BIOGRAPHICAL SKETCH

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NAME: Darst, Seth A.

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

POSITION TITLE: Professor, Head of Laboratory

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 Colorado, Boulder, CO	B.S.	06/1982	Chemical Engineering
Stanford University, Stanford, CA	M.S.	06/1984	Chemical Engineering
Stanford University, Stanford, CA	Ph.D.	06/1987	Chemical Engineering
Stanford University, Stanford, CA	Postdocoral	06/1987 – 09/1993	Structural Biology

Please refer to the Biographical Sketch sample in order to complete sections A, B, C, and D of the Biographical Sketch.

A. Personal Statement

I obtained rigorous training in quantitative approaches with a B.S. and Ph.D. in chemical engineering. In my Ph.D., I specialized in biochemical engineering but came to realize I was more interested in science rather than engineering. I therefore undertook a postdoc in the laboratory of Roger D. Kornberg, where I began my training as a biochemist and structural biologist and developed an obsession with the process of transcription. There, I contributed to the development of novel approaches to produce two-dimensional crystals of macromolecular complexes suitable for electron microscopy analysis (at the time, obtaining three-dimensional crystals of RNA polymerase suitable for X-ray crystallography seemed impossible), generated the first two-dimensional crystals of cellular RNA polymerases (1, 2), and used electron microscopy methods to determine the first low-resolution structures of RNA polymerases (RNAPs). I also showed that RNAP could grow three-dimensional crystals, setting the stage for future advances in RNAP structural biology. I established my own group at The Rockefeller University in 1992, focusing almost exclusively on bacterial transcription due to the relative simplicity of the bacterial system despite high structural and functional homology with eukaryotic RNAPs. Initially, we continued to use electron microscopy, but in 1999 we established the first high-resolution structure of a cellular RNAP by X-ray crystallography. Since then, my group has made many key contributions, including determining the structural mechanism for rifampicin inhibition of RNAP, structures of RNAP holoenzyme alone and bound to promoter DNA, determining the structural mechanism for σ factor function, and determining the structural basis for the regulation of RNAP by accessory factors. Thus, I played a major role in establishing the field of RNAP structural biology, and my group has a long standing record of commitment to this field and to solving challenging problems.

During my postdoc and initial years at The Rockefeller University, electron microscopy provided the only structural information on cellular RNAPs (low-resolution) until 1999 when X-ray crystallography became the primary method of choice. In 2010, my group completely stopped using electron microscopy. Nevertheless, the fact that X-ray crystallography requires the analysis of samples prepared as high-quality three-dimensional crystals imposes many challenges to producing structures as well as interpreting them (due to crystal packing effects). Advances in direct electron detectors and image processing have revolutionized structural biology, opening up new avenues for high-resolution structural analysis of macromolecular complexes by electron

microscopy that do not require crystallization. We are now using these new approaches in combination with X-ray crystallography, biochemical, biophysical, and genetic approaches, to provide unprecedented insight into the structure, function, and regulation of the bacterial transcription cycle (3, 4).

During this COVID-19 pandemic, a small sub-group of my laboratory is using our expertise in biochemistry and structural biology of nucleic acid polymerases to study the COVID-19 replicase/transcriptase complexes.

Since establishing my laboratory at The Rockefeller University 27 years ago, I have mentored 16 Postdocs (currently in the following positions: 1 M.D., 10 Profs., 13 in academics, 2 in industry) and 7 Graduate Students (currently: 1 M.D., 2 Profs., 5 in academics, 1 in industry, 1 practicing lawyer, 2 school teachers). Through the Rockefeller Summer Undergraduate Research Program, we have hosted roughly on average two undergraduates in the laboratory every summer, for a total of more than 50 undergraduates – most of these have gone on to graduate school (not necessarily at Rockefeller) and further academic careers, and 7 have co-authored manuscripts from our laboratory. I have also mentored (often with members of my group) 7 SMART teams (Students Modeling A Research Topic; http://cbm.msoe.edu/smartTeams/), teams of high school students and their teachers who work with research scientists to design and construct 3D physical models of the proteins being investigated in their laboratories.

1. **Darst SA**, Ribi HO, Pierce DW, Kornberg RD (1988) Two-dimensional Crystals of *Escherichia coli* RNA Polymerase Holoenzyme on Positively Charged Lipid Layers, *J. Mol. Biol.* **203**, 269-273.
2. Edwards AM, **Darst SA**, Feaver WJ, Thompson NE, Burgess RR, Kornberg RD (1990) Purification and Lipid Layer Crystallization of Yeast RNA Polymerase II, *Proc. Natl. Acad. Sci. USA* **87**, 2122-2126.
3. Kang JY, Mooney RA, Nedialkov Y, Saba J, Mishanina TV, Artsimovitch I, Landick R, **Darst SA** (2018) Structural basis for transcript elongation control by NusG/RfaH universal regulators, *Cell* **173**, 1650-1662.e14 (PMCID: PMC6003885].
4. Boyaci H, Chen J, Jansen R, **Darst SA**, Campbell EA (2019) Structures of an RNA polymerase promoter melting intermediate elucidate DNA unwinding, *Nature* **565**, 382-385 [PMCID: PMC6399747]

