

Stanford



Ellen Yeh

Assistant Professor of Biochemistry, of Pathology and of Microbiology and Immunology

Bio

ACADEMIC APPOINTMENTS

- Assistant Professor, Biochemistry
- Assistant Professor, Pathology
- Assistant Professor, Microbiology & Immunology
- Member, Bio-X
- Member, Maternal & Child Health Research Institute (MCHRI)
- Faculty Fellow, Stanford ChEM-H

HONORS AND AWARDS

- Medical Scientist Training Program (MSTP), NIH (2001-2008)
- Career Award for Medical Scientists, Burroughs-Wellcome Fund (2012-2017)
- Early Career Independence Award (DP5), NIH (2012-2017)

PROFESSIONAL EDUCATION

- MD, Harvard Medical School , Medicine (2008)
- PhD, Harvard Medical School , Biophysics (2006)
- BA, Harvard University , Biochemical Sciences (2001)

LINKS

- YEH LAB website: <http://yehlab.stanford.edu/>

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

Lab website: <http://yehlab.stanford.edu/>

The chemistry and biology of the unique plastid organelle, the apicoplast, in malaria parasites

Malaria caused by Plasmodium spp parasites has an enormous disease burden that disproportionately affects the world's poorest and youngest. New anti-malarials with novel drug mechanisms are desperately needed in the face of existing or emerging drug resistance to all available therapies. Investigation of Plasmodium biology offers

both the potential for important biomedical impact and an opportunity to explore fascinating eukaryotic biology. Given the challenges of genetic and other approaches to studying this complex organism, the development of chemical tools will be especially critical in pushing forward basic research.

My research focuses on the apicoplast, a prokaryotically-derived plastid organelle unique to Plasmodium (and other pathogenic Apicomplexa parasites) and a key anti-malarial drug target. My laboratory's goal is to elucidate apicoplast biology, function, and role in pathogenesis with the ultimate goal of realizing the potential of the apicoplast as a therapeutic target. In a major step toward this goal, my previous work has demonstrated that the sole essential function of the apicoplast in blood-stage *P. falciparum* parasites is the biosynthesis of isoprenoid precursors. As such, I was able to generate parasites completely devoid of this essential organelle but chemically rescued by supplementation of the growth media with isopentenyl pyrophosphate (IPP), the pathway product. Chemical rescue and "apicoplast(-)" parasites are innovative tools for investigating apicoplast biology and for advancing apicoplast-directed drug and vaccine development. Our research takes advantage of these new tools and our newfound understanding of apicoplast function to explore a variety of topics, including protein trafficking to the apicoplast and the protein "prenylome" in Plasmodium. We employ a variety of methods but have a particular focus on the use of chemical tools to overcome the current challenges in studying this organelle. Our exploration of the Plasmodium apicoplast are likely to reveal both unique biology and targets for anti-malarial drug development.

Teaching

STANFORD ADVISEES

Doctoral Dissertation Reader (AC)

Sabrina Ergun, Abel Ferrel, Daniel Mokhtari, Makenna Morck, Margaux Pinney, Suchita Rastogi, Cole Sitron

Postdoctoral Faculty Sponsor

Michael Pulkoski-Gross, Marta Walczak, Yili Zhu

Doctoral Dissertation Advisor (AC)

Stephanie Kabeche, Thomas Meister, Yong Tang

GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Biochemistry (Phd Program)
- Infectious Diseases (Fellowship Program)
- Microbiology and Immunology (Phd Program)

Publications

PUBLICATIONS

- **A mutagenesis screen for essential plastid biogenesis genes in human malaria parasites.** *PLoS biology*
Tang, Y., Meister, T. R., Walczak, M., Pulkoski-Gross, M. J., Hari, S. B., Sauer, R. T., Amberg-Johnson, K., Yeh, E.
2019; 17 (2): e3000136
- **Host Cell Metabolism Contributes to Delayed-Death Kinetics of Apicoplast Inhibitors in *Toxoplasma gondii*** *ANTIMICROBIAL AGENTS AND CHEMOTHERAPY*
Amberg-Johnson, K., Yeh, E.
2019; 63 (2)
- **A mutagenesis screen for essential plastid biogenesis genes in human malaria parasites** *PLOS BIOLOGY*
Tang, Y., Meister, T. R., Walczak, M., Pulkoski-Gross, M. J., Hari, S. B., Sauer, R. T., Amberg-Johnson, K., Yeh, E.
2019; 17 (2)
- **Disruption of Apicoplast Biogenesis by Chemical Stabilization of an Imported Protein Evades the Delayed-Death Phenotype in Malaria Parasites.** *mSphere*
Boucher, M. J., Yeh, E.
2019; 4 (1)

