Stanford

Le Cong

Associate Professor of Pathology (Pathology Research) and of Genetics

Bio

BIO

Dr. Cong's research program spans from foundational genome engineering to building agentic AI and autonomous laboratories for biomedical discovery. His group develops advanced technologies for large-scale genome editing and cell therapy, while also leveraging these tools for single-cell functional screening to probe the mechanisms of innate immunity in cancer and neuro-immune diseases. To accelerate these efforts, the team pioneers the integration of AI foundation models into biology. Recent innovations include RNAGenesis foundation model for generative design of RNA, CRISPR-GPT as an AI agent system that automates complex gene-editing workflows, and LabOS, an AI-XR co-scientist platform that embeds reasoning directly into physical laboratory. Alongside upcoming initiatives like the MedOS, the group is building a vision to unify computational design with robotic execution to turn the lab into a programmable, AI-native environment.

The team's work led to one of the first CRISPR/Cas9 gene-editing tools for in vivo gene therapy. More recently, his group invented tools for cleavage-free large gene insertion using novel recombination proteins (SSAP editor) and developed machine-learning optimized single-cell methods (DAISY) for studying complex immune diseases. These tools are also being deployed with collaborators to study stem cell regeneration and brain aging.

Dr. Cong is a recipient of the NHGRI Genomic Innovator Award, and a Baxter Foundation Faculty Scholar. He has also been recognized among the Genetic Engineering and Biotechnology News (GEN) Top 10 Under 40, Clinical OMICs Pioneers Under 40, and is a Clarivate Web of Science Highly Cited Researcher.

ACADEMIC APPOINTMENTS

- Associate Professor, Pathology
- Associate Professor, Genetics
- Member, Bio-X
- Member, Cardiovascular Institute
- Member, Stanford Medicine Children’s Health Center for IBD and Celiac Disease
- Member, Stanford Cancer Institute
- Member, Wu Tsai Neurosciences Institute

HONORS AND AWARDS

- Genomic Innovator Award, National Institute of Health (NIH), National Human Genome Research Institute (NHGRI)
- Donald and Delia Baxter Foundation Faculty Scholar, Baxter Foundation

- CRI Irvington Fellow, Cancer Research Institute
- HHMI International Fellow, Howard Hughes Medical Institute

BOARDS, ADVISORY COMMITTEES, PROFESSIONAL ORGANIZATIONS

- Genome Editing and New Investigator Committee Member, American Society of Gene & Cell Therapy (ASGCT) (2019 - present)
- Editorial Board, Gene and Genome Editing (2021 - present)

PROFESSIONAL EDUCATION

- PhD, Harvard University, Harvard Medical School. , Biological and Biomedical Sciences (2014)
- LHB, Harvard Medical School. , Certificate in Leder Human Biology and Translational Medicine
- B.S., Tsinghua University , Biological Sciences, Electronic Engineering (2009)

COMMUNITY AND INTERNATIONAL WORK

- Neuro-engineering and Gene-editing., Cold Spring Harbor Laboratory

PATENTS

- Feng Zhang, Le Cong, Patrick Hsu, Fei Ann Ran. "United States Patent 8,906,616 Engineering of systems, methods and optimized guide compositions for sequence manipulation"
- Le Cong, Feng Zhang. "United States Patent 8,932,814 CRISPR-Cas nickase systems, methods and compositions for sequence manipulation in eukaryotes."
- Feng Zhang, LeCong, Randall Platt, Neville Sanjana, Fei Ann Ran. "United States Patent 8,993,233 Engineering and optimization of systems, methods and compositions for sequence manipulation with functional domains"
- Cong, Egloff, Garraway, Grandis, Lander, Stransky, Tward, Zhang.. "United States Patent 9,370,551. Compositions and methods of treating head and neck cancer."
- Le Cong, Feng Zhang, Patrick Hsu, Fei Ann Ran. "United States Engineering of systems, methods and optimized guide compositions for sequence manipulation."

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

Our lab develops gene-editing technologies like novel CRISPR systems and large gene insertion techniques for gene and cell therapy. We also leverage these gene-editing tools for single-cell functional screening to probe mechanisms of cancer, immunological, and aging-associated diseases. To accelerate our work, we integrate AI and machine learning to design and evolve therapeutic RNAs/proteins, and build AI-XR co-scientists like LabOS that bridge AI computation and biomedical experimentation.