B. Positions and Honors

1982-1987	Graduate Student with Channing R. Robertson, Department of Chemical Engineering, Stanford University, Stanford, CA
1987-1990	American Cancer Society Postdoctoral Fellow with Roger D. Kornberg, Department of Cell Biology, Stanford University, Stanford, CA
1990-1992	Lucille P. Markey Postdoctoral Scholar with Roger D. Kornberg, Department of Cell Biology, Stanford University, Stanford, CA
1992-1997	Assistant Professor, Head of Laboratory, The Rockefeller University, New York, NY
1997-2000	Associate Professor, Head of Laboratory, The Rockefeller University, New York, NY
2000-	Professor, The Rockefeller University, New York, NY

Honors

Undergraduate

1980	Dean's Club Fellow
1981	Giroux Fellow
1982-1983	Chevron Fellow
1983-1987	Kodak Fellow

Postdoctoral

1987-1990	American Cancer Society Postdoctoral Fellow

Postdoctoral & PI

1990-1996	Lucille P. Markey Award in Biomedical Science

PI

1994-1999	Career Scientist of the Irma T. Hirschl Charitable Trust
1995-1999	Pew Scholar in the Biomedical Sciences
2008	American Academy of Microbiology Fellow
	National Academy of Sciences Fellow

Service (selected)

1997	NIH BBCB study section, *ad hoc*
1998	NIH special review panels (served on two separate panels)
2000	NIH BBCA study section, *ad hoc*
	NIH special review panel
2001	NSLS PSP review panel
	NIH special review panel
2002	NSLS PSP review panel, chair
	NIH PB study section, *ad hoc*
	NIH special review panel (served on four separate panels)
2003	APS reviewer
	NIH special review panel
	NIH MBC2 study section, *ad hoc*
	NIH BBCA study section, *ad hoc*
2004	APS reviewer
	NIH transcription cluster review panel
	NIH study section for members
2005	NIH BBCA study section, *ad hoc*
	Co-chair, 2005 FASEB Summer Research Conference – Mechanisms and Regulation of Prokaryotic Transcription
2005-2018	APS SBC Scientific Advisory Committee
2006	NIH NRSA study section, *ad hoc*
	Chair, 2007 FASEB Summer Research Conference – Mechanisms and Regulation of Prokaryotic Transcription
2008	NIH MSFC study section, *ad hoc*
2009	NIH BCMB study section, *ad hoc*
2010	NIH special review panel
2011	NCI PO1 review panel
	NIH MSFC study section, *ad hoc*
	NIH ZRG1 MSFC-K(02)S panel
2012–2016	MSFC study section, standing member
	NSLS II AMX/FMX beamline advisory team
2017	NIH K99 review panel
	NIH Review panel for Regional Consortia for High Resolution Cryoelectron Microscopy (U24) applications
2018	NIH ZRG1 BST-T(40) review panel
	NIH ZRG1 CB B55 (MIRA) review panel

Frequent reviewer for: *Cell*, *Elife*, *J. Mol. Biol., Mol. Cell*, *Nature*, *Nature Chem. Biol.*, *Nature Com., Nature Struct. Mol. Biol.*, *Nucleic Acids Research*, *Proc. Natl. Acad. Sci. U.S.A.*, *Science*.

C. Contribution to Science

1. As a postdoc (a, b) and then as an independent investigator (c), I used electron microscopy to provide the first (low-resolution) reconstructions of cellular RNAPs. These studies revealed the 'crab-claw' shape of RNAP and provided the first structural framework used by the field to interpret decades of accumulated biochemical data. We determined the first X-ray structure in 1999, but we continued to use electron microscopy to examine RNAP complexes with accessory factors to gain mechanistic understanding (d).
    a. **Darst SA**, Kubalek EW, Kornberg RD (1989) Three-dimensional Structure of *Escherichia coli* RNA Polymerase Holoenzyme Determined by Electron Crystallography, *Nature* **340**, 730-732.
    b. **Darst SA**, Edwards AM, Kubalek EW, Kornberg RD (1991) Three-dimensional Structure of Yeast RNA Polymerase II at 16 Å Resolution, *Cell* **66**, 121-128.
    c. Polyakov A, Severinova E, **Darst SA** (1995) Three-dimensional structure of *Escherichia coli* core RNA polymerase: Promoter recognition and elongation conformations of the enzyme, *Cell*, **83**, 365-373.
    d. Opalka N, Chlenov M, Chacon P, Rice WJ, Wriggers W, **Darst SA** (2003) Structure and function of the transcription elongation factor GreB bound to bacterial RNA polymerase, *Cell* **114**, 335-345.

