Kai-Yuan Chen, Ph.D.

Foster City, CA
Phone: 607-793-0198 • E-Mail: kaiyuan.kyle.chen@gmail.com

PROFESSIONAL SUMMARY

Strategic and results-driven computational biologist with over a decade of expertise in AI/ML-driven target discovery, multi-omics, cancer and cardiometabolic diseases. Proven leadership in applying cutting-edge computational techniques to drive drug discovery, translational medicine, and clinical research. Extensive experience in human genetics, single-cell transcriptomics, and high-dimensional omics data analysis. Adept at managing and mentoring high-performance teams, fostering cross-functional collaboration, and delivering innovative AI/ML solutions in the biopharmaceutical industry.

EXPERIENCE

Director, Head of Computational Genomics and Data Science 2023-present
Scribe Therapeutics

- Leading cross-functional teams in Next Generation Sequencing (NGS), Bioinformatics, and Data Science to advance Lab-In-A-Loop R&D strategies and accelerate CRISPR-based drug development with a focus on cardiometabolic diseases.
- Drive biomarker discovery strategies and off-target discovery strategies using advanced AI/ML approaches in multi-omics data and genomics sciences.
- Designed and executed a computational biology strategy to prioritize multiple therapeutic targets for cardiometabolic diseases, leveraging genetics and causal disease biology insights
- Leading the development of Machine Learning (ML) and Artificial Intelligence (AI) algorithms for protein design, preclinical research, and genomics, while optimizing high-throughput automation and R&D operations to improve NGS efficiency by 140% and increase screening accuracy by over 50%.
- Spearheading the deployment of advanced protein generative AI models, such as RFDiffusion, HyenaDNA, Evo, and ProteinMPNN, along with in-house development of predictive deep learning models and fine-tuning of large language models (LLMs), to transform protein design, facilitate AI-driven protein screening and validation, and enhance precision and therapeutic efficacy.
- Presented complex AI-driven genomic insights to stakeholders via compelling visualizations, facilitating cross-functional decision-making in drug discovery programs.
- Fostering strategic partnerships with external technology providers, accelerating AI innovation.
- Establish advanced computational environments with scalable cloud infrastructure, GPU computing, and AI/ML engineering platforms, enabling cross-functional collaboration in Computation Biology, Lab Automation, and Machine Learning.

Director, Head of Data Science and Computation Biology 2023
Associate Director, Head of Data Science and Computation Biology 2021-2023
Omega Therapeutics

- Led the analysis, integration, and AI/ML-driven modeling of complex genomics and epigenomics data to accelerate the translation of therapeutic targets to clinical applications. Responsible for data analytics across all pipelines, including multi-omic disease characterization, gene targeting specificity, target discovery, and drug formulation quality control.

- Managed and built a team of PhD-level computational biologists, data scientists, and engineers specializing in genomics discovery and lipid nanoparticle (LNP)/mRNA drug design.
- Built cloud strategy for hybrid genomic computation and AI/ML modeling, overseeing data analytics for preclinical R&D, mRNA production, and drug delivery. Implemented state-of-the-art ML/AI architectures using Deep Learning frameworks, Natural Language Processing (NLP), and Transformer models.
- Drove AI/ML strategies for Omega's technical platforms, developing an in-house knowledgebase using NLP, data mining, and big data for business development, target identification. Built GNN/CNN/Transformer models for novel protein design and genomic target discovery.
- Supported Investigational New Drug (IND) filings and led Next-Generation Sequencing (NGS) analytics for preclinical programs, integrating multi-genomic data with direct impact on Omega's clinical and preclinical pipelines.
- Designed and implemented scalable, reproducible NGS pipeline workflows integrated with cloud infrastructure, covering whole-genome methylation sequencing, RNA-Seq, ATAC-Seq, ChIP-Seq, single-cell RNA sequencing (scRNASeq), multi-omics integration, and more.
- Collaborated with cross-functional project teams and external partners to drive innovation and streamline AI-powered genomic solutions.

Principal Bioinformatics Scientist, 2019-2021
Engine Biosciences

- Led a global team in the creation of an AI-driven knowledgebase for cancer target discovery, utilizing advanced machine learning (ML) and data science techniques to streamline drug development processes.
- Spearheaded the pipeline development and optimization of whole-genome dual-CRISPR screening, integrating AI-driven analysis to enhance the precision and efficiency of gene editing research.
- Drove the development of cutting-edge AI/ML frameworks and Natural Language Processing (NLP) models to accelerate drug discovery, leveraging deep learning algorithms to identify novel therapeutic targets.
- Designed and led the implementation of a robust, enterprise-level data lake system, enabling real-time data ingestion, transformation, and business intelligence (BI) reporting to support AI-driven decision-making.
- Architected biotech enterprise cloud infrastructure on AWS, integrating scalable, big-data solutions optimized for AI/ML projects across global research and development pipelines.
- Led external collaborations with leading academic institutions and industry partners, driving innovation through AI and fostering breakthroughs in drug discovery and cancer research.

