BIOGRAPHICAL SKETCH

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NAME	POSITION TITLE
Gira Bhabha	Assistant Professor
eRA COMMONS USER NAME (credential, e.g., agency login) gbhabha	

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

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
The University of Chicago	B.A.	09/01-06/05	Cell & Molecular Biology
The Scripps Research Institute, La Jolla, CA	Ph.D.	09/06-08/11	Structural Biology
The University of California, San Francisco	postdoc	02/12-12/16	Structural & Cell Biology

A. Personal Statement:

I have a long-standing interest in protein structure, dynamics and mechanism, and in studying how structural interactions and coordinated movements within proteins and between proteins facilitate biological function. I began my independent lab in 2017, and currently, my lab focuses on unraveling the structural basis of transport mechanisms in eukaryotic (motor proteins) and prokaryotic (lipid transport) systems. We have previously used cryo EM to characterize the mechanism by which the motor protein dynein moves along microtubules. My experience in the cytoskeleton field as well as cryo EM drive a strong interest in the collaborative project with Sabine Petry's lab to understand the structural basis of how the γ-Tubulin Ring Complex (γ-TuRC) initiates and facilitates microtubule nucleation. γ-TuRC is an ~2 MDa protein complex, well suited for single particle EM. My lab consists of five lab members, including a staff scientist, Nicolas Coudray, dedicated to single particle cryo EM data processing, and would be able to provide a good environment for this project.

B. Positions and Honors:

Positions

06/2005-05/2006	Research Assistant (full-time). Dept. Of Medicine, Section of Cardiology, The University of Chicago. Supervisor: Elizabeth McNally
06/2006-08/2011	Graduate Student (full-time). Dept. of Molecular Biology, The Scripps Research Institute. Supervisor: Peter Wright
09/2011-01/2012	Postdoc (full-time). Dept. of Molecular Biology, The Scripps Research Institute. Supervisor: Peter Wright
02/2012-12/2016	Postdoctoral Fellow (full-time). Dept. of Cellular and Molecular Pharmacology, University of California, San Francisco. Supervisor: Ron Vale
01/2017-present	Assistant Professor (full-time). Skirball Institute of Biomolecular Medicine, New York University School of Medicine.

Honors

2004	Howard Hughes Medical Institute (HHMI) Undergraduate Fellowship
2011	Travel award, IXth European Symposium of the Protein Society
2012	NIH NRSA postdoctoral fellowship (declined)

2012 Jane Coffin Childs postdoctoral fellowship (declined)
2012 Merck fellow of the Damon Runyon Cancer Research Foundation
2015 K99/R00 Pathway to Independence grant, NIH/NIGMS
2017 Damon Runyon Dale F. Frey award for breakthrough scientists
2018 Searle Scholar

Professional Societies and Public Advisory Committees
2008-2015 Faculty of 1000, Associate faculty member
2011-present Technical Consultant, “Global Online Fight Against Malaria”, World Community Grid

C. **Contributions to Science**

1. Role of protein dynamics in enzyme catalysis

Understanding the role that protein conformational changes play in enzyme catalysis is an area of intense research. Describing the dynamics of a protein in detail on many timescales can be quite feasible using NMR spectroscopy. However, assigning a role to the observed dynamics is challenging. As a graduate student, I worked with Peter Wright at The Scripps Research Insitute to study the role of protein dynamics in the model enzyme, dihydrofolate reductase (DHFR). DHFR is found in almost all cells, and reduces dihydrofolate to tetrahydrofolate (THF), most often being the sole source of THF in a cell. Much work has been done on E. coli DHFR using X-ray crystallography (Kraut and others), NMR (Wright and others) and kinetic measurements (Benkovic and others), making it a paradigm for studying catalytic mechanisms. As part of my graduate work I was able to show that conformational fluctuations on the millisecond timescale can have an important influence on the chemical step of an enzymatic reaction. In subsequent collaborative work, we harnessed recently developed methods in room temperature crystallography coupled with novel computational tools to gain further insights into how our mutant impacts *ec*DHFR catalysis. These results led to our current view: the mutation inhibits millisecond timescale conformational fluctuations that are conducive to formation of an optimal transition state configuration.

- **Bhabha G**, Lee J, Ekiert DC, Gam J, Wilson IA, Dyson HJ, Benkovic SJ, Wright PE (2011). A dynamic knockout reveals that conformational fluctuations influence the chemical step of enzyme catalysis. *Science*. 332:234-8

- van den Bedem H, **Bhabha G**, Yang K, Wright PE, Fraser JS (2013). Automated identification of functional dynamic contact networks from X-ray crystallography. *Nature Methods.* 10(9):896-902

2. Evolution of protein dynamics at an atomic level

As a graduate student, I was particularly interested in understanding how not just protein structures, but also protein dynamics have been shaped by evolution. A detailed study of human DHFR (hDHFR) revealed that both the timescale and nature of the dynamic motions (and therefore the dynamic mechanism underlying function) in hDHFR differ from that of its bacterial counterpart, E. coli DHFR (ecDHFR). A comparison of DHFRs from a number of different species revealed that although the 3-dimensional structure of DHFR is very similar across all kingdoms of life, the dynamics of the enzyme are indeed divergent. Moreover, while both the hDHFR and *ec*DHFR are highly active *in vitro*, hDHFR cannot complement an *E. coli* DHFR knockout cell. In a comprehensive analysis of available DHFR sequences, we were able to identify several keys features at the primary sequence level that dictate the dynamic mechanisms of the enzymes. Notably, we found that the sequence features that modulate DHFR dynamics are not randomly distributed across species but correlate with the position of an organism in the tree of life. Our results suggest that changes in the intracellular environment in some lineages may have driven the divergent evolution of dynamics, and thereby differences in the kinetics of ligand flux in the DHFR family (perhaps due to changes in the ratio of NADPH to $NADP^+$ between bacteria and higher eukaryotes). We were able to demonstrate that enzyme dynamics, like protein structure, are subject to evolutionary pressure and environmental influences, leading us to a model for how protein dynamics in the DHFR protein family have evolved. This work provides unprecedented and exciting new glimpses into the evolution of protein dynamics, and many novel details remain to be elucidated.