Teaching

COURSES

2022-23

- Advanced Genetics: GENE 205 (Win)

STANFORD ADVISEES

Doctoral Dissertation Reader (AC)

Freja Ekman, Kathryn Hanson, Yannick Lee-Yow

Postdoctoral Faculty Sponsor

Xuefeng Liu, Xiaotong Wang, Yingcheng Wu, Guangxue Xu, Di Yin

Doctoral Dissertation Advisor (AC)

Hannah Chung

Doctoral (Program)

Michal Gerasimiuk

GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Biochemistry (Phd Program)
- Bioengineering (Phd Program)
- Biology (School of Humanities and Sciences) (Phd Program)
- Biomedical Data Science (Masters Program)
- Biomedical Data Science (Phd Program)
- Biophysics (Phd Program)
- Cancer Biology (Phd Program)
- Chemical and Systems Biology (Phd Program)
- Cytopathology (Fellowship Program)
- Developmental Biology (Phd Program)
- Genetics (Phd Program)
- Hematopathology (Fellowship Program)
- Immunology (Phd Program)
- Microbiology and Immunology (Phd Program)
- Molecular and Cellular Physiology (Phd Program)
- Neuropathology (Fellowship Program)
- Neurosciences (Phd Program)
- Stem Cell Biology and Regenerative Medicine (Phd Program)
- Structural Biology (Phd Program)

Publications

PUBLICATIONS

- **Programmable RNA translation through deep learning-driven IRES discovery and de novo generation** *NATURE MACHINE INTELLIGENCE*
  Chu, Y., Yin, D., Yu, D., Xu, G., Zhang, J., Wang, X., Shen, Y., Li, Y., Zhao, N., Zhu, Y., Zhang, J., Goodarzi, H., Wang, et al
  2026; 8 (4)

- **Minimizing far-extending chromatin perturbation in genome editing preserves stem cell identity.** *Cell stem cell*
  Zhu, M., Yuan, J., Meng, Q., Yu, J., Xu, X., Xu, M., Ren, X., Hu, Y., Wei, G., Jia, Z., Yuan, G., Zang, L., Liu, et al
  2026

- **Compact bacterial recombination complexes drive efficient kilobase-scale knock-in in mammalian cells.** *Nucleic acids research*
  Luo, Y., Jiang, Q., Qu, Y., Li, W., Liu, R., Zhu, Y., Xie, Y., Jiang, C., Chen, C., Cong, L., Han, F., Bao, J., Wang, et al
  2026; 54 (2)

- **Autonomous AI Agents Discover Aging Interventions from Millions of Molecular Profiles.** *bioRxiv : the preprint server for biology*
  Ying, K., Tyshkovskiy, A., Moldakozhayev, A., Wang, H., De Magalhães, C. G., Iqbal, S., Garza, A. E., Tskhay, A., Poganik, J. R., Huang, K., Qu, Y., Glubokov, D., Jin, et al
  2025

- **CRISPR-GPT for agentic automation of gene-editing experiments.** *Nature biomedical engineering*
  Qu, Y., Huang, K., Yin, M., Zhan, K., Liu, D., Yin, D., Cousins, H. C., Johnson, W. A., Wang, X., Shah, M., Altman, R. B., Zhou, D., Wang, et al

2025

- **Membrane-wide screening identifies potential tissue-specific determinants of SARS-CoV-2 tropism.** *PLoS pathogens*
  Dinesh, R. K., Wang, C., Qu, Y., Rustagi, A., Cousins, H., Zengel, J., Wang, X., Barnard, T. R., Johnson, W. A., Xu, G., Zhang, T., Magazine, N., Beck, et al
  2025; 21 (7): e1013157

- **Biomni: A General-Purpose Biomedical AI Agent.** *bioRxiv : the preprint server for biology*
  Huang, K., Zhang, S., Wang, H., Qu, Y., Lu, Y., Roohani, Y., Li, R., Qiu, L., Li, G., Zhang, J., Yin, D., Marwaha, S., Carter, et al
  2025

- **Efficient and multiplexed somatic genome editing with Cas12a mice.** *Nature biomedical engineering*
  Hebert, J. D., Xu, H., Tang, Y. J., Ruiz, P. A., Detrick, C. R., Wang, J., Hughes, N. W., Donosa, O., Siah, V. P., Andrejka, L., Karmakar, S., Aboiralor, I., Tang, et al
  2025

- **A call for built-in biosecurity safeguards for generative AI tools.** *Nature biotechnology*
  Wang, M., Zhang, Z., Bedi, A. S., Velasquez, A., Guerra, S., Lin-Gibson, S., Cong, L., Qu, Y., Chakraborty, S., Blewett, M., Ma, J., Xing, E., Church, et al
  2025

