Xueqiu Lin

Department of Bioengineering, Stanford University
Phone: +1-713-240-6422; Email: xqlin@stanford.edu

RESEARCH INTEREST

Deep examinations of whole genomes in tumors highlight that the majority of DNA mutations occur in non-coding regions. It remains unclear how their functions converge in a non-coding regulatory network to lead to cancer. Our lab focuses on developing cutting-edge computational and experimental approaches to uncover interactive rules within these regulatory networks, and to understand the functional consequences of non-coding mutations through these networks. We focus on the development of multiplexed CRISPR screening to study the functional interaction network of enhancers. The use of this approach, combined with deep learning and statistical modeling, will reveal the genetic code, discover novel genetic biomarkers, and develop epistasis-aware genomic risk prediction schemes for precision cancer medicine.

EDUCATION AND TRAINING

Postdoctoral training, Computational biology Synthetic biology	Stanford University	03/2017 ~ present
Ph.D., Bioinformatics	Tongji University, China & Baylor College of Medicine	03/2011 ~ 06/2016

- The first two years were trained in Tongji University; The last three years were trained in Baylor College of Medicine.
- Dissertation: Developing bioinformatics tool, detecting novel regulatory elements and studying regulatory mechanism of DNA methyltransferase based on bisulfite sequencing data.

B.S., Biological Sciences	Sun Yat-Sen University, China	09/2007 ~ 06/2011

APPOINTMENTS

Assistant Professor, Computational Biology Program and Public Health Sciences Division, Fred Hutchinson Cancer Center, WA (September 2023 -).

Postdoctoral Scholar, Department of Bioengineering, Stanford University, CA (March 2017 - August 2023). Advisor: Lei Stanley Qi. Link.

Graduate Research Assistant, Dan L. Duncan Cancer Center, Department of Molecular and Cellular Biology, Baylor College of Medicine, TX (February 2014 - February 2017). Advisor: Wei Li. Link.

Graduate Research Assistant, Department of Bioinformatics, School of life sciences and Technology, Tongji University, Shanghai, China (September 2011 - January 2014). Advisor: Wei Li, Xiaole Shirley Liu, and Yong Zhang. Link1. Link2

MOST SIGNIFICANT SCIENTIFIC CONTRIBUTIONS

Citation information (Link)
#Co-first author. *Co-corresponding author

1. **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 JN, La Russa M, Wong WH, Zhao K, Qi LS. Nested Epistasis Enhancer Networks for Robust Genome Regulation. **Science** (2022). Link.

   Commented by Nature "News & Views". Link.

2. **Lin X#**, Liu Y#, Chemparathy A#, Pande T, Russia ML, Qi LS. A comprehensive analysis and resource to use CRISPR-Cas13 for broad-spectrum targeting of RNA viruses. **Cell Reports Medicine** (2021). Link.

3. Abbott TR#, Dhamdhere G#, Liu Y#, **Lin X#**, Goudy L#, Zeng L, Chemparathy A, Chmura S, Heaton NS, Debs R, Pande T, Endy d, Russa ML*, Lewis DB*, Qi LS*. Development of CRISPR as a prophylactic strategy to combat novel coronavirus and influenza. **Cell** (2020). Link.

   Media coverage: Link1, Link2, Link3.

4. Gu T#, **Lin X#**, Cullen S, Luo M, Jeong M, Estecio M, Shen J, Hardikar S, Sun D, Su J, Rux D, Guzman A, Lee M, Qi L, Chen J, Kyba M, Huang Y, Chen T, Li W*, Goodell MA*. DNMT3A and TET1 cooperate to regulate promoter epigenetic landscapes in mouse embryonic stem cells. **Genome Biology** (2018). Link.

5. **Lin X**, Su J, Chen K, Rodrigues B, Li W. Sparse conserved under-methylated CpGs are associated with high-order chromatin structure. **Genome Biology** (2017). Link.

6. **Lin X**, Sun D, Rodriguez B, Zhao Q, Sun H, Zhang Y, Li W. BSeQC: Quality Control of Bisulfite Sequencing Experiments. **Bioinformatics** (2013). Link.

OTHER PUBLICATIONS

7. Guo L#*, Bian J#, Davis AE, Liu P, Kempton HR, Zhang X, Chemparathy A, Gu B, **Lin X**, Rane DA, Xu X, Jamiolkowski RM, Hu Y, Wang S*, Qi LS*. Multiplexed genome regulation in vivo with hyper-efficient Cas12a. **Nature Cell Biology** (2022). Link.

8. Gu T#, Hao D#, Woo J, Huang TW, Guo L, **Lin X**, Guzman AG, Tovy A, Rosas C, Jeong M, Zhou Y, Deneen B, Huang Y, Li W, Goodell MA. The disordered N-terminal domain of DNMT3A recognizes H2AK119ub and is required for postnatal development. **Nature Genetics** (2022). Link.