- **Bhabha G**, Ekiert DC, Jennewein M, Zmasek CM, Tuttle LM, Kroon G, Dyson HJ, Godzik A, Wilson IA, Wright PE (2013). Divergent evolution of protein conformational dynamics in dihydrofolate reductase. *Nat Struct Mol Biol.* 20 (11):1243-9

- **Bhabha G,** Tuttle L, Martinez-Yamout MA, and Wright PE (2011). Identification of endogenous ligands bound to bacterially expressed human and *E. coli* dihydrofolate reductase by 2D NMR. FEBS Lett. 585(22):3528-32

3. Mechanism of the motor protein dynein

Dynein is a large microtubule based, minus-end directed AAA motor protein that is critical for the proper functioning of most eukaryotic cells. Cytoplasmic dynein actively transport cargos and plays a role in the cell cycle. Dyneins were first discovered over 50 years ago by Ian Gibbons, and since then much work has been done on understanding dynein function. Understanding the structural basis and mechanism of dynein howver, was more challenging, due to the large size and inherent flexibility of the motor proteins. Initial breakthroughs were made by imaging axonemal dynein using negative stain EM (Burgess), and then obtaining the first crystal structures for cytoplasmic dyneins (Carter, Vale and co-workers, and Sutoh, Kon and coworkers) as recently as 2011. Beginning in 2012, my postdoctoral work focused on using hybrid methods to capture snapshots of yeast cytoplasmic dynein in different in different stages of its ATP cycle, and understand the conformational changes that correlate with its chemical cycle. In an exciting effort led together with my colleague, Hui-Chun Cheng, we were able to use X-ray crystallography, EM, biochemical and functional assays to generate a model for dynein's mechanochemical cycle, and dissect the roles of it's individual AAA domains.

- **Bhabha G**, Zhang N, Moeller A, Liao M, Speir J, Cheng Y, Vale RD, Cheng HC (2014). Allosteric communication in the dynein motor domain. *Cell.* 159(4):857-68

- **Bhabha G**, Johnson GT, Schroeder CM, Vale RD (2016). How dynein moves along microtubules. *Trends Biochem Sci*. 41(1):94-105

- Niekamp S., Coudray N., Zhang N., Vale RD and **Bhabha G** (2018). Dynein stalk length controls ATPase activity and directional movement (BioRxiv preprint)

4. Architectures of the MCE family of bacterial lipid transporters

How phospholipids are trafficked between the bacterial inner and outer membranes through the intervening hydrophilic space of the periplasm is not known. We recently discovered that members of the mammalian cell entry (MCE) protein family form structurally diverse hexameric rings and barrels with a central channel capable of mediating lipid transport. The *E. coli* MCE protein, MlaD, forms a ring as part of a larger ABC transporter complex in the inner membrane, and employs a soluble lipid-binding protein to ferry lipids between MlaD and an outer membrane protein complex. In contrast, our cryo EM structures of two other *E. coli* MCE proteins show that YebT forms an elongated tube consisting of seven stacked MCE rings, and PqiB adopts a syringe-like architecture. Both YebT and PqiB create channels of sufficient length to span the entire periplasmic space. This work has revealed for the first time the diverse architectures of highly conserved protein-based channels implicated in the transport of lipids between the inner and outer membranes of bacteria and some eukaryotic organelles. This work was a close collaboration with Damian Ekiert; we conceived the research together, I carried out cryo EM experiments, while Damian solved several crystal structures, and we discussed and analyzed data together throughout the project. This work has resulted in a plethora of questions, several of which we plan to address through a long term collaboration.

- Ekiert DC*, **Bhabha G***, Isom GL, Greenan G, Ovchinnikov S, Henderson IR, Cox JS, Vale RD. Architectures of lipid transport systems for the bacterial outer membrane. *Cell.* In Press. *Pre-print posted on BioRxiv. July 18 (2016). doi: 110.1101/064360.*

Complete list of published works:
https://www.ncbi.nlm.nih.gov/pubmed/?term=bhabha+g

D. Research Support

Ongoing Research Support Bhabha (PI) 07/01/2018 – 06/30/2021
SSP-2018-2737
Searle Scholars Program
How ballistic organelles invade host cells
The objective of this grant is to understand the mechanistic basis of how ballistic organelles, such as the polar tube from microsporidia parasites invade host cells to initiate infection.

Ongoing Research Support Bhabha (PI) 01/01/2017 – 12/31/2020
R00GM112982
NIH/NIGMS
Structure and mechanism of cytoplasmic and axonemal dyneins
The objective of this grant is twofold: first, to characterize the dynamics of cytoplasmic dynein using SAXS, single molecule light microscopy and electron microscopy, and second, to structurally characterize axonemal dyneins using cryo electron microscopy. Thus far, we have completed a comprehensive study on the stalk element of cytoplasmic dynein, which sheds light on allosteric communication in the protein. This work is currently being completed, and will be ready for publication shortly.

Ongoing Research Support Bhabha (PI) 01/01/2017 – 12/31/2019
DFS-20-16
Damon Runyon Cancer Research Foundation
High-resolution studies of dynein structure and mechanism
The goal of this project is to characterize how dynein mechanisms relate to ciliary function. Both motile and primary cilia are dependent on dynein 2 for retrograde intraflagellar transport. Motile cilia are additionally dependent on several axonemal dyneins that facilitate microtubule sliding in axonemes, which results in ciliary beating. We will use hybrid methods to address how both kinds of dyneins function in the context of cilia.

Completed Research Support Bhabha (PI) 03/01/2015 – 02/28/2016
K99GM112982
NIH/NIGMS
Structure and mechanism of cytoplasmic and axonemal dyneins
The objective of this grant is twofold: first, to characterize the dynamics of cytoplasmic dynein using SAXS, single molecule light microscopy and electron microscopy, and second, to structurally characterize axonemal dyneins using cryo electron microscopy.

Completed Research Support Bhabha (PI) 07/01/2012 – 02/28/2015
DRG-2136-12
Damon Runyon Cancer Research Foundation
High-resolution studies of dynein structure and mechanism
The goal of this project was to understand the structural mechanism of the dynein, a negative end directed microtubule based motor protein. A hybrid approach, including X-ray crystallography and cryo electron microscopy, was used to elucidate conformational changes in yeast cytoplasmic dynein as it steps along a microtubule. This work resulted in a new model and mechanistic insights into how cytoplasmic dynein works, published in *Cell* (2014).

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
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NAME: Sabine Petry

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

POSITION TITLE: Assistant Professor, Department of Molecular Biology

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
Goethe Universität Frankfurt am Main, Germany	B.S.	07/2000	Biochemistry
Goethe Universität Frankfurt am Main and Max-Planck Institute of Biophysics, Germany	M.Sc.	07/2003	Biophysics
University of Cambridge and MRC Laboratory of Molecular Biology, UK	Ph.D.	07/2007	Structural Studies
UCSF/HHMI, San Francisco, CA	Postdoc	08/2013	Cell Biology

A. Personal Statement

The mission of my lab is to understand how cells acquire their shape, position organelles, move materials, and segregate chromosomes during cell division. These features are organized by the microtubule (MT) cytoskeleton, which resembles the skeletal system that supports our human body. Its biological function relies on the precise arrangement of MTs in the cell. To achieve this organization, MTs are generated at defined locations and then organized by proteins, which sever, polymerize, shrink, bundle, anchor, or move MTs. We want to understand these functionalities mechanistically and study them by combining methods of cell biology, biochemistry, biophysics, structural biology and engineering. This will ultimately reveal how the MT cytoskeleton builds structures to support essential functions of the cell, and enable us to address malfunction of the MT cytoskeleton, which lie at the heart of many diseases involving cell proliferation and cancer.
My training in X-ray crystallography, biochemistry, cell biology and high-resolution microscopy methods is ideal to tackle these research questions via a novel, multidisciplinary approach. My lab consists of eight outstanding lab members, specifically five Ph.D. students, two post-doctoral scholars and a senior thesis student. Besides the NIH Pathways to Independence Award, I received the Pew Award for Biomedical Research, the Sidney Kimmel Award for Cancer Research, the Packard Award for Science and Engineering, and most recently the NIH New Innovator Award (DP2).

