

# Han Sun, PhD

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## EXPERIENCE

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### Research Scientist/Senior Computational Biologist

2020 –

Department of Pediatrics, School of Medicine, Stanford University, [Prof. Anna Gloy](#)

### Postdoc

2015 – 2019

Department of Genetics, School of Medicine, Stanford University, [Prof. Lars Steinmetz](#)

## EDUCATION

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### PhD, Bioinformatics

2009 – 2014

University of Chinese Academy of Sciences, [Prof. Yixue Li](#) and [Prof. Lu Xie](#)

### Bachelor, Software Engineering

2004 – 2008

East China Normal University

## PROJECTS

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- **Splicing-mediated transcript fusion and oncogene activation in multiple cancers**

With the aim of exploring gene fusion events at the transcriptional level, rather than the traditional genomic level in cancer patients, I reanalyzed both whole exome sequencing (WES) and RNA-Seq data from over 10,000 patients across 33 cancer types from the TCGA project using a negative binomial-based generalized linear model. I discovered significant correlations between somatic mutations and the splicing of adjacent genes (transcript fusion) in several cohorts. Notably, a mutation within CDKN1A and the splicing between CDKN1A and RAB44 were prominent in bladder, stomach, and skin cancers. To establish causality, I collaborated with other labs and introduced the mutation into cell lines using CRISPR/Cas9, successfully reproducing the between-gene splicing and gene activation. This was confirmed through RT-PCR, Sanger sequencing, qPCR, and RNA-Seq. Further functional and phenotypic assays demonstrated a connection between RAB44 activation and MDM2 upregulation (and consequently, TP53 downregulation). I proposed a splicing-mediated readthrough stabilization (SRS) model as a novel mechanism for oncogene activation.

- **RNA-binding protein RBM20-deficient dilated cardiomyopathy**

Starting with a family affected by dilated cardiomyopathy, I analyzed whole exome sequencing (WES) and whole genome sequencing (WGS) data from the family members and identified a suspicious missense mutation in RBM20 through linkage analysis. Given that RBM20 is an RNA-binding protein, I further identified its splicing targets using RNA-Seq data from humans and pigs. We validated this finding by performing CRISPR/Cas9 editing in human induced pluripotent stem (iPS) cells and differentiating them into cardiomyocytes. By integrating gene expression data from thousands of tissues in the GTEx project, I proposed a model for the tissue-specific splicing of a mitochondrial inner membrane protein, IMMT, suggesting a molecular link between energy supply deficiencies and dilated cardiomyopathy.

- **Mutation and regulatory elements underlying neonatal diabetes**

By analyzing whole genome sequencing (WGS) and array-based genotyping data from mice, I identified a suspicious intronic mutation that correlates with neonatal diabetes. We validated that the mutation causes diabetes by introducing it into both B6 and NOD mice using CRISPR/Cas9 editing. I proposed a mechanism where the mutation creates a novel splice site, resulting in a longer transcript but truncated protein, which has been verified. We are now working with bulk and single-cell data (scRNA-Seq and scATAC-Seq) throughout development to investigate additional regulatory elements and understand why the phenotype is specific to the pancreas. I am also working on large-scale QTL mapping (eQTL, caQTL, and pQTL) on multiomics datasets of human islets to study the genetic architecture of diabetes.

- **Machine Learning/Deep Learning of tissue-specific splicing, genetic ancestry, selenocysteine element, etc.**

After reproducing the state-of-the-art model in splice site prediction, SpliceAI, using both TensorFlow and PyTorch, I developed new models with attention and GPT backbone to predict tissue-specific splicing from long reads (PacBio).

## RESEARCH INTERESTS

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- Disease Genetics (Cancer, Cardiomyopathy, Diabetes, ...)
- Multiomics (WGS, WES, RNA-Seq, ATAC-Seq, ChIP-Seq, MS/MS, bulk and single cell)
- AI 4 Life Science and Drug Discovery

## SCIENTIFIC SKILLS

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- Python, R, C, git, Linux, and High Performance Computing
- statsmodels, scikit-learn, Tensorflow, and PyTorch
- Bioinformatics and Biostatistics
- Machine Learning and Deep Learning
- Genomics, Transcriptomics, Proteomics, and Epigenomics
- Linkage analysis, QTL mapping, and GWAS

## CERTIFICATIONS

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- Machine Learning Specialization, Andrew Ng, [Coursera](#)
- Deep Learning Specialization, Andrew Ng, [Coursera](#)

## PATENTS

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- Methods of Treatment, Genetic Screening, and Disease Models for Heart Conditions Associated with RBM20 Deficiency. Francesca Briganti, Lars M. Steinmetz, Han Sun, and Wu Wei. WO 2020/092171.