Kai-Yuan Chen, Ph.D.

Computational Scientist, 2018-2019
Intellia Therapeutics

- Developed scalable computational pipelines to quantify genome-wise targets/off-targets of CRISPR editing
- Developed analytical pipelines for immune cell engineering design using high throughput CRISPR screening platform.
- Comprehensive Immunogenicity analysis on TCGA metadata for immunotherapy target discovery.
- Designed and initiated single-cell analytic pipelines on gene expression and immune profiling from 10X Chromium platform.

Postdoctoral Research Associate, 2016-2018
Dept. of Biomedical Engineering & Center for Genomic and Computational Biology, Duke University

- Led a research team with 2 post-docs, 2 graduate students, and 2 technicians
- Developed epigenomic profiling and epigenomic editing platform (CRISPR/dCas9-Krab/p300) to identify intestinal stem cell drivers, drug-resistant factors in colon cancer, and liver metastasis.
- Developed high-throughput drug screening of 3D organoid system for personalized therapy.
- Investigated drug responses of the colorectal tumor using single-cell RNASeq.
- Led and mentored 2 graduate students to investigate microbiome in response to intestine inflammation and neural modulation

Irwin M. and Joan K. Jacobs Fellow/Research Associate 2010-2015
School of Electrical and Computer Engineering, Cornell University

- Integrated transcriptomics and metabolomics data to identify the metabolic signatures in liver metastasis of colorectal cancer.
- Developed mathematical and computational models, applied ChIP-Seq, and CRISPR/Cas9 system to predict and characterize the intestine stem cell-niche interaction.
- Developed mathematical microRNA model to predict cancer stem cell control.

EDUCATION

Ph.D.	School of Electrical and Computer Engineering, Cornell University, USA
M.Eng.	Department of Biomedical Engineering, Cornell University, USA
M.S.	Department of Electrical Engineering, National Taiwan University, Taiwan
B.A.	Department of Electrical Engineering, National Cheng Kung University, Taiwan

PUBLICATION (selected) [Google Scholar]

- Wang, L., Wang, E., Prado Balcazar, J., Wu, Z., Xiang, K., Wang, Y., Huang, Q., Negrete, M., **Kai-Yuan Chen**, Li, W. and Fu, Y., 2021. Chromatin Remodeling of Colorectal Cancer Liver Metastasis is Mediated by an HGF-PU. 1-DPP4 Axis. Advanced Science, 8(19), p.2004673.
- Lin, C.C., Ding, C.K.C., Sun, T., Wu, J., **Kai-Yuan Chen**, Zhou, P. and Chi, J.T., 2021. The regulation of ferroptosis by MESH1 through the activation of the integrative stress response. Cell Death & Disease, 12(8), pp.1-10.

