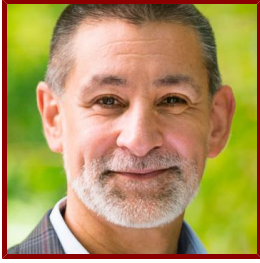


# Stanford

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## Manuel R. Amieva

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

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**Fax** (650) 725-8040

### Bio

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### CLINICAL FOCUS

- Infectious Diseases, Pediatric
- Pediatric Infectious Diseases

### ACADEMIC APPOINTMENTS

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

### PROFESSIONAL EDUCATION

- Residency: Stanford Health Care at Lucile Packard Children's Hospital (1999) CA
- Internship: Stanford Health Care at Lucile Packard Children's Hospital (1998) CA
- Medical Education: Stanford University School of Medicine (1997) CA
- Board Certification: Pediatric Infectious Diseases, American Board of Pediatrics (2005)
- Fellowship: Stanford University Pediatric Infectious Disease Fellowship (2004) CA

### LINKS

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

### Research & Scholarship

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### 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 our 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 epithelial junctions as host factors involved in the pathogenesis of one of *Staphylococcus aureus* major toxins.

## Teaching

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### COURSES

#### 2022-23

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

#### 2021-22

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

#### 2020-21

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

#### 2019-20

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

### STANFORD ADVISEES

#### Doctoral Dissertation Reader (AC)

Suchita Rastogi

**Postdoctoral Faculty Sponsor**

Benedikt Geier, Sophia Parks Berry

**Doctoral Dissertation Advisor (AC)**

Youlim Kim

**GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS**

- Microbiology and Immunology (Phd Program)

**Publications**

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**PUBLICATIONS**

- **Controlling the polarity of human gastrointestinal organoids to investigate epithelial biology and infectious diseases.** *Nature protocols*  
Co, J. Y., Margalef-Catala, M., Monack, D. M., Amieva, M. R.  
2021
- **Progenitor identification and SARS-CoV-2 infection in human distal lung organoids.** *Nature*  
Salahudeen, A. A., Choi, S. S., Rustagi, A., Zhu, J., van Unen, V., de la O, S. M., Flynn, R. A., Margalef-Catala, M., Santos, A. J., Ju, J., Batish, A., Usui, T., Zheng, et al  
2020
- **High-resolution mapping reveals that microniches in the gastric glands control *Helicobacter pylori* colonization of the stomach** *PLOS BIOLOGY*  
Fung, C., Tan, S., Nakajima, M., Skoog, E. C., Camarillo-Guerrero, L., Klein, J. A., Lawley, T. D., Solnick, J. V., Fukami, T., Amieva, M. R.  
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- **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.  
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- ***Helicobacter pylori* senses bleach (HOCl) as a chemoattractant using a cytosolic chemoreceptor.** *PLoS biology*  
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- **A Dock-and-Lock Mechanism Clusters ADAM10 at Cell-Cell Junctions to Promote alpha-Toxin Cytotoxicity.** *Cell reports*  
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- **Stanley Falkow (1934-2018)** *NATURE*  
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- **Multiple Acid Sensors Control *Helicobacter pylori* Colonization of the Stomach.** *PLoS pathogens*  
Huang, J. Y., Goers Sweeney, E., Guillemin, K., Amieva, M. R.  
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- **Stromal R-spondin orchestrates gastric epithelial stem cells and gland homeostasis.** *Nature*  
Sigal, M. n., Logan, C. Y., Kapalczynska, M. n., Mollenkopf, H. J., Berger, H. n., Wiedenmann, B. n., Nusse, R. n., Amieva, M. R., Meyer, T. F.  
2017; 548 (7668): 451–55
- **Pathobiology of *Helicobacter pylori*-Induced Gastric Cancer** *GASTROENTEROLOGY*  
Amieva, M., Peek, R. M.  
2016; 150 (1): 64-78
- **The adherens junctions control susceptibility to *Staphylococcus aureus* a-toxin.** *Proceedings of the National Academy of Sciences of the United States of America*  
Popov, L. M., Marceau, C. D., Starkl, P. M., Lumb, J. H., Shah, J., Guerrero, D., Cooper, R. L., Merakou, C., Bouley, D. M., Meng, W., Kiyonari, H., Takeichi, M., Galli, et al