2. In bacteria, the initiation-specific σ factor combines with the RNAP catalytic core to form the holoenzyme, which is required to direct promoter-specific transcription initiation. A major mechanism through which bacteria regulate transcription initiation is through regulation of σ activity. Starting with the structure of a σ fragment (a), my group has determined high-resolution structures of σ factor domains (a, c). These studies provided the first insights into σ factor function in promoter recognition and melting, and greatly facilitated our understanding of the first holoenzyme structures. Our structural and functional studies of σ factor complexes with their cognate regulatory anti-σ factors (for example, b, d) have elucidated regulatory principles governing a major mechanism to control gene expression in bacteria.
    a. Malhotra A, Severinova E, **Darst SA** (1996) Crystal structure of an *Escherichia coli* RNA polymerase σ^{70} subunit fragment, *Cell* **87**, 127-136.
    b. Campbell EA, Masuda S, Sun JL, Olson CA, Wang S, Muzzin O, **Darst SA** (2002) Crystal structure of the *Bacillus stearothermophilus* anti-σ factor SpoIIAB with the sporulation σ factor σ^{F}, *Cell* **108**, 795-807.
    c. Campbell EA, Muzzin O, Chlenov M, Sun JL, Olson CA, Weinman O, Trester-Zedlitz ML, **Darst SA** (2002) Structure of the bacterial RNA polymerase promoter specificity σ subunit, *Mol. Cell* **9**, 527-539.
    d. Campbell EA, Greenwell R, Anthony JR, Wang S, Lim L, Das K, Sofia HJ, Donohue TJ, **Darst SA** (2007) A conserved structural module regulates transcriptional responses to diverse stress signals in eubacteria, *Mol. Cell* **27**, 793-805 [PMCID: PMC2390684].
3. We revolutionized the transcription field with the first high-resolution X-ray crystal structure of a cellular RNAP (a), providing the first detailed structural framework for the interpretation of decades of functional and genetic data, and enabling the design of much more incisive experiments moving forward. Important among the new studies made possible by this advance, structural and mechanistic studies of bacterial RNAP inhibitors (such as rifamycins, a key component of tuberculosis treatment) revealed the molecular mechanism of inhibition (b-d).
    a. Zhang G, Campbell E, Minakhin L, Richter C, Severinov K, **Darst SA** (1999) Crystal structure of *Thermus aquaticus* core RNA polymerase at 3.3 Å resolution, *Cell* **98**, 811-824.
    b. Campbell EA, Korzheva N, Mustaev A, Murakami K, Goldfarb A, **Darst SA** (2001) Structural mechanism for rifampicin inhibition of bacterial RNA polymerase, *Cell* **104**, 901-912.
    c. Bae B, Nayak D, Mustaev A, Landick R, **Darst SA** (2015) CBR antimicrobials inhibit RNA polymerase via at least two bridge-helix cap-mediated effects on nucleotide addition, *Proc. Natl. Acad. Sci. USA* **112**, E4178-87 [PMCID: 4534225].
    d. Boyaci H, Chen J, Lilic M, Palka M, Mooney RA, Landick R, **Darst SA***, Campbell EA* (2018) Fidaxomicin jams *M. tuberculosis* RNA polymerase motions needed for initiation via RbpA contacts, *Elife* **7**, e34823 [PMCID: PMC5837556].
4. RNAP holoenzyme & transcription initiation. Our studies of RNAP holoenzyme and complexes with promoters have revealed the organization of σ/RNAP interactions in the holoenzyme (a), the overall architecture of the holoenzyme/promoter complex (b), how σ initiates the formation of the transcription bubble (c), and how the holoenzyme stabilizes the final open promoter complex.
    a. Murakami KS, Masuda S, **Darst SA** (2002) Structural basis of transcription initiation: RNA polymerase holoenzyme at 4 Å resolution, *Science* **296**, 1280-1284.
    b. Murakami KS, Masuda S, Campbell EA, Muzzin O, **Darst SA** (2002) Structural basis of transcription initiation: An RNA polymerase holoenzyme/DNA complex, *Science* **296**, 1285-1290.
    c. Feklistov A, **Darst SA** (2011) Structural basis for promoter –10 element recognition by the bacterial RNA polymerase σ subunit, *Cell* **147**, 1257-1269 [PMCID: PMC3245737].
    d. Boyaci H, Chen J, Jansen R, **Darst SA**, Campbell EA (2019) Structures of an RNA polymerase promoter melting intermediate elucidate DNA unwinding, *Nature* **565**, 382-385 [PMCID: in process].
5. The bacterial transcription cycle is regulated by hundreds of accessory factors. In addition to regulation of σ factor activity, transcription initiation in bacteria is modulated by extrinsic factors (a, d). RNAP function can also be co-opted by extrinsic factors during bacteriophage infection (b, c). Structural and mechanistic analyses of such regulators elucidate the function and regulation of the RNAP itself.

a. Jain D, Nickels BE, Sun L, Hochschild A, **Darst SA** (2004) Structure of a ternary transcription activation complex, *Mol. Cell* **13**, 45-53.

b. Osmundson J, Montero-Diez C, Westblade LF, Hochschild A, **Darst SA** (2012) Promoter-specific transcription inhibition in *Staphylococcus aureus* by a phage protein, *Cell* **151**, 1005-1016 [PMCID: PMC3604623].

c. Chen J, Wassarman KM, Feng S, Leon K, Feklistov A, Winkelman JT, Li Z, Walz T, Campbell EA, **Darst SA** (2017) 6S RNA mimics B-form DNA to regulate *Escherichia coli* RNA polymerase, *Mol. Cell* **68**, 388-397 [PMCID: PMC5683422].

d. Kang JY, Mooney RA, Nedialkov Y, Saba J, Mishanina TV, Artsimovitch I, Landick R, **Darst SA** (2018) Structural basis for transcript elongation control by NusG/RfaH universal regulators, *Cell* **173**, 1650-1662.e14 [PMCID: PMC6003885].

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/seth.darst.1/bibliography/41155375/public/?sort=date&direction=ascending

D. Research Support

Active

R35 GM118130 Seth A. Darst (PI) 5/1/16 - 4/30/21 NIH/NIGMS

Structure, function, and regulation of the bacterial transcription cycle

We will use cryo-electron microscopy, in combination with X-ray crystallography and other approaches, to provide a complete characterization of the bacterial transcription cycle.