B. Positions and Honors

Positions and Employment

2013 - **Assistant Professor, Department of Molecular Biology, Princeton University** *NJ USA*
Associated Faculty Member, Department of Chemical and Biological Engineering
Associated Faculty Member, Department of Chemistry

2008-13 **Post-doctoral Fellow, University of California at San Francisco** *CA USA*
Mentor: Prof. Ronald D. Vale
Topic: Structural and Functional Analysis of Microtubule Nucleation within the Mitotic Spindle

2009-12 (Summers) Marine Biological Laboratory, Woods Hole *MA USA*
Collaborators: Prof. Timothy Mitchison (Harvard Medical School), Dr. Francois Nedelec (EMBL)
Topic: Functional Studies of the Augmin Complex in Xenopus Egg Extracts

2003-07 **Ph.D. Student, MRC Laboratory of Molecular Biology** *Cambridge, UK*
Advisor: Dr. Venki Ramakrishnan
Ph.D. Thesis: Structural Studies of the Termination of Translation

2002-03 Diploma (M.Sc.) Student, Max Planck Institute of Biophysics *Frankfurt am Main, Germany*
Advisors: Prof. Carola Hunte and Prof. Hartmut Michel. Diploma Thesis: Generation and Characterization of Single-Chain-Fv Fragments specific for the Cytochrome bc1 Complex

07 – 08/03 **World Health Organization**, Geneva, Switzerland
Summer Associate, solely responsible for the section UV Radiation in the Department for the Protection of the Human Environment

07/01 **Genoscope**, the National Sequencing Center *Evry, France*
Research Associate involved in high-throughput sequencing and genome analysis

08 – 10/00 **Max-Planck-Institute of Biophysics** *Frankfurt am Main, Germany*
Research Associate with Dr. Guenter Frisch and Prof. Dr. Hartmut Michel
Biochemical and X-ray crystallographic studies of the bacterial reaction center

07 – 08/99 **Merck KGaA** *Darmstadt, Germany*
Summer Associate in the Environmental Protection Department

Other Experience and Professional Memberships

Professional Memberships

2008 – present Member, American Society for Cell Biology
2017 – present Member, American Society for Biochemistry and Molecular Biology
2015 – present Member, American Association for the Advancement of Science
2014 – 2015 Member, American Genetics Society
2007 RNA society

Other Experience

1996 - 1998 Professional basketball player with the Aschaffenburg Wild Cats, Germany,
1998 2nd place in the 1st Federal League of Germany; participation in the 2nd European League
1997 2nd place in the 1st Federal League of Germany; 1st European League participation
1996 Oregon State Championships (Gladstone Glad Gals), 1st All Tourney & 2nd All State Teams
1996 State Champion in Shot Put, Oregon, USA
1994 – 1995 German Youth National Team, Basketball, 7th place at European Championships, Poland
1992 – 1993 German Youth National Team, Pentathlon
1992 German Champion, Pentathlon

Honors

2017 – 2019 Humboldt University – Princeton University Partnership Grant, co-PI
2016 **NIH New Innovator Award (DP2)**
2016 **Schmidt Fund Transformative Technology Award**, co-PI, Princeton University *NJ*
2015 – 2016 Innovation Award, co-PI, Department of Molecular Biology Princeton University *NJ*
2015 – 2016 Humboldt University – Princeton University Partnership Grant, co-PI
2014 – 2019 **Packard Fellowship for Science and Engineering**
2014 – 2016 **Pew Scholar in the Biomedical Sciences**
2014 – 2016 **Kimmel Scholar for Cancer Research**
2012 - 2016 **NIH Pathway to Independence Award (K99/R00)**
2009 - 2011 **Postdoctoral HHMI Fellow of the Life Science Research Foundation**
2009 Postdoctoral Fellowship of the Helen Hay Whitney Foundation (declined)
2009 Postdoctoral Fellowship of the Human Science Frontier Program (declined)
2008 **EMBO Long-term Fellowship for Postdoctoral Research**
2007 **FEBS Young Scientist Prize** for best presentation, 7th FEBS Young Scientist Forum *Vienna, Austria*
2006 Young Investigator Award for best poster and best lecture, 40th Anniversary Meeting *Spetses, Greece*

2005 **Max Perutz Student Price for Outstanding Research**, MRC Lab. of Molecular Biology *Cambridge, UK*
2003 - 2006 **Ph.D. Scholarship by Boehringer Ingelheim Fonds**
2003 - 2006 College Scholarship for University of Cambridge from Medical Research Council, *UK*
2003 World Health Organization Scholarship, Bureau for Leaders in International Organizations, *Germany*
2001 - 2003 **German National Merit Foundation / Studienstiftung des Deutschen Volkes**

C. Contributions to Science

1. Together with Venki Ramakrishnan, I solved the first crystal structures of a classical translation factor bound to the entire ribosome, work which substantially increased our knowledge of how class I release factors recognize stop codons and stimulate peptide release. Shortly after, I was part of the team that solved the high-resolution structure of the 70S ribosome complexed with mRNA and tRNA ligands. Those first structures of functional ribosomal complexes explain many aspects of protein synthesis and are important steps towards obtaining a complete picture of how translation factors drive protein synthesis in the ribosome.
    a. **Petry S**, Brodersen DE, Murphy FV IV, Dunham CM, Selmer M, Tarry MJ, Kelley AC, Ramakrishnan V (2005) Crystal structures of the ribosome in complex with release factors RF1 and RF2 bound to a cognate stop codon. **Cell** 123, 1255-1266. [Evaluated by Faculty 1000] https://DOI.org/10.1016/j.cell.2005.09.039

    b. Selmer M, Dunham CM, Murphy FV IV, Weixlbaumer A, **Petry S**, Kelley AC, Weir JR, Ramakrishnan V (2006) Structure of the 70S ribosome complexed with mRNA and tRNA. **Science** 313, 1935-1942. [Evaluated by Faculty 1000] https://DOI.org/10.1126/science.1131127

    c. **Petry S**, Weixlbaumer A, Ramakrishnan V (2008) The termination of translation. **Curr Opin Struct Biol** 18, 70-77. https://DOI.org/10.1016/j.sbi.2007.11.005

    d. Weixlbaumer A, Jin H, Neubauer C, Voorhees RM, **Petry S**, Kelley AC, Ramakrishnan V (2009) Insights into translational termination from the structure of RF2 bound to the ribosome. **Science** 322, 953-6. [Evaluated by Faculty 1000] PMCID: PMC2642913

