BIOGRAPHICAL SKETCH

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NAME: OLSON, RICHARD A

eRA COMMONS USER NAME (credential, e.g., agency login): ROLSON

POSITION TITLE: Associate Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	END DATE MM/YYYY	FIELD OF STUDY
Cornell University, Ithaca, NY	BA	05/1997	Biology, Conc. in Biochemistry
Columbia University, New York, NY	PHD	06/2003	Biochemistry and Molecular Biophysics
California Institute of Technology, Pasadena, CA	Postdoctoral Fellow	08/2009	Structural studies of immune molecules

A. Personal Statement

The long-term goal of my research program is to gain structural and functional insight into how virulence factors from pathogenic bacteria contribute to pathogenicity and threaten human health. My lab uses a combination of X-ray crystallography and biophysical/biochemical techniques and has focused recently on biofilm matrix proteins and pore-forming toxins. As a graduate student in Dr. Eric Gouaux's laboratory, I gained experience in X-ray crystallography while studying ionotropic glutamate receptors, P2X receptors, and bacterial pore-forming toxins. While at Columbia, I also learned biophysical and biochemical techniques including analytical ultracentrifugation, membrane protein expression and purification, and the development of ligand-binding assays. I next worked with Dr. Pamela Björkman as a Beckman Fellow at Caltech where I developed skills in mammalian and insect cell culture while continuing to practice X-ray crystallography. At Caltech, I worked on projects relating to MHC homologs while continuing to work on toxins, collaborating with a fellow postdoc on a three-dimensional EM study of the *Vibrio cholerae* cytolysin pore. My work at Wesleyan has expanded to include an interest in the role of glycobiology in pathogen/host interactions. To gain additional expertise in this area, in 2019 I spent a sabbatical semester working with Dr. Ursula Neu (in Dr. Markus Wahl's laboratory at the Freie Universität in Berlin), whose expertise is in viral-glycan interactions. We employ a diverse set of biophysical techniques in our research, including isothermal titration calorimetry, fluorescence-based binding studies, and surface plasmon resonance and have recently collaborated with an NMR spectroscopist (Dr. Andre Alexandrescu at UConn) to solve structures of a toxin targeting domain. In summary, I have over 25-years of experience in studying bacterial virulence factors and the desire to understand the complex mechanism that governs their structure and function. In my almost 15 years at Wesleyan, I have gained extensive experience mentoring undergraduate researchers and have included undergraduate authors on many of my papers (including as first author). Students can obtain credit for research during the school year and participate in summer research as part of Wesleyan's Research in Sciences Summer Research Program. I am strongly committed to increasing diversity in the sciences and have been the faculty director of the Wesleyan Science and Mathematics Scholars Program (WesMaSS) for the past three years, supporting underrepresented and FGLI STEM students transition to and suceed in college. I currently have several WesMaSS students conducting research in my laboratory. In addition to undergraduates, Wesleyan has a fifth year Master's program as well as a Ph.D. program in five STEM degree-awarding departments.

1. Tai JB, Mukherjee S, Nero T, Olson R, Tithof J, Nadell CD, Yan J. Social evolution of shared biofilm matrix components. Proc Natl Acad Sci U S A. 2022 Jul 5;119(27):e2123469119. PubMed Central PMCID: PMC9271185.
2. Jiang Z, Nero T, Mukherjee S, Olson R, Yan J. Searching for the Secret of Stickiness: How Biofilms Adhere to Surfaces. Front Microbiol. 2021;12:686793. PubMed Central PMCID: PMC8295476.

