BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors. Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Christina R. Bourne

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

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)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Oklahoma, Norman OK	BS	05/1997	Biochemistry
Oklahoma Medical Research Foundation and OU Health Sciences Center, Oklahoma City OK	PhD	10/2003	Biochemistry, Mol Biol and Structural Biology
OU Health Sciences Center, Oklahoma City OK	Postdoctoral Fellow	10/2007	Structural Virology

A. Personal Statement

I have more than 20 years of experience in biochemistry and structural biology that I apply to reveal insights and methods for targeting macromolecules important to maintaining human health and combating disease. My experience spans structure determination of human proteins (publication a), anti-viral development (publication b), and anti-bacterial development (detailed in Contributions section), with additional expertise in biochemical and biophysical measurements and assays.

I have formal training and experience in X-ray macromolecular crystallography and have expanded my training to cryo-electron microscopy single particle analysis. Through embedded training at the National Center for CryoEM Access and Training (NCCAT) and multiple visits to the Pacific Northwest CryoEM Center (PNCC), including during Sabbatical leave in Spring 2023, I have learned how to reproducibly prepare high quality grids, screen and collect data, and progress in the data processing pipeline. This is facilitated by institutional investments in infrastructure, expanding our computational resources beyond our HPC with installation of two GPU workstations (one currently dedicated for my research group) and the installation of a cryoEM instrument (TF Tundra 100 kV) at OU, with a soft opening scheduled for June 2024.

My research program is highly collaborative with recent co-authorship with the Singh group (publication c), and with the Burgett group (publication d) supporting structural studies of macromolecules. Based on my broad scientific training and experience in laboratory management and mentorship, I contribute strong team leadership to deliver impactful results within a defined time frame and budget.

a. Ramsland PA, Terzyan SS, Cloud G, **Bourne CR**, Farrugia W, Tribbick G, Geysen HM, Moomaw C R, Slaughter CA, Edmundson AB. Crystal structure of a glycosylated Fab from an IgM cryoglobulin with properties of a natural proteolytic antibody. Biochem. J. (2006) 395(3): 473-81. PMCID: PMC1462693

b. **Bourne CR**, Finn MG, Zlotnick A. Global structural changes in hepatitis B virus capsids induced by the assembly effector HAP1. J Virol. 2006 Nov;80(22):11055. PMID: 16943288; PMCID: PMC1642186.

c. Johnson BP, Kumar V, Scull EM, Thomas LM, **Bourne CR**, Singh S. Molecular basis for the substrate promiscuity of isopentenyl phosphate kinase from *Candidatus methanomethylophilus* alvus. ACS Chem Biol. 2022 Jan 21;17(1):85-102. PMID: 34905349; PMCID: PMC9745668.

d. Severance ZC, Nuñez JI, Le-McClain AT, Malinky CA, Bensen RC, Fogle RS, Manginelli GW, Sakers SH, Falcon EC, Bui RH, Snead KJ, **Bourne CR**, Burgett AWG. Structure-activity relationships of ligand

binding to Oxysterol-Binding Protein (OSBP) and OSBP-Related Protein 4. J Med Chem. 2023 Mar 23;66(6):3866-3875. PMID: 36916802. PMCID: PMC10786236

Ongoing and completed projects that I would like to highlight:

NIH NIGMS P30-GM145423 (Pilot, PI: A. Burgett, co-I: C. Bourne) 09/22 – 5/24

"Structure/function of oxysterol-binding protein to guide therapeutic development"
This project provided funding for preliminary data in the current proposal, including methods to recombinantly product both full length and the only the ligand binding domain of the OSBP protein, as well as further development of methods in the current proposal