2. Working with Ron Vale, I uncovered that a microtubule (MT) can be nucleated from the sides of a preexisting MT (branching) and identified its key players using light microscopy. Until this discovery, it was still unknown whether this process even existed in metazoan organisms or in a mitotic spindle of any organism. It explains how MTs are amplified with a defined geometry: a low branch angle and local preservation of polarity make branching MT nucleation well suited for rapid assembly of the spindle and kinetochore fibers, prerequisites for a successful cell division. Microtubule branching helps explain many unresolved aspects of how the mitotic spindle is assembled, and raises new questions about its role in building the microtubule cytoskeleton of the cell.
    a. Uehara R, Nozawa RS, Tomioka A, **Petry S**, Vale RD, Obuse C, Goshima G (2008) The augmin complex plays a critical role in spindle microtubule generation for mitotic progression and cytokinesis in human cells. **Proc Natl Acad Sci** USA 106(17):6998-7003. PMCID: PMC2668966

    b. **Petry S**, Pugieux C, Nedelec F, Vale RD (2011) Augmin promotes meiotic spindle formation and bipolarity in Xenopus egg extracts. **Proc Natl Acad Sci** USA 108(35):14473-8. PMCID: PMC3167534

    c. **Petry S**, Vale RD (2011) A new cap for kinetochore fibre minus ends. **Nat Cell Biol** 13(12):1389-91. PMCID: PMC3532025

    d. **Petry S**, Groen AC, Ishihara K, Mitchison TJ, Vale RD (2013) Branching microtubule nucleation in Xenopus egg extract mediated by augmin and TPX2. **Cell** 152, 768-777. [Evaluated by Faculty F1000] PMCID: PMC3680348

3. The goal of my lab is to understand how cells obtain their shape, position organelles, move materials, and segregate chromosomes during cell division. These essential functions rely on a specific architecture of the microtubule (MT) cytoskeleton. For instance, long and stable MTs are required in an axon, whereas short and dynamic MTs are arranged in a spindle to segregate chromosomes. Despite its central biological role, it is not well understood how such a particular MT architecture is established. My lab tackles this problem by investigating how MT nucleation is locally activated to build the MT cytoskeleton. By combining cell biology, biochemistry, biophysics, structural biology and engineering, my goal is to illuminate how the MT nucleation machinery builds cellular structures.
    a. Petry S (2016) Mechanisms of Mitotic Spindle Assembly. Annual Rev Biochem. Jun 2; 85:659-83. PMCID: PMC5016079

    b. Alfaro-Aco R, Thawani A and Petry S (2017) Structural Analysis of the Role of TPX2 in Branching Microtubule Nucleation. J Cell Biol. Apr 3;216(4):983-997. Epub 2017 Mar 6. PMCID: PMC5379942

    c. Song J, King MR, Zhang R, Kadzik R, Thawani A and Petry S (2018) Mechanism of how Augmin directly targets the γ-tubulin ring complex to microtubules. J Cell Biol 217(7):2417-2428.

    d. Thawani A, Kadzik R and Petry S (2018) XMAP215 is a microtubule nucleation factor that acts synergistically with the gamma tubulin ring complex. Nat Cell Biol 20(5):575-585.

Complete List of Published Work in MyBibliography
https://www.ncbi.nlm.nih.gov/myncbi/browse/collection/43169023/?sort=date&direction=ascending

D. Additional Information: Research Support and/or Scholastic Performance

Source: NIH (PI: Petry) ID: 1DP2GM123493-01
Title: Building the Chromosome Segregation Machinery from Scratch
Total Period: 09/30/2016 – 05/31/2021
Major Goals: The goal of this grant is to advance our understanding of chromosome segregation and its errors to a biochemical level. This will be achieved by studying individual microtubule nucleation pathways in isolation, before combining them to build the mitotic spindle and thereby elucidating its molecular organization.

Source: 2014 Pew Scholars Program in the Biomedical Sciences ID: 00027340
Title: Building the Microtubule Cytoskeleton via Microtubule Nucleation
Total Period: 8/1/14-7/31/19
Major Goals: The objective of this career award is to understand how cells obtain their shape, position organelles, move materials, and segregate chromosomes during cell division. Each of these functions relies on a specific architecture of the microtubule (MT) cytoskeleton. Yet, it is unknown how the MT nucleator gammatubulin, which is abundant in the cytoplasm, is activated at a certain time and location within the cell to generate a functional MT architecture. My overall research goal is to illuminate how the MT nucleation machinery builds cellular structures.

Source: The Lucile & David Packard Foundation ID: #2014-40376
Title: Building the Microtubule Cytoskeleton via Microtubule Nucleation
Total Period: 10/30/14-10/29/19
Major Goals: The biological function of the microtubule (MT) cytoskeleton relies on the precise arrangement of MTs in the cell. To achieve this organization, MTs are generated at defined locations and then organized by proteins, which sever, polymerize, shrink, bundle, anchor, or move MTs. We want to understand these functionalities mechanistically and study them by combining methods of cell biology, biochemistry, biophysics, structural biology and engineering. This will ultimately reveal how the MT cytoskeleton builds structures to support essential functions of the cell, and enable us to address malfunction of the MT cytoskeleton, which lie at the heart of many diseases involving cell proliferation and cancer.

Source: Princeton University E&W Schmidt Transformative Technology Fund (PIs: Shaevitz, Petry, and Yang)
Title: Princeton University E&W Schmidt Transformative Technology Fund
Total Period: 05/19/2016 – 04/18/2020
Major Goals: To design and build a new type of microscope that can view a living cell's interior in 3-D while simultaneously allowing investigators to manipulate chromosomes and other internal structures in ways that were previously impossible.

Source: Princeton University Molecular Biology Innovation Fund
Title: Segregating Chromosomes in vitro using Optical Tweezers
Total Period: 03/1/2015 – 2/28/2018
Major Goals: The faithful segregation of genetic material between dividing cells is of critical for sustaining life. It relies on finding and aligning chromosomes, before segregating them into the two daughter cells. The goal of this proposal is to study how chromosomes are segregated. This will help explain how cells divide and thus procreate life, and may provide new treatments for diseases that lie at the heart of cell proliferation, such as cancer and cell regeneration.