- **CRISPR-GPT: LLM Agents for Automated Design of Gene-Editing Experiments**
  Qu, Y., Huang, K., Yin, M., Zhan, K., Liu, D., Yin, D., Cousins, H., Johnson, W., Wang, X., Altman, R., Zhou, D., Wang, M., Cong, et al
  CELL PRESS.2025

- **Surfaceome CRISPR Activation Screens to Delineate Determinants of Natural Killer Cell Killing towards Cancer Cells**
  Wang, X., Dinesh, R., Mohammad, I., Sunwoo, J., Cong, L.
  CELL PRESS.2025

- **FoldMark: Protecting Protein Generative Models with Watermarking.** *bioRxiv : the preprint server for biology*
  Zhang, Z., Jin, R., Fu, K., Cong, L., Zitnik, M., Wang, M.
  2024

- **Computationally guided high-throughput engineering of an anti-CRISPR protein for precise genome editing in human cells.** *Cell reports methods*
  Marsiglia, J., Vaalavirta, K., Knight, E., Nakamura, M., Cong, L., Hughes, N. W.
  2024; 4 (10): 100882

- **Systematic Discovery, In Vivo Delivery, and DNA Repair Mechanism of Single-Strand Annealing Protein for Precision Integration of Large DNA Sequences**
  Cong, L., Yin, D., Xu, G., Qu, Y., Wang, C., Wang, X., Johnson, W., Filsinger, G., Wannier, T., Church, G. M., Phoon, L., Gao, B., Lan, et al
  CELL PRESS.2024: 9-10

- **A 5′ UTR language model for decoding untranslated regions of mRNA and function predictions** *NATURE MACHINE INTELLIGENCE*
  Chu, Y., Yu, D., Li, Y., Huang, K., Shen, Y., Cong, L., Zhang, J., Wang, M.
  2024

- **A 5' UTR Language Model for Decoding Untranslated Regions of mRNA and Function Predictions.** *Nature machine intelligence*
  Chu, Y., Yu, D., Li, Y., Huang, K., Shen, Y., Cong, L., Zhang, J., Wang, M.
  2024; 6 (4): 449-460

- **APOE loss-of-function variants: Compatible with longevity and associated with resistance to Alzheimer's disease pathology.** *Neuron*
  Chemparathy, A., Le Guen, Y., Chen, S., Lee, E. G., Leong, L., Gorzynski, J. E., Jensen, T. D., Ferrasse, A., Xu, G., Xiang, H., Belloy, M. E., Kasireddy, N., Peña-Tauber, et al
  2024

- **Long sequence insertion via CRISPR/Cas gene-editing with transposase, recombinase, and integrase.** *Current opinion in biomedical engineering*
  Wang, X., Xu, G., Johnson, W. A., Qu, Y., Yin, D., Ramkissoon, N., Xiang, H., Cong, L.
  2023; 28

- **Long sequence insertion via CRISPR/Cas gene-editing with transposase, recombinase, and integrase** *CURRENT OPINION IN BIOMEDICAL ENGINEERING*
  Wang, X., Xu, G., Johnson, W. A., Qu, Y., Yin, D., Ramkissoon, N., Xiang, H., Cong, L.
  2023; 28

- **Integrative analysis of functional genomic screening and clinical data identifies a protective role for spironolactone in severe COVID-19.** *Cell reports methods*
  Cousins, H. C., Kline, A. S., Wang, C., Qu, Y., Zengel, J., Carette, J., Wang, M., Altman, R. B., Luo, Y., Cong, L.
  2023; 3 (7): 100503

- **APOE loss-of-function variants: Compatible with longevity and associated with resistance to Alzheimer's Disease pathology.** *medRxiv : the preprint server for health sciences*
  Chemparathy, A., Guen, Y. L., Chen, S., Lee, E. G., Leong, L., Gorzynski, J., Xu, G., Belloy, M., Kasireddy, N., Tauber, A. P., Williams, K., Stewart, I., Wingo, et al
  2023

- **Gene set proximity analysis: expanding gene set enrichment analysis through learned geometric embeddings, with drug-repurposing applications in COVID-19.** *Bioinformatics (Oxford, England)*
  Cousins, H., Hall, T., Guo, Y., Tso, L., Tzeng, K. T., Cong, L., Altman, R. B.
  2022

- **Single-cell transcriptome analysis of regenerating RGCs reveals potent glaucoma neural repair genes.** *Neuron*
  Li, L., Fang, F., Feng, X., Zhuang, P., Huang, H., Liu, P., Liu, L., Xu, A. Z., Qi, L. S., Cong, L., Hu, Y.
  2022