Role: PI

Completed

None

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
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NAME: CAMPBELL, ELIZABETH

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

POSITION TITLE: Research Associate Professor

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)	Completion Date MM/YYYY	FIELD OF STUDY
Swarthmore College, Swarthmore, PA	BA	06/1992	Biology
The Rockefeller University, New York, NY	PHD	06/1998	Microbial Pathogenesis
The Rockefeller University, New York, NY	Post-doctoral	07/2003	Structural Biology

A. Personal Statement

PhD – natural transformation in *Streptococcus pneumoniae*: My interests in studying approaches to combat bacterial pathogens began during undergraduate research at Stanford University with Dr. Bruce Stocker, whose work with Salmonella led to the development of vaccines to prevent typhoid. The following year, I worked on purifying macromolecular complexes as a summer research student in Dr. Roger Kornberg's lab, also at Stanford. There, I discovered the power of structural biology as a method for elucidating biochemical mechanisms. As a PhD student at The Rockefeller University, I was trained in the laboratory of Molecular Genetics of Pathogenesis, headed by Drs. Elaine Tuomonen and Robert Masure. There, I learned how to genetically manipulate the pathogen *Streptococcus pneumonia*e by modifying the then current protocols of molecular biology *for Escherichia coli* (*E. coli*) and developing genetic screens to identify genes in *S. pneumoniae* required for competence (DNA transformation), a mechanism this pathogen uses to acquire drug resistance. It was during the attempted purification and characterization of a competence σ factor and a growing interest in structural biology, that I realized a post-doctoral fellowship in the laboratory of Dr. Seth Darst at The Rockefeller University would be of great benefit.

Postdoctoral studies – structural and biophysical training in bacterial transcription: My principal research as a post-doctoral fellow and research associate used a structure-based approach to understand the diverse features of regulators that mediate the basic and pathogenic mechanisms of transcription in bacteria, including *E. coli* and *Bacillus sp*. To understand the molecular mechanisms of regulators, I determined three-dimensional structures of transcription factors and inhibitors, and their complexes with RNA polymerase (RNAP). My structural training was supplemented with biochemical, genetic and *in vivo* techniques, often in highly productive collaborations with leaders in the bacterial transcription field, to gain comprehensive understanding of the molecular mechanisms that modulate transcription. My biophysical training led to the first structures of bacterial σ factors and the proteins that regulate them (anti-σ factors) from several different bacteria, including pathogens such as *Bacillus* sp., *Mycobacterium* sp. and *Enterobacter* sp. In collaborative studies, I defined the structural basis for rifampicin inhibition of bacterial RNAP, and for other RNAP inhibitors (e.g., sorangicin) relevant to drug design against tuberculosis and other infectious diseases (see contributions). It was during these studies that I realized the potential of applying the structural and biophysical techniques I learned in Dr. Darst's lab towards understanding transcription in pathogens. I applied to be a senior research associate with the understanding that I will employ my training towards directing projects aimed at understanding transcription in mycobacteria with the overarching goal to help in the development of therapeutics.

Current- Structure/function studies of transcription in *Mycobacterium tuberculosis* with the goal of providing new therapeutics against tuberculosis: Upon promotion to Senior Research Associate and later to Research Associate Professor, I shifted my focus to the structure and function of RNAPs from mycobacteria, and the essential transcription factors that regulate this enzyme. My group has found that unlike *E. coli*, where the overwhelming majority of biochemical characterizations have focused, *Mycobacterium sp*. are substantially different at various kinetic steps of initiation and several essential transcription factors (which are absent in

E. coli) are critical to boost the mycobacteria enzyme. Our structural and biochemical studies have revealed the mechanisms by which two essential transcription factors, CarD and RbpA, activate mycobacteria RNAP. It is our recent success in achieving the first structures of mycobacteria RNAP at high resolution, critical for drug-guided studies, that has facilitated my focus on characterizing the mechanisms of inhibitors with the goal to provide therapeutics to treat the disease tuberculosis. One of the significant outcomes of our research has led to the first X-ray crystal and cryo-EM structures of mycobacteria RNAP, positioning us for the proposed research (see contributions). In summary, our structural and biochemical advances encourage future structure/function studies with the goal to dissect the general mechanism of transcription in pathogenic bacteria such as mycobacteria, as well as contributing to insights that could lead to new therapeutics that target the RNAP.

Expertise My expertise in the field of bacterial transcription and pathogenesis is evidenced by the chairing of multiple sessions at FASEB meetings on Mechanisms of Prokaryotic Transcription from 2009 to 2017 (most recently, for the session 'Alternate Mechanisms of Transcription Regulation in Pathogens'). I served as co-organizer for the 2017 meeting. I also served as convener and speaker at the ASM microbe 2017 meeting in the symposium 'Structural Basis of Antibiotic Mechanism of Action and Resistance' and will speak this year again. I am a repeat invited speaker at the IAS Focused Program on Mechanisms of Transcription and Its Regulation, an invited seminar speaker at The University of Wisconsin-Madison (a hub of bacterial transcription studies), and served on the scientific advisory board on of the European ERASynBio initiative. I have also served as an *ad hoc* reviewer for many peer-reviewed journals and the NIH PCMB panel. More recently, as chair I have initiated a Gordon Research Conference on Microbial Transcription, which has been approved and will take place in 2019. Finally, my recent (2018) election to the American Academy of Microbiology affirms my expertise in the field of bacteria transcription. In addition, to my research expertise, I have enthusiastically and successfully mentored over 30 high school and undergraduate students, seven graduate students, four post-doctoral fellows, and eight research scientists.