U.S. Army, Department of Defense W81XWH2010121 (PI: C. Bourne) 02/20 – 05/23

"Unlocking the potential of bacterial ParE toxins: developing a blueprint for co-opting molecular time bombs that impact bacterial cell survival"
This project is examining the phenotypic outcomes for four human bacterial pathogens when their native chromosomal ParE toxins are over-expressed within the native host cells. A proof-of-concept study design will assess the efficiency of antitoxin removal from these ParE toxins in an *E. coli* host.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2023 - 2027	Member, American Crystallographic Association Communications Committee (elected)
2021 - *current*	Associate Professor, U. of Oklahoma, Dept. of Chemistry and Biochemistry, Norman, OK
2021 – (*2023)*	U. of Oklahoma, Dept. of Chemistry and Biochemistry, Executive Comm. Member (elected)
2021 - *current*	Member, User Review Committee, National Center for CryoEM Access and Training (NCCAT)
2017 - *current*	Member (Chair, effective 2021), Advisory Committee, OU Biomolecular Structure Core Facility
2015 - *current*	Member, OU Institutional Biosafety Committee
2014 - 2021	Assistant Professor, U. of Oklahoma, Dept. of Chemistry and Biochemistry
2011 - 2013	Member, BEI Resources Focus Group for Biodefense and High Containment Bacteria
2007 – 2013	Associate Research Scientist, Oklahoma State U., Center for Veterinary Health Sciences
2005 – 2007	American Cancer Society Postdoctoral Fellow, U. of Oklahoma Health Sciences Center

Other Experience and Professional Memberships

Ad Hoc manuscript reviewer (previous 5 years): *ACS Medicinal Chemistry, ACS Omega, Frontiers in Microbiology, Frontiers in Genetics, Genes, Journal of Biochemistry, mBio, Medicinal Research Reviews, Microorganisms, Molecular Microbiology, Nature Communications, Nature Reviews in Microbiology, Nucleic Acids Research, Protein Science, Spectrum, Structure, Toxins*

Proposal reviews (previous 5 years): French National Research Agency, BBSRC, US Army Research Office, NIH Special Emphasis Panel ZRG1 BST-M, U. of Missouri Research Board, European Research Council Starting Grants panel, Joint Canada-Israel Health Research Program Phase II

Member, American Crystallographic Association (2001-present), American Society for Biochemistry and Molecular Biology (2003-present), American Society for Microbiology (2008-present), American Association for the Advancement of Science (2017-present)

2023	American Crystallographic Association Session Chair, DEI: Expanding Access and Opportunities in Structural Science
2023	Representative User for the NY National Center from Cryo-EM Access and Training, NIH Common Fund CryoEM Centers Annual Meeting
2021 - *current*	Member, Editorial Board, *Frontiers in Microbiology* Microbial Physiology and Metabolism
2014 - 2017	Member, Editorial Board, *Scientific Reports*
2011 - 2017	Member, Editorial Advisory Board, *Journal of Molecular Recognition*
2015	Tech to Trek guest promoting science careers to young women, Southwestern Okla State Uni.
2015	Participant, BioCAT Advanced SAXS Training Course, Argonne National Laboratory
2000, 2014	Participant, RapiData X-ray Diffraction Data Collection and Structure Solving, Brookhaven National Laboratory
2012 - 2013	Mentor, Oklahoma State University Women's Mentorship Program

2010	Guest Scientist, Community outreach program "Born To Do Science"
2009	Participant, MolSoft2009 Workshop on Modern Drug Target Crystallography and Structure Based Drug Discovery, San Diego, CA

Honors

2022	OU Ed Cline Faculty Fellowship
2020	Nancy L. Mergler Faculty Mentor Award for Undergraduate Research
2020	Peggy Cotter Branch Travel Award, American Society of Microbiology
2018	OK - Louis Stokes Alliance for Minority Participation (LSAMP) Outstanding Faculty Mentor Award (Norman campus)
2014, 2015	VPR Summer Faculty Fellowship, University of Oklahoma
2005 - 2007	Mary Horton Postdoctoral Fellowship, American Cancer Society
2005	Travel Grant, US National Committee for Crystallography
2003	Pauling Poster Prize, American Crystallographic Association
2001	Ludo Frevel Crystallography Scholarship, International Centre for Diffraction Data