2015; 112 (46): 14337-14342

- **Chemodetection and Destruction of Host Urea Allows *Helicobacter pylori* to Locate the Epithelium** *CELL HOST & MICROBE*  
Huang, J. Y., Sweeney, E. G., Sigal, M., Zhang, H. C., Remington, S. J., Cantrell, M. A., Kuo, C. J., Guillemin, K., Amieva, M. R.  
2015; 18 (2): 147-156
- ***Helicobacter pylori* Activates and Expands Lgr5(+) Stem Cells Through Direct Colonization of the Gastric Glands.** *Gastroenterology*  
Sigal, M., Rothenberg, M. E., Logan, C. Y., Lee, J. Y., Honaker, R. W., Cooper, R. L., Passarelli, B., Camorlinga, M., Bouley, D. M., Alvarez, G., Nusse, R., Torres, J., Amieva, et al  
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- ***Helicobacter pylori* Activates and Expands Lgr5(+) Stem Cells Through Direct Colonization of the Gastric Glands** *GASTROENTEROLOGY*  
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- **Three-Dimensional Human Skin Models to Understand *Staphylococcus aureus* Skin Colonization and Infection.** *Frontiers in immunology*  
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- **Three-Dimensional Human Skin Models to Understand *Staphylococcus aureus* Skin Colonization and Infection.** *Frontiers in immunology*  
Popov, L., Kovalski, J., Grandi, G., Bagnoli, F., Amieva, M. R.  
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- **Iron deficiency accelerates *Helicobacter pylori*-induced carcinogenesis in rodents and humans** *JOURNAL OF CLINICAL INVESTIGATION*  
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- **ChePep Controls *Helicobacter pylori* Infection of the Gastric Glands and Chemotaxis in the Epsilonproteobacteria** *MBIO*  
Howitt, M. R., Lee, J. Y., Lertsethtakarn, P., Vogelmann, R., Joubert, L., Ottemann, K. M., Amieva, M. R.  
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- ***Helicobacter pylori* Perturbs Iron Trafficking in the Epithelium to Grow on the Cell Surface** *PLOS PATHOGENS*  
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- ***Listeria monocytogenes* Internalin B Activates Junctional Endocytosis to Accelerate Intestinal Invasion** *PLOS PATHOGENS*  
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- ***Helicobacter pylori* Usurps Cell Polarity to Turn the Cell Surface into a Replicative Niche** *PLOS PATHOGENS*  
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- **Host-bacterial interactions in *Helicobacter pylori* infection** *GASTROENTEROLOGY*  
Amieva, M. R., El-Omar, E. M.  
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- ***Listeria monocytogenes* invades the epithelial junctions at sites of cell extrusion** *PLOS PATHOGENS*  
Pentecost, M., Otto, G., Theriot, J. A., Amieva, M. R.  
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- ***Helicobacter pylori* CagA induces a transition from polarized to invasive phenotypes in MDCK cells** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*  
Bagnoli, F., Buti, L., Tompkins, L., Covacci, A., Amieva, M. R.  
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- **Important bacterial gastrointestinal pathogens in children: A pathogenesis perspective** *PEDIATRIC CLINICS OF NORTH AMERICA*  
Amieva, M. R.  
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- **Breaking into the epithelial apical-junctional complex - news from pathogen hackers** *CURRENT OPINION IN CELL BIOLOGY*  
Vogelmann, R., Amieva, M. R., FALKOW, S., Nelson, W. J.  
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- **Disruption of the epithelial apical-junctional complex by *Helicobacter pylori* CagA** *SCIENCE*  
Amieva, M. R., Vogelmann, R., Covacci, A., Tompkins, L. S., NELSON, W. J., FALKOW, S.  
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- **Engineered Matrices Enable the Culture of Human Patient-Derived Intestinal Organoids** *ADVANCED SCIENCE*  
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- **Enteroaggregative *E. coli* Adherence to Human Heparan Sulfate Proteoglycans Drives Segment and Host Specific Responses to Infection.** *PLoS pathogens*  
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Ding, S. n., Song, Y. n., Brulois, K. F., Pan, J. n., Co, J. Y., Ren, L. n., Feng, N. n., Yasukawa, L. L., Sánchez-Tacuba, L. n., Wosen, J. E., Mellins, E. D., Monack, D. M., Amieva, et al  
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- **IgE Effector Mechanisms, in Concert with Mast Cells, Contribute to Acquired Host Defense against *Staphylococcus aureus*.** *Immunity*  
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Wosen, J. E., Ilstad-Minnihan, A., Co, J. Y., Jiang, W., Mukhopadhyay, D., Fernandez-Becker, N. Q., Kuo, C. J., Amieva, M. R., Mellins, E. D.  
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- **A Multi-Institution Collaboration to Define Core Content and Design Flexible Curricular Components for a Foundational Medical School Course: Implications for National Curriculum Reform** *ACADEMIC MEDICINE*

- Chen, S. F., Deitz, J., Batten, J. N., DeCoste-Lopez, J., Adam, M., Alspaugh, J., Amieva, M. R., Becker, P., Boslett, B., Carline, J., Chin-Hong, P., Engle, D. L., Hayward, et al  
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- **Profiling of rotavirus 3'UTR-binding proteins reveals the ATP synthase subunit ATP5B as a host factor that supports late-stage virus replication** *JOURNAL OF BIOLOGICAL CHEMISTRY*  
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  - **A Multi-Institution Collaboration to Define Core Content and Design Flexible Curricular Components for a Foundational Medical School Course: Implications for National Curriculum Reform.** *Academic medicine : journal of the Association of American Medical Colleges*  
Chen, S. F., Deitz, J., Batten, J. N., DeCoste-Lopez, J., Adam, M., Alspaugh, J. A., Amieva, M. R., Becker, P., Boslett, B., Carline, J., Chin-Hong, P., Engle, D. L., Hayward, et al  
2019
  - **Profiling of rotavirus 3'UTR-binding proteins reveals the ATP synthase subunit ATP5B as a host factor that supports late-stage virus replication.** *The Journal of biological chemistry*  
Ren, L., Ding, S., Song, Y., Li, B., Ramanathan, M., Co, J., Amieva, M. R., Khavari, P. A., Greenberg, H. B.  
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  - **The Use of Short, Animated, Patient-Centered Springboard Videos to Underscore the Clinical Relevance of Preclinical Medical Student Education.** *Academic medicine*  
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  - **Quantitative Imaging of Gut Microbiota Spatial Organization** *CELL HOST & MICROBE*  
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