- **Machine-learning-optimized Cas12a barcoding enables the recovery of single-cell lineages and transcriptional profiles.** *Molecular cell*
  Hughes, N. W., Qu, Y., Zhang, J., Tang, W., Pierce, J., Wang, C., Agrawal, A., Morri, M., Neff, N., Winslow, M. M., Wang, M., Cong, L.
  2022

- **Editorial: CRISPR and alternative approaches.** *Biotechnology journal*
  Kapusi, E., Cong, L., Stoger, E.
  2022: e2200290

- **dCas9-based gene editing for cleavage-free genomic knock-in of long sequences.** *Nature cell biology*
  Wang, C., Qu, Y., Cheng, J. K., Hughes, N. W., Zhang, Q., Wang, M., Cong, L.
  2022

- **Neural Bandits for Protein Sequence Optimization**
  Wang, C., Kim, J., Cong, L., Wang, M., IEEE
  IEEE.2022: 188-193

- **The role of p53 in the development of pancreatic ductal adenocarcinoma.**
  Hanson, K. J., Flowers, B. M., Hughes, N., Vogel, H., Cong, L., Attardi, L. D.
  AMER ASSOC CANCER RESEARCH.2021: 58

- **Deciphering pathogenicity of variants of uncertain significance with CRISPR-edited iPSCs.** *Trends in genetics : TIG*
  Guo, H., Liu, L., Nishiga, M., Cong, L., Wu, J. C.
  2021

- **Conventional type I dendric cells maintain a reservoir of proliferative tumor-antigen specific TCF-1+ CD8+ Tcells in tumor-draining lymph nodes.** *Immunity*
  Schenkel, J. M., Herbst, R. H., Canner, D., Li, A., Hillman, M., Shanahan, S., Gibbons, G., Smith, O. C., Kim, J. Y., Westcott, P., Hwang, W. L., Freed-Pastor, W. A., Eng, et al
  2021

- **CRISPR-Cas12a System With Synergistic Phage Recombination Proteins for Multiplex Precision Editing in Human Cells.** *Frontiers in cell and developmental biology*
  Wang, C., Xia, Q., Zhang, Q., Qu, Y., Su, S., Cheng, J. K., Hughes, N. W., Cong, L.
  2021; 9: 719705

- **Cleavage-Free dCas9 Knock-In Gene-Editing Tool Leveraging RNA-Guided Targeting of Recombineering Proteins**

Cong, L., Wang, C., Cheng, J. K. W., Qu, Y., Zhang, Q.
CELL PRESS.2021: 107

- **A CRISPR Landing for Genome Rewriting at Locus-Scale.** *The CRISPR journal*
  Hughes, N. W., Cong, L.
  2021; 4 (2): 163–66

- **Microbial single-strand annealing proteins enable CRISPR gene-editing tools with improved knock-in efficiencies and reduced off-target effects.** *Nucleic acids research*
  Wang, C., Cheng, J. K., Zhang, Q., Hughes, N. W., Xia, Q., Winslow, M. M., Cong, L.
  2021

- **A functional taxonomy of tumor suppression in oncogenic KRAS-driven lung cancer.** *Cancer discovery*
  Cai, H. n., Chew, S. K., Li, C. n., Tsai, M. K., Andrejka, L. n., Murray, C. W., Hughes, N. W., Shuldiner, E. G., Ashkin, E. L., Tang, R. n., Hung, K. L., Chen, L. C., Lee, et al
  2021

- **Adeno-associated viral vector-mediated immune responses: Understanding barriers to gene delivery.** *Pharmacology & therapeutics*
  Nidetz, N. F., McGee, M. C., Tse, L. V., Li, C., Cong, L., Li, Y., Huang, W.
  2019: 107453

- **Take Risks and Constantly Challenge the Status Quo** *STEM CELLS AND DEVELOPMENT*
  Cong, L.
  2019

- **Combined Computational-Experimental Approach to Explore the Molecular Mechanism of SaCas9 with a Broadened DNA Targeting Range** *JOURNAL OF THE AMERICAN CHEMICAL SOCIETY*
  Luan, B., Xu, G., Feng, M., Cong, L., Zhou, R.
  2019; 141 (16): 6545–52