3. Kaus K, Biester A, Chupp E, Lu J, Visudharomn C, Olson R. The 1.9 Å crystal structure of the extracellular matrix protein Bap1 from *Vibrio cholerae* provides insights into bacterial biofilm adhesion. J Biol Chem. 2019 Oct 4;294(40):14499-14511. PubMed Central PMCID: PMC6779443.
4. De S, Kaus K, Sinclair S, Case BC, Olson R. Structural basis of mammalian glycan targeting by *Vibrio cholerae* cytolysin and biofilm proteins. PLoS Pathog. 2018 Feb;14(2):e1006841. PubMed Central PMCID: PMC5825169.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2016 -	Associate Professor, Wesleyan University, Middletown, CT
2010 -	Member, American Society for Biochemistry and Molecular Biology
2010 -	Member, Biophysical Society
2009 - 2016	Assistant Professor, Wesleyan University, Middletown, CT
2006 - 2009	Beckman Postdoctoral Fellowship, Caltech, Pasadena, CA
2004 - 2005	Rosalind Alcott Postdoctoral Fellowship, Caltech, Pasadena, CA

Honors

2019	Article designated "Editors Pick", Journal of Molecular Biology
2005	Outstanding Poster Award, Caltech Biology Departmental Retreat
2003	Ph.D. Thesis deemed "with distinction", Columbia University

C. Contribution to Science –

Undergraduate student authors bold underlined, *=graduate students

1. *How biofilm matrix proteins from Vibrio cholerae (Vc) adhere to biotic and abiotic surfaces*: Biofilms serve to organize and protect communities of bacteria and play an important role in pathogenesis and environmental persistence. Vc biofilms are composed of a secreted polysaccharide, matrix proteins, and extracellular DNA. A complex array of molecular interactions between these various components determine the macroscale properties of secreted biofilms. We are employing a combination of structural, biophysical, and biochemical methods to characterize these interactions at the molecular level. We seek to understand the structural mechanism for how biofilm components interact with each other and with surfaces to which biofilms attach. Thus far, our work in this area includes the identification and structural characterization of glycan receptors found on mammalian cell surfaces that are targeted by Vc biofilm matrix proteins (d). Recently, we also solved the near-complete high-resolution crystal structure of the Bap1 biofilm matrix protein revealing a unique abiotic surface targeting sequence with functional homology to mussel adhesion proteins (c). Our work provides a beginning framework for understanding how Vc biofilms attach to surfaces in the environment and in the human host; our proposed work in this application will continue and expand this line of inquiry. We expect that this early work will have a significant influence on the study of biofilm proteins from Vc, and in biofilms in general. I served as the PI on these studies. Additionally, through a collaboration with the Yan lab at Yale, we are making progress on understanding the mechanism for how biofilms adhere to surfaces (a,b).

    a. Tai JB, Mukherjee S, Nero T, Olson R, Tithof J, Nadell CD, Yan J. Social evolution of shared biofilm matrix components. Proc Natl Acad Sci U S A. 2022 Jul 5;119(27):e2123469119. PubMed Central PMCID: PMC9271185.
    b. Jiang Z, Nero T, Mukherjee S, Olson R, Yan J. Searching for the Secret of Stickiness: How Biofilms Adhere to Surfaces. Front Microbiol. 2021;12:686793. PubMed Central PMCID: PMC8295476.
    c. *Kaus K, **Biester A, Chupp E, Lu J, Visudharomn C**, Olson R. The 1.9 Å crystal structure of the extracellular matrix protein Bap1 from *Vibrio cholerae* provides insights into bacterial biofilm adhesion. J Biol Chem. 2019 Oct 4;294(40):14499-14511. PubMed Central PMCID: PMC6779443.

d. *De S, *Kaus K, **Sinclair S**, *Case BC, Olson R. Structural basis of mammalian glycan targeting by *Vibrio cholerae* cytolysin and biofilm proteins. PLoS Pathog. 2018 Feb;14(2):e1006841. PubMed Central PMCID: PMC5825169.

