Stanford

Howard Y. Chang, MD, PhD

Virginia and D. K. Ludwig Professor of Cancer Genomics and of Genetics

Dermatology

Curriculum Vitae available Online

CLINICAL OFFICES

- **Stanford Dermatology Clinic**

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  Pavilion B

  Redwood City, CA 94063

  Tel (650) 723-6316 **Fax** (650) 721-3476

ACADEMIC CONTACT INFORMATION

- **Alternate Contact**

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Bio

BIO

I am a physician-scientist who has trained in genome science. My research has focused on mechanisms that coordinate the activities of large number of genes in cell fate control. We made a series of discoveries that introduced the important and pervasive roles of long noncoding RNAs in biological regulation. My group has substantial experience in epigenetics and RNA biology, including invention of new methods for epigenomic profiling, map RNA occupancy on chromatin, and define RNA structures genome-wide. My group pioneered methods to identify key regulators of large-scale transcriptional programs; these methods have been highly fruitful for studies of development, cancer, and aging. The long term goal of my laboratory is to decipher the regulatory information in the human genome for disease diagnosis and therapy.

CLINICAL FOCUS

- Cancer > Cutaneous (Dermatologic) Oncology
- Dermatology
- General Dermatology

ACADEMIC APPOINTMENTS

- Professor, Dermatology
- Professor, Genetics
- Member, Bio-X
- Member, Maternal & Child Health Research Institute (MCHRI)
- Member, Stanford Cancer Institute
- Faculty Fellow, Stanford ChEM-H
- Member, Wu Tsai Neurosciences Institute

ADMINISTRATIVE APPOINTMENTS

- Member, Stanford Diabetes Research Center, (2018- present)

- Director, NIH Center of Excellence in Genomic Science: Center for Personal Dynamic Regulome, (2014-2019)

HONORS AND AWARDS

- Investigator, Howard Hughes Medical Institute (2018)
- NAS Award in Molecular Biology, National Academy of Science (2018)
- Member, National Academy of Medicine (2017)
- Outstanding Investigator Award, National Cancer Institute (2016)
- Paul Marks Prize for Cancer Research, Memorial Sloan Kettering Cancer Institute (2015)

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BOARDS, ADVISORY COMMITTEES, PROFESSIONAL ORGANIZATIONS

- Editorial Board, Molecular Cell (2014 - present)

PROFESSIONAL EDUCATION

- Fellowship: Stanford University Dept of Dermatology (2004) CA
- Residency: Stanford University Dermatology Residency (2003) CA
- Internship: Santa Clara Valley Medical Center Dept of Medicine (2001) CA
- Board Certification: Dermatology, American Board of Dermatology (2004)
- Medical Education: Harvard Medical School (2000) MA

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LINKS

- Chang Lab, Stanford University: http://changlab.stanford.edu

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

The same genetic blueprint gives rise to thousands of cell types that make up the human body. Intricate mechanisms govern the choice to make skin, heart, or brain cells. These different cell types must be correctly arranged in spatial patterns to make functioning tissues and organs. In many organisms with continual turnover of cells, the genome faces the additional challenge of ensuring the faithful transmission of information throughout a lifetime#over decades in the case of humans. Thus, how one genome encodes thousands of patterns in space and time is of central importance to biology and medicine. Inappropriate activation of genes can give rise to birth defects, premature aging, or cancer, among many other diseases. Restoration of proper organ function often requires restoring homeostatic gene regulation.

Long Noncoding RNAs and Positional Identity

As a practicing dermatologist, I am fascinated by what makes human skin from different parts of the body different, a fact that guides the diagnosis and treatment of many skin diseases. Why do long hairs grow on the scalp but not on our palms or soles? How do cells know where they are located in the body, and how do they remember this information?

We discovered that one class of skin cells, the fibroblasts, encode the positional identity of skin via specific markings on their chromatin, the DNA-protein complex where genes reside. Based on the chromatin configurations of specific genes, most notably the HOX genes, fibroblasts differentially activate hundreds of genes based on their the cell’s location along three anatomic axes#anterior-posterior (head to tail), proximal-distal (close or far away from the trunk), and dermal-nondermal (surface or internal organ). This in effect creates a global positioning system for all cells to navigate.

