HAN, CUIJUAN

418 Farmington Ave, New Britain, CT, 06053 | +1 (619)-306-4478 | cuijuan.hanhan@gemail.com

EDUCATIONAL EXPERIENCE

Year	Institute	Department	Major or Position
2022.9-Now	The Jackson Laboratory	Genomic Medicine	Postdoctoral Associate
2021.9-2022.8	University of California in San Diego	Department of Medicine	Postdoctoral
2019.9-2021.8	Northwestern University (Chicago)	Biochemistry and molecular genetics	Postdoctoral
2016.9-2019.6	Wuhan University	Medical Research Institute	Basic Medicine （Ph.D.）
2014.9-2016.7	Wuhan University	College of Life Sciences	Biochemistry and Molecular Biology （Master）
2010.9-2014.7	Henan University of Urban Construction	School of life sciences and engineering	Biological engineering （Bachelor）

RESEARCH EXPERIENCE

In The Jackson Laboratory for Genomic Medicine in Farmington

- **Overcoming Drug Resistance in Hematologic Malignancies**

Drug resistance continues to be the main limiting factor to achieving cures in cancer patients. My project focuses on investigating both genetic and non-genetic mechanisms of therapy resistance in hematologic malignancies. We apply a broad range of genetic tools including CRISPR-Cas9 genetic screens to identify drug-gene interactions and multi-modal single-cell technologies to reveal cell intrinsic and extrinsic (i.e., immune microenvironment) mechanisms of resistance. Overall, these studies will provide a blueprint for clinically relevant biomarkers and developing new therapeutic strategies to overcome drug resistance in cancer.

In Department of Medicine, University of California in San Diego (Post-doctoral, 2021.9-now):

- **Identifying targets in Hepatic Stellate Cells to treat NASH:**

Nonalcoholic fatty liver disease (NAFLD) is one of the most global metabolic diseases that contains a broad liver dysfunctions spectrum ranging from steatosis (nonalcoholic fatty liver, **NAFL**) to non-alcoholic steatohepatitis (**NASH**) with fibrosis. Hepatic Stellate Cells (HSCs) play a key role in the pathogenesis of NASH. In response to chronic toxic injury, quiescent HSCs (qHSCs) activate into active HSCs (aHSCs) /myofibroblasts, that secrete the extracellular matrix to generate the liver fibrous scar. The characteristic and mechanism of NASH-mediated activation of human HSCs are not well understood. Phenotypic changes in HSCs occur without a change in the DNA sequence but are regulated on an epigenetic level, e.g. specific modifications in the chromatin structure, which affect DNA accessibility of the regulatory transcription factors (TFs), causing transcriptional activation or repression of their target genes. We are now analyzing and comparing gene expression of normal hHSCs to activated HSCs from patients with NAFLD or NASH by snRNA seq and snATAC-seq. To identify the marker genes that distinguish NASH- from Normal HSCs and study the function in liver fibrosis. 3D cell culture and 3D bioprinting were used to validate novel target genes or drugs in human disease and provide a powerful

evidence in liver disease study field.

In Feinberg School of Medicine, Northwestern University (Post-doctoral, 2019.9-2021.8):

- **Alternative splicing and its posttranslational regulation in T-ALL:**

Aberrant splicing is an important cancer causality and the production of non-canonical mRNA transcripts might associate with the progression of malignancy. T-cell acute lymphoblastic leukemia (T-ALL) does not present with mutations in the splicing machinery, in contrast to myeloid malignancies. We have previously identified that the serine/arginine-rich splicing factors (SRSFs), and SRSF6 in particular, that controls exon skipping, is critical for T-ALL growth (*Zhou YL, **Han CJ** et al., Cancer Discovery, 2020*). The ubiquitin-specific peptidase 7 (USP7) regulates SRSF6 protein levels via active deubiquitination.

As the first author, I discovered that the splicing factor SF3B1 is posttranslational regulated and is highly expressed in T cell acute lymphoblastic leukemia. I identified that SF3B1 inhibition perturbs exon skipping, especially checkpoint kinase 2 (CHEK2) which is related to DNA damage response. I further demonstrate that clinically used SF3B1 inhibitors synergize with CHEK2 inhibitors and chemotherapeutic drugs to block leukemia growth. My study provides the proof of principle for posttranslational regulation of splicing components and associated roles and therapeutic implications for the U2 complex in T cell leukemia (***Han CJ** et al, Science advances, 2022*).

My other study identified that CCCTC-binding factor (CTCF) binding events are related to altered chromatin interaction, partially with DNA methylation changes. My study validated that oncogenic NOTCH1 induced specific CTCF binding and they cooperatively activate expression of targets genes in leukemia cell (*Fang C, **Han CJ** et al, Genome biology, 2021*).

