



Manuel Amieva

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

 NIH Biosketch available Online

CLINICAL OFFICES

- **Pediatric Infectious Disease**

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Bio

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

- Board Certification: Pediatric Infectious Diseases, American Board of Pediatrics (2005)
- 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

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 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

COURSES

2019-20

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

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)

STANFORD ADVISEES

Doctoral Dissertation Reader (AC)

Susan Brewer, Spencer Cesar, Andrew Guzman, Kyler Lugo, Suchita Rastogi, Terence Theisen

Postdoctoral Faculty Sponsor

Jessica Klein, Maria del Mar Margalef Catala

GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Microbiology and Immunology (Phd Program)

Publications

PUBLICATIONS

- **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.
2019; 17 (5)
- **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
- ***Helicobacter pylori* senses bleach (HOCl) as a chemoattractant using a cytosolic chemoreceptor.** *PLoS biology*
Perkins, A., Tudorica, D. A., Amieva, M. R., Remington, S. J., Guillemin, K.
2019; 17 (8): e3000395
- **A Dock-and-Lock Mechanism Clusters ADAM10 at Cell-Cell Junctions to Promote alpha-Toxin Cytotoxicity.** *Cell reports*
Shah, J., Rouaud, F., Guerrero, 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
- **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
2015; 148 (7): 1392-404 e21
- ***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
2015; 148 (7): 1392-?
- **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.
2014; 5: 41-?
 - **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.
2014; 5: 41-?
 - **Iron deficiency accelerates Helicobacter pylori-induced carcinogenesis in rodents and humans** *JOURNAL OF CLINICAL INVESTIGATION*
Noto, J. M., Gaddy, J. A., Lee, J. Y., Piazuolo, M. B., Friedman, D. B., Colvin, D. C., Romero-Gallo, J., Suarez, G., Loh, J., Slaughter, J. C., Tan, S., Morgan, D. R., Wilson, et al
2013; 123 (1): 479-492
 - **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.
2011; 2 (4)
 - **Helicobacter pylori Perturbs Iron Trafficking in the Epithelium to Grow on the Cell Surface** *PLOS PATHOGENS*
Tan, S., Noto, J. M., Romero-Gallo, J., Peek, R. M., Amieva, M. R.
2011; 7 (5)
 - **Listeria monocytogenes Internalin B Activates Junctional Endocytosis to Accelerate Intestinal Invasion** *PLOS PATHOGENS*
Pentecost, M., Kumaran, J., Ghosh, P., Amieva, M. R.
2010; 6 (5)
 - **Helicobacter pylori Usurps Cell Polarity to Turn the Cell Surface into a Replicative Niche** *PLOS PATHOGENS*
Tan, S., Tompkins, L. S., Amieva, M. R.
2009; 5 (5)
 - **Host-bacterial interactions in Helicobacter pylori infection** *GASTROENTEROLOGY*
Amieva, M. R., El-Omar, E. M.
2008; 134 (1): 306-323
 - **Listeria monocytogenes invades the epithelial junctions at sites of cell extrusion** *PLOS PATHOGENS*
Pentecost, M., Otto, G., Theriot, J. A., Amieva, M. R.
2006; 2 (1): 29-40
 - **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.
2005; 102 (45): 16339-16344
 - **Important bacterial gastrointestinal pathogens in children: A pathogenesis perspective** *PEDIATRIC CLINICS OF NORTH AMERICA*
Amieva, M. R.
2005; 52 (3): 749-?
 - **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.
2004; 16 (1): 86-93
 - **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.
2003; 300 (5624): 1430-1434
 - **Helicobacter pylori enter and survive within multivesicular vacuoles of epithelial cells** *CELLULAR MICROBIOLOGY*
Amieva, M. R., Salama, N. R., Tompkins, L. S., FALKOW, S.
2002; 4 (10): 677-690