1. Bae B, Chen J, Davis E, Leon K, Darst SA, **Campbell EA**. CarD uses a minor groove wedge mechanism to stabilize the RNA polymerase open promoter complex. Elife. 2015 Sep 8;4 PMCID: PMC4593161.
2. Hubin EA, Tabib-Salazar A, Humphrey LJ, Flack JE, Olinares PD, Darst SA, **Campbell EA***, Paget MS*(* Co-corresponding authors). Structural, functional, and genetic analyses of the actinobacterial transcription factor RbpA. Proc Natl Acad Sci U S A. 2015 Jun 9;112(23):7171-6. PMCID: PMC4466734.
3. Hubin EA, Lilic M, Darst SA, **Campbell EA**. Structural insights into the mycobacteria transcription initiation complex from analysis of X-ray crystal structures. Nature communications. 2017; 8:16072. PMCID:PMC5511352.
4. E. Peek J, Lilic M, Montiel D, Mishteyn A, Woodworth I, Biggins JB, Ternei MA, Calle P, Danziger M, Warrier T, Saito K, Braffman N, Fay A, Glickman MS, Darst SA, **Campbell EA***, Brady SF*. Rifamycin congeners kanglemycins are active against rifampicin-resistant bacteria via a distinct mechanism. *Nature Communications* (2018); 9:4147. PMCID:PMC6175910.

B. Positions and Honors

Positions and Employment

2018 - current Research Associate Professor, The Rockefeller University, New York, NY
2011 – 2018 Senior Research Associate, The Rockefeller University, New York, NY
2003 – 2011 Research Associate, The Rockefeller University, New York, NY

Select Experience and Professional Memberships

2017-2019 Chair, Gordon Research Conference on the Mechanism and Regulation of Microbial Transcription
Ongoing- Contributing member, American Society of Microbiology

Ongoing-	Peer Reviewer: mBio, Molecular Microbiology, Proceedings of the National Academy of Sciences, Journal of Bacteriology, Journal of Biochemistry, Nucleic Acids Research and Acta Crystallographica, PLOS Genetics, Genes and Development, Frontiers in Molecular Biosciences, Journal of Molecular Biology, ACS Chemical Biology, Nature Structure and Molecular Biology
2013-2018	Member of the scientific advisory board of a translational research consortium under the umbrella of the European ERASynBio initiative
2009-2017	Session Chair, Federation of American Societies for Experimental Biology Conference on the Mechanism and Regulation of Prokaryotic Transcription Conference on the Mechanism and Regulation of Prokaryotic Transcription
2015-2017	Co-chair organizer, Federation of American Societies for Experimental Biology Conference on the Mechanism and Regulation of Prokaryotic Transcription Conference on the Mechanism and Regulation of Prokaryotic Transcription
2016, 2018	Invited speaker at the IAS Focused Program on Mechanisms of Transcription in HKST
2017	Convener and speaker at Symposium entitled Structural Basis of Antibiotic Mechanism of Action and Resistance, American Society of Microbiology, Microbe 2017 Meeting
2017	NIH PCMB panel reviewer, ad hoc

Honors

1991 - 1992	Hunter Grubb Foundation Scholar, Swarthmore College
1991 - 1992	Pew Minority Undergraduate Fellow, Swarthmore College
1992 - 1992	Distinction in Biology in Graduation, Swarthmore College
1992	Sigma Xi Fellow, Swarthmore College
1992 - 1993	John Kluge Graduate Fellow, The Rockefeller University
1993 - 1996	NSF Minority Graduate Fellow, National Science Foundation
1995 - 1996	American Society for Microbiology Student Travel Grantee, American Society for Microbology
1996 - 1996	Segal Travel Grantee, The Rockefeller University
1999 - 2000	The Rockefeller Postdoctoral Fellowship award
2000 – 2003	Individual National Research Service award, National Institutes of Health
2017	Structural Genomics Consortium research award
2018	Elected to Fellowship in the American Academy of Microbiology
2019	Keystone Symposia Early Career Investigator Travel Award

C. Contribution to Science

Transcription in bacteria is performed by the enzyme RNA polymerase (RNAP) and is highly regulated at several stages, including initiation. Factors regulating which genes are transcribed in response to specific signals include σ factors, subunits of RNAP critical for promoter recognition and melting, as well as other transcription factors such as activators and repressors. RNAP is a proven target for antibiotic therapy against pathogens, most notably *Mycobacterium tuberculosis*, the causative agent of tuberculosis. My path in science started as a graduate student studying genetic mechanisms of how pathogens acquire antibiotic resistance. I then switched disciplines to learn biochemistry and structural biology and to apply these approaches to understanding basic mechanisms in transcription, including the basis of antibiotic inhibition of RNAP. The culmination of this training has now allowed me to apply these fundamental disciplines of structural biology, biophysics and biochemistry toward understanding the mechanisms of current and novel antibiotics against mycobacteria RNAP with the goal to contribute to the development of new therapeutics against tuberculosis.

