Stanford

Antonio J. Pagán

Assistant Professor of Microbiology and Immunology

Bio

BIO

Antonio J. Pagán, PhD is an Esther Ehrman Lazard Faculty Scholar and Assistant Professor in the Department of Microbiology and Immunology at Stanford School of Medicine.

Antonio received his doctorate in Immunology from the University of Minnesota and completed postdoctoral studies at the University of Washington and the University of Cambridge. His laboratory studies the regulation of immunity and pathogenesis in tuberculosis (TB). TB is characterized by the formation of multicellular aggregates of immune cells called granulomas. His lab leverages powerful genetics and imaging capabilities of genetically diverse fish models of TB, which capture key features of human TB granulomas, to address fundamental questions in mycobacterial pathogenesis and granuloma immunobiology.

ACADEMIC APPOINTMENTS

- Assistant Professor, Microbiology and Immunology

HONORS AND AWARDS

- Esther Ehrman Lazard Faculty Scholar, Stanford (2025 - 2026)
- BATS Rising Star Award, Bay Area Tuberculosis Science (BATS) Symposium (2024)

PROFESSIONAL EDUCATION

- PhD, University of Minnesota, Minneapolis, MN
- BS, Haverford College, Haverford, PA

LINKS

- Pagán Lab website: https://med.stanford.edu/paganlab.html

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

Granulomas are organized aggregates of immune cells which form in response to particulate matter that the body cannot readily clear. Granulomas evolved as protective responses to destroy or sequester harmful particles but become pathological in numerous medically important infectious and non-infectious inflammatory diseases, such as tuberculosis (TB), schistosomiasis, sarcoidosis, Crohn’s disease, and foreign body reactions which constitute serious complications of medical implants, necessitating their removal.

In tuberculosis (TB), the granuloma exerts both host-beneficial and -detrimental functions which shape disease severity and outcomes. Mycobacterium tuberculosis, the causative agent of human TB, has evolved mechanisms to manipulate the granulomatous response for its advantage. My lab seeks to understand how host-mycobacterium interactions shape TB pathogenesis. We study the virulence mechanisms that mycobacteria utilize to adapt to or manipulate the granuloma as well as the immune mechanisms that mediate host defense versus immunopathology.

Zebrafish infected with Mycobacterium marinum, a natural fish pathogen closely related to M. tuberculosis, develop TB-like disease characterized by the formation of necrotic granulomas like those found in humans with severe TB. We have identified another small freshwater fish species that is naturally resistant to M. marinum and forms granulomas that seldom become necrotic. We exploit the unique genetic and imaging capabilities of these complementary fish models and integrate this work with studies of human TB. We believe that by investigating the cues governing TB granuloma form and function, our studies will specifically illuminate TB pathogenesis, uncover new concepts in immunobiology, and may produce medically relevant insights for a wide range of inflammatory diseases.

Teaching

STANFORD ADVISEES

Doctoral Dissertation Advisor (AC)

Jonathan Castro

GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Immunology (Phd Program)
- Microbiology and Immunology (Phd Program)

Publications

PUBLICATIONS

- **mTOR-regulated mitochondrial metabolism limits mycobacterium-induced cytotoxicity.** *Cell*
  Pagán, A. J., Lee, L. J., Edwards-Hicks, J., Moens, C. B., Tobin, D. M., Busch-Nentwich, E. M., Pearce, E. L., Ramakrishnan, L.
  2022; 185 (20): 3720-3738.e13
- **The C terminus of the mycobacterium ESX-1 secretion system substrate ESAT-6 is required for phagosomal membrane damage and virulence.** *Proceedings of the National Academy of Sciences of the United States of America*
  Osman, M. M., Shanahan, J. K., Chu, F., Takaki, K. K., Pinckert, M. L., Pagán, A. J., Brosch, R., Conrad, W. H., Ramakrishnan, L.
  2022; 119 (11): e2122161119
- **Elevated cerebrospinal fluid cytokine levels in tuberculous meningitis predict survival in response to dexamethasone.** *Proceedings of the National Academy of Sciences of the United States of America*
  Whitworth, L. J., Troll, R., Pagán, A. J., Roca, F. J., Edelstein, P. H., Troll, M., Tobin, D. M., Phu, N. H., Bang, N. D., Thwaites, G. E., Thuong, N. T., Sewell, R. F., Ramakrishnan, et al
  2021; 118 (10)
- **Schistosoma mansoni Eggs Modulate the Timing of Granuloma Formation to Promote Transmission.** *Cell host & microbe*
  Takaki, K. K., Rinaldi, G., Berriman, M., Pagán, A. J., Ramakrishnan, L.
  2021; 29 (1): 58-67.e5
- **Tumor Necrosis Factor and Schistosoma mansoni egg antigen omega-1 shape distinct aspects of the early egg-induced granulomatous response.** *PLoS neglected tropical diseases*
  Takaki, K. K., Roca, F. J., Schramm, G., Wilbers, R. H., Ittiprasert, W., Brindley, P. J., Rinaldi, G., Berriman, M., Ramakrishnan, L., Pagán, A. J.
  2021; 15 (1): e0008814
- **Mycobacterium marinum phthiocerol dimycocerosates enhance macrophage phagosomal permeabilization and membrane damage.** *PloS one*
  Osman, M. M., Pagán, A. J., Shanahan, J. K., Ramakrishnan, L.