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: **Nicolas Coudray**

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

POSITION TITLE: **Research Scientist**

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 Haute-Alsace, Mulhouse, France	**B.Eng.**	**06/2003**	**Electrical Engineering, Electronics and Automatism**
University of Haute-Alsace, Mulhouse, France & Concordia University, Montréal, Canada.	**Master**	**06/2004**	
University of Haute-Alsace, Mulhouse, France	**DEA (MPhil equivalent)**	**06/2005**	**Automatism & Image Processing**
	PhD	**11/2008**	**Image Processing**

A. Personal Statement

As a research scientist in the Skirball Institute of Biomolecular Medicine (Bhabha Lab), I am also working on the resolution of the 3D structure of proteins using single particles. Among those are YebT and MlaFEDB, proteins involved in the trafficking of lipids between the bacterial inner and outer membranes, contributing to their resistance to antibiotics. As part of the Bhabha lab, I also interface with collaborators at Princeton, UCSF and Rockefeller University.

As an Image Processing Scientist in the Applied Bioinformatics Laboratories, I am currently working on the development of deep-learning tools for the processing of biomedical images. My main projects include the analysis of Histopathology images of lung cancer and of melanoma. For the analysis lung cancer, the current toolchain is able to automatically identify the sub-type with accuracy slightly better than the one of a pathologist. Furthermore, mutations can be predicted solely from the images, offering a fast and new way to identify important gene mutations. Similar study applied to the analysis of melanoma metastasis in lymph nodes have shown that we can also predict the response to a certain treatment by proper training of histopathology image analysis.

From 2010 to 2016, I have been participating in the development, maintenance and supervision of a high-throughput toolchain within the TEMIMPS consortium. This consortium was dedicated to the development of tools for the structure determination of a variety of membrane protein targets. In particular, we have developed a pipeline that includes two-dimensional crystallization of membrane proteins, electron cryo-microscopy and image analysis to achieve this goal. Over 10 technologies have been submitted to the PSI technology portal. We have planned, set and coordinated crystallization screening projects of more than 50 proteins and thanks to novel screening strategies, over 10 proteins have given crystalline hits, most of them forming helical crystals. The structure of two of those crystals have been published so far: yiiP, a zinc transporter, and Bor1p, a boron transporter.

Previously, I have been working on the HT-3DEM (High Throughput Three Dimensional Electron Microscope) project as a PhD student first, and then as a Research Associate in the MIPS Laboratory, at the University of Haute Alsace, France. During this project, an automated platform has been successfully developed to enable high throughput screening and analysis of native protein complexes and protein crystals by electron microscopy. I have been mainly working on the automation of the microscope through the development of

image processing algorithms, and through this project (granted by the European Union), I had the opportunity to collaborate with prestigious collaborators working in the fields of microscopy and of membrane proteins research. During these years, I have also been participating in discussions, milestones, progress reports and collaborative work processes.

B. Positions and Honors

Positions and Employment

2017-current Senior Bioinformatics Programmer & Image Analysis Specialist at NYU, New York, USA
2015-03/2017 Associate research scientist at NYU
2010-2014 Post-doc, project Manager at NYSBC, New York, USA
2010-2010 Post-doctoral fellow, at the C-CINA, University of Basel, Basel, Switzerland
2008-2010 Research and Teaching Associate, in the MIPS laboratory
2005-2008 PhD in the MIPS laboratory, TROP Group, UHA
and Supply Teacher (Master level, UHA)
2004-2005 DEA (MPhil equivalent) internship in the MIPS laboratory, LabEl Group, University of Haute-Alsace (UHA), Mulhouse, France

C. Contribution to Science

1. *Deep-learning tools for the analysis of biomedical images* – I established in our Lab the use of deep-learning for biomedical images, developing a toolchain (github.com/ncoudray/DeepPATH) trained on several projects. Deep-learning architectures are able to process a high number of images, extract and sort highly complex information from them. We have shown proper training of these tools not only lead to performances better or equivalent to pathologists on sub-type classification of cancer, but it can also extract information such as mutation status that pathologists cannot distinguish without the help of such a tool.

a. Classification and Mutation Prediction from Non-Small Cell Lung Cancer Histopathology Images using Deep Learning. *N. Coudray, A. L. Moreira, T. Sakellaropoulos, S. Fenyo, N. Razavian, A. Tsirigos*. bioRxiv (2018). Nature Medicine.

2. *Development of high-throughput crystallization tools* - During the first project dedicated to the development of High-Throughput technologies for 2D-crystals, I actively participated in the creation of a Matlab-based toolbox called ANIMATED-TEM. It includes several image processing tools dedicated to the analysis of protein crystals acquired with a transmission electron microscope (TEM) equipped with 96-grid autoloader. These tools allowed to successfully automate the acquisition of images of crystals from a 2D crystallization trials, allowing the TEM to target regions of interest, analyze them and create a database of images which permits the characterization of an experiment.

b. Automated Screening of 2D Crystallization Trials Using Transmission Electron Microscopy: A High-Throughput Tool-Chain for Sample Preparation and Microscopic Analysis*. N. Coudray, G. Hermann, D. Caujolle-Bert, A. Karathanou, F. Erne-Brand, J.-L. Buessler, P.Daum, J. Plitzko, M. Chami, U. Mueller, H. Kihl, J.-P. Urban, A. Engel, H.-W. Rémigy*. Journal of Structural Biology, Feb 2011, 173(2), pp 365-374
c. ANIMATED-TEM: a toolbox for electron microscope automation based on image analysis. *G. Hermann, N. Coudray, J.-L. Buessler, D. Caujolle-Bert, H.-W. Rémigy, J.-P. Urban*. Machine Vision and Applications, July 2011, pp 1-21

3. *Growing new crystals using novel high-throughput 2D crystallization tools and strategies* - Automated tools and screening strategies were improved as we designed a sparse and an incomplete factorial matrix to cover a wide range of factors which appeared to be successful in the literature. Combining high-throughput tools with these new screening strategies proved to accelerate considerably the success rate of membrane protein crystallization. Several tubular crystals are in the different stages of the pipelines: some need to be improved, other are ready for cryo-imaging and 3D reconstruction.

a. Sparse and incomplete factorial matrices to screen membrane protein 2D crystallization. *R.Lasala, N.Coudray, A.Abdine, A.Zhang, M.Lopez-Redondo, R.Kirshenbbaum, J.Alexopoulos, Z.Zolnai, D.Stokes, I.Ubarretxena.* Journal of Structural Biology, 2015, vol. 189(2), pp 123-134

4. *Analysis of Helical crystals* - The tubular crystals of yiiP, a zinc transporter, have been used to achieve a 3D reconstruction of the protein. To achieve the reconstruction, we used both the traditional Fourier-Bessel method and the IHRSR method recently developed by Pawel Penczek. Our 13 Å model published in 2013, in an inward-facing conformation, shows a conformation change relative to the 3X-ray structure, a change which reflects the alternating access mechanism of transport. We have acquired images acquired on a direct-electron camera and increased the resolution to ~4 Å (manuscript in preparation).