- **Human Intestinal Enteroids Model MHC-II in the Gut Epithelium** *FRONTIERS IN IMMUNOLOGY*
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.
2019; 10
- **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
2019; 94 (6): 819–25
- **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*
Ren, L., Ding, S., Song, Y., Li, B., Ramanathan, M., Co, J., Amieva, M. R., Khavari, P. A., Greenberg, H. B.
2019; 294 (15): 5993–6006
- **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.
2019
- **Identification of a S. aureus virulence factor by activity-based protein profiling (ABPP).** *Nature chemical biology*
Lentz, C. S., Sheldon, J. R., Crawford, L. A., Cooper, R., Garland, M., Amieva, M. R., Weerapana, E., Skaar, E. P., Bogoy, M.
2018
- **The soluble extracellular domain of E-cadherin interferes with EPEC adherence via interaction with the Tir:intimin complex.** *FASEB journal : official publication of the Federation of American Societies for Experimental Biology*
Login, F. H., Jensen, H. H., Pedersen, G. A., Amieva, M. R., Nejsum, L. N.
2018; fj201800651
- **A dual function antibiotic-transporter conjugate exhibits superior activity in sterilizing MRSA biofilms and killing persister cells.** *Journal of the American Chemical Society*
Antonoplis, A., Zang, X., Huttner, M. A., Chong, K., Lee, Y. B., Co, J. Y., Amieva, M., Kline, K., Wender, P. A., Cegelski, L.
2018
- **The Use of Short, Animated, Patient-Centered Springboard Videos to Underscore the Clinical Relevance of Preclinical Medical Student Education.** *Academic medicine*
Adam, M., Chen, S. F., Amieva, M., Deitz, J., Jang, H., Porwal, A., Prober, C.
2017
- **The basolateral vesicle sorting machinery and basolateral proteins are recruited to the site of enteropathogenic E. coli microcolony growth at the apical membrane.** *PloS one*
Pedersen, G. A., Jensen, H. H., Schelde, A. B., Toft, C., Pedersen, H. N., Ulrichsen, M., Login, F. H., Amieva, M. R., Nejsum, L. N.
2017; 12 (6): e0179122
- **Quantitative Imaging of Gut Microbiota Spatial Organization** *CELL HOST & MICROBE*
Earle, K. A., Billings, G., Sigal, M., Lichtman, J. S., Hansson, G. C., Elias, J. E., Amieva, M. R., Huang, K. C., Sonnenburg, J. L.
2015; 18 (4): 478-488
- **Helicobacter pylori CheZHP and ChePep form a novel chemotaxis-regulatory complex distinct from the core chemotaxis signaling proteins and the flagellar motor.** *Molecular microbiology*
Lertsethtakarn, P., Howitt, M. R., Castellon, J., Amieva, M. R., Ottemann, K. M.
2015; 97 (6): 1063-1078
- **Regulation of Helicobacter pylori Virulence Within the Context of Iron Deficiency** *JOURNAL OF INFECTIOUS DISEASES*
Noto, J. M., Lee, J. Y., Gaddy, J. A., Cover, T. L., Amieva, M. R., Peek, R. M.

2015; 211 (11): 1790-1794

- **A Pediatric Case of New Delhi Metallo- β -Lactamase-1-Producing Enterobacteriaceae in The United States.** *Pediatric infectious disease journal*
Green, D. A., Srinivas, N., Watz, N., Tenover, F. C., Amieva, M., Banaei, N.
2013; 32 (11): 1291-1294
- **The intestinal stem cell markers *Bmi1* and *Lgr5* identify two functionally distinct populations** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
Yan, K. S., Chia, L. A., Li, X., Ootani, A., Su, J., Lee, J. Y., Su, N., Luo, Y., Heilshorn, S. C., Amieva, M. R., Sangiorgi, E., Capecchi, M. R., Kuo, et al
2012; 109 (2): 466-471
- ***Shigella* navigates tight corners.** *Cell host & microbe*
Amieva, M.
2012; 11 (4): 319-20
- **Tolerance Rather Than Immunity Protects From *Helicobacter pylori*-Induced Gastric Preneoplasia** *GASTROENTEROLOGY*
Arnold, I. C., Lee, J. Y., Amieva, M. R., Roers, A., Flavell, R. A., Sparwasser, T., Mueller, A.
2011; 140 (1): 199-?
- **The Complete Genome Sequence of *Helicobacter pylori* Strain G27** *JOURNAL OF BACTERIOLOGY*
Baltrus, D. A., Amieva, M. R., Covacci, A., Lowe, T. M., Merrell, D. S., Ottemann, K. M., Stein, M., Salama, N. R., Guillemin, K.
2009; 191 (1): 447-448
- **The role of bacterial pathogens in cancer** *CURRENT OPINION IN MICROBIOLOGY*
Vogelmann, R., Amieva, M. R.
2007; 10 (1): 76-81
- ***Helicobacter pylori* and gastric cancer: What can be learned by studying the response of gastric epithelial cells to the infection?** *AACR Special Conference on Colorectal Cancer - Molecular Pathways and Therapies*
Mueller, A., FALKOW, S., Amieva, M. R.
AMER ASSOC CANCER RESEARCH.2005: 1859-64
- **Jarisch-Herxheimer reaction associated with ciprofloxacin administration for tick-borne relapsing fever** *PEDIATRIC INFECTIOUS DISEASE JOURNAL*
Webster, G., Schiffman, J. D., Dosanjh, A. S., Amieva, M. R., Gans, H. A., Sectish, T. C.
2002; 21 (6): 571-573
- **Imaging of dynamic changes of the actin cytoskeleton in microextensions of live NIH3T3 cells with a GFP fusion of the F-actin binding domain of moesin.** *BMC cell biology*
Litman, P., Amieva, M. R., FURTHMAYR, H.
2000; 1: 1-?
- **Disruption of dynamic cell surface architecture of NIH3T3 fibroblasts by the N-terminal domains of moesin and ezrin: in vivo imaging with GFP fusion proteins** *JOURNAL OF CELL SCIENCE*
Amieva, M. R., Litman, P., Huang, L. Q., Ichimaru, E., Furthmayr, H.
1999; 112 (1): 111-125
- **The plasma membrane-actin linking protein, ezrin, is a glomerular epithelial cell marker in glomerulogenesis, in the adult kidney and in glomerular injury** *KIDNEY INTERNATIONAL*
Hugo, C., Nangaku, M., Shankland, S. J., Pichler, R., Gordon, K., Amieva, M. R., Couser, W. G., FURTHMAYR, H., JOHNSON, R. J.
1998; 54 (6): 1934-1944
- **Hypoxia increases human keratinocyte motility on connective tissue** *56th Annual Meeting of the Society-for-Investigative-Dermatology*
O'Toole, E. A., Marinkovich, M. P., Peavey, C. L., Amieva, M. R., FURTHMAYR, H., Mustoe, T. A., Woodley, D. T.
AMER SOC CLINICAL INVESTIGATION INC.1997: 2881-91
- **Phosphorylation of T-558 of moesin detected by site-specific antibodies in RAW264.7 macrophages** *BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS*
Nakamura, F., Amieva, M. R., Hirota, C., Mizuno, Y., FURTHMAYR, H.
1996; 226 (3): 650-656
- **The cytoskeletal linking proteins, moesin and radixin, are upregulated by platelet-derived growth factor, but not basic fibroblast growth factor in experimental mesangial proliferative glomerulonephritis** *JOURNAL OF CLINICAL INVESTIGATION*