9. Zeng L#, Liu Y#, Nguyenla XH, Abbott TR, Han M, Zhu Y, Chemparathy A, **Lin X**, Chen X, Wang H, Rane DA, Spatz JM, Jain S, Rustagi A, Pinsky B, Zepeda AE, Kadina AP, Walker JA, Holden K, Temperton N, Cochran JR, Barron AE, Connolly MD, Blish CA, Lewis DB, Stanley SA*, Russa ML*, Qi LS*. Broad-spectrum CRISPR-mediated

inhibition of SARS-CoV-2 variants and endemic coronaviruses in vitro. **Nature Communications** (2022). Link.

10. **Lin X**, Chemparathy A, Russa ML, Daley T, Qi LS. Computational Methods for Analysis of Large-Scale CRISPR Screens. **Annual Review of Biomedical Data Science** (2020). Link.

11. Bodapati S, Daley TP, **Lin X**, Zou J*, Qi LS*. A benchmark of algorithms for the analysis of pooled CRISPR screens. **Genome Biology** (2020). Link.

12. Wang H, Xu X, Nguyen CM, Liu Y, Gao Y, **Lin X**, Daley T, Kipniss NH, La Russa M, Qi LS. CRISPR-mediated programmable 3D genome positioning and nuclear organization. **Cell** (2018). Link.

13. Liu Y#, Yu C#, Daley T#, Wang F, Cao WS, Bhate S, **Lin X**, Still II C, Liu H, Zhao D, Wang H, Xie X, Ding S, Wong WH, Wernig M, Qi LS. CRISPR Activation Screens Systematically Identify Factors that Drive Neuronal Fate and Reprogramming. **Cell Stem Cell** (2018). Link.

14. Daley T#*, Lin Z, **Lin X**, Liu Y, Wong WH, Qi LS. CRISPhieRmix: a hierarchical mixture model for CRISPR pooled screens.**Genome Biology** (2018). Link.

15. Su J#, Huang Y#, Cui X, Zhang X, Wang X, Xin Y, **Lin X**, Chen K, Lv J, Xu J, Goodell MA* and Li W*. Homeobox oncogene activation by pan-cancer DNA hypermethylation. **Genome Biology** (2018). Link.

16. Xu J, Zhang W, Yan X, **Lin X,** Li W, Mi J, Li J, Zhu J, Chen Z, Chen S. DNMT3A mutation leads to leukemia extramedullary infiltration mediated by TWIST1. **Journal of Hematology & Oncology** (2016). Link.

17. Yang L#, Rodriguez B#, Mayle A, Park HJ, **Lin X,** Luo M, Jeong M, Curry CV, Kim S, Ruau D, Zhang X, Zhou T, Zhou M, Rebel VI, Challen GA, Gottgens B, Lee JS, Rau R, Li W*, Goodell MA*. DNMT3A loss drives enhancer hypomethylation in FLT3-ITD-associated leukemias. **Cancer Cell** (2016). Link.

18. Chen K, Chen Z, Wu D, Zhang L, **Lin X,** Su J, Rodriguez B, Xi Y, Xia Z, Chen X, Shi X, Wang Q, Li W. Broad H3K4me3 is associated with increased transcription elongation and enhancer activity at tumor-suppressor genes. **Nature Genetics** (2015). Link.

19. Ho JWK#, Jung YL#, Liu T#, Alver B. H, Lee S, Ikegami K, Sohn K, Minoda A, Tolstorukov MY, Appert A, Parker SCJ, Gu T, Kundaje A, Riddle NC, Bishop E, Egelhofer TA, Hu SS, Alekseyenko AA, Rechtsteiner A, Asker D, Belsky JA, Bowman SK, Chen QB, Chen RAJ, Day DS, Dong Y, Dose AC, Duan X, Epstein CB, Ercan S, Feingold EA, Ferrari F, Garrigues JM, Gehlenborg N, Good PJ, Haseley P, He D, Herrmann M, Hoffman MM, Jeffers TE, Kharchenko PV, Kolasinska-Zwierz P, Kotwaliwale CV, Kumar N, Langley SA, Larschan EN, Latorre I, Libbrecht MW, **Lin X,** Park R, Pazin MJ, Pham HN, Plachetka A, Qin B, Schwartz YB, Shoresh N, Stempor P, Vielle A, Wang C, Whittle CM, Xue H, Kingston RE, Kim JH, Bernstein BE, Dernburg AF, Pirrotta V, Kuroda MI, Noble WS, Tullius TD, Kellis M, MacAlpine DM*, Strome S*, Elgin SCR*, Liu XS*, Lieb

JD*, Ahringer J*, Karpen GH*, Park PJ*. Comparative analysis of metazoan chromatin organization. **Nature** (2014). Link.

