Dr. Yaqiang Cao *Curriculum Vitae*

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Education

- **Ph.D. in Computational Biology** (M.S. included), CAS-MPG Partner Institute for Computational Biology, University of Chinese Academy of Sciences, with Prof. Jing-Dong Jackie Han (2012.09 - 2018.11)

- **B.S. in Bioengineering**, East China University of Science and Technology (2008.09 - 2012.06)

Professional Experience

- **Research Fellow**, NHLBI, NIH, with Dr. Keji Zhao (2024.04 – Present, hire freeze in the transition to Staff Scientist)

- **Visiting Fellow/Postdoctoral Researcher**, NHLBI, NIH, with Dr. Keji Zhao (2019.04 - 2024.04)

Research Interests

Bioinformatics, Epigenetics, T-cells, immune cell exhausting & aging

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Research Summary

My research elucidates how epigenetic regulatory mechanisms govern normal development and contribute to diseases like leukemia. By synergistically combining computational and experimental strategies, I dissect the molecular language of chromatin interactions, histone modifications, and nucleosome positioning, with a specific focus on $CD4^+$ T cells. Utilizing innovative bioinformatics tools and bulk/single-cell sequencing, I reveal how genomic instructions define cellular identity. Furthermore, strategic multidisciplinary collaborations bridge data science and functional genomics, propelling precision medicine innovations for immunological and age-related disorders. Ultimately, I advocate for accessibility, ensuring these powerful bioinformatics tools are user-friendly and broadly available to the research community.

Studies in Preparation

1. Tao Zhen *, Yaqiang Cao *, Tongyi Dou, Yun Chen, Guadalupe Lopez, Ana Catarina Menezes, Xufeng Wu, John A. Hammer, Jun Cheng, Lisa Garrett, Stacie Anderson, Martha Kirby, Stephen Wincovitch, Bayu Sisay, Abdel G. Elkahloun, Di Wu, Lucio Castilla, Wei Yang, Jiansen Jiang, Keji Zhao, Pu Paul Liu#: Enhancing RUNX1-DNA binding affinity is a critical step for leukemogenesis by CBFβ-SMMHC (under review)
2. Guangzhe Ge *, Yaqiang Cao *, Danping Wei *, Jinfang Zhu, and Keji Zhao [#]: Deciphering chromatin priming of T cell lineage by single-cell micrococcal nuclease sequencing
3. Yaqiang Cao *, Guangzhe Ge * and Keji Zhao [#]: VINCE: single-cell nucleosomes explorer

Selected First or Co-first Publications

1. Ma, F. *, *Cao, Y.* *, Du, H., Braikia, F., Zong, L., Ollikainen, N., Bayer, M., Qiu, X., Park, B., Roy, R., Nandi, S., Sarantopoulou, D., Ziman, A., Bianchi, A., Beerman, I., Zhao, K., Grosschedl, R., Sen, R. [#]. (2024) Three-dimensional chromatin reorganization regulates B cell development during ageing. *Nat Cell Biol*. 1-12.
2. Liu, S. *, *Cao, Y.* *, Cui, K*., Ren, G., Zhao, T., Wang, X., Wei, D., Chen, Z., Gurram, R.K., Liu, C. and Wu, C., Zhu, J., & Zhao, K. [#] (2024) Regulation

of T helper cell differentiation by the interplay between histone modification and chromatin interaction. *Immunity*. *57*(5), 987-1004.

3. *Cao, Y.* *, Liu, S. *, Cui, K. *, Tang, Q., & Zhao, K. # (2023). Hi-TrAC detects active sub-TADs and reveals internal organizations of super-enhancers. *Nucleic Acids Research*, gkad378.

4. Cui, K. *, Chen, Z. *, *Cao, Y.* *, Liu, S. *, Ren, G., Hu, G., Fang, D., Wei, D., Liu, C., Zhu, J., Wu, C. #, & Zhao, K. # (2023). Restraint of IFN-γ expression through a distal silencer CNS–28 for tissue homeostasis. *Immunity*, 56(5), 944-958 (**selected as cover**)

5. *Cao, Y.* *, Liu, S. *, Ren, G. *, Tang, Q., & Zhao, K. # (2022). cLoops2: a full-stack comprehensive analytical tool for chromatin interactions. *Nucleic Acids Research*, 50(1), 57-71.