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- Hugo, C., Hugo, C., Pichler, R., Gordon, K., Schmidt, R., Amieva, M., Couser, W. G., FURTHMAYR, H., JOHNSON, R. J.
1996; 97 (11): 2499-2508
- **Phosphorylation of threonine 558 in the carboxyl-terminal actin-binding domain of moesin by thrombin activation of human platelets** *JOURNAL OF BIOLOGICAL CHEMISTRY*
Nakamura, F., Amieva, M. R., FURTHMAYR, H.
1995; 270 (52): 31377-31385
 - **SUBCELLULAR-LOCALIZATION OF MOESIN IN DYNAMIC FILOPODIA, RETRACTION FIBERS, AND OTHER STRUCTURES INVOLVED IN SUBSTRATE EXPLORATION, ATTACHMENT, AND CELL-CELL CONTACTS** *EXPERIMENTAL CELL RESEARCH*
Amieva, M. R., FURTHMAYR, H.
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 - **MOESIN, EZRIN, AND P205 ARE ACTIN-BINDING PROTEINS ASSOCIATED WITH NEUTROPHIL PLASMA-MEMBRANES** *MOLECULAR BIOLOGY OF THE CELL*
Pestonjamp, K., Amieva, M. R., Strassel, C. P., Nauseef, W. M., FURTHMAYR, H., LUNA, E. J.
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 - **RADIXIN IS A COMPONENT OF HEPATOCYTE MICROVILLI IN-SITU** *EXPERIMENTAL CELL RESEARCH*
Amieva, M. R., Wilgenbus, K. K., FURTHMAYR, H.
1994; 210 (1): 140-144
 - **CDNA SEQUENCE AND INTRACELLULAR LOCALIZATION OF HUMAN RADIXIN** *78th Meeting of the Deutschen-Gesellschaft-fur-Pathologie*
Wilgenbus, K. K., Amieva, M., FURTHMAYR, H.
GUSTAV FISCHER VERLAG.1994: 245-245
 - **MOESIN, A NEW CYTOSKELETAL PROTEIN AND CONSTITUENT OF FILOPODIA - ITS ROLE IN CELLULAR FUNCTIONS** *FOREFRONTS IN NEPHROLOGY SYMP ON MESANGIAL CELL AND EXTRACELLULAR MATRIX*
FURTHMAYR, H., Lankes, W., Amieva, M.
BLACKWELL SCIENCE INC.1992: 665-70
 - **EARLY NEUROGENESIS OF THE MOUSE OLFATORY NERVE - GOLGI AND ELECTRON-MICROSCOPIC STUDIES** *JOURNAL OF COMPARATIVE NEUROLOGY*
MARINPADILLA, M., Amieva, M. R.
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