Stanford

Manuel Amieva

Associate Professor of Pediatrics (Infectious Diseases) and of Microbiology and Immunology

Pediatrics - Infectious Diseases

NIH Biosketch available Online

CLINICAL OFFICES

- **Pediatric Infectious Disease**

  730 Welch Rd

  MC 5884 2nd Fl

  Palo Alto, CA 94304

  Tel (650) 721-5805 **Fax** (650) 725-8040

Bio

CLINICAL FOCUS

- Infectious Diseases, Pediatric
- Pediatric Infectious Diseases

ACADEMIC APPOINTMENTS

- Associate Professor, Pediatrics - Infectious Diseases
- Associate Professor, Microbiology & Immunology
- Member, Maternal & Child Health Research Institute (MCHRI)

PROFESSIONAL EDUCATION

- Fellowship: Stanford University Pediatric Infectious Disease Fellowship (2004) CA
- Residency: Stanford University Pediatric Residency (1999) CA
- Internship: Stanford University Pediatric Residency (1998) CA
- Medical Education: Stanford University School of Medicine Registrar (1997) CA
- Board Certification: Pediatric Infectious Diseases, American Board of Pediatrics (2013)

LINKS

- Amieva Lab Website: http://amievalab.stanford.edu

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

My laboratory studies how bacteria colonize our bodies for long periods of time, and how interactions between bacteria and the epithelial surfaces of the gastrointestinal tract and skin may lead to disease. Epithelial surfaces are the first barrier against infection, but they also where our bodies meet and co-evolve with the microbial world.. Several of our studies have focused on the epithelial junctions as a target for bacterial pathogens. The host epithelium uses its epithelial junctions to form a

tight but dynamic barrier with an external surface that is inhospitable to microbial attachment, secretes anti-microbial compounds, and has a rapid rate of self-renewal. The balance in the microbe-epithelial relationship results in silent commensalism or symbiosis; an imbalance results in diseases ranging from acute bacterial invasive disease to chronic ulcers or carcinoma.

Our laboratory has developed novel microscopy applications such as quantitative 3D confocal microscopy, electron microscopy, time-lapse imaging, microinjection and micromanipulation to visualize the interaction of pathogens with epithelial cells in culture and in animal and human tissues. Many of out studies focus on the gastric pathogen Helicobacter pylori, but we have also expanded our investigations to include the intestinal pathogens Listeria monocytogenes and Salmonella enterica, and the skin pathogen and colonizer Staphylococcus aureus. I believe that elucidating how microbes communicate with and alter our epithelial cells at a molecular level will be important for finding novel therapeutic targets to control mucosal colonization and prevent invasive disease.

Using this perspective, we have uncovered several novel concepts of how bacteria colonize and breach our epithelial surfaces. For example, we discovered that Helicobacter pylori target the intercellular junctions, and in particular that the virulence factor CagA affects junction assembly and cell polarity. This confers H. pylori the ability to extract nutrients and grow directly on the epithelial surface. We also found that these properties of CagA have consequences for cellular transformation of the epithelium. For instance, we showed that H. pylori affect the activity and state of epithelial stem cells in the stomach by colonizing the epithelial surface deep in the gastric glands. This gland-associated population is essential for pathological inflammation and hyperplasia in animal models, and confers significant colonization advantages to the bacteria. Our Listeria research uncovered a new mechanism and site where bacteria can breach the gastrointestinal epithelial barrier to invade. We found that Listeria find their receptor for invasion at sites of epithelial senescence, where the epithelial junctions undergo dynamic turnover. To study Salmonella and H. pylori we have developed a human organoid model to study their interactions with human gut epithelium in vitro. To study Staphylococcus aureus pathogenesis, we have developed methods to visualize infection at the scale of a single bacterial microcolony using an organoid culture system of human keratinocytes and fibroblasts that grow into a 3D skin-equivalent. We recently identified several proteins at the eptithelial junctions as host factors involved in the pathogenesis of one of Staphylococcus aureus major toxins.

Teaching

COURSES

2018-19

- Microbiology and Infectious Diseases I: INDE 263 (Win)
- Microbiology and Infectious Diseases III: INDE 265 (Aut)

2017-18

- Microbiology and Infectious Diseases I: INDE 263 (Win)
- Microbiology and Infectious Diseases III: INDE 265 (Aut)

2016-17

- Microbiology and Infectious Diseases I: INDE 263 (Win)
- Microbiology and Infectious Diseases III: INDE 265 (Aut)

2015-16

- Microbiology and Infectious Diseases I: INDE 263 (Win)

STANFORD ADVISEES

Doctoral Dissertation Reader (AC)

Susan Brewer, Kyler Lugo, Suchita Rastogi

Postdoctoral Faculty Sponsor

Jessica Klein, Maria del Mar Margalef Catala

GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Microbiology and Immunology (Phd Program)

Publications

PUBLICATIONS

- **Controlling Epithelial Polarity: A Human Enteroid Model for Host-Pathogen Interactions.** *Cell reports*
  Co, J. Y., Margalef-Catala, M., Li, X., Mah, A. T., Kuo, C. J., Monack, D. M., Amieva, M. R.
  2019; 26 (9): 2509

- **A Dock-and-Lock Mechanism Clusters ADAM10 at Cell-Cell Junctions to Promote alpha-Toxin Cytotoxicity.** *Cell reports*
  Shah, J., Rouaud, F., Guerrera, D., Vasileva, E., Popov, L. M., Kelley, W. L., Rubinstein, E., Carette, J. E., Amieva, M. R., Citi, S.
  2018; 25 (8): 2132

- **Stanley Falkow (1934-2018)** *NATURE*
  Amieva, M. R.
  2018; 558 (7709): 190

- **Multiple Acid Sensors Control Helicobacter pylori Colonization of the Stomach.** *PLoS pathogens*
  Huang, J. Y., Goers Sweeney, E., Guillemin, K., Amieva, M. R.
  2017; 13 (1)

- **Stromal R-spondin orchestrates gastric epithelial stem cells and gland homeostasis.** *Nature*
  Sigal, M., Logan, C. Y., Kapalczynska, M., Mollenkopf, H. J., Berger, H., Wiedenmann, B., Nusse, R., Amieva, M. R., Meyer, T. F.
  2017; 548 (7668): 451–55

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