In Medical Research Institute of Wuhan University:

- **Mechanism of hepatic metabolic pathology:**

To explore the molecular mechanism of nonalcoholic hepatic steatosis and nonalcoholic steatohepatitis; special attention is paid to the molecular mechanisms by which natural immunity, ubiquitination/deubiquitination are involved in metabolic regulation and thus affect the occurrence of such metabolic diseases. Through public database mining and in vivo experiments, we identified a new functional transcription factor IRF6 that plays an important regulatory role in nonalcoholic steatohepatitis and confirmed the epigenetic modification of its promoter region on its expression level by methylation sequencing. After that, in vitro and in vivo experiments have proved that IRF6 regulates fatty acids synthesis through downstream target PPARγ (*Tong JJ, **Han CJ**, Hepatology, 2019*).

In College of Life Sciences of Wuhan University:

- **Mechanism of megakaryocyte production and acute myeloid leukemia:**

Study of signal transduction, transcriptional regulation, epigenetic regulation in megakaryocyte development and differentiation; Molecular basis and targeted interventions; identification of key factors and new biomarkers for proliferation, survival and malignancy of acute leukemia cells.

Publications & poster:

Postdoctoral

1. **Cuijuan Han***, Alireza Khodadadi-Jamayran, Adam Hartman Lorch, Qi Jin, Valentina Serafin, Ping Zhu, Yuliya Politanska, Limin Sun, Blanca T. Gutierrez-Diaz, Hiam Abdala-Valencia, Elizabeth Thomas Bartom, Barbara Buldini, Giuseppe Basso, Sadanandan E. Velu, Kavitha Sarma, Basil Baby Mattamana, Rebecca C. Obeng, Young Ah Goo, Aristotelis Tsirigos, Yalu Zhou, and Panagiotis Ntziachristos* **SF3B1 homeostasis is critical for survival and therapeutic response in T cell leukemia.** ***Science Advances,*** *2022 Jan 21;8(3):eabj8357. doi:10.1126/sciadv.abj8357.*

2. Wang E, Pineda JMB, Kim WJ, Chen S, Bourcier J, Stahl M, Hogg SJ, Bewersdorf JP, **Han C,** Singer ME, Cui D, Erickson CE, Tittley SM, Penson AV, Knorr K, Stanley RF, Rahman J, Krishnamoorthy G, Fagin JA, Creger E, McMillan E, Mak CC, Jarvis M, Bossard C, Beaupre DM, Bradley RK, Abdel-Wahab O. **Modulation of RNA splicing enhances response to BCL2 inhibition in leukemia.** ***Cancer Cell.*** *2023 Jan 9;41(1):164-180.e8. DOI:10.1016/j.ccell.2022.12.002. PMID: 36563682; PMCID: PMC9839614.*

3. Raquel Carvalho-Gontijo*****, **Cuijuan Han***, Lei Zhang, Vivian Zhang, Mojgan Hosseini, Kristin Mekeel, Bernd Schnabl, Rohit Loomba, Michael Karin, David A Brenner, Tatiana Kisseleva. ***Metabolic Injury of Hepatocytes Promotes Progression of NAFLD and AALD. Seminar Liver Disease,*** *2022; 42(03): 233-249*

4. **Cuijuan Han,** Panagiotis Ntziachristos. ***T-ALL and the talented Mr.IL7Ra. Commentary, 2021. Blood.***

5. **Cuijuan Han***, Alireza Khodadadi Jamayran, Adam Hartmann Lorch, Qi Jin, Valentina Serafin, Ping Zhu, Yuliya Politanska, Limin Sun, Yohhei Takahashi, Hiam Abdala-Valencia, Elizabeth Bartom, Kavitha Sarma, Giuseppe Basso, Sadanandan Velu, Aristotelis Tsirigos, Yalu Zhou, and Panagiotis Ntziachristos* **U2 spliceosome proteostasis controls the transcriptome and therapeutic response in leukemia.** ***ePoster of Keystone,*** *Hematopoiesis EK37, 2021.*

6. Yalu Zhou*, **Cuijuan Han**, Eric Wang, Adam H. Lorch, Valentina Serafin, Byoung-Kyu Cho, Blanca T. Gutierrez Diaz, Julien Calvo, Celestia Fang, Alireza Khodadadi-Jamayran, Tommaso Tabaglio, Christian Marier, Anna Kuchmiy, Limin Sun, George Yacu, Szymon K. Filip, Qi Jin, Yoh-Hei Takahashi, David R. Amici, Emily J. Rendleman, Radhika Rawat, Silvia Bresolin, Maddalena Pagani, Cheng Zhang, Hu Li, Irawati Kandela, Yuliya Politanska, Hiam Abdala-Valencia, Marc L. Mendillo, Ping Zhu, Bruno Palhais, Pieter Van Vlierberghe, Tom Taghon, Iannis Aifantis, Young Ah Goo, Ernesto Guccione, Adriana Heguy, Aristotelis Tsirigos, Keng Boon Wee, Rama K. Mishra, Francoise Pflumio, Benedetta Accordi4, Giuseppe Basso4, and Panagiotis Ntziachristos. **Posttranslational Regulation of the Exon Skipping Machinery Controls Aberrant Splicing in Leukemia.** ***Cancer Discovery.*** *2020. DOI: 10.1158/2159-8290.CD-19-1436.*