1. My initial contribution to science occurred as a PhD candidate where I identified competence-regulated genes in the pathogen *S. pneumoniae*, the causative agent of many diseases including meningitis, otitis media, pneumonia, and septicemia. The bacteria are able to acquire resistance through natural transformation, where DNA is exchanged between bacteria. I developed a genetic screen which led to the identification of a novel promoter element which regulates the expression of competence genes as well as the identification of competence regulated genes and operons. I subsequently went on to show these genes

are critical for natural transformation. I served as a primary and contributing experimental investigator on these projects.

a. **Campbell EA**, Choi SY, Masure HR. A competence regulon in Streptococcus pneumoniae revealed by genomic analysis. Mol Microbiol. 1998 Mar;27(5):929-39.

b. Cheng Q, **Campbell EA**, Naughton AM, Johnson S, Masure HR. The com locus controls genetic transformation in Streptococcus pneumoniae. Mol Microbiol. 1997 Feb;23(4):683-92.

2. When I joined the Darst lab as a postdoctoral fellow, the understanding of the structural mechanisms of σ factor function was limited due to the lack of structures. Using my previous training in microbial genetics, I was able to identify the σ factor from the thermophilic bacterium, *Thermus aquaticus*, and purify sufficient quantities (despite toxicity when expressed in the host *E. coli* cells) for crystallization, leading to the first structures of discrete σ domains, including bound to substrate promoter DNA and RNAP. This work led to the understanding of how σ /promoter recognition occurs. I served as experimental investigator, first author and a contributing author on this work.

   a. Camarero JA, Shekhtman A, **Campbell EA**, Chlenov M, Gruber TM, Bryant DA, Darst SA, Cowburn D, Muir TW. Autoregulation of a bacterial sigma factor explored by using segmental isotopic labeling and NMR. Proc Natl Acad Sci U S A. 2002 Jun 25;99(13):8536-41. PMCID: PMC124302.

   b. Murakami KS, Masuda S, **Campbell EA**, Muzzin O, Darst SA. Structural basis of transcription initiation: an RNA polymerase holoenzyme-DNA complex. Science. 2002 May 17;296(5571):1285-90.

   c. **Campbell EA**, Muzzin O, Chlenov M, Sun JL, Olson CA, Weinman O, Trester-Zedlitz ML, Darst SA. Structure of the bacterial RNA polymerase promoter specificity sigma subunit. Mol Cell. 2002 Mar;9(3):527-39.

3. An additional step of regulation in bacterial transcription is mediated by a class of factors (anti-σ's) which negatively regulate σ factors. As a postdoctoral fellow, I elucidated their mechanism of inhibition by solving the first structures of anti-σ's in complex with their cognate σ factors. I showed that anti-σ's function in a variety of ways, including preventing the σ factor from binding RNAP and binding promoter DNA. This work led to the definition of a conserved anti-σ structural domain in all bacteria, revealing the mechanism of inhibition within a wide spectrum of bacterial σ/anti-σ pairs. I served as the primary experimental investigator/first author and principal investigator on these projects.

   a. **Campbell EA**, Masuda S, Sun JL, Muzzin O, Olson CA, Wang S, Darst SA. Crystal structure of the Bacillus stearothermophilus anti-sigma factor SpoIIAB with the sporulation sigma factor sigmaF. Cell. 2002 Mar 22;108(6):795-807.

   b. **Campbell EA**, Tupy JL, Gruber TM, Wang S, Sharp MM, Gross CA, Darst SA. Crystal structure of Escherichia coli sigmaE with the cytoplasmic domain of its anti-sigma RseA. Mol Cell. 2003 Apr;11(4):1067-78.

   c. Masuda S, Murakami KS, Wang S, Anders Olson C, Donigian J, Leon F, Darst SA, **Campbell EA**. Crystal structures of the ADP and ATP bound forms of the Bacillus anti-sigma factor SpoIIAB in complex with the anti-anti-sigma SpoIIAA. J Mol Biol. 2004 Jul 23;340(5):941-56.

   d. **Campbell EA**, Greenwell R, Anthony JR, Wang S, Lim L, Das K, Sofia HJ, Donohue TJ, Darst SA (2007) A conserved structural module regulates transcriptional responses to diverse stress signals in eubacteria, *Mol. Cell* **27**, 793-805. PMCID: PMC2390684.

4. After my training in structural biology, I decided to apply this approach towards combating bacterial pathogenesis. I therefore solved the first structures of RNAP bound to the inhibitors rifampicin (a current antimicrobial therapeutic for treating tuberculosis) and sorangicin, thus elucidating the mechanisms of inhibition as well as understanding the molecular nature of resistance to the medically important antibiotic rifampicin. An important finding was that rifampicin kills bacteria by inhibiting transcription via steric clash with the nascent RNA transcript. Our subsequent work with sorangicin suggested that sorangicin, despite occupying the Rif pocket, inhibits RifR RNAP because of its flexible nature, suggesting a desirable feature of future antibiotics. I served as the primary experimental investigator/first author on these projects.

   a. **Campbell EA**, Korzheva N, Mustaev A, Murakami K, Nair S, Goldfarb A, Darst SA. Structural mechanism for rifampicin inhibition of bacterial RNA polymerase. Cell. 2001 Mar 23;104(6):901-12.

b. **Campbell EA**, Pavlova O, Zenkin N, Leon F, Irschik H, Jansen R, Severinov K, Darst SA. Structural, functional, and genetic analysis of sorangicin inhibition of bacterial RNA polymerase. EMBO J. 2005 Feb 23;24(4):674-82. PubMed Central PMCID: PMC549610.