- Tung, K.L., **Kai-Yuan Chen***, Negrete, M., Chen, T., Safi, A., Aljamal, A.A., Song, L., Crawford, G.E., Ding, S., Hsu, D.S. and Shen, X., 2021. Integrated chromatin and transcriptomic profiling of patient-derived colon cancer organoids identifies personalized drug targets to overcome oxaliplatin resistance. Genes & diseases, 8(2), pp.203-214.
- Altunel, E., Roghani, R. S., **Kai-Yuan Chen**, et al., 2020. Development of a precision medicine pipeline to identify personalized treatments for colorectal cancer. *BMC Cancer*.
- Ding, C.K.C., Rose, J., Sun, T., Wu, J., Chen, P.H., Lin, C.C., Yang, W.H., **Kai-Yuan Chen**, et al., 2020. MESH1 is a cytosolic NADPH phosphatase that regulates ferroptosis. *Nature Metabolism*, pp.1-8.
- Wang, L., Wang, E., Wang, Y., Mines, R., Xiang, K., Sun, Z., Zhou, G., **Kai-Yuan Chen**, et al., 2018. miR-34a is a microRNA safeguard for Citrobacter-induced inflammatory colon oncogenesis. *Elife*, 7, p.e39479.
- Ziyang Gao, **Kai-Yuan Chen**, et al. "Microbiota of Inflammatory Bowel Disease Models." *Conf Proc IEEE Eng Med Biol Soc* 2018
- **Kai-Yuan Chen**, T. Srinivasan, et al. "Single-Cell Transcriptomics Reveals Heterogeneity and Drug Response of Human Colorectal Cancer Organoids." *Conf Proc IEEE Eng Med Biol Soc* 2018
- **Kai-Yuan Chen**, Xiling Shen, and Anna Mae Diehl. "Prometheus revisited." *The Journal of clinical investigation*128.6 (2018).
- P. Bu*, **Kai-Yuan Chen***, C. Johnson*, N. Rakhilin, Y. Ai, L. Wang, et al. "Aldolase B-Mediated Fructose Metabolism Drives Metabolic Reprogramming of Colon Cancer Liver Metastasis." *Cell Metabolism*, (2018)
- **Kai-Yuan Chen***, T. Srinivasan*, K.-L. Tung, J. Choi, et al. "A Notch positive feedback in intestinal stem cell niche." *Molecular Systems Biology*, 13.4 (2017): 927.
- Y. Wang, D. Huang, **Kai-Yuan Chen**, M. Cui, W. Wang, et al. "Fucosylation Deficiency in Mice Leads to Colitis and Adenocarcinoma", *Gastroenterology.* (2016), doi: 10.1053/j.gastro.2016.09.00
- Srinivasan T, Walters J, Bu P, Than EB, Tung KL, **Kai-Yuan Chen**, et al. NOTCH Signaling Regulates Asymmetric Cell Fate of Fast-and Slow-Cycling Colon Cancer–Initiating Cells. *Cancer research.* 2016 Jun 1;76(11):3411-21.
- Srinivasan T, Than EB, Bu P, Tung KL, **Kai-Yuan Chen**, et al. Notch signalling regulates asymmetric division and inter-conversion between lgr5 and bmi1 expressing intestinal stem cells. *Scientific reports.* 2016;6.
- Bu, P., Wang, L., **Kai-Yuan Chen**, Srinivasan, T., Murthy, P. K. L., et al. (2016). A miR-34a-Numb Feedforward Loop Triggered by Inflammation Regulates Asymmetric Stem Cell Division in Intestine and Colon Cancer. *Cell stem cell*, *18*(2), 189-202.
- Chen, H. J., J. Sun, Z. Huang, H. Hou, Jr., M. Arcilla, N. Rakhilin, D. J. Joe, J. Choi, P. Gadamsetty, J. Milsom, G. Nandakumar, R. Longman, X. K. Zhou, R. Edwards, J. Chen, **Kai-Yuan Chen**, P. Bu, L. Wang, et al. (2015). "Comprehensive models of human primary and metastatic colorectal tumors in immunodeficient and immunocompetent mice by chemokine targeting." *Nat Biotechnol* 33(6): 656-660.
- Bu, P., L. Wang, **Kai-Yuan Chen**, N. Rakhilin, J. Sun, et al. (2015). "miR-1269 promotes metastasis and forms a positive feedback loop with TGF-beta." *Nat Commun* 6: 6879.
- **Kai-Yuan Chen**, X. Liu, P. Bu, C. S. Lin, N. Rakhilin, J. W. Locasale and X. Shen (2014). "A metabolic signature of colon cancer initiating cells." *Conf Proc IEEE Eng Med Biol Soc* 2014: 4759-4762.
- Bu, P., **Kai-Yuan Chen**, J. H. Chen, L. Wang, J. Walters, et al. (2013). "A microRNA miR-34a-regulated bimodal switch targets Notch in colon cancer stem cells." *Cell Stem Cell* 12(5): 602-615.
- Bu, P., **Kai-Yuan Chen**, S. M. Lipkin and X. Shen (2013). "Asymmetric division: a marker for cancer stem cells in early stage tumors?" *Oncotarget* 4(7): 950-951

EXPERTISE AND SKILLS

- AWS architecture, cloud computation, lake formation, pipeline development.
- Programming skills: R; Python; Matlab; C++; Java; Mathematica.
- NGS analysis & High-Throughput Analysis
    - Epigenomic Sequencing (ChIP-Seq; ATAC-Seq; DNase-Seq),

  - Transcriptomic Sequencing (single-cell RNA-Seq; RNA-Seq; MicroArray)
  - Ribosomal Profiling (Ribo-Seq)
  - Microbiome (qiime)
  - Metabolomics (LCMS)
  - 3D genome (HiC, capture HiC, HiChIP)
  - The Cancer Genome Atlas (TCGA) analysis
  - CITE-Seq, Perturb-Seq, scATACSeq, 10X immune profiling
  - DepMap analysis
  - Pathway Analysis
- Genomic/Epigenomic Editing system
  - CRISPR/Cas9; dCas9-Krab; Whole-Genome sgRNA design
- Systems biology
  - Deterministic/Stochastic modeling; Nonlinear dynamics analysis; Hybrid modeling; 3D tissue modeling
- ML/AI
  - NLP modeling
  - LLM, deep learning, graph neural network, CNN, RNN, Graph Neural Network
  - Diffusion Model/Generative Model
  - Keras, Tensorflow, PyTorch, Nvidia BioNeMO, AWS Sagemaker, etc.