

Kim Orth

Curriculum Vitae

Howard Hughes Medical Institute
Department of Molecular Biology
University of Texas Southwestern Medical Center
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Education

1993 Ph.D., Biochemistry and Molecular Biology
University of Texas Southwestern Medical Center

1986 Master of Science, Biological Chemistry
UCLA School of Medicine

1984 Bachelor of Science, Biochemistry
Texas A & M University

Positions and Employment

1985 - 1986 Master Student, Dept. of Bio. Chem., UCLA School of Medicine

1987 - 1990 Research Associate, HHMI & UT Southwestern Medical Center

1991 - 1995 Ph.D. Student/Postdoc Fellow, UT Southwestern Med. Center

1995 - 2001 Postdoc Fellow and Research Inv., Dept of Bio. Chem., Univ. of Mich.

2001 - 2007 Assistant Professor, Dept. of Molecular Biology, UT Southwestern Med. Center

2007 - 2011 Associate Professor, Dept. of Molecular Biology, UT Southwestern Med. Center

2010 –present Secondary Appointment, Department of Biochemistry

2011 – present Professor, Dept. of Molecular Biology, UT Southwestern Med. Center

2015 – present HHMI, Investigator

Honors and Awards

1986 NIH Predoctoral Training Grant, Cell and Molecular Biology. UCLA

1993-1998 NCI Postdoctoral Fellowship, Molecular Genetics, U. of Michigan

1998-2001 Walther Cancer Institute, Dawson Research Fellowship

2001-present W.W. Caruth Jr. Scholar in Biomedical Research

2003-2006 Arnold and Mabel Beckman Young Investigator Award

2006-2013 Burroughs Wellcome Investigator in Pathogenesis of Infectious Disease

2010 Welch Foundation Norman Hackerman Award in Chemical Science

2011 TAMEST; 2011 Edith & Peter O'Donnell Award in Science

2012 ASBMB Young Investigator Award

2013 Earl A. Forsythe Chair in Biomedical Science

2016 American Academy of Microbiology

Peer-Reviewed Publications (43 out 120)