I have also been working on helical crystals of Borp, a borate transporter, solving the structure at ~7 Å. To achieve the indexing of those helical crystals, we have developed new techniques to validate that step and could be beneficial for other types of helical crystals

a. Inward-facing conformation of the zinc transporter YiiP revealed by cryoelectron microscopy. *N. Coudray, S. Valvo, M. Hu, R. Lasala, C. Kim, M. Vink, M. Zhou, D. Provasi, M. Filizola, J. Tao, J. Fang, P.A. Penczek, I. Ubarretxena-Belandia, D.L. Stokes.* Proceedings of the National Academy of Sciences of the United States of America, 2013, vol. 110(1), pp 2140-2145
b. Structure of the SLC4 transporter Bor1p in an inward-facing conformation. Coudray, *N., Seyler, S., Lasala, R., Zhang, Z., Clark, K.M., Dumont, M., Rohou, A., I., Beckstein, O., Stokes, D.L.*. Protein Science, 2017, 26(1) pp130-145
c. Deducing the symmetry of helical assemblies: Applications to membrane proteins. *Coudray, N. Lasala, R., Zhang, Z. Clark, K. Dumont, M., Stokes D.* Journal of Structural Biology, 2016, vol. 195(2), pp 167-178

Complete List of Published Work:

http://www.scopus.com/authid/detail.url?authorId=23492220900

D. Research Support

Completed Research Supports

U54 GM094598 S.Stokes (PI) 09/30/2010-06/30/2015
Transcontinental EM Initiative for Membrane Protein Structure
The goal was to apply high-throughput methods to 2D crystallization and to modernize the methods for structure determination.
Role: Project manager

FP6-Lifescihealth 1881 A.Engel 10/01/2005-09/30/2008
Founded by the European Union, an automated platform was developed to enable high throughput screening and analysis of native protein complexes and two-dimensional membrane protein crystals by Electron Microscopy.
Role: PhD Student

BIOGRAPHICAL SKETCH

NAME: Brian Patrick Mahon

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

POSITION TITLE: Postdoctoral Research Associate

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)*	Start Date MM/YYYY	Completion Date MM/YYYY	FIELD OF STUDY
Wesley College	B.S.	08/2006	05/2011	Biological Chemistry
University of Florida	Ph.D.	08/2012	05/2016	Biomedical Sciences
NIDDK/NIH		08/2016	12/2017	Biophysics
Princeton University		02/2018	Current	Structural Biology

A. Personal Statement

My career goal is to become a principle investigator (PI) in at an academic institution where I can contribute to the progression of science and provide valuable mentoring to students and trainees. My long-term research goals are to understand the dynamic structures and functions of large multi-subunit cytoskeletal protein complexes that govern specific cellular processes important for sustaining life. My previous academic training and research, will provide me the necessary background to develop a research program that combines advanced structural biology techniques in single-particle cryo-EM and X-ray crystallography, with advanced light microscopy and biochemical assays to decipher structure-function relationships of these cytoskeletal proteins. As an undergraduate I worked in the lab of Dr. Malcolm D'Souza and used chemical kinetics to understanding reaction mechanisms of thioester solvolysis. I determined the influence of functional group diversity on solvolytic mechanism of these compounds which resulted in 3 co-authored publications. From here, I spent 1 year at the pharmaceutical company Merck, where I learned to express, purify and biochemically characterize proteins. I also identified novel inhibitors for several enzyme drug targets and received good-manufacturing practices (GMP) training. I completed my doctoral training with Dr. Robert McKenna and applied my knowledge of protein chemistry and enzymology to understand structure-function relationships of several enzymes, such as carbonic anhydrase (CA) and HIV-1 protease for medical applications. Here, I gained expertise in X-ray crystallography, mass spectroscopy, small-angle X-ray scattering, and *in silico* modeling. My doctoral work was highly successful with 10 first-author and 6 co-author publications, 6 reviews and book chapters, several conference presentations, and a number of awards. After graduating, I joined the NIDDK/NIH Laboratory of Chemical Physics as an IRTA Postdoctoral Fellow in the lab of Dr. Philip Anfinrud. Here, I was able to build on my previous experiences and learn methods to study structural dynamics of proteins. This included time-resolved X-ray diffraction and scattering (TRXD and TRXS, respectively) techniques, and microfluidics instrumentation development for synchrotrons and X-ray free electron lasers (XFEL). In addition, in collaboration with Dr. Alexandra Lucas at Arizona State University I was able to use my background in X-ray crystallography to determine the structure of the serpin from *Myxomavirus*, Serp-1. This work resulted in a first-author publication, a review, and a book chapter. After a successful year at the NIH/NIDDK, I joined Dr. Sabine Petry's lab at Princeton University, where I will apply all of my previous experiences to develop an atomic level understanding of the molecules of the cytoskeleton. Dr. Petry is an expert in molecular imaging and the cell division field, with a lab uniquely equipped to directly study cytoskeletal processes at both the molecular and cellular level. Here, I am able to hone in my skill sets as a structural biologist and transition to an independent role. From the skills and mentoring gained in Dr. Petry's lab, I will be able to reach my career goal and construct a research platform that links molecular structure to cellular function with the ultimate goal of understanding biology at the most fundamental level.

B. Positions and Honors

Positions and Employment

2008-2011	Undergraduate Research Assistant (Wesley College)
2011	Summer Research Intern (Merck & Co.)
2011-2012	Chemist II (contractor) (Joulè Scientific/Merck & Co.)
2012	Summer Research Intern (Merck & Co.)
2012-2016	Graduate Research Assistant/Doctoral Candidate (University of Florida)
2015	Teaching Assistant (University of Florida)
2016-2017	IRTA Postdoctoral Fellow (NIDDK/NIH)
2018-	Prison Teaching Initiative – Instructor for BIO 111: Introduction to Biology
2018-	Postdoctoral Research Associate (Princeton University)
2018-	Instructor for Molecular Biology Junior Tutorials Course (Princeton University)

Other Experience and Professional Membership

2010-2011	Wesley College Society Member (2010 – 2011)
2010	Spring, Volunteer, Kids in Chemistry Outreach Program
2011-2012	Current Good Manufacturing Practices (cGMP) Training
2012	Volunteer Instructor, Cade Museum for Creativity and Invention
2012-2016	Student mentor - seven undergraduate and three high school students (University of Florida)
2014-2016	American Chemical Society (ACS) Member
2014-2017	American Crystallographic Association (ACA) Member
2015-2016	Graduate Student Officers – College of Medicine (University of Florida)
2017	'Scientist Teaching Science' Workshop – Office of Intramural Training & Education (FAES/NIH)
2017	'Summer Science Skills Bootcamp' – Office of Intramural Training & Education (FAES/NIH)
2017	Guest Lecturer for Montgomery College (MD) Intro to Biotechnology Course
2018	Molecular Biology Departmental Retreat – Poster presentation (Princeton University)