- **Disruption of Apicoplast Biogenesis by Chemical Stabilization of an Imported Protein Evades the Delayed-Death Phenotype in Malaria Parasites** *MSPHERE*
Etoucher, M. J., Yeh, E.
2019; 4 (1)
- **Plastid-endomembrane connections in apicomplexan parasites.** *PLoS pathogens*
Boucher, M. J., Yeh, E.
2019; 15 (6): e1007661
- **Host cell metabolism contributes to delayed-death kinetics of apicoplast inhibitors in Toxoplasma gondii.** *Antimicrobial agents and chemotherapy*
Amberg-Johnson, K., Yeh, E.
2018
- **The Toxoplasma gondii Active Serine Hydrolase 4 Regulates Parasite Division and Intravacuolar Parasite Architecture.** *mSphere*
Foe, I. T., Onguka, O., Amberg-Johnson, K., Garner, R. M., Amara, N., Beatty, W., Yeh, E., Bogyo, M.
2018; 3 (5)
- **Integrative proteomics and bioinformatic prediction enable a high-confidence apicoplast proteome in malaria parasites.** *PLoS biology*
Boucher, M. J., Ghosh, S., Zhang, L., Lal, A., Jang, S. W., Ju, A., Zhang, S., Wang, X., Ralph, S. A., Zou, J., Elias, J. E., Yeh, E.
2018; 16 (9): e2005895
- **The Toxoplasma gondii Active Serine Hydrolase 4 Regulates Parasite Division and Intravacuolar Parasite Architecture** *MSPHERE*
Foe, I. T., Onguka, O., Amberg-Johnson, K., Garner, R. M., Amara, N., Beatty, W., Yeh, E., Bogyo, M.
2018; 3 (5)
- **The Toxoplasma gondii Active Serine Hydrolase 4 Regulates Parasite Division and Intravacuolar Parasite Architecture (vol 3, e00393-18, 2018)** *MSPHERE*
Foe, I. T., Onguka, O., Amberg-Johnson, K., Garner, R. M., Amara, N., Beatty, W., Yeh, E., Bogyo, M.
2018; 3 (5)
- **The Toxoplasma gondii Active Serine Hydrolase 4 Regulates Parasite Division and Intravacuolar Parasite Architecture (vol 3, e00393-18, 2018)** *MSPHERE*
Foe, I. T., Onguka, O., Amberg-Johnson, K., Garner, R. M., Amara, N., Beatty, W., Yeh, E., Bogyo, M.
2018; 3 (5)
- **Specific Inhibition of the Bifunctional Farnesyl/Geranylgeranyl Diphosphate Synthase in Malaria Parasites via a New Small-Molecule Binding Site** *CELL CHEMICAL BIOLOGY*
Gisselberg, J. E., Herrera, Z., Orchard, L. M., Llinas, M., Yeh, E.
2018; 25 (2): 185-+
- **ATG8 Is Essential Specifically for an Autophagy-Independent Function in Apicoplast Biogenesis in Blood-Stage Malaria Parasites.** *mBio*
Walczak, M., Ganesan, S. M., Niles, J. C., Yeh, E.
2018; 9 (1)
- **Erratum for Foe et al., "The Toxoplasma gondii Active Serine Hydrolase 4 Regulates Parasite Division and Intravacuolar Parasite Architecture".** *mSphere*
Foe, I. T., Onguka, O., Amberg-Johnson, K., Garner, R. M., Amara, N., Beatty, W., Yeh, E., Bogyo, M.
2018; 3 (5)
- **Small molecule inhibition of apicomplexan FtsH1 disrupts plastid biogenesis in human pathogens** *ELIFE*
Amberg-Johnson, K., Hari, S. B., Ganesan, S. M., Lorenzi, H. A., Sauer, R. T., Niles, J. C., Yeh, E.
2017; 6
- **The Prenylated Proteome of Plasmodium falciparum Reveals Pathogen-specific Prenylation Activity and Drug Mechanism-of-action** *MOLECULAR & CELLULAR PROTEOMICS*
Gisselberg, J. E., Zhang, L., Elias, J. E., Yeh, E.
2017; 16 (4): S54-S64
- **The apicoplast: now you see it, now you don't** *INTERNATIONAL JOURNAL FOR PARASITOLOGY*
McFadden, G. I., Yeh, E.
2017; 47 (2-3): 137-144