7. Celestia Fang*, Zhenjia Wang*, **Cuijuan Han**, Stephanie L Safgren, Kathryn A Helmin, Emmalee R Adelman, Kyle P Eagen, Alexandre Gaspar-Maia, Maria E Figueroa, Benjamin D Singer, Aakrosh Ratan, Panagiotis Ntziachristos, Chongzhi Zang. ***Cancer-specific CTCF binding facilitates oncogenic transcriptional dysregulation. Genome biology,*** *2020, DOI: 10.1186/s13059-020-02152-7.*

8. Qi Jin*, Blanca Gutierrez Diaz*, Tim Pieters, Yalu Zhou, Sonali Narang, Igor Fijalkwoski, Cristina Borin, Jolien Van Laere, Monique Payton, Byoung-Kyu Cho, **Cuijuan Han**, Limin Sun, Valentina Serafin, George Yacu, Wouter Von Loocke, Giuseppe Basso, Giulia Veltri 11, Ingrid Dreveny, Issam Ben-Sahra, Young Ah Goo, Stephanie L Safgren, Yi-Chien Tsai, Beat Bornhauser, Praveen Kumar Suraneni, Alexandre Gaspar-Maia, Irawati Kandela, Pieter Van Vlierberghe, John D Crispino, Aristotelis Tsirigos, Panagiotis Ntziachristos*. **Oncogenic deubiquitination controls tyrosine kinase signaling and therapy response in acute lymphoblastic leukemia,** ***Science Advances.*** *2022 Dec 9;8(49):eabq8437. DOI: 10.1126/sciadv.abq8437.*

Master and Ph.D.

9. Tong J*, **Han CJ***, Zhang JZ, He WZ, Zhao GJ, Cheng X, Zhang L, Deng KQ, Liu Y, Fan HF, Tian S, Cai J, Huang Z, She ZG, Zhang P5, Li H. **Hepatic IRF6 alleviates liver steatosis and metabolic disorder by transcriptionally suppressing PPARγ.** ***Hepatology. DOI:10.1002/hep.30559.***

10. Sun X*, Lu B*, **Han C***, Qiu W, Jin Q, Li D, Li Q, Yang Q, Wen Q, Opal P, Kini AR, Crispino JD, Huang Z. **ANP32A dysregulation contributes to abnormal megakaryopoiesis in acute megakaryoblastic leukemia.** ***Blood cancer journal. DOI: 10.1038/s41408-017-0031-x.***

11. Lu B*, Ren Y*, Sun X*, **Han C**, Wang H, Chen Y, Peng Q, Cheng Y, Cheng X, Zhu Q, Li W, Li HL, Du HN, Zhong B, Huang Z. **Induction of INKIT by Viral Infection Negatively Regulates Antiviral Responses through Inhibiting Phosphorylation of p65 and IRF3.** ***Cell Host Microbe. 2017;22(1):86-98 e84.***

12. Yang X*, Lu B*, Sun X*, **Han C**, Fu C, Xu K, Wang M, Li D, Chen Z, Opal P, Wen Q, Crispino JD, Wang QF & Huang Z. **ANP32A regulates histone H3 acetylation and promotes leukemogenesis.** ***Leukemia. 2018; doi:10.1038/s41375-018-0010-7.***

Presentation:

- **Cuijuan Han*,** Xiao Liu, Sara Brin Rosenthal, Huayi Zhao, Lei Zhang, Leon Fan Xiao Lin, Raquel Carvalho Gontijo Weber, Vivian Zhang, David Brenner, Kristin Mekeel and Tatiana Kisseleva. **Single-nucleus transcriptome reveals potential targets in NASH-activated human Hepatic Stellate Cells. May 3-4.2022, Department of Surgery Virtual Annual Research Symposium.**
- **Cuijuan Han*,** Xiao Liu, Sara Brin Rosenthal, Huayi Zhao, Leon Fan Xiao Lin, Raquel Carvalho Gontijo Weber, Vivian Zhang, David Brenner and Tatiana Kisseleva. **Identification of novel therapeutic targets in NASH-activated human Hepatic Stellate Cells (hHSCs). May 21-24.2022. Digestive Disease Week, San Diego.**
- **Cuijuan Han***, Alireza Khodadadi-Jamayran, Adam Hartman Lorch, Qi Jin, Valentina Serafin, Ping Zhu, Yuliya Politanska, Limin Sun, Blanca T. Gutierrez-Diaz, Hiam Abdala-Valencia, Elizabeth Thomas Bartom, Barbara Buldini, Giuseppe Basso, Sadanandan E. Velu, Kavitha Sarma, Basil Baby Mattamana, Rebecca C. Obeng, Young Ah Goo, Aristotelis Tsirigos, Yalu Zhou, and Panagiotis Ntziachristos*. **SF3B1 homeostasis is critical for survival and therapeutic response in T cell leukemia. May 23. 2021, Seminar of Department of Biochemistry and Molecular genetics.**

The work of tutoring and teaching students

Guiding and teaching an undergraduate student of an independent research study class BISP199 in 2021-2022.