6. Liu, S. *, *Cao, Y*. *, Cui, K., Tang, Q., & Zhao, K. # (2022). Hi-TrAC reveals division of labor of transcription factors in organizing chromatin loops. *Nature communications*, 13(1), 1-17.

7. Zhen, T. *, *Cao, Y.* *, Ren, G., Zhao, L., Hyde, R. K., Lopez, G., Feng, D., Alemu, L., Zhao, K., & Liu, P. P. # (2020). RUNX1 and CBFβ-SMMHC transactivate target genes together in abnormal myeloid progenitors for leukemia development. *Blood*, The Journal of the American Society of Hematology, 136(21), 2373-2385. (**selected as Plenary Paper**)

8. Han, M. *, Li, J. *, *Cao, Y.* *, Huang, Y., Li, W., Zhu, H., Zhao, Q., Han, J., Wu, Q., Li, J., Feng, J., & Wong, J. (2020). A role for LSH in facilitating DNA methylation by DNMT1 through enhancing UHRF1 chromatin association. *Nucleic Acids Research*, *48*(21), 12116-12134.

9. *Cao, Y.* *, Chen, Z. *, Chen, X. *, Ai, D. *, Chen, G., McDermott, J., Huang, Y., Guo, X., & Han, J. # (2020). Accurate loop calling for 3D genomic data with cLoops. *Bioinformatics*, 36(3), 666-675.

10. *Cao, Y.* *, Chen, G. *, Wu, G. *, Zhang, X. *, McDermott, J., Chen, X., Xu, C., Jiang, Q., Chen, Z., Zeng, Y., Ai, D., Huang, Y., &Han, J. # (2019). Widespread roles of enhancer-like transposable elements in cell identity and long-range genomic interactions[J]. *Genome research*, 2019, 29(1): 40-52.

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Other Contributed Publications

For a full list of publications: Google Scholar

1. Hong, S., Huang, Y., ***Cao, Y.***, Chen, X., & Han, J. D. J. (2014). Approaches to uncovering cancer diagnostic and prognostic molecular signatures. ***Molecular & Cellular Oncology***, *1*(2), e957981.
2. Chen, W., Qian, W., Wu, G., Chen, W., Xian, B., Chen, X., ***Cao, Y***. Green, C.D., Zhao, F., Tang, K., & Han, J. (2015). Three-dimensional human facial morphologies as robust aging markers. ***Cell research***, *25*(5), 574-587.
3. Huang, Y., Yu, X., Sun, N., Qiao, N., ***Cao, Y.***, Boyd-Kirkup, J. D., Shen, Q., & Han, J. (2015). Single-cell-level spatial gene expression in the embryonic neural differentiation niche. ***Genome research***, *25*(4), 570-581.
4. Wang, L. *****, Xu, X. *****, ***Cao, Y***. *****, Li, Z., Cheng, H., Zhu, G., Duan, F., Na, J., Han, J., & Chen, Y. G. (2016). Activin/Smad2-induced H3K27me3 reduction is crucial to initiate mesendoderm differentiation of human embryonic stem cells. ***Journal of Biological Chemistry***, jbc-M116.
5. Xu, C., Ai, D., Shi, D., Suo, S., Chen, X., Yan, Y., ***Cao, Y.***, Zhang, R., Sun, N., Chen, W., McDermott, J., Zhang, S., Zeng, Y. & Han, J.(2018). Accurate Drug Repositioning through Non-tissue-Specific Core Signatures from Cancer Transcriptomes. ***Cell reports***, 25(2), 523-535.
6. Chen, X., Xu, C., Hong, S., Xia, X., ***Cao, Y.***, McDermott, J., Mu, Y., & Han, J. (2019). Immune Cell Types and Secreted Factors Contributing to Inflammation-to-Cancer Transition and Immune Therapy Response. ***Cell reports***, 26(7), 1965-1977.
7. Huang, F. *****, ***Cao, Y***. *****, Wu, G., Chen, J., Lin, W., Lan, R., Wu, B., Xie, X., Hong, J., & Fu, L. (2020). BMP2 signaling activation enhances bone metastases of non-small cell lung cancer. ***Journal of cellular and molecular medicine***, 24(18), 10768-10784.
8. Zeng, Y. *****, ***Cao, Y***. *****, Halevy, R. S. *****, Nguyen, P., Liu, D., Zhang, X., Ahituv, N., & Han, J. (2020). Characterization of functional transposable element enhancers in acute myeloid leukemia. ***Science China Life Sciences***, 1-13.
9. Xia, X., Chen, X., Wu, G., Li, F., Wang, Y., Chen, Y., Chen, M., Wang, X., Chen, W., Xian, B., Chen, W., ***Cao, Y.***, Xu, C., Gong, W., Chen, G., Cai, D., Wei, W., Yan, Y., Liu, K., Qiao, N., Zhao, X., Jia, J., Wang, W., Kennedy, B., Zhang, K., Cannistraci, C., Zhou, Y., & Han, J. (2020). Three-dimensional facial-image analysis to predict heterogeneity of the human ageing rate and the impact of lifestyle. ***Nature Metabolism***, 2(9), 946-957.
10. Qiu, X., Ma, F., Zhao, M., ***Cao, Y.***, Shipp, L., Liu, A., Dutta, A., Singh, A., Braikia, F.Z., De, S., Wood, W. H., Becker, K.G., Zhou, W., Ji, H., Zhao, K., Atchison, M.L., & Sen, R. (2020). Altered 3D chromatin structure permits inversional recombination at the IgH locus. ***Science advances***, 6(33), eaaz8850.
11. Huang, F., ***Cao, Y.***, Wang, C., Lan, R., Wu, B., Xie, X., Hong, J., Fu, L., & Wu, G. (2021). PNMA5 promotes bone metastasis of non-small-cell lung