## PUBLICATIONS

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1. **Han Sun**, Huiying Yan, Kathryn Biegling-Rolett, Michelle Nguyen, William F. Mueller, Zhuanfen Cheng, Hong Zeng, Laura Attardi, Wu Wei, and Lars M. Steinmetz et al. "CDKN1A-RAB44 transcript fusion and oncogene activation in cancers.", [bioRxiv](#).
2. Francesca Briganti, **Han Sun**, Wu Wei, Jingyan Wu, Chencheng Zhu, Martin Liss, Ioannis Karakikes et al. "iPSC Modeling of RBM20-Deficient DCM Identifies Upregulation of RBM20 as a Therapeutic Strategy." [Cell Reports](#) 32, no. 10 (2020): 108117, **co-first author**.
3. **Han Sun**, Seth A Sharp, Nicole A J Krentz, Anna Gloyn et al., "Deep learning prediction of selenocystine element and its application in diabetes and cancers", in preparation.
4. Kolic, Jelena, WenQing Grace Sun, Haoning Howard Cen, Jessica D. Ewald, Jason C. Rogalski, Shugo Sasaki, **Han Sun**, et al. "Proteomic predictors of individualized nutrient-specific insulin secretion in health and disease." [Cell Metabolism](#) 36, no. 7 (2024): 1619-1633.
5. Rottner, Antje K., Yingying Ye, Elena Navarro-Guerrero, Varsha Rajesh, Alina Pollner, **Han Sun**, Romina J. Bevacqua, Jing Yang et al. "A genome-wide CRISPR screen identifies CALCOCO2 as a regulator of beta cell function influencing type 2 diabetes risk." [Nature Genetics](#) 55, no. 1 (2023): 54-65.
6. Lau, Hwee Hui, Nicole AJ Krentz, Fernando Abaitua, Marta Perez-Alcantara, **Han Sun**, Jun-Wei Chan, Jila Ajeian, Soumita Ghosh et al. "PAX4 loss of function increases diabetes risk by altering human pancreatic endocrine cell development." [Nature Communications](#) 14, no. 1 (2023): 6119.
7. Mattis, Katia K., Nicole AJ Krentz, Christoph Metzendorf, Fernando Abaitua, Aliya F. Spigelman, **Han Sun**, Jennifer M. Ikle et al. "Loss of RREB1 in pancreatic beta cells reduces cellular insulin content and affects endocrine cell gene expression." [Diabetologia](#) 66, no. 4 (2023): 674-694.
8. Cortez, Briana N., Hui Pan, Samuel Hinthorn, **Han Sun**, Nicola Neretti, Anna L. Gloyn, and Cristina Aguayo-Mazzucato. "Heterogeneity of increased biological age in type 2 diabetes correlates with differential tissue DNA methylation, biological variables, and pharmacological treatments." [GeroScience](#) (2023): 1-21.
9. Torres, Jason M., **Han Sun**, Vibe Nylander, Damien J. Downes, Martijn van de Bunt, Mark I. McCarthy, Jim R. Hughes, and Anna L. Gloyn. "Inferring causal genes at type 2 diabetes GWAS loci through chromosome interactions

in islet cells.” [Wellcome Open Research](#) 8 (2023).

