizhen Wu*, **Jian Cao***, Wesley Cai, Sabine Lang, John Horton, Daniel Jansen, Zongzhi Liu, Jocelyn Chen, Meiling Zhang, Bryan Mott, Katherine Pohida, Ganesha Rai, Stephen Kales, Stephen Kales, Mark Henderson, Xin Hu, Ajit Jadhav, David Maloney, Anton Simeonov, Shu Zhu, Akiko Iwasaki, Matthew Hall, Xiaodong Cheng, Gerald Shadel, and Qin Yan. KDM5 histone demethylases repress immune response via suppression of STING. ***PLoS Biol.*** 2018 Aug 6;16(8). (*** contribute equally**) PMC6095604.

3. I have made significant contributions to the analysis of viral integration in tumors. There are seven well-accepted human oncoviruses, cumulatively responsible for approximately 10% of human cancer cases. The most virus-caused tumors carry viral integrations in the tumor genome. My colleagues and I have developed VIcaller, a novel platform for identifying viral integrations that are derived from any characterized viruses and shared by a large proportion of tumor cells using whole-genome sequencing (WGS) data. The sensitivity and precision were confirmed with simulated and benchmark cancer data sets. By applying this platform to cancer WGS data sets with proven or speculated viral etiology, we identified new or confirmed clonal integrations of hepatitis B virus (HBV), human papillomavirus (HPV), Epstein-Barr virus (EBV), and BK Virus (BKV), suggesting the involvement of these viruses in early stages of tumorigenesis in affected tumors, such as HBV in *TERT* and *KMT2B* gene loci in liver cancer, HPV and BKV in bladder cancer, and EBV in non-Hodgkin's lymphoma. Specifically, we found 10% of HBV+ hepatocellular carcinoma carry clonal integrations of HBV in the *KMT2B* gene between exons 3 and 6. It was the foundation of the proposed study.

a. Xun Chen, Jason Kost, Arvis Sulovari, Nathalie Wong, Winnie S. Liang, **Jian Cao #** and Dawei Li **#**. A virome-wide clonal integration analysis platform for discovering cancer viral etiology. ***Genome Res.*** 2019 May;29(5):819-830. (**# correspondence**) PMC6499315.
b. **Jian Cao #** and Dawei Li **#**. Searching for human oncoviruses: Histories, challenges, and opportunities. ***J Cell Biochem.*** 2018 Jun;119(6):4897-4906. (**# correspondence**) PMID: 29377246.

4. I have developed a simple and robust CRISPR/Cas9 toolbox for inducible and multiplexing genome editing. This is the first inducible genome editing system with very high efficiency in a polyclonal setting. Furthermore, this inducible system allowed us to dramatically decrease off-target effects. Combined with my one-step strategy to assemble a targeting vector for up to 6 genes simultaneously, this system can be used to study functional redundancy of gene families and gene-gene interactions *in vitro* and *in vivo*. As a proof of concept, I have demonstrated the functional redundancy of the KDM5 family of epigenetic regulators. Taken together, this user-friendly and highly-efficient toolbox provides a solution for easy genome editing with tight temporal control, minimal off-target effects, and multiplex targeting. Since published, this system has been requested by and distributed to dozens of laboratories around the world, including Yale, Harvard, Stanford, Cambridge, McGill, Emory, UNC Chapel Hill, and RIKEN.

a. **Jian Cao**, Lizhen Wu, Shang-Min Zhang, Min Lu, William K.C. Cheung, Wesley Cai, Molly Gale, Qi Xu,

and Qin Yan. An easy and efficient inducible CRISPR/Cas9 platform with improved specificity for multiple gene targeting. ***Nucleic Acids Res*** 2016 Nov 2;44(19):e149. PMC5100567.

b. **Jian Cao**, Qian Xiao, and Qin Yan. The multiplexed CRISPR targeting platforms. ***Drug Discov Today Technol.*** 2018 Aug;28:53-61. PMID: 30205881.

5. I contributed to the medical genetic field by identifying disease-associated genes. Using SNP genotype datasets, I performed meta-analysis and identified three genes strongly associated with substance abuse, including *HTR1B* with alcohol, cocaine, and heroin abuse, *SLC6A4* with substance use disorder, and *HTR2A* with alcohol and heroin addiction.

a. **Jian Cao**, Xiangtao Liu, Shizhong Han, Clarence K. Zhang, Zongzhi Liu, and **Dawei Li**. Association of the HTR2A gene with alcohol and heroin abuse. ***Human Genetics*** 2014 Mar: 133(3): 357-365. PMC4085799.

b. **Jian Cao**, James J Hudziak and **Dawei Li**. Multi-cultural association of the serotonin transporter gene (SLC6A4) with substance use disorder. ***Neuropsychopharmacology*** 2013 Aug; 38(9):1737–1747. PMC3717550.

c. **Jian Cao**, Emily LaRocque, and **Dawei Li**. Associations of the 5-hydroxytryptamine (serotonin) receptor 1B gene (HTR1B) with alcohol, cocaine, and heroin abuse. ***American Journal of Medical Genetics Part B: Neuropsychiatric Genetics*** 2013 Mar; 162(2):169-76. PMC4089973.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/1BKl6kmNgkyQf/bibliography/48493861/public/?sort=date&direction=ascending