2. *How pathogenic pore-forming toxins utilize lipid/glycan receptors to target cell-membranes*: Bacterial virulence factors, including pore-forming toxins, utilize cell-surface receptors to increase their potency against target cells. These receptors may include protein, lipid, or carbohydrate moieties. It is important to understand these interactions to develop therapies to mitigate the action of microbial pathogens. We used a combination of glycan-screening, mutagenesis, and X-ray crystallography to determine how several pore-forming toxins from *Vibrio cholerae* utilize glycans to target cellular membranes. For *Vibrio cholerae* cytolysin, we identified complex N-glycans as the targeted moiety (d) and showed how glycan targeting and direct membrane interactions (b) work together to facilitate cellular lysis. For *Vibrio vulnificus* hemolysin, we showed that terminal N-acetyl lactosamine moieties on cell-surface glycans are utilized as receptors (c). Our work was innovative, because we utilized glycan-chip technologies, cellular assays, and high-resolution X-ray crystallographic techniques to offer a complete understanding of the role of cellular glycans in toxin activity. I served as the PI in these studies. Additionally, we collaborated with the Alexandrescu lab at UConn to determine the structure of an accessory domain of Hemolysin II from *Bacillus cereus* (a).

   a. *Kaplan AR, Olson R, Alexandrescu AT. Protein yoga: Conformational versatility of the Hemolysin II C-terminal domain detailed by NMR structures for multiple states. Protein Sci. 2021 May;30(5):990-1005. PubMed Central PMCID: PMC8040871.
   b. *De S, **Bubnys A**, Alonzo F 3rd, Hyun J, Lary JW, Cole JL, Torres VJ, Olson R. The Relationship between Glycan Binding and Direct Membrane Interactions in *Vibrio cholerae* Cytolysin, a Channel-forming Toxin. J Biol Chem. 2015 Nov 20;290(47):28402-28415. PubMed Central PMCID: PMC4653697.
   c. *Kaus K, Lary JW, Cole JL, Olson R. Glycan specificity of the *Vibrio vulnificus* hemolysin lectin outlines evolutionary history of membrane targeting by a toxin family. J Mol Biol. 2014 Jul 29;426(15):2800-12. PubMed Central PMCID: PMC4102649.
   d. **Levan S**, *De S, Olson R. *Vibrio cholerae* cytolysin recognizes the heptasaccharide core of complex N-glycans with nanomolar affinity. J Mol Biol. 2013 Mar 11;425(5):944-57. PubMed Central PMCID: PMC3578121.

3. *How secreted pore-forming toxins assemble to form transmembrane channels*: Pore-forming toxins are secreted as water soluble monomers and assemble into transmembrane channels on susceptible cell membranes. How a water-soluble protein can assemble into a membrane protein is a fascinating question that we were able to address structurally for a related class of beta-barrel pore-forming toxins. The water-soluble structure of Staph LukF (d) showed how amphipathic beta-sheets are folded up in the water-soluble form of the toxin. Along with the previously published structure of homologous Staph alpha-hemolysin, we were able to show the structural changes that occur upon toxin assembly. Further work with Vibrio cholerae cytolysin (a, b, c) outlined water-soluble and oligomeric pore structures of a multi-domain toxin with attached lectin and pro-domains. Our structures represented the first pair of any type of pore-forming toxin with high-resolution structures for both water soluble and transmembrane pores. These contributions were made over twelve years, spanning my time as a graduate student, postdoc, and PI.

   a. *De S, Olson R. Crystal structure of the *Vibrio cholerae* cytolysin heptamer reveals common features among disparate pore-forming toxins. Proc Natl Acad Sci U S A. 2011 May 3;108(18):7385-90. PubMed Central PMCID: PMC3088620.
   b. He Y, Olson R. Three-dimensional structure of the detergent-solubilized *Vibrio cholerae* cytolysin (VCC) heptamer by electron cryomicroscopy. J Struct Biol. 2010 Jan;169(1):6-13. PubMed PMID: 19616104.
   c. Olson R, Gouaux E. Crystal structure of the *Vibrio cholerae* cytolysin (VCC) pro-toxin and its assembly into a heptameric transmembrane pore. J Mol Biol. 2005 Jul 29;350(5):997-1016. PubMed PMID: 15978620.

d. Olson R, Nariya H, Yokota K, Kamio Y, Gouaux E. Crystal structure of staphylococcal LukF delineates conformational changes accompanying formation of a transmembrane channel. Nat Struct Biol. 1999 Feb;6(2):134-40. PubMed PMID: 10048924.