Honors

2010	Moor's Music Award (Wesley College)
2010	Alumni Scholarship (Wesley College)
2010	Theodore O'Brien Award (Wesley College)
2011	Award for Excellence in Biological Chemistry (Wesley College)
2011	Student Award in Environmental Chemistry (ACS)
2011	Posters on the Hill (Council on Undergraduate Research)
2012	Graduate School Fellowship, (University of Florida)
2014	Margaret C. Etter Student Lecturer Award, Young Scientist (ACA)
2014, 2015	Conference Travel Awards (ACA)
2015	Medical Guild Advancement to Candidacy Award (University of Florida)
2015	Margaret C. Etter Student Lecturer Award, Industrial Section (ACA)
2015	GSAC Graduate Student Mentoring Award (University of Florida)
2016	Richard Boyce Award for Graduate Research in Biochemistry (University of Florida)
2016	Medical Guild Graduate Student Competitions – 1st Place (University of Florida)
2017	Intramural AIDS Research Fellowship Recipient – Office of AIDS Research (NIH)

C. Contributions to Science

1. Early Career: My early career contributions are divided between my undergraduate and post-baccalureate careers. As an undergraduate, I worked in the lab of Dr. Malcolm D'Souza. Our research focused on characterizing solvolytic mechanisms of thiol- and thionocarbonyl ester compounds to be used in drug synthesis. We proved that the addition of "bulkier" chemical groups to these compounds resulted in a shift in their solvolytic mechanism. In addition, we were able to suggest a unique substitution mechanism for some compounds. My role in these experiments was to analyze kinetic data and using linear-free energy relationships, propose a mechanism for solvolysis for several compounds. After graduation, I joined Merck Research Laboratories (MRL) as a summer intern in 2011 under the direction of Dr. Brian Beyer in the *In vitro* Pharmacology department. My project focused on the biochemical and biophysical characterizations of β-secretase isoforms I and II (BACE I & II), established drug targets for Alzhemier's Disease. I used assays to measure enzyme maturation and activity and identified potent inhibitors. Since the compounds being used were proprietary, results could only be summarized internally within the company. From here, I transitioned to Dr. Steve Liang's group in the Analytical Chemistry in Development and Supply department (ACDS), where I

developed methods validated Standard Operating Procedures (SOPs) used for testing physical and chemical properties of clinically approved drugs such as Zontivity™ (vorapaxar) and ELOCON®. Next, I rejoined Dr. Beyer's group in MRL and completed a project focused on the expression, purification, and screening of isoforms of β-lactamase that are linked to antibiotic resistance.

Research Papers

a. Kyong, J. B., Lee, Y., D'Souza, M. J., **Mahon, B.P**., and Kevill, D. N. (2012) Correlation of the rates of solvolysis of tert-butyl chlorothioformate and observations concerning the reaction mechanism. *Eur. J. Chem*. 3, 267–272. doi: http://dx.doi.org/10.5155/eurjchem.3.3.267-272.624
b. D'Souza, M.J., Hailey, S., **Mahon, B.P.,** and Kevill, D. (2011) Understanding Solvent Effects in the Solvolyses of 4-Fluorophenyl Chlorothionoformate. *Chem. Sci. J*. PMCID: PMC3172719
c. D'Souza, M.J., **Mahon, B.P.,** and Kevill, D. N. (2010) Analysis of the nucleophilic solvation effects in isopropyl chlorothioformate solvolysis. *Int. J. Mol. Sci*. 11, 2597–2611. doi:10.3390/ijms11072597.

Abstracts and Presentations

a. **Mahon, B.P.,** McAneny, M.J., and D'Souza, M.J. "Analysis of Sulfur Containing Intermediates for Potential Drug-Candidates to Treat Many Diseases", Council on Undergraduate Research: Posters on the Hill, Washington, D.C. (2011)
b. **Mahon, B.P.,** D'Souza, M.J., and Kevill, D.N. "Insights into the Solvolytic Mechanism of Aklyl Thiolesters", 240th National ACS Meeting, Anaheim, CA (2011)
c. **Mahon B.P.,** McAneny, M.J., Hailey, S.M., and D'Souza, M.J. "Understanding Solvent Effects on Akyl Thioesters", Third Biennial National IDeA Symposium of Biomedical Research Excellence (NISBRE), Bethesda, MD (2010).
d. **Mahon, B.P.,** Hailey, S.M., D'Souza, M.J., and Kevill, D.N. "The importance of Linear Free Energy Relationships (LFER) in Studying Solvolytic Behavior in Thio- and Thionocarbonyl Esters", 239th National ACS Meeting, San Francisco, CA (2010).
e. **Mahon, B.P.,** D'Souza, M.J., and Kevill, D.N. "Correlation of the Rates of Solvolysis of Isopropyl Chlorothioformate", 237th National ACS Meeting, Salt Lake City, UT (2009)
f. **Mahon, B.P.,** Reed, D.N., D'Souza, M.J., and Kevill, D.N., "Solvolytic Reactions of Thiolesters", Undergraduate Summer Research Symposium, University of Delaware, Newark, DE (2008).

2. Graduate Career: In the lab of Robert McKenna, I worked on several projects focusing on CA. The majority of my work was using a structure-guided approach to design inhibitors against CA isoform IX (CA IX), an established cancer target. CA IX is highly homologous to other human CAs (especially isoform II), so identifying inhibitors that selective target the enzyme has been challenging. In addition, wild-type CA IX is notoriously difficult to crystallize so for a majority of the studies I utilized a variant of CA isoform II that "mimicked" CA IX. Results from these studies achieved several hallmarks in the field of CA IX inhibitor design. This includes the identification of carbohydrates and carbohydrate-based inhibitors as compounds that preferential bind to CA IX, and the "mapping" of key active site residues that are responsible for isoform selective inhibition amongst human CAs. In addition, I have performed work that has identified the common artificial sweetener, saccharin, as a potential lead compound for CA IX inhibitor design. This work led to me receiving an award from the American Crystallographic Association and has been highlighted several news outlets including *Yahoo News, Fox News,* and *National Geographic* among others. Aside from this, I have also engineered a form of wild-type CA IX that is more easily crystallized. As a result, I was able to determine the first high-resolution structure of wild-type CA IX that reveals features of its active site that can be correlated to its catalytic mechanism (PDB ID: 5DVX).