C. Contributions to Science

1. **Toxin Antitoxin systems as targets to control bacterial growth:** My team has structurally characterized and compared the extensive interaction interfaces between the toxin and antitoxin proteins with an aim of manipulating them to alter bacterial growth, with a focus on gyrase-inhibiting ParE toxins and their cognate ParD antitoxins (structure 6xrw, publication e). We recently reported a pervasive response limiting inducible toxin production by modulating plasmid copy number and find this arises directly through a specific point mutation in the *polA* gene (publication f). In other work we identified different *in vitro* IC_{50} values for inhibition of the gyrase enzyme from *E. coli* versus that from *P. aeruginosa* by the same ParE toxin protein, suggesting a complex structure-function relationship (publication g). Through our studies we have also characterized the YoeB RNase-type toxins and identified a promiscuous nuclease activity and species-specific toxicity (structure 6n90, publication h).

   e. Snead, K.J., Moore, L.L., **Bourne, C.R.** ParD antitoxin hotspot alters a disorder-to-order transition upon binding to its cognate ParE toxin, lessening its interaction affinity and increasing its protease degradation kinetics. Biochemistry. 2022 Jan; 61(1):34. PMID: 34914387; PMCID: PMC9805013

   f. Ruan S, **Bourne C.R.** *Escherichia coli* cells evade inducible ParE toxin expression by reducing plasmid copy number. Microbiol Spectr. 2024 May 3:e0397323. Epub ahead of print. PMID: 38700352.

   g. Muthuramalingam M, White JC, Murphy, T., Ames, J.R., **Bourne C.R.** The toxin from a ParDE toxin-antitoxin system found in *Pseudomonas aeruginosa* offers protection to cells challenged with anti-gyrase antibiotics. Mol. Microbiol. 2019 Feb; 111(2):441. PMID: 30427086; PMCID: PMC6368863.

   h. Ames, J.R., McGillick, J., Murphy, T., Reddem, E., **Bourne, C.R.** Identifying a molecular mechanism that imparts species-specific toxicity to YoeB toxins. Front. Micro. 2020 May; 11:959. PMID: 32528435; PMCID: PMC7256200.

2. **New inhibitors of bacterial biosynthetic folate pathway:** I carried out extensive structure-function studies to characterize a series of inhibitors derived from the structure of the antibiotic trimethoprim, including whole cell MIC measurements, *in vitro* enzyme activity inhibition, and three-dimensional structure determinations. This work produced structures of the dihydrofolate (DHFR) from three different bacteria, resulting in 13 deposited crystal structures (publications i, j, k). This work has expanded in recent years to a collaborative effort (publication l).

   i. Muddala, P.N., White, J.C., Nammalwar, B., Pratt, I., Thomas, L.M., Bunce, R.A., Berlin, K.D., **Bourne, C.R.** Inhibitor design to target a unique feature in the folate pocket of *Staphylococcus aureus* dihydrofolate reductase. 2020 Eur. J. Med. Chem. 200:112412. PMID: 32502861; PMCID: PMC7932028.

   j. **Bourne CR**, Wakeham N, Nammalwar B, Tseitin V, Bourne PC, Barrow EW, Mylvaganam S, Ramnarayan K, Bunce RA, Berlin KD, Barrow WW. Structure-activity relationship for enantiomers of

potent inhibitors of *B. anthracis* dihydrofolate reductase. Biochim Biophys Acta. 2013 Jan;1834(1):46. PMID: 22999981; PMCID: PMC3530638.

k. **Bourne CR**, Wakeham N, Webb N, Nammalwar B, Bunce RA, Berlin KD, Barrow WW. The structure and competitive substrate inhibition of dihydrofolate reductase from *Enterococcus faecalis* reveal restrictions to cofactor docking. Biochemistry. 2014 Feb 25;53(7):1228. PMID: 24495113; PMCID: PMC3985486.

l. Boyer ZW, Kessler H, Brosman H, Ruud KJ, Falkowski AF, Viollet C, **Bourne CR**, O'Reilly MC. Synthesis and characterization of functionalized amino dihydropyrimidines toward the analysis of their antibacterial structure-activity relationships and mechanism of action. ACS Omega. 2022 Oct 13;7(42):37907. PMID: 36312355; PMCID: PMC9607683.