2020; 15 (7): e0233252

- **The Formation and Function of Granulomas.** *Annual review of immunology*
  Pagán, A. J., Ramakrishnan, L.
  2018; 36: 639-665
- **TORmented macrophages spontaneously form granulomas.** *Nature immunology*
  Pagán, A. J., Ramakrishnan, L.
  2017; 18 (3): 252-253
- **Most microbe-specific naïve CD4# T cells produce memory cells during infection.** *Science (New York, N.Y.)*
  Tubo, N. J., Fife, B. T., Pagan, A. J., Kotov, D. I., Goldberg, M. F., Jenkins, M. K.
  2016; 351 (6272): 511-4
- **Myeloid Growth Factors Promote Resistance to Mycobacterial Infection by Curtailing Granuloma Necrosis through Macrophage Replenishment.** *Cell host & microbe*
  Pagán, A. J., Yang, C. T., Cameron, J., Swaim, L. E., Ellett, F., Lieschke, G. J., Ramakrishnan, L.
  2015; 18 (1): 15-26
- **Chronic parasitic infection maintains high frequencies of short-lived Ly6C+CD4+ effector T cells that are required for protection against re-infection.** *PLoS pathogens*
  Peters, N. C., Pagán, A. J., Lawyer, P. G., Hand, T. W., Henrique Roma, E., Stamper, L. W., Romano, A., Sacks, D. L.
  2014; 10 (12): e1004538
- **Immunity and Immunopathology in the Tuberculous Granuloma.** *Cold Spring Harbor perspectives in medicine*
  Pagán, A. J., Ramakrishnan, L.
  2014; 5 (9)
- **Single naive CD4+ T cells from a diverse repertoire produce different effector cell types during infection.** *Cell*
  Tubo, N. J., Pagán, A. J., Taylor, J. J., Nelson, R. W., Linehan, J. L., Ertelt, J. M., Huseby, E. S., Way, S. S., Jenkins, M. K.
  2013; 153 (4): 785-96
- **Tracking antigen-specific CD4+ T cells throughout the course of chronic Leishmania major infection in resistant mice.** *European journal of immunology*
  Pagán, A. J., Peters, N. C., Debrabant, A., Ribeiro-Gomes, F., Pepper, M., Karp, C. L., Jenkins, M. K., Sacks, D. L.
  2013; 43 (2): 427-38
- **Acute gastrointestinal infection induces long-lived microbiota-specific T cell responses.** *Science (New York, N.Y.)*
  Hand, T. W., Dos Santos, L. M., Bouladoux, N., Molloy, M. J., Pagán, A. J., Pepper, M., Maynard, C. L., Elson, C. O., Belkaid, Y.
  2012; 337 (6101): 1553-6
- **CD28 promotes CD4+ T cell clonal expansion during infection independently of its YMNM and PYAP motifs.** *Journal of immunology (Baltimore, Md. : 1950)*
  Pagán, A. J., Pepper, M., Chu, H. H., Green, J. M., Jenkins, M. K.
  2012; 189 (6): 2909-17
- **ADAP regulates cell cycle progression of T cells via control of cyclin E and Cdk2 expression through two distinct CARMA1-dependent signaling pathways.** *Molecular and cellular biology*
  Srivastava, R., Burbach, B. J., Mitchell, J. S., Pagán, A. J., Shimizu, Y.
  2012; 32 (10): 1908-17
- **Opposing signals from the Bcl6 transcription factor and the interleukin-2 receptor generate T helper 1 central and effector memory cells.** *Immunity*
  Pepper, M., Pagán, A. J., Igyártó, B. Z., Taylor, J. J., Jenkins, M. K.
  2011; 35 (4): 583-95
- **Cutting edge: CD28 and c-Rel-dependent pathways initiate regulatory T cell development.** *Journal of immunology (Baltimore, Md. : 1950)*
  Vang, K. B., Yang, J., Pagán, A. J., Li, L. X., Wang, J., Green, J. M., Beg, A. A., Farrar, M. A.
  2010; 184 (8): 4074-7
- **Control of alpha4beta7 integrin expression and CD4 T cell homing by the beta1 integrin subunit.** *Journal of immunology (Baltimore, Md. : 1950)*

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  Pepper, M., Linehan, J. L., Pagán, A. J., Zell, T., Dileepan, T., Cleary, P. P., Jenkins, M. K.
  2010; 11 (1): 83-9
- **Efficient help for autoreactive B-cell activation requires CD4+ T-cell recognition of an agonist peptide at the effector stage.** *European journal of immunology*
  Hondowicz, B. D., Batheja, A. O., Metzgar, M. H., Pagán, A. J., Perng, O. A., Willms, S., Caton, A. J., Erikson, J.
  2009; 39 (9): 2377-82
- **Tracking epitope-specific T cells.** *Nature protocols*
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- **The role of BLyS/BLyS receptors in anti-chromatin B cell regulation.** *International immunology*
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- **T cell-mediated activation and regulation of anti-chromatin B cells.** *Autoimmunity reviews*
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- **Thymopoiesis independent of common lymphoid progenitors.** *Nature immunology*
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