20. Wang J, **Lin X,** Wang S, Wang C, Wang Q, Duan X, Lu P, Wang Q, Wang C, Liu XS, Huang J. PHF8 and REST/NRSF co-occupy gene promoters to regulate proximal gene expression. **Scientific Reports** (2014). Link.

21. Sun H, Qin B, Liu T, Wang Q, Liu J, Wang J, **Lin X,** Yang Y, Taing L, Rao PK, Brown M, Zhang Y, Long HW, Liu XS. CistromeFinder for ChIP-seq and DNase-seq data reuse. **Bioinformatics** (2013). Link.

MANUSCRIPT IN PREPARATION

22. Chen Yu#, **Lin X#**, Liu Y#, Zhu X, Qi LS. Systematic assessment of regulatory elements in control of pluripotency by CRISPR-based multi-dimension datasets.

23. Wu L#, **Lin X#,** Zhu X#, Liu Y Qi LS. Genome-wide CRISPR screen identifies novel aging regulator.

PRESENTATIONS

1. Nested Enhancer Networks Link Multiple Non-coding Variants to Disease Risk (Oral presentation)
    a. 4DN Scientific Webinar, Aug 2022
    b. University of California Irvine, Oct 2022
    c. Stanford Center of Excellence in Genomic Science (CEGS) Seminar, Nov 2022
2. Enhancer-enhancer interaction networks involved in ultralong-distance genome regulation link multiple non-coding variants to function (Oral presentation and Poster), Virtual ASHG, Oct 2021

3. Computational analysis on model organisms and non-model organisms (Oral presentation). ChEM-H Retreat, Stanford University, May 2017

4. Computational analysis on DNA methylome: Tool Development, Data Mining and Collaborative Study (Invited oral presentation).
    a. University of California, Los Angeles, Nov 2016
    b. University of Washington, Nov 2016
    c. Stanford University, Nov 2016

5. BSeQC: Quality Control of Bisulfite Sequencing Experiments (Poster). Cold Spring Harbor Asia (CSHA): Frontiers in Bioinformatics and Computational Biology, Suzhou, China, 2013

HONORS AND AWARDS

- Reviewers Choice Awards, ASHG, 2021

- Excellent Ph.D. students Scholarship, Tongji University, 2013~2015
- Guanghua Scholarship, Tongji University, 2013
- Excellent master students Scholarship, Tongji University, 2011~2013

GRANT

NIH R01 CA266470: High resolution dissection of oncogene enhancer networks via CRISPR screening and live-cell imaging (Role: Researcher; Contributed data and writing)

TEACHING AND MENTORING

Augustine George Chemparathy, MD student, 2021-Present
- Develop web to provide resources of predicted enhancer pairs with synergistic interaction within multi-layer enhancer network

Augustine George Chemparathy, Master student, 2019-2021
- Package the codes of computational algorithms that is used to design sgRNA to aid Cas13 platform (PAC-MAN) for pan-virus inhibition and degradation
- Develop web to provide resources of sgRNAs designed to aid Cas13 platform (PAC-MAN) for pan-virus inhibition and degradation
- Build RNA-seq analysis pipeline
- Build analysis pipeline for genome editing experiments
- Write some sections for a review focusing on computational methods for analysis of large-scale CRISPR screens.

Tanye Wen, Undergraduate student, 2021
- Build a manching model to predict efficient sgRNA in CRISPRa system

Liqun Zhou, Undergraduate student, 2020
- Build a manching model to predict efficient sgRNA in CRISPRi system

Teaching assistant for the operation of bioinformatics tools, 2013 DragonStar course, Shanghai, China, 2013

ACADEMIC SERVICE

- Journal peer-review
  Genome Biology, Briefings in Bioinformatics, Genomics, Biomedicine & Pharmacotherapy, IEEE/ACM Transactions on Computational Biology and Bioinformatics, Nucleic Acids Research, Journal for ImmunoTherapy of Cancer, Frontiers in Genetics, Frontiers in Oncology

- Principal member of the conference organizer
  2011 Tongji-Novartis Cancer and Epigenetics Symposium, Shanghai, China

SCIENTIFIC SOFTWARE AND RESOURCE

SRE_Predictor for predicting enhancer epistatic interactions for pathogenic genes

BSeQC for quality control of bisulfite sequencing experiments

CRISPhieRmix for using a hierarchical mixture model to resolve issues in CRISPRi/a screens

EnhancerNet for providing a useful resource to study enhancer interactions for gene regulation and multiple non-coding variants for complex diseases

PACMAN crRNA Repository for providing a comprehensive analysis and resource to use CRISPR-Cas13 for broad-spectrum targeting of RNA viruses