These studies also revealed a surprising abundance of long intergenic long noncoding RNAs (also known as lincRNAs, a newly recognized type of genes that do not code forencode proteins) that are involved in programming chromatin states. We are particularly fascinated by HOTAIR, the first known lincRNA that can regulate the chromatin state of genes on distantly located chromosomes. We now appreciate that the genome is pervasively transcribed to give rise to thousands of lincRNAs, which are likely to play key roles in the gene regulation of diverse biological states and disease. We are interested in understanding how lincRNAs control gene activity, and in deciphering the rules that will allow the functions of thousands of lincRNAs to be predicted and studied.

Large-Scale Gene Regulatory Programs in Cancer Metastasis and Self-Renewal
In contrast to the orderly acquisition of positional identity, cancer progression is characterized by abrogation of normal positional boundaries, especially in metastasis, which is the leading cause of cancer death. We and many others have previously identified gene expression signatures (GES), composed of dozens to hundreds of genes, that distinguish indolent human cancers from those prone to metastasis; these signatures can provide improved prognostic prediction for cancer patients. Furthermore, we have developed methods to pinpoint master regulators of GES#singular control points that can toggle the activity of the entire genetic program. This allows complex gene programs observed in human cancers to be easily recapitulated in the laboratory as models for drug development. This has enabled the creation of faithful laboratory models of human cancer types, identified specific drugs that can target these cancers, and revealed the hierarchy of transcriptional programs involved in the generation of cancer stem cells#the cells that continually repopulate a tumor or its metastases.

CLINICAL TRIALS

- A Pilot Study of Imatinib Mesylate in Steroid Refractory Chronic Graft Versus Host Disease, Not Recruiting

Teaching

STANFORD ADVISEES

Doctoral Dissertation Reader (AC)

Maurice Youzong Lee

Postdoctoral Faculty Sponsor

Chun-Kan Chen, Diana Dou, Furqan Fazal, Katerina Kraft, Qing Ma, Bingfei Yu

Doctoral Dissertation Advisor (AC)

Laura Amaya, Kevin Parker

Doctoral (Program)

Julia Belk

Postdoctoral Research Mentor

Katerina Kraft, Yuning Wei

GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Cancer Biology (Phd Program)
- Dermatology (Fellowship Program)

Publications

PUBLICATIONS

- **Promoter of lncRNA Gene PVT1 Is a Tumor-Suppressor DNA Boundary Element.** *Cell*
  Cho, S. W., Xu, J., Sun, R., Mumbach, M. R., Carter, A. C., Chen, Y. G., Yost, K. E., Kim, J., He, J., Nevins, S. A., Chin, S., Caldas, C., Liu, et al
  2018; 173 (6): 1398

- **Transcript-indexed ATAC-seq for precision immune profiling.** *Nature medicine*
  Satpathy, A. T., Saligrama, N., Buenrostro, J. D., Wei, Y., Wu, B., Rubin, A. J., Granja, J. M., Lareau, C. A., Li, R., Qi, Y., Parker, K. R., Mumbach, M. R., Serratelli, et al
  2018

- **The chromatin accessibility landscape of primary human cancers.** *Science (New York, N.Y.)*
  Corces, M. R., Granja, J. M., Shams, S., Louie, B. H., Seoane, J. A., Zhou, W., Silva, T. C., Groeneveld, C., Wong, C. K., Cho, S. W., Satpathy, A. T., Mumbach, M. R., Hoadley, et al
  2018; 362 (6413)

- **RNA Duplex Map in Living Cells Reveals Higher-Order Transcriptome Structure** *CELL*
  Lu, Z., Zhang, Q. C., Lee, B., Flynn, R. A., Smith, M. A., Robinson, J. T., Davidovich, C., Gooding, A. R., Goodrich, K. J., Mattick, J. S., Mesirov, J. P., Cech, T. R., Chang, et al
  2016; 165 (5): 1267-1279

- **Long Noncoding RNAs in Cancer Pathways.** *Cancer cell*
  Schmitt, A. M., Chang, H. Y.
  2016; 29 (4): 452-463

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