5. More recently, as a Senior Research Associate and Research Associate Professor, I have directed an independent research program to characterize the transcriptional properties of RNAP from the pathogen *M. tuberculosis*, the causative agent of tuberculosis. *M. tuberculosis* contains two essential transcription factors not found in *E. coli* and our biochemical and structural studies led to the finding that the paradigm of transcription initiation, previously defined by studies in *E. coli*, does not apply to mycobacteria. In addition, an impediment to drug design and optimization as well as studies in basic transcriptional mechanisms, was the lack of structures of RNAP from "gram-positive" bacteria, including those in the Actinobacteria phylum to which *M. tuberculosis* belongs. My most recent work has provided the first structure of RNAP from the actinobacteria clade (also known as the high GC content gram-positive bacteria), *M. smegmatis*, in complex with promoter DNA and the initiation factor RbpA. In addition, using the structure to guide us, we compared the kinetics of transcription between *M. tuberculosis* RNAP and *E. coli* and found critical differences in their function. Importantly, recently we applied the unique kinetic properties of *M. tuberculosis* RNAP to capture a promoter melting intermediate revealing the pathway of DNA unwinding. This work is significant for understanding how RNAPs in general work, the specific structural and kinetic properties of RNAP from this pathogen, as well as setting up a platform for studying and devising molecules to target this enzyme. One of our most recent cryo-EM structures reveals how the Actinobacteria specific transcription factor, RbpA, interacts with the antibiotic Fidaxomicin and confers clade specific sensitivity of this antibiotic to *M. tuberculosis*. This work is especially relevant to the medical community as RNAP is the target for first-line treatment against tuberculosis. Here, I served as the principal investigator and corresponding author for these projects.

   a. Davis E, Chen J, Leon K, Darst SA, **Campbell EA**. Mycobacterial RNA polymerase forms unstable open promoter complexes that are stabilized by CarD. Nucleic Acids Res. 2015 Jan;43(1):433-45. PMCID: PMC4288152.

   b. Hubin EA, Fay A, Xu C, Bean JM, Saecker RM, Glickman MS, Darst SA, **Campbell EA**. Structure and function of the mycobacterial transcription initiation complex with the essential regulator RbpA. eLife. 2017 Jan 9;6. PMCID:PMC5302886.

   c. Boyaci H, Chen J, Lilic M, Palka M, Mooney RA, Landick R, Darst SA*, **Campbell EA*** Fidaxomicin Jams Myocbacterium tuberculosis RNA polymerase motions needed for initiation via RbpA contacts. eLife 2018;7:e34823. PMCID:PMC5837556

   d. Boyaci H, Chen J, Jansen R, Darst SA, **Campbell EA***. Structures of an RNA polymerase promoter melting intermediate elucidate DNA unwinding. Nature (2018); **565**:382-385.NIHMSID:1007841

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/1n_ekkuzXr25P/bibliography/47915347/public/?sort=date&direction=ascending

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

Ongoing Research Support

2 R01 GM114450-06 CAMPBELL, ELIZABETH A (PI) 04/01/20-03/31/24 NIH/NIGMS
Structural and functional characterization of RNA polymerase and its regulators from Mycobacerium tuberculosis and Clostridioides difficile

Goals: To elucidate the structure and function of essential transcription factors from major human pathogens M. tuberculosis and C. difficile.

Role: PI

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: James Chen

eRA COMMONS USER NAME (credential, e.g., agency login): jchen91

POSITION TITLE: Graduate Research Fellow

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 Pennsylvania	B.A.	05/2013	Biophysics
The Rockefeller University	Ph.D.	03/2020	Molecular Biophysics

A. Personal Statement

The proposed research project involves the use of structural methods to characterize SARS-Cov-2 RNA dependent RNA polymerase complexes. I have the knowledge, expertise and motivation to achieve the goals of this project. During my undergraduate and graduate coursework, I have obtained a broad background in biochemistry and biophysics, specifically knowledge about structural methods such as crystallography and cryo-electron microscopy. I have an extensive background in studying proteins that interact with DNA or RNA. During my high school years, I took the initiative to join a protein crystallography lab under the mentorship of Gregory Van Duyne, Ph.D. to study Cre recombination and to develop my skills in structural biology. This interest in nucleic acid interacting proteins has led me to pursue further training under Seth A. Darst, Ph.D. (studying prokaryotic transcription) and Shelley L. Berger, Ph.D. (studying epigenetic modifications in mammalian cells) during my undergraduate education at the University of Pennsylvania. The culmination of my research experiences has allowed me to layout the foundation for the proposed research project by training me in protein structure determination and nucleic acid biochemistry. Upon entering the Rockefeller University as a graduate research fellow, I joined the Laboratory of Molecular Biophysics under the mentorship of Seth A. Darst, Ph.D. and Elizabeth A. Campbell, Ph.D. During my graduate studies, I developed protocols for protein and RNA purification and single particle cryo-electron microscopy methodologies, which I hope to apply in the proposed research project.