- **IL-33 Signaling Alters Regulatory T Cell Diversity in Support of Tumor Development.** *Cell reports*
  Li, A. n., Herbst, R. H., Canner, D. n., Schenkel, J. M., Smith, O. C., Kim, J. Y., Hillman, M. n., Bhutkar, A. n., Cuoco, M. S., Rappazzo, C. G., Rogers, P. n., Dang, C. n., Jerby-Arnon, et al
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- **Efficient Generation of Transcriptomic Profiles by Random Composite Measurements.** *Cell*
  Cleary, B., Cong, L., Cheung, A., Lander, E. S., Regev, A.
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- **A Distinct Gene Module for Dysfunction Uncoupled from Activation in Tumor-Infiltrating T Cells** *CELL*
  Singer, M., Wang, C., Cong, L., Marjanovic, N. D., Kowalczyk, M. S., Zhang, H., Nyman, J., Sakuishi, K., Kurtulus, S., Gennert, D., Xia, J., Kwon, J. Y., Nevin, et al
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- **RBPJ Controls Development of Pathogenic Th17 Cells by Regulating IL-23 Receptor Expression.** *Cell reports*
  Meyer Zu Horste, G., Wu, C., Wang, C., Cong, L., Pawlak, M., Lee, Y., Elyaman, W., Xiao, S., Regev, A., Kuchroo, V. K.
  2016; 16 (2): 392-404

- **Definitive localization of intracellular proteins: Novel approach using CRISPR-Cas9 genome editing, with glucose 6-phosphate dehydrogenase as a model.** *Analytical biochemistry*
  Spencer, N. Y., Yan, Z., Cong, L., Zhang, Y., Engelhardt, J. F., Stanton, R. C.
  2016; 494: 55-67

- **In vivo gene editing in dystrophic mouse muscle and muscle stem cells** *SCIENCE*
  Tabebordbar, M., Zhu, K., Cheng, J. K., Chew, W. L., Widrick, J. J., Yan, W. X., Maesner, C., Wu, E. Y., Xiao, R., Ran, F. A., Cong, L., Zhang, F., Vandenberghe, et al
  2016; 351 (6271): 407-411

- **Crystal Structure of Staphylococcus aureus Cas9** *CELL*
  Nishimasu, H., Cong, L., Yan, W. X., Ran, F. A., Zetsche, B., Li, Y., Kurabayashi, A., Ishitani, R., Zhang, F., Nureki, O.
  2015; 162 (5): 1113-1126

- **Sequence determinants of improved CRISPR sgRNA design.** *Genome research*
  Xu, H., Xiao, T., Chen, C. H., Li, W., Meyer, C. A., Wu, Q., Wu, D., Cong, L., Zhang, F., Liu, J. S., Brown, M., Liu, X. S.
  2015; 25 (8): 1147-57

- **In vivo genome editing using Staphylococcus aureus Cas9** *NATURE*
  Ran, F. A., Cong, L., Yan, W. X., Scott, D. A., Gootenberg, J. S., Kriz, A. J., Zetsche, B., Shalem, O., Wu, X., Makarova, K. S., Koonin, E. V., Sharp, P. A., Zhang, et al
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- **Genome engineering using CRISPR-Cas9 system.** *Methods in molecular biology (Clifton, N.J.)*
  Cong, L., Zhang, F.
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- **Global microRNA depletion suppresses tumor angiogenesis.** *Genes & development*
  Chen, S., Xue, Y., Wu, X., Le, C., Bhutkar, A., Bell, E. L., Zhang, F., Langer, R., Sharp, P. A.
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  2013; 500 (7463): 472-6

- **Multiplex Genome Engineering Using CRISPR/Cas Systems** *SCIENCE*
  Cong, L., Ran, F. A., Cox, D., Lin, S., Barretto, R., Habib, N., Hsu, P. D., Wu, X., Jiang, W., Marraffini, L. A., Zhang, F.
  2013; 339 (6121): 819-823

- **Comprehensive interrogation of natural TALE DNA-binding modules and transcriptional repressor domains** *NATURE COMMUNICATIONS*
  Cong, L., Zhou, R., Kuo, Y., Cunniff, M., Zhang, F.
  2012; 3

- **A transcription activator-like effector toolbox for genome engineering.** *Nature protocols*
  Sanjana, N. E., Cong, L., Zhou, Y., Cunniff, M. M., Feng, G., Zhang, F.
  2012; 7 (1): 171-92

- **Efficient construction of sequence-specific TAL effectors for modulating mammalian transcription** *NATURE BIOTECHNOLOGY*
  Zhang, F., Cong, L., Lodato, S., Kosuri, S., Church, G. M., Arlotta, P.
  2011; 29 (2): 149-U90