Research Papers

a. **Mahon, B. P.,** Bhatt, A., Socorro, L., Driscoll, J.M., Okoh, C., Lomelino, C.L., Mboge, M.Y., Kurian, J., Tu, C., Frost, S.C., and McKenna, R. The structure of carbonic anhydrase IX is adapted for low-pH catalysis. *Biochemistry*. 2016 Aug 23;55(33): 4642-53. DOI: 10.1021/acs.biochem.6b00243.
b. **Mahon, B.P.**, Lomelino, C.L., Moeker, J., Driscoll, J.M., Salguero, A.L., Pinard, M.A., Vullo, D., Supuran, C.T., Poulsen, S.A., McKenna, R., (2015) Mapping Selective Inhibition of the Cancer-Related Carbonic Anhydrase IX using Structure-Activity Relationships of Glucosyl-Based Sulfamates. *J. Med Chem.*2015 Aug 27;58(16): 6630-8. DOI: 10.1021/acs.jmedchem.5b00845

c. **Mahon, B.P.,** Lomelino, C.L., Salguero, S.L., Driscoll, J.M., Pinard, M.A., McKenna, R. (2015) Observed Surface Lysine Acetylation of Human Carbonic Anhydrase II Expressed in Escherichia Coli. *Protein Science*. 2015 Nov;24(11): 1800-7. doi: 10.1002/pro.2771

d. Pinard, M.A., Aggarwal, M., **Mahon, B.P.**, Tu, C., McKenna, R., (2015) Sucrose binding site provides lead towards an isoform specific inhibitor for the cancer associated enzyme carbonic anhydrase IX. *Acta Crystallogr. F. Struc. Biol. Commun*., 71 (10) DOI: 10.1107/S2053230X1501239X

e. **Mahon, B.P.,** Driscoll, J.M, Hendon, A.M., Poulsen, S., Supuran, C.T., and McKenna, R., (2014) Saccharin: a Lead Compound for Structure-Based Drug Design of Carbonic Anhydrase IX Inhibitors. *Bioorg. Med. Chem*. 2015 Feb 15;23(4):849-54. doi: 10.1016/j.bmc.2014.12.030.
f. Moeker, J., **Mahon, B.P.**, Bornaghi, L.F., Vullo, D., Supuran, C.T., McKenna, R., Poulsen, S.A. (2014) Structural Insights into Carbonic Anhydrase IX Isoform Specificity of Carbohydrate-Based Sulfamates. *J. Med. Chem*. Oct 23;57(20):8635-45. doi: 10.1021/jm5012935.

Reviews

a. **Mahon, B.P.,** Okoh, C., McKenna, R., (2015) Targeting Aggressive Cancers with an Artificial Sweetner: Can Saccharin be a Lead Compound in Anticancer Therapy? *Expert Opinion* Front. Oncol. 15, 2117-2119. doi: 10.2217/fon.15.137.
b. **Mahon, B.P.,** Pinard, M.A., and McKenna, R. (2015) Targeting Carbonic Anhydrase IX Expression and Activity. *Molecules.* Jan 30;20(2):2323-2348.
c. Pinard, M.A., **Mahon, B.P**., and McKenna, R. (2014) Probing the Surface of Human Carbonic Anhydrase for Clues towards Designing Isoform Specific Inhibitors. *BioMed Res. Int*. Article ID 453543 1-15.

Conference Abstracts

a. **Mahon B. P.,** Bennett, A., Tondnevis, F., Socorro, L., Driscoll, J.M., and McKenna, R., "High Resolution Crystal Structure of the Cancer-Associated Carbonic Anhydrase IX," American Crystallographic Association, Philadelphia, PA (2015). *Student Lecturer Award, Industrial (YSSIG)*
b. **Mahon, B.P.,** Ladwig, J., Driscoll, J.M., Bornaghi, L., Vullo, D., Poulsen, S.A., Supuran, C.T., McKenna, R., "Isoform selective inhibition of tumor-associated carbonic anhydrase IX using carbohydrate-based sulfamates for the treatment of several cancers," 249th National ACS Meeting, Denver, CO (2015).
c. **Mahon, B.P.,** Hendon, A.M., Driscoll, J.M., and McKenna, R. "Saccharin as a Potential Lead Compound for Anti-cancer Targeting of Carbonic Anhydrase IX", American Crystallographic Association, Albuquerque, NM (2014). *Student Lecturer Award, Young Scientist (YSSIG).*

3. Postdoctoral Career: In the lab of Dr. Philip Anfinrud, At the NIH/NIDDK, my project focused on developing and optimizing a microfluidics system that could be used for protein crystallization and sample delivery during TRXD data collection. In addition, I designed TRXD and TRXS experiments to capture structural intermediates of enzyme reactions of HIV-1 protease and RNase, and temperature dependent changes of the protein cyclophilin A. This required, optimizing sample preparation, developing software and delivery schemes for data collection and analysis. From here, I engineering and designed microfluidics devices for crystal growth and delivery for data collection (In preparation). Also, I worked on several side projects. Here, I lead a study, in collaboration with Dr. Alexandra Lucas, that focused on the structural determination of the serine-protease inhibitor I from Myxomavirus (Serp-1), which is a clinically for severe inflammation. From the structure of Serp-1 we rationally designed peptides that "mimicked" parts of the protein responsible for its therapeutic effect. We were able to identify three peptides that display similar behavior to the full-length protein when tested *in vivo*.

Research Paper

Mahon, B. P., Ambadapadi, S., Taron, J., Lomelino, C.L., Pinard, M., Keinan, S., Kurnikov, I., Colin, M., Liqiang, Z., Reeves, W., McFadden G., Tibbets, S., McKenna, R., and Lucas, A.R. Crystal Structure of Cleaved Serp-1, a Myxomavirus-derived Immune Modulating Serpin; Structural Design of Serpin Reactive Center Loop (RCL). *Biochemistry*. 2018 Dec 11;57(7): 1096-1107. doi: 10.1021/acs.biochem.7b01171.

Review

Lucas, A.R., Ambadapadi, S., **Mahon, B.P**., Viswanathan, K., Chen, H., Liu, L., Dai, E., Munuswami-Ramanujam, G., Kwiecien, J.M., Yaron, J., Narute, P.S., McKenna, R., Keinan, S., Reeves, W., Brantly, M., Pepine, C., and McFadden, G. *J. Clin. Exp. Cardiolog.* 8:e150.doi:10.4172/2155-9880.1000e150**.**

Book Chapter

Mahon, B. P., and McKenna, R. (2018) Chapter 2: Methods for determining and understanding serpin structure and function: X-ray crystallography: Methods and Protocols. In Lucas, A. (Eds.), *Methods in Molecular Biology: Serpins,* Springer, 2018, ISBN: 978-1-4939-8645-3. DOI: 10.1007/978-1-4939-8645-3_2.

Conference Abstract

Mahon B. P.,Cho, H.S., Schotte, F., Anfinrud, P.A. “A Microfluidics-based Approach for Time-resolved Serial Crystallography,” American Crystallographic Association, New Orleans, LA (2017).

Complete List of published work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/1vyEntOks_IAh/bibliography/48756067/public/?sort=date&direction=ascending