1. Casey, A.K., Moelman, A., Zhang, J., Servage, K., Kramer, H. & **Orth, K.** Fic-mediated deAMPylation of BiP is not dependent on homo-dimerization and rescues toxic AMPylation in flies. *J Biol Chem.* (Under review)
2. de Souza Santos, M., Salomon, D. & **Orth, K.** T3SS effector VopL inhibits the host ROS response, promoting the intracellular survival of *Vibrio parahaemolyticus*. *PLoS Pathog* (2017) 13(6): e1006438. <https://doi.org/10.1371/journal.ppat.100643>
3. Casey, A.K. & **Orth, K.** Enzymes involved in AMPylation and deAMPylation *Chemical Reviews (In Press)*
4. Li, P., Salomon, D., Kinch, L.N., Ray, A., Dalia, A.B., Cong, Q., Ninan, L., Camilli, A., Grishin, N.V. & **Orth, K.** Acute Hepatopancreatic Necrosis Disease (AHPND) causing *Vibrio parahaemolyticus* contains a virulent Type VI Secretion System (T6SS) with anti-bacterial activities. *Appl Environ Microbiol.* (2017) Apr 21. pii: AEM.00737-17. doi: 10.1128/AEM.00737-17
5. Cancel-Rivera, G. & **Orth, K.** Biochemical basis for activation of virulence genes by bile salts in *Vibrio parahaemolyticus*. *Gut Microbes Gut Microbes.* 2017 Jan 27:0. doi: 10.1080/19490976.2017.1287655
6. De Nisco, N.J., Kanchwala, M., Li, P., Fernandez, J., Xing, C. & **Orth, K.** Cytotoxic Vibrio T3SS1 Rewires Host Gene Expression to Subvert Cell Death Signaling and Activate Cell Survival Networks. (Under Review)
7. Huebinger, R.M., Stones, D.H., de Souza Santos, M., Carlson, D.L., Song, J., Vaz, D.P., Keen, E., Wolf, S.E., **Orth, K.** & Krachler, A. M. Targeting bacterial adherence inhibits multidrug-resistant *Pseudomonas aeruginosa* infection following burn injury. (2016) *Scientific Reports* Dec 20;6:39341. doi: 10.1038/srep39341
8. Ray, A., Kinch, L.N., de Souza Santos, M., Grishin, N.V., **Orth, K.** & Salomon, D. Proteomics analysis reveals previously uncharacterized virulence factors in *Vibrio proteolyticus*. (2016) *mBio* 7(4):e01077-16. doi:10.1128/mBio.01077-16.
9. Li, P., Rivera-Cancel, G., Kinch, L.N., Salomon, D., Tomchick, D. R., Grishin, N.V., & **Orth, K.** Bile salt receptor complex activates pathogenic Type III secretion system. (2016) *eLife* 5:e15718
10. Salomon, D., Klimko, J.A., Trudgian, D.C., Kinch, L.N., Grishin, N.V., Mirzaei, H & **Orth, K.** Type VI secretion system toxins horizontally shared between marine bacteria (2015) *PLoS Pathogen* Aug 25;11(8):e1005128.
11. Sreelatha, A., Bennett, T.L., Carpinone, E.M., O'Brien, K.M., Jordan, K.D., Burdette, D.L., **Orth, K.** & Starai, V.J. The *Vibrio* effector protein, VopQ, inhibits fusion of V-ATPase containing membranes. (2015) *PNAS.* 112(1):100-5 PMID:25453092 PubMed in process.
12. de Souza Santos M., Salomon, D. Li, P., Krachler, A-M. & **Orth, K.** *Vibrio parahaemolyticus* Virulence Determinants (2015) *The Comprehensive Sourcebook of Bacterial Protein Toxins, Fourth Edition*
13. de Souza Santos, M. & **Orth, K.** Subversion of the cytoskeleton by intracellular bacteria: lessons from *Listeria*, *Salmonella* and *Vibrio*. (2015) *Cell Microbiology* 17(2):164-73 PMID: 25440316 PubMed in process
14. Ham H., Woolery A.R., Tracy C., Stenesen D., Krämer H. & **Orth, K.** Unfolded protein response-regulated dFic reversibly AMPylates BiP during ER homeostasis. (2014) *JBC* 289(52):36059-69 PMID: 25395623. PubMed in process.
15. Woolery, A.R., Yu, X., LaBaer, J. & **Orth, K.** AMPylation of Rho GTPases subverts multiple host signaling processes. (2014) *JBC* 289(47):32977-88.
16. Calder, T., Santos, M.S., Attah, V., Klimko, J., Fernandez, J., Salomon, D., Krachler, A.M., & **Orth, K.** Structural and regulatory mutations in *Vibrio parahaemolyticus* type III secretion systems display variable effects on virulence. (2014) *FEMS* 361(2):107-14..
17. de Souza Santos, M.S. & **Orth, K.** Intracellular *Vibrio parahaemolyticus* Escapes the Vacuole and Establishes a Replicative Niche in the Cytosol of Epithelial Cells. (2014) *mBio* 9;5(5):e01506-14.
18. Yu, X., Woolery, A.R., Luong, P., Hao, Y.H., Grammel, M., Westcott, N., Park, J., Wang, J., Bian, X., Demirhan, G., Hang, H.C., **Orth, K.** & LaBaer, J. Click chemistry-based detection of global pathogen-host AMPylation on self-assembled human protein microarrays. (2014) *Mol & Cell Proteomics* 13(11):3164-76. PMID 25073739 PubMed in process.
19. Calder, T., Kinch, L.N., Fernandez, J., Salomon, D., Grishin, N.V., & **Orth, K.** *Vibrio* type III effector VPA1380 is related to the cysteine protease domain of large bacterial toxin. (2014) *PLoS ONE* 6;9(8):e104387 PMID 25099122 PubMed in process.

