Stanford

Rogelio A. Hernández-López

Assistant Professor of Bioengineering and of Genetics

Bio

ACADEMIC APPOINTMENTS

- Assistant Professor, Bioengineering
- Assistant Professor, Genetics
- Member, Bio-X
- Member, Stanford Cancer Institute
- Member, Wu Tsai Neurosciences Institute

HONORS AND AWARDS

- Chan-Zuckerberg Biohub Investigator, Chan-Zuckerberg Biohub- San Francisco (2022)
- Reid and Polly Anderson Faculty Fellow, Stanford University (2022)
- V Scholar, V Foundation (2022)
- Career Award at the Scientific Interface, Burroughs Wellcome Fund (2021)
- Merck Postdoctoral Fellowship, Cancer Research Institute (2017-2021)
- Postdoctoral Fellowship, UC MEXUS (2016-2017)
- Christensen Prize for Outstanding Research Achievement, Harvard University (2012)

BOARDS, ADVISORY COMMITTEES, PROFESSIONAL ORGANIZATIONS

- Co-founder and board member, Science Clubs International (2016 - present)
- Co-founder and board member, Clubes de Ciencia Mexico (2014 - present)

PROFESSIONAL EDUCATION

- Postdoctoral Fellow, University of California San Francisco , Synthetic Biology, Immune engineering (2022)
- Ph.D., Harvard University , Chemical Physics (2015)
- B.S., National Autonomous University of Mexico , Chemistry (2008)

LINKS

- Hernandez-Lopez Lab website: https://www.hl-lab.org

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

Cell engineering has become an exciting field that leverages the power of synthetic and natural biological systems to carry out complex behaviors with important applications in human health, energy, and the environment. For example, T cells can be redirected to kill cancer cells using synthetic receptors and this approach has shown remarkable success against hematologic cancers. Nonetheless, many challenges still remain unsolved to apply this therapy to a broader range of cancers. Our research integrates mechanistic cell biology and synthetic biology to understand and engineer fundamental cellular behaviors such as recognition and communication. We are currently interested in developing novel receptors and therapeutic T cells targeted to solid tumors. We are also launching new research programs to expand our approach to other molecules, cells and tissues for a variety of applications.

1) Programming enhanced cellular recognition in T cells
A fundamental behavior in biology is cellular recognition. In cancer immunotherapy, highly discriminatory cell recognition would expand the applications of engineered T cells to treat solid cancers. Current CAR T cells, while effective at killing cells expressing the target antigen, fail to discriminate between high and low antigen-expressing cells. Therefore, common antigens (e.g. HER2, EGFR, and GD2) that are overexpressed in solid tumor cells cannot currently be used as good targets, as this has led in some cases to the lethal off-target killing of bystander tissues expressing lower levels of antigen.

We are using principles of molecular recognition to understand and compare the limits among different strategies for engineering cellular discrimination. We recently built a two-step circuit that links a low-affinity recognition event with a subsequent high-affinity activation event. In this circuit, transcription activation, via a synthetic Notch (synNotch) receptor induces expression of a high-affinity CAR. This low-to-high synNotch to CAR circuit leads to an ultrasensitive antigen density response that allows robust discrimination of high and low HER2 expressing target cells in vitro and in vivo.

2) Uncovering the principles of cell-cell communication in the tumor microenvironment
How a tissue structure affects its function and the progression of disease are outstanding questions in cell and developmental biology with fundamental applications in cancer treatment. Tumor heterogeneity and the immunosuppressive tumor microenvironment, which affects T cell migration and infiltration, remain some of the major barriers to effective solid tumor immunotherapy. Addressing these problems is challenging because tumors are complex multicellular systems. We know that T cells can recognize tumors with high specificity, and we also know that tumors modulate T cell activity via the so-called tumor microenvironment. However, we understand little about the tumor microenvironment, in particular, we do not know how tumor composition and organization mechanistically affect the response of engineered cell therapies. Our group is interested in understanding how the organization of a solid tumor affects immune cell response.

We are combining cellular and tissue engineering to systematically interrogate the activity of immune cells targeted to solid tumors. We are interested in deconstructing features of tumors such as composition, structure and organization and aim for designing and building synthetic circuits that can program biomedical useful cellular behaviors to treat solid tumors.

Teaching

COURSES

2023-24

- Fundamentals for Engineering Biology Lab: BIOE 44 (Aut)

2022-23

- Fundamentals for Engineering Biology Lab: BIOE 44 (Aut)

STANFORD ADVISEES

Doctoral Dissertation Reader (AC)

Jon Bezney, Xinyi Chen, Vandon Duong, Cindy Sandoval Espinoza

Postdoctoral Faculty Sponsor

Daniel Hoces Burga, Jesus Miguens Blanco, Celine Prange, Qian Xue

Doctoral Dissertation Advisor (AC)

Jaclyn Ng, Julian Perez

Doctoral Dissertation Co-Advisor (AC)

Yixin Hu

Master's Program Advisor

Nikita Mishra

Doctoral (Program)

Louise Gabrielle Lima, Yuxuan Wu

GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Bioengineering (Phd Program)
- Cancer Biology (Phd Program)
- Genetics (Phd Program)

Publications

PUBLICATIONS

- **A synthetic biology approach to engineering circuits in immune cells.** *Immunological reviews*
  Hoces, D., Miguens Blanco, J., Hernandez-Lopez, R. A.
  2023
- **T cell circuits that sense antigen density with an ultrasensitive threshold** *SCIENCE*
  Hernandez-Lopez, R. A., Yu, W., Cabral, K. A., Creasey, O. A., Lopez Pazmino, M., Tonai, Y., De Guzman, A., Makela, A., Saksela, K., Gartner, Z. J., Lim, W. A.
  2021; 371 (6534): 1166-+
- **DNA scaffolds enable efficient and tunable functionalization of biomaterials for immune cell modulation.** *Nature nanotechnology*
  Huang, X., Williams, J. Z., Chang, R., Li, Z., Burnett, C. E., Hernandez-Lopez, R., Setiady, I., Gai, E., Patterson, D. M., Yu, W., Roybal, K. T., Lim, W. A., Desai, et al
  2021; 16 (2): 214-223