10. Alghamdi, Tamadher A., Nicole AJ Krentz, Nancy Smith, Aliya F. Spigelman, Varsha Rajesh, Alok Kumar Jha, **Han Sun**, Mourad Ferdaoussi et al. “Zmiz1 is required for mature  $\beta$ -cell function and mass expansion upon high fat feeding.” [Molecular Metabolism](#) 66 (2022): 101621.
11. Chenchen Zhu, Jingyan Wu, **Han Sun**, Francesca Briganti, Benjamin Meder, Wu Wei, and Lars M. Steinmetz. “Single-molecule, full-length transcript isoform sequencing reveals disease-associated RNA isoforms in cardiomyocytes.” [Nature Communications](#) 12, no. 1 (2021): 1-9.
12. Benedikt Rauscher, William F Mueller, Sandra Clauder-Münster, Petra Jakob, M Saiful Islam, **Han Sun**, Sonja Ghidelli-Disse, Markus Boesche, Marcus Bantscheff, Hannah Pflaumer, Paul Collier, Bettina Haase, Songjie Chen, Rene Hoffman, Guangwen Wang, Vladimir Benes, Gerard Drewes, Michael Snyder, Lars M Steinmetz. “Patient-derived gene and protein expression signatures of NGLY1 deficiency”, [Journal of Biochemistry](#), 2021
13. Semih Calamak, Menekse Ermis, **Han Sun**, Saiful Islam, Michael Sikora, Michelle Nguyen, Vasif Hasirci, Lars M. Steinmetz, and Utkan Demirci. “A Circulating Bioreactor Reprograms Cancer Cells Toward a More Mesenchymal Niche.” [Advanced Biosystems](#) 4, no. 2 (2020): 1900139, **co-first author**.
14. Jay W Schneider, Saji Oommen, Muhammad Y Qureshi, Sean C Goetsch, Rhianna S Sundsbak, Wei Guo, Mingming Sun, **Han Sun**, Dennis A Webster, Alex W Coutts, Francesca Briganti, Wu Wei, Lars Steinmetz, Daniel F Carlson, and Timothy J. Nelson et al. “Dysregulated ribonucleoprotein granules promote cardiomyopathy in RBM20 gene-edited pigs”, [Nature Medicine](#) (2020): 1-13.
15. William F. Mueller, Petra Jakob, **Han Sun**, Sandra Clauder-Münster, Sonja Ghidelli-Disse, Diana Ordonez, Markus Boesche, Marcus Bantscheff, Paul Collier, Bettina Haase, Vladimir Benes, Malte Paulsen, Peter Sehr, Joe Lewis, Gerard Drewes, Lars M. Steinmetz. “Loss of N-glycanase 1 Alters Transcriptional and Translational Regulation in K562 Cell Lines.” [G3: Genes, Genomes, Genetics](#) (2020).
16. Arne H. Smits, Frederik Ziebell, Gerard Joberty Nico Zinn, William F. Mueller, Sandra Clauder-Munster, Paola Grandi, Petra Jakob, Anne-Marie Michon, **Hanice Sun**, Karen Tessmer, Tilmann Burckstummer, Marcus Bantscheff, Lars M. Steinmetz, Gerard Drewes, and Wolfgang Huber. “Biological plasticity rescues target activity in CRISPR knock outs.”, [Nature Methods](#) 2019 Oct 28:1-7.
17. Suo, Lun, Yu Xiao Zhou, Li Ling Jia, Hai Bo Wu, Jin Zheng, Qi Feng Lyu, Li Hua Sun, **Han Sun**, and Yan Ping Kuang. “Transcriptome profiling of human oocytes experiencing recurrent total fertilization failure.” [Scientific Reports](#) 8, no. 1 (2018): 17890.
18. **Han Sun**, Chen Chen, Baofeng Lian, Menghuan Zhang, Xiaojing Wang, Bing Zhang, Yixue Li, Pengyuan Yang, and Lu Xie. 2015. “Identification of HPV Integration and Gene Mutation in HeLa Cell Line by Integrated Analysis of RNA-Seq and MS/MS Data.” [Journal of Proteome Research](#) 14 (4): 1678–86, **co-first author**.
19. **Han Sun**, Chen Chen, Meng Shi, Dandan Wang, Mingwei Liu, Daixi Li, Pengyuan Yang, Yixue Li, and Lu Xie. 2014. “Integration of Mass Spectrometry and RNA-Seq Data to Confirm Human Ab Initio Predicted Genes and lncRNAs.” [Proteomics](#) 14 (23-24): 2760–68, **co-first author**.
20. **Han Sun**, Xiaobin Xing, Jing Li, Fengli Zhou, Yunqin Chen, Ying He, Wei Li, et al. 2013. “Identification of Gene Fusions from Human Lung Cancer Mass Spectrometry Data.” [BMC Genomics](#) 14 Suppl 8 (December): S5, **co-first author**.
21. Zhen-Hao Liu, Bao-Feng Lian, Qiong-Zhu Dong, **Han Sun**, Jin-Wang Wei, Yuan-Yuan Sheng, Wei Li, et al. 2018. “Whole-Exome Mutational and Transcriptional Landscapes of Combined Hepatocellular Cholangiocarcinoma and Intrahepatic Cholangiocarcinoma Reveal Molecular Diversity.” [Biochimica et Biophysica Acta](#) 1864 (6 Pt B): 2360–68.
22. Menghuan Zhang, Hong Li, Ying He, **Han Sun**, Li Xia, Lishun Wang, Bo Sun, et al. 2015. “Construction and Deciphering of Human Phosphorylation-Mediated Signaling Transduction Networks.” [Journal of Proteome Research](#) 14 (7): 2745–57.
23. Wei Li, Jian Yu, Baofeng Lian, **Han Sun**, Jing Li, Menghuan Zhang, Ling Li, Yixue Li, Qian Liu, and Lu Xie. 2015. “Identifying Prognostic Features by Bottom-up Approach and Correlating to Drug Repositioning.” [PloS One](#) 10 (3): e0118672.
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27. Jian Yu, Xiaobin Xing, Lingyao Zeng, Jiehuan Sun, Wei Li, **Han Sun**, Ying He, et al. 2012. "SyStemCell: A Database Populated with Multiple Levels of Experimental Data from Stem Cell Differentiation Research." PloS One 7 (7): e35230.
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29. Xiao Chang, Yun Li, Jie Ping, Xiao-Bin Xing, **Han Sun**, Peng Jia, Chuan Wang, Yuan-Yuan Li, and Yi-Xue Li. 2011. "EcoBrowser: A Web-Based Tool for Visualizing Transcriptome Data of Escherichia Coli." BMC Research Notes 4 (October): 405.
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