20. Salomon, D., Klimko, & **Orth, K.** H-NS regulates the *Vibrio parahaemolyticus* type VI secretion system 1. (2014) *Microbiology* 160(Pt9):1867-73. PMID:24987102 PubMed in process.
21. Salomon, D., Kinch, L.N., Trudgian, D.C., Guo, X., Klimko, J.A., Grishin, N.V., Mirzaei, H & **Orth, K.** Marker for Type VI Secretion System effectors (2014) *PNAS USA* 111(25):9271-6 PMID 24927539.
22. Lewallen, D.M., Sreelatha, A., Dharmarajan, V., Madoux, F., Chase, F., Griffin, P.R., **Orth, K.**, Hoddler, p. & Thompson, P.R. Inhibiting AMPylation: a novel screen to identify the first small molecule inhibitors of protein AMPylation. (2014) *ACS Chem Biol* 9(2): 433-432 PMC3944102.
23. Sreelatha, A., **Orth, K.**, & Starai, V.J. The pore-forming bacterial effector, VopQ, halts autophagic turnover. (2013) *Autophagy* 9(12): 2169-70. PMID:24145145 PubMed in process.
24. Salomon D., Guo, Y., Kimch, L.N., Grishin, N.V., Mirzaei, H. & **Orth, K.** Effectors of animal and plant pathogens use a common domain to bind host phosphoinositides. (2013) *Nature Communications* 4:2973. Doi:10.1038/ncomms3973.
25. Hawley, C.A., Watson, C., **Orth, K.** & Krachler, A-M. High-affinity binding of bacterial fibronectin-binding proteins to host cells inhibits critical steps in wound healing. (2013) *PloS ONE* 8.11:e81216
26. Sreelatha, A., Bennett, T. L., Zheng, H., Jiang, Q.X., **Orth, K.***, & Starai, V.J.* *Vibrio* VopQ forms a gated outward rectifying channel that disrupts host ion homeostasis. (2013) *PNAS USA* 110(28):11559-64
27. Altura, M.A., Heath-Heckman, E.A., Gillette, A. Kremer, A-M, Krachler, A.M. Brennean, c., Ruby, E.G., **Orth, K.**, McFall-Ngai, M.J. (2013) The first engagement of partners in the Euprymna scolopes-Vibrio fischeri symbiosis is a two-step process initiated by a few environmental symbiont cells. (2013) *Environ Microbiol.* Jun 11. doi: 10.1111/1462-2920.12179 (Epub ahead of print).
28. Salomon, D. & **Orth, K.** What Pathogens Have Taught Us About Posttranslational Modifications (2013) *Cell Host Microbes* 14:3 269-279.
29. Krachler, A-M. & **Orth, K.** Made to stick: Anti-adhesion therapy for bacterial infections as an alternative to conventional antimicrobials. (2013) *Microbe* 8:286-290.
30. Krachler, A-M. & **Orth, K.** Targeting the bacteria-host interface: strategies in anti-adhesion therapy (2013) *Virulence* 4(4): 284-94.
31. Salomon, D. & **Orth, K.** Lost after translation: post-translational modifications by bacterial type III effectors. (2013) *Current Opinions in Microbiology* 6(2):213-20.
32. Zhang, L.L & **Orth, K.** Virulence Determinants for *Vibrio parahaemolyticus* Infection. (2013) *Current Opinions in Microbiology* 16(1):70-7.
33. Salomon, D., Gonzalez, H., Updegraff, B.L. & **Orth, K.** *Vibrio parahaemolyticus* Type VI Secretion System 1 is Activated in Marine Conditions to Target Bacteria, and is Differentially Regulated from System 2. (2013) *PLoS ONE* 8:4 e61086.
34. Ham, H. & **Orth, K.** The Role of Type III Secretion System 2 in *Vibrio parahaemolyticus* Pathogenicity. (2012) *J Microbiol.* Oct;50(5):719-25. PMID:23124738[PubMed - in process]
35. Krachler AM, Mende, K, Murray, C. & **Orth K.** In vitro characterization of Multivalent Adhesion Molecule 7-based inhibition of multidrug-resistant bacteria isolated from wounded military personnel. (2012) *Virulence* 3(4):389-99. PMC3478241
36. Alto, N.M. & **Orth, K.** Subversion of cell signaling by pathogens. (2012) In Signal Transduction Textbook. Cold Spring Harbor Press.
37. Zhang, L.L, Krachler, A-M, Broberg, CA, Li, Y, Mirzaei, H, Gilpin, CJ & **Orth, K.** Type III effector VopC mediates invasion for *Vibrio* species. (2012) *Cell Reports* DOI 10.1016/j.celrep.2012.04.004.
38. Rahman, M., Ham, H., Liu, X., Sugiura, Y., **Orth, K.** and Krämer, H. Visual neurotransmission in *Drosophila* requires expression of dFic in glial capitate projections. (2012) *Nature Neuroscience* Apr 29. doi: 10.1038/nn.3102. [Epub ahead of print] PMID:22544313
39. Krachler, A-M, Ham, H. & **Orth, K.** Turnabout is fair play: Use of the bacterial Multivalent Adhesion Molecule 7 as an antimicrobial agent. (2012) *Virulence* 1;3(1).
40. Krachler AM & **Orth K.** Functional characterization of the interaction between bacterial adhesin multivalent adhesion molecule 7 (MAM7) protein and its host cell ligands. (2011) *J Biol Chem.* 286(45): 38939-47.