- **A Chemical Rescue Screen Identifies a Plasmodium falciparum Apicoplast Inhibitor Targeting MEP Isoprenoid Precursor Biosynthesis.** *Antimicrobial agents and chemotherapy*
Wu, W., Herrera, Z., Ebert, D., Baska, K., Cho, S. H., DeRisi, J. L., Yeh, E.
2015; 59 (1): 356-364
- **Chemical Rescue of Malaria Parasites Lacking an Apicoplast Defines Organelle Function in Blood-Stage Plasmodium falciparum** *PLOS BIOLOGY*
Yeh, E., DeRisi, J. L.
2011; 9 (8)
- **Immediate Incubation Reduces Indeterminate Results for QuantiFERON-TB Gold In-Tube Assay** *JOURNAL OF CLINICAL MICROBIOLOGY*
Herrera, V., Yeh, E., Murphy, K., Parsonnet, J., Banaei, N.
2010; 48 (8): 2672-2676
- **Real-Time PCR Testing for mecA Reduces Vancomycin Usage and Length of Hospitalization for Patients Infected with Methicillin-Sensitive Staphylococci** *JOURNAL OF CLINICAL MICROBIOLOGY*
Nguyen, D. T., Yeh, E., Perry, S., Luo, R. F., Pinsky, B. A., Lee, B. P., Sisodiya, D., Baron, E. J., Banaei, N.
2010; 48 (3): 785-790
- **Preferential Lower Respiratory Tract Infection in Swine-Origin 2009 A(H1N1) Influenza** *CLINICAL INFECTIOUS DISEASES*
Yeh, E., Luo, R. F., Dynner, L., Hong, D. K., Banaei, N., Baron, E. J., Pinsky, B. A.
2010; 50 (3): 391-394
- **Hair Sheep Blood, Citrated or Defibrinated, Fulfills All Requirements of Blood Agar for Diagnostic Microbiology Laboratory Tests** *PLOS ONE*
Yeh, E., Pinsky, B. A., Banaei, N., Baron, E. J.
2009; 4 (7)
- **Chlorination by a long-lived intermediate in the mechanism of flavin-dependent halogenases** *BIOCHEMISTRY*
Yeh, E., Blasiak, L. C., Koglin, A., Drennan, C. L., Walsh, C. T.
2007; 46 (5): 1284-1292
- **Characterization of the aminocarboxycyclopropane-forming enzyme CmaC** *BIOCHEMISTRY*
Kelly, W. L., Boyne, M. T., Yeh, E., Vosburg, D. A., Galonic, D. P., Kelleher, N. L., Walsh, C. T.
2007; 46 (2): 359-368
- **Enzymatic generation of the antimetabolite gamma,gamma-dichloroaminobutyrate by NRPS and mononuclear iron halogenase action in a streptomycete** *CHEMISTRY & BIOLOGY*
Ueki, M., Galonic, D. P., Vaillancourt, F. H., Garneau-Tsodikova, S., Yeh, E., Vosburg, D. A., Schroeder, F. C., Osada, H., Walsh, C. T.
2006; 13 (11): 1183-1191
- **Nature's inventory of halogenation catalysts: Oxidative strategies predominate** *CHEMICAL REVIEWS*
Vaillancourt, F. H., Yeh, E., Vosburg, D. A., Garneau-Tsodikova, S., Walsh, C. T.
2006; 106 (8): 3364-3378
- **Flavin redox chemistry precedes substrate chlorination during the reaction of the flavin-dependent halogenase RebH** *BIOCHEMISTRY*
Yeh, E., Cole, L. J., Barr, E. W., Bollinger, J. M., Ballou, D. P., Walsh, C. T.
2006; 45 (25): 7904-7912
- **Dichlorination of a pyrrolyl-S-carrier protein by FADH(2)-dependent halogenase PltA during pyoluteorin biosynthesis** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
Dorrestein, P. C., Yeh, E., Garneau-Tsodikova, S., Kelleher, N. L., Walsh, C. T.
2005; 102 (39): 13843-13848
- **Cryptic chlorination by a non-haem iron enzyme during cyclopropyl amino acid biosynthesis** *NATURE*
Vaillancourt, F. H., Yeh, E., Vosburg, D. A., O'Connor, S. E., Walsh, C. T.
2005; 436 (7054): 1191-1194
- **Robust in vitro activity of RebF and RebH, a two-component reductase/halogenase, generating 7-chlorotryptophan during rebeccamycin biosynthesis** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
Yeh, E., Garneau, S., Walsh, C. T.
2005; 102 (11): 3960-3965

- **Enhanced macrocyclizing activity of the thioesterase from tyrocidine synthetase in presence of nonionic detergent** *CHEMISTRY & BIOLOGY*
Yeh, E., Lin, H. N., Clugston, S. L., Kohli, R. M., Walsh, C. T.
2004; 11 (11): 1573-1582
- **Type II thioesterase restores activity of a NRPS module stalled with an aminoacyl-S-enzyme that cannot be elongated** *CHEMBIOCHEM*
Yeh, E., Kohli, R. M., Bruner, S. D., Walsh, C. T.
2004; 5 (9): 1290-1293