3. **A new strategy for antiviral therapy using misdirection of capsid assembly:** As a post-doc I contributed to a novel approach to anti-viral therapies by altering the assembly pathway of the Hepatitis B virus capsid assembly. Using biophysical measurements and biochemical assays, we determined this compound mis-directed HBV assembly (publication m) and I identified a lab-derived genotype that could mimic these effects (publication n). I was awarded a fellowship from the American Cancer Society to pursue structural studies, and these resulted in two crystal structures (2g33, 2g34) identifying the binding pocket for these compounds, contributed to structure-guided compound modifications, and subsequently tested derivatized compounds to validate the compound orientation (publication o).

m. Stray SJ, **Bourne CR**, Punna S, Lewis WG, Finn MG, Zlotnick A. A heteroaryldihydropyrimidine activates and can misdirect hepatitis B virus capsid assembly. Proc Natl Acad Sci U S A. 2005 Jun 7;102(23):8138. PMID: 15928089; PMCID: PMC1149411.

n. **Bourne CR**, Katen SP, Fulz MR, Packianathan C, Zlotnick A. A mutant hepatitis B virus core protein mimics inhibitors of icosahedral capsid self-assembly. Biochemistry. 2009 Mar 3;48(8):1736. PMID: 19196007; PMCID: PMC2880625.

o. **Bourne C**, Lee S, Venkataiah B, Lee A, Korba B, Finn MG, Zlotnick A. Small-molecule effectors of hepatitis B virus capsid assembly give insight into virus life cycle. J Virol. 2008 Oct;82(20):10262. PMID: 18684823; PMCID: PMC2566253.

4. **Structure and function of human antibodies:** My graduate work focused on mechanisms of protein crystal growth and their application to the structural properties of human antibodies. I participated in studies conducted on flight missions STS-95 and STS-107 to evaluate the effect of microgravity on protein crystal quality (publication p, q). Other work identified an inherent proteolytic capacity of a subset of neoplastic-derived human IgM antibodies (publications r, s, crystal structure 2agj), a revolutionary finding that is still an active area of research, for example in the Ramsland lab at RMIT, Melbourne, AU.

p. Alverado UR, **DeWitt CR**, Shultz BB, Ramsland PA, Edmundson AB. A method for growing protein crystals in capillary tubes. J Cryst Growth 2001; 233:407-414.

q. Terzyan SS, **Bourne CR**, Ramsland PA, Bourne PC, Edmundson AB. Comparison of the three-dimensional structures of a human Bence-Jones dimer crystallized on Earth and aboard US Space Shuttle Mission STS-95. J Mol Recognit. 2003 Mar-Apr;16(2):83. PMID: 12720277.

r. Ramsland PA, Upshaw JL, Shultz BB, **DeWitt CR**, Chissoe WF, Raison RL, Edmundson AB. Interconversion of different crystal forms of Fabs from human IgM cryoglobulins. J Cryst Growth 2001; 232:204-214.

s. Ramsland PA, Terzyan SS, Cloud G, **Bourne CR**, Farrugia W, Tribbick G, Geysen HM, Moomaw CR, Slaughter CA, Edmundson AB. Crystal structure of a glycosylated Fab from an IgM cryoglobulin with properties of a natural proteolytic antibody. Biochem J. 2006 May 1;395(3):473. PMID: 16422668; PMCID: PMC1462693.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/10usXwuC15FAk/bibliography/47974641/public/?sort=date&direction=descending