41. Grammel M, Luong P, **Orth K**, Hang HC. A chemical reporter for protein AMPylation. (2011) *J Am Chem Soc.* 133(43):17103-5.
42. Krachler, A-M, Woolery, A.R. & **Orth, K.** Host-pathogen interactions: Manipulation of kinase signaling by bacterial pathogens. (2011) *J. Cell Biol* 195(7):1083-92.
43. Krachler, A-M, Ham, H. & **Orth, K.** Outer membrane adhesion factor multivalent adhesion molecule 7 initiates host cell binding during infection by Gram-negative pathogens. (2011) *PNAS USA* 108(28):11614-9
44. Ham H., Sreelatha, A. & **Orth, K.** Manipulation of Host Membranes by Bacterial Effectors. (2011) *Nature Reviews Microbiology* 9(9):635-46.
45. Li, Y., Al-Eryani, R., Yarbrough, M.L., Orth, K., & Ball, H.L. Characterization of AMPylation on threonine, serine, and tyrosine using mass spectrometry. (2011) *J. Am Soc Mass Spectrom* 22(4):753-761. Ham H & **Orth K.** De-AMPylation unmasked: modulation of host membrane trafficking 2011) *Sci Signal.* (Oct 11;4(194).
46. Broberg, C. A., Zhang, L.L., Gonzalez, H., Laskowski-Arce, M.A. & **Orth, K.** A Vibrio Effector Protein is an Inositol Phosphatase and Disrupts Host Cell Membrane Integrity. (2010) *Science* 329:1660-2. (Epub, Aug. 2010).
47. Luong, P., Kinch, L.N., Brautigam, C.A., Grishin, N.V., Tomchick, D.R. & **Orth, K.** VopS Fic Domain uses direct transfer mechanism for AMPylation. (2010) *J Biol Chem.* 285(26): 20155-63
48. Yarbrough ML, Orth K. AMPylation is a new post-translational modification. 2009) *Nat Chem Biol.* (6):378-9.
49. Yarbrough, M., Li, Y., Kinch, L.N., Grishin, N.V., Hall B.E., & **Orth, K.** AMPylation of Rho GTPases by *Vibrio* VopS disrupts effector binding and downstream signaling. (2009) *Science* 323: 269-272. (Epub, Nov. 2008).