BIOGRAPHICAL SKETCH

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NAME: McLaughlin, Krystle Jenelle Williams

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

POSITION TITLE: Assistant 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
Colgate University	BA	05/2006	Physics
University of Rochester	MS	10/2008	Biophysics
University of Rochester	PHD	08/2011	Biophysics
University of North Carolina at Chapel Hill	Postdoctoral Fellow	06/2014	Chemistry

A. Personal Statement

I am an Assistant Professor of Chemistry and my research investigates the structural and biochemical basis of several microbial protein mechanisms. I have broad training in biophysics and biochemistry, with an emphasis on structural biology specializing in x-ray crystallography. My lab currently is focused on elucidating the structural basis for the spread of antibiotic resistant genes via conjugative plasmid transfer (CPT). Antibiotic resistant bacterial strains pose a major threat to human health and CPT is a major route for the spread of antibiotic resistant genes. Resistance genes are contained on extrachromosomal pieces of DNA called conjugative multiresistance plasmids (cMRPs) which are processed for transfer by an essential complex of proteins called the relaxosome. cMRPs also encode most of the genes to direct their own cell-to-cell transfer such as the relaxosome, as well as genes for plasmid replication and other maintenance. Both the relaxosome and many essential plasmid maintenance processes like replication are still not fully understood. My research is focused on understanding plasmid propagation and replication using cRMPs found in Salmonella Typhimurium and Staphylococcus aureus. Additionally, as a PI at a primarily undergraduate institution, integrating teaching and research is also a main focus of my scholarship. I have recently been awarded external funding for these projects and have published papers on the structural and biophysical investigations of various proteins as an independent investigator. In summary, I have the expertise, and resources to carry out this project, and I am highly motivated to expand my structural biology training to cryo-EM to further my research. The ongoing project that I would like to highlight is:

Cottrell Scholar Award #28277 McLaughlin (PI) 07/01/2022 – 06/30/2025 Structural Basis for the Conjugative Spread of Antibiotic Resistance

This project has generated three publications so far for (1) the research proposal to understand conjugative proteins from S. aureus pSK41, and (2) as part of the education proposal which created a new protein crystallography undergraduate course, with five undergraduates as lead or co-author.

1. Ran X, Parikh P, Abendroth J, Arakaki TL, Clifton MC, Edwards TE, Lorimer DD, Mayclin S, Staker BL, Myler P, McLaughlin KJ. Structural and functional characterization of FabG4 from Mycolicibacterium smegmatis. Acta Crystallogr F Struct Biol Commun. 2024 Apr 1;80(Pt 4):82-91. PubMed Central PMCID: PMC11058512.
2. Sarosh A, Kwong SM, Jensen SO, Northern F, Walton WG, Eakes TC, Redinbo MR, Firth N, McLaughlin KJ. pSK41/pGO1-family conjugative plasmids of Staphylococcus aureus encode a cryptic repressor of replication. Plasmid. 2023 Sep-Nov;128:102708. PubMed PMID: 37967733.
3. Moorefield J, Konuk Y, Norman JO, Abendroth J, Edwards TE, Lorimer DD, Mayclin SJ, Staker BL, Craig JK, Barett KF, Barrett LK, Van Voorhis WC, Myler PJ, McLaughlin KJ. Characterization of a family I inorganic pyrophosphatase from Legionella pneumophila Philadelphia 1. Acta Crystallogr F Struct Biol Commun. 2023 Oct 1;79(Pt 10):257-266. PubMed Central PMCID: PMC10565794.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2017 -	Assistant Professor , Vassar College, Poughkeepsie, NY
2014 - 2017	Professor Of Practice, Lehigh University, Bethlehem, PA
2013 - 2013	Adjunct Lecturer, University of North Carolina at Pembroke, Pembroke, NC
2011 - 2014	SPIRE Postdoctoral Scholar, University of North Carolina at Chapel Hill, Chapel Hill, NC

Honors

2022 - 2025	Cottrell Scholar Award, Research Corporation for Science Advancement
2011 - 2014	Seeding Postdoctoral Innovators in Research and Education (SPIRE) Postdoctoral Fellowship, University of North Carolina at Chapel Hill
2012	George V. Metzger Award for most outstanding biophysics PhD thesis, University of Rochester
2010	Elon Huntington Hooker Graduate Fellowship, University of Rochester
2009	William F. Neuman Award, for most outstanding biophysics student , University of Rochester