cancer as a target of BMP2 signaling. ***Frontiers in cell and developmental biology***, (2021): 1400.

12. Ku, W. L., Pan, L., ***Cao, Y.***, Gao, W., & Zhao, K. (2021). Profiling single-cell histone modifications using indexing chromatin immunocleavage sequencing. ***Genome Research***, gr-260893.

13. Fang, D., Cui, K., ***Cao, Y.***, Zheng, M., Kawabe, T., Hu, G., Khillan, J., Li, D., Zhong, C., Jankovic, D., Sher, A., Zhao, K., & Zhu, J. (2022). Differential regulation of transcription factor T-bet induction during NK cell development and T helper-1 cell differentiation. ***Immunity***, 55(4), 639-655.

14. Pan, L., Ku, W. L., Tang, Q., ***Cao, Y.***, & Zhao, K. (2022). scPCOR-seq enables co-profiling of chromatin occupancy and RNAs in single cells. ***Communications biology***, 5(1), 1-9.

15. Ren, G., Lai, B., Harly, C., Baek, S., Ding, Y., Zheng, M., ***Cao, Y.***, Cui, K., Yang, Y., Zhu, J., Hager, G., Bhandoola, A., & Zhao, K. (2022). Transcription factors TCF-1 and GATA3 are key factors for the epigenetic priming of early innate lymphoid progenitors toward distinct cell fates. ***Immunity,*** 55(8), 1402-1413.

16. Lin, X., Liu, Y., Liu, S., Zhu, X., Wu, L., Zhu, Y., Zhao, D., Xu, X., Chemparathy, A., Wang, H., ***Cao, Y.***, Nakamura, M., Noordermeer, J., Russa, M., Wong, W., Zhao, K., & Qi, L. S. (2022). Nested epistasis enhancer networks for robust genome regulation. ***Science***, 377(6610), 1077-1085.

17. Zhang, X., Jiang, Q., Li, J., Zhang, S., ***Cao, Y.***, Xia, X., Cai, D., Tan, J., Chen, J., & Han, J. D. J. (2022). KCNQ1OT1 promotes genome-wide transposon repression by guiding RNA–DNA triplexes and HP1 binding. ***Nature Cell Biology***, 1-13.

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Academic Software Development

- **cLoops**: accurate and flexible loops calling tool for 3D genomic data (released in 2017)
- **cLoops2**: full stack analysis tool for chromatin interaction data such as Hi-TrAC, HiChIP and Hi-C (released in 2021)
- **astroBoy**: streamlined NGS data automatic processing web service for in-house data and public data (GEO database), in-house service within NIH since December 2022; processed nearly 195 billion reads (more than 6000 samples and 400 jobs)

Awards & Honors

- **2024 NHLBI Director's Award for Innovation** – Discovery of a novel regulatory element for IFN-γ expression

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Mentoring Experience

- **Hannah Zhu**, NIH Summer Internship Program (2023, 2024)
- **Emily Yu**, High School Senior Project, The Bryn Mawr School (2024)

Review Contributions

Reviewer for: *Bioinformatics, Communications Biology, BMC Genomics, F1000Research, Frontiers in Immunology, Frontiers in Bioinformatics, Genes, Cells*, and more.