4. *Structural understanding of non-classical MHC molecules in the immune system*: MHC class I molecules are essential factors in the functioning of the adaptive immune system that display cell-derived peptides to receptors on T-cells. A number of MHC-like molecules with similar structures, yet non-traditional functions, have been identified in mammals. We undertook a study of a class of MHC-homologs expressed in the mammalian olfactory system. These molecules are exclusively expressed in the vomeronasal organ, which is responsible for the detection of pheromones by mammals and may act as a chaperone for class C G-protein coupled-receptors involved in pheromone detection. Our structure of a mouse MHC molecule identified a structure similar to traditional MHC molecules, but with an open groove devoid of bound peptides. This was the first example of a classical MHC-class I molecule with an open and empty groove. I had the primary research role in the project as a postdoctoral fellow.

   a. Arnon TI, Kaiser JT, West AP Jr, Olson R, Diskin R, Viertlboeck BC, Göbel TW, Bjorkman PJ. The crystal structure of CHIR-AB1: a primordial avian classical Fc receptor. J Mol Biol. 2008 Sep 12;381(4):1012-24. PubMed Central PMCID: PMC2603183.
   b. Olson R, Dulac C, Bjorkman PJ. MHC homologs in the nervous system--they haven't lost their groove. Curr Opin Neurobiol. 2006 Jun;16(3):351-7. PubMed PMID: 16698261.
   c. Olson R, Huey-Tubman KE, Dulac C, Bjorkman PJ. Structure of a pheromone receptor-associated MHC molecule with an open and empty groove. PLoS Biol. 2005 Aug;3(8):e257. PubMed Central PMCID: PMC1174912.

5. *The structural mechanism of ion channel selectivity and desensitization*: Gated ion channels play an essential role in the nervous system facilitating many aspects of learning, sensory perception, locomotion, and memory. As a graduate student, I studied in a lab working on the structure and function of ion channels, primarily ionotropic glutamate receptors. In those early years of ion channel structural biology (the first high-resolution ion channel structure was published in 1998), there were many outstanding questions about the structural underpinnings of phenomena observed by electrophysiologists. I contributed to the understanding of how ligand-gated ion channels recognize small molecules and how structural changes in these channels lead to their activation and desensitization. The key paper in this study (b) outlined the structural and functional mechanism for how ionotropic glutamate receptors desensitize (close while remaining bound to agonists) and has been cited over 700 times. In this work, I primarily studied how oligomeric interactions between ligand-binding domains lead to activation and desensitization using analytical ultracentrifugation. I contributed similarly to the study of a primordial glutamate receptor (c) and HCN pacemaker channels (a).

   a. Zagotta WN, Olivier NB, Black KD, Young EC, Olson R, Gouaux E. Structural basis for modulation and agonist specificity of HCN pacemaker channels. Nature. 2003 Sep 11;425(6954):200-5. PubMed PMID: 12968185; NIHMSID: NIHMS198060.
   b. Sun Y, Olson R, Horning M, Armstrong N, Mayer M, Gouaux E. Mechanism of glutamate receptor desensitization. Nature. 2002 May 16;417(6886):245-53. PubMed PMID: 12015593.
   c. Mayer ML, Olson R, Gouaux E. Mechanisms for ligand binding to GluR0 ion channels: crystal structures of the glutamate and serine complexes and a closed apo state. J Mol Biol. 2001 Aug 24;311(4):815-36. PubMed PMID: 11518533.

Complete List of Published Work in My Bibliography:
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