C. Contribution to Science

1. Structural and biochemical characterization of Conjugative Proteins. During conjugative plasmid transfer, genetic material is transmitted between bacterial cells in part by a complex of proteins called the relaxosome, conferring virulence factors and antibiotic resistance. In order for the plasmid to be maintained in daughter cells it must be replicated each time the bacteria divides. The relaxosome proteins as wel las replication proteins are plasmid-encoded. Characterizing these plasmid-encoded conjugative proteins will help to shed light on the CPT and plasmid maintenance. Successful conjugative DNA transfer depends on key catalytic relaxosome components to nick one strand of the duplex DNA plasmid and separate the DNA strands while cell-to-cell transfer occurs. The TraI protein from the conjugative Salmonella plasmid pCU1 fulfills these key catalytic roles, as it contains both single-stranded DNA-nicking relaxase and ATP-dependent helicase domains within a single, 1,078-residue polypeptide. We characterized the helicase determinants of Salmonella pCU1 TraI and my work revealed a previously uncharacterized C-terminal functional domain that uncouples ATP hydrolysis from strand separation activity. This domain may facilities TraI serving as a unique potential drug target. The plasmid-encoded replication protein Rep is key to keeping the plasmid present in bacterial cells. We solved the crystal structure and functionally characterized Cop, a cryptic regulator of Rep that is conserved in pSK41-family conjugative plasmids from Staphylococcus.

    a. Sarosh A, Kwong SM, Jensen SO, Northern F, Walton WG, Eakes TC, Redinbo MR, Firth N, McLaughlin KJ. pSK41/pGO1-family conjugative plasmids of Staphylococcus aureus encode a cryptic repressor of replication. Plasmid. 2023 Sep-Nov;128:102708. PubMed PMID: 37967733.
    b. McLaughlin KJ, Nash RP, Redinbo MR. Unique helicase determinants in the essential conjugative TraI factor from Salmonella enterica serovar Typhimurium plasmid pCU1. J Bacteriol. 2014 Sep;196(17):3082-90. PubMed Central PMCID: PMC4135661.

2. Structural Biology Education of Undergraduates. While x-ray crystallography is one of the most commonly used techniques for obtaining three-dimensional structures of proteins, it is rarely taught to students at the undergraduate level. Course-based Undergraduate Research Experiences (CUREs) have been shown to be an effective way to integrate authentic research projects into the curriculum, however there are currently no CUREs available for adoption that include protein crystallography. I have developed a protein X-ray crystallography focused biochemistry lab, which exposes students to an authentic research experience. This project is partially funded by my Cottrell Scholar Award and has generated three publications so far, one editorial describing the CURE for wide use and two student led research projects.

    a. Ran X, Parikh P, Abendroth J, Arakaki TL, Clifton MC, Edwards TE, Lorimer DD, Mayclin S, Staker BL, Myler P, McLaughlin KJ. Structural and functional characterization of FabG4 from Mycolicibacterium smegmatis. Acta Crystallogr F Struct Biol Commun. 2024 Apr 1;80(Pt 4):82-91. PubMed Central PMCID: PMC11058512.

b. Moorefield J, Konuk Y, Norman JO, Abendroth J, Edwards TE, Lorimer DD, Mayclin SJ, Staker BL, Craig JK, Barett KF, Barrett LK, Van Voorhis WC, Myler PJ, McLaughlin KJ. Characterization of a family I inorganic pyrophosphatase from Legionella pneumophila Philadelphia 1. Acta Crystallogr F Struct Biol Commun. 2023 Oct 1;79(Pt 10):257-266. PubMed Central PMCID: PMC10565794.

c. McLaughlin KJ. Developing a macromolecular crystallography driven CURE. Struct Dyn. 2021 Mar;8(2):020406. PubMed Central PMCID: PMC8012065.

d. Rodarte JV, Abendroth J, Edwards TE, Lorimer DD, Staker BL, Zhang S, Myler PJ, McLaughlin KJ. Crystal structure of acetoacetyl-CoA reductase from Rickettsia felis. Acta Crystallogr F Struct Biol Commun. 2021 Feb 1;77(Pt 2):54-60. PubMed Central PMCID: PMC7900926.

3. Recognition of the 3' Splice Site by Essential Splicing Factor U2AF65. As part of the Kielkopf Lab at the University of Rochester, we elucidated the structural basis of which the essential splicing factor U2AF65 recognizes the polypyrimidine tract at the 3' splice site during splicing initiation. I demonstrated the unique thermodynamic signature of U2AF65 when it binds its cognate RNA sequence, as compared to other RNA binding proteins. This unique signature allows U2AF65 to tolerate purine interruptions more easily in its natural binding site without loss of affinity. I solved multiple x-ray crystallographic structures that helped show the structural basis for how U2AF65 can tolerate purine substitutions in the polypyrimidine tract, which maintaining binding affinity. This is relevant to polypyrimidine tracts containing mutations that may lead to a disease state because of aberrant splicing as U2AF65 may not bind, and this work also showed how creating mutations in U2AF65 can rescues some aberrant splicing.

   a. Agrawal AA, McLaughlin KJ, Jenkins JL, Kielkopf CL. Structure-guided U2AF65 variant improves recognition and splicing of a defective pre-mRNA. Proc Natl Acad Sci U S A. 2014 Dec 9;111(49):17420-5. PubMed Central PMCID: PMC4267390.

   b. McLaughlin KJ, Jenkins JL, Kielkopf CL. Large favorable enthalpy changes drive specific RNA recognition by RNA recognition motif proteins. Biochemistry. 2011 Mar 8;50(9):1429-31. PubMed Central PMCID: PMC3050080.

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