Invited Talks

1. **Epigenetics Retreat, November 2017, Ningbo, China;** Accurate loop calling for 3D genomic data with cLoops.
2. **DECODE Seminar Series, August 2023, NIH, Bethesda, USA;** Fine-scale dynamic chromatin loops and domains: beyond cohesin.
3. **Invited by Prof. Lei Hou, August 2023, Boston University, Boston, USA:** Fine-scale dynamic chromatin loops and domains: beyond cohesin.
4. **Invited by Dr. Gordon L. Hager, September 2024, NCI, Bethesda, USA:** Decoding chromatin structures sequencing data with cLoops2.
5. **Invited by NICHD Bioinformatics and Scientific Programming Core, November 2024, NICHD, Bethesda, USA:** Rock The Fine-scale Dynamic Chromatin Loops and Domains.

Conference Presentations & Posters

1. **Otto Warburg Summer School, September 2015, Max Planck Institute for Molecular Genetics, Berlin, German;** Yaqiang Cao (2015) iDBSCAN: An improvement to density-based clustering method for ultrafast detection of chromosomal interactions
2. **The 3th International Symposium on 3D genomics, November 2016, Huazhong Agricultural University, Wuhan, China;** Yaqiang Cao (2016) Widespread Associated Retrotransposons MIR and L2 Function as Seeds of Cis-regulatory Units Marking Cell Identities
3. **The First Chromatin Biology Conference of the Chinese Society for Cell Biology, April 2017, Shenzhen, China;** Yaqiang Cao (2017) Widespread Associated Retrotransposons MIR and L2 Function as Seeds of Cis-regulatory Units
4. **Cold Spring Harbor Asia Conferences on Chromatin, Epigenetics & Transcription, April 2018, Suzhou, China;** Yaqiang Cao (2018) cLoops-A clustering-based loops calling method for ChIA-PET, HiChIP and Hi-C
5. **4D Nucleosome Annual Meeting, December 2019, DC, USA;** Shuai Liu, Yaqiang Cao, Qingsong Tang, Keji Zhao (2019) TrAC-looping2 – A Highly Sensitive Technique for Detecting Multiple Levels of Chromatin Interactions
6. **SCBA DC-Baltimore chapter annual scientific symposium, December 2022, University of Maryland, USA:** Yaqiang Cao (2022) Hi-TrAC reveals internal organizations of super-enhancers
7. **NHLBI Fellow Festival, April 2023, NIH, Bethesda, USA:** Yaqiang Cao (2023) Hi-TrAC reveals internal organizations of super-enhancers
8. **Gordon Research Conference, Genome Architecture in Cell Fate and Disease, June 2023, Ventura, California, USA:** Yaqiang Cao (2023) Hi-TrAC: Revealing Fine-Scale Dynamic Chromatin Loops and Domains
9. **NIH/FDA IMMUNOLOGY INTEREST GROUP 2024 RETREAT, January 2024, DC, USA**: Yaqiang Cao (2024) T Helper Cell Fate Orchestrated by H3K4me1–Chromatin Loop–GATA3 Tangos
10. **NHLBI Fellow Festival, March 2024, NIH, Bethesda, USA:** Yaqiang Cao (2024) T Helper Cell Fate Orchestrated by H3K4me1–Chromatin Loop–GATA3 Tangos
11. **Epigenetics & Chromatin, September 2024, Cold Spring Harbor Laboratory, New York, USA:** Yaqiang Cao (2024) T Helper Cell Fate Orchestrated by H3K4me1–Chromatin Loop–GATA3 Tangos
12. **NCI Histone Modifications and Chromatin Structure Symposium (2024), Bethesda, Maryland, USA:** Yaqiang Cao (2024) T Helper Cell Fate Orchestrated by H3K4me1–Chromatin Loop–GATA3 Tangos

Technical Skills

- Epigenomic/Gene Expression Data Analysis (Hi-C, ATAC-seq, ChIP-seq, MNase-seq, Hi-TrAC, RNA-seq, 10x single-cell RNA-seq)
- Programming (Python, Bash)
- High-Performance Computing
- Servers maintenance
- Web-application Development
- Deep-learning
- Machine-learning