B. Positions and Honors

Positions and Employment

2006-2013 High School/Undergraduate Research Fellow, Department of Biochemistry and Biophysics (Gregory Van Duyne, Ph.D.), University of Pennsylvania, Philadelphia, PA

2010-2013 Undergraduate Tutor (Calculus), The Tutoring Center, University of Pennsylvania, Philadelphia, PA

2010-2013 Science Fair Judge, Pennsylvania Junior Academy of Science and George Washington Carver Science Fairs, Philadelphia, PA

2012-2012 Summer Undergraduate Research Fellow, Laboratory of Molecular Biophysics (Seth A. Darst, Ph.D.), The Rockefeller University, New York, NY

2012-2013 Undergraduate Research Fellow, Department of Cell and Developmental Biology (Shelley L Berger, Ph.D.), University of Pennsylvania, Philadelphia, PA
2012-2013 Founding Chapter Member, Phi Sigma Biological Science Honor Society, University of Pennsylvania, Philadelphia, PA
2013-2020 Graduate Student, Laboratory of Molecular Biophysics (Seth A. Darst), The Rockefeller University, New York, NY

Honors
2009 Guggenheim Scholarship, Central High School, Philadelphia, PA
2009 Lindsay G. Dunham Scholarship, University of Pennsylvania, Philadelphia, PA
2009 Philadelphia's Mayor's Scholarship, University of Pennsylvania, Philadelphia, PA
2012 Inducted into Phi Sigma Biological Science Honor Society, University of Pennsylvania, Philadelphia, PA

C. Contributions to Science

1. Transcription initiation requires the formation of the open promoter complex, RPo. To generate RPo, the RNA polymerase enzyme (RNAP) unwinds the DNA duplex to form the transcription bubble and then loads the DNA into the RNAP active site. RPo formation is a multi-step process with transient intermediates of unknown structures. In this study, single particle cryo-electron microscopy (cryo-EM) was used to visualize RPo formation by *Escherichia coli* (*Eco*) RNAP on a promoter, *rpsT* P2, that forms an unstable RPo compared to many *Eco* promoters. To facilitate visualization of RPo intermediates, TraR, a transcription factor that inhibits *rpsT* P2 activity, was added. TraR binds directly to RNAP rather than to promoter DNA, altering the RNAP conformation and increasing the occupancy of intermediates on the RPo formation pathway. Using image classification approaches, seven intermediates formed by RNAP on the *rpsT* P2 promoter were visualized. The structures span the RPo formation pathway from initial recognition of the duplex promoter in a closed complex (unmelted DNA) to the final RPo. The structures and supporting biochemical data define RNAP and promoter DNA conformational changes that delineate steps on the pathway, including previously undetected transient promoter-RNAP interactions that contribute to populating the intermediates but do not occur in RPo. Features of the structures allow their placement in an ordered pathway that provides a structural basis for understanding RPo formation in all organisms, a major point of regulation for gene expression.

   Structures of bacterial RPos have been well characterized (both X-ray crystallography and cryo-EM), but the structural basis for RPo formation is poorly understood due to the transient nature of the intermediates along the RPo formation pathway. In this study, seven different intermediate structures were observed that delineate changes in the conformation of both RNAP and the promoter DNA on the pathway to forming transcription-capable RPo. These structures are the first "snapshots" to detail the DNA opening process by any cellular RNAP. They document how the duplex DNA is first engaged outside the active site channel and then disrupted to form the "nucleated" bubble. DNA opening then propagates through a series of increasingly unwound intermediates. These initial steps place DNA inside the channel where the final unwinding steps form transcriptionally-functional RPo. Analysis of the structures of RPo intermediates provides details about the mechanism of transcription initiation. Given the conservation of the global architecture of RNAP, these structures are relevant to how this fundamental process occurs in all kingdoms of life. In particular these structures illustrate how large-scale protein and DNA conformational changes serve as key "checkpoints" in this tightly regulated process. These findings will be of great interest to scientists interested in (i) the regulation of gene expression, (ii) mechanisms of RNAP and transcription initiation, and (iii) biophysical mechanisms of the function of macromolecular machines.

   a. Chen J, Gopalkrishnan S, Chiu C, Chen AY, Campbell EA, Gourse RL, Ross W, Darst SA. E. coli TraR allosterically regulates transcription initiation by altering RNA polymerase conformation. Elife. 2019 Dec 16;8. doi: 10.7554/eLife.49375.
   b. Chen J, Chiu C, Gopalkrishnan S, Chen AY, Olinares PDB, Saecker RM, Winkelman JT, Maloney MF, Chait BT, Ross W, Gourse RL, Campbell EA, Darst SA. Stepwise Promoter Melting by Bacterial RNA Polymerase. Mol Cell. 2020 Mar 2;. doi: 10.1016/j.molcel.2020.02.017.

2. The bacterium *Mycobacterium tuberculosis (Mtb)* is the causative agent of the devastating disease TB, and multi-drug resistance has become a major threat. One of the first line antibiotics to treat TB, Rif, targets the

bacterial RNAP. The bacterial RNAP is a proven target for antibiotics. The rifamycin (Rif) class of antibiotics, which inhibit RNAP function, is a lynchpin of modern tuberculosis (TB) treatment. Fidaxomicin (Fdx) is an antimicrobial RNAP inhibitor highly effective against *Mtb* RNAP *in vitro*, but clinical use of Fdx is limited to treating *Clostridium difficile* intestinal infections due to poor bioavailability. Addressing this limitation requires understanding the structural and mechanistic basis for Fdx inhibition, which is heretofore unknown. A structure of this class of antibiotic bound to any RNAP was not available, but an Fdx-RNAP structure is essential to understand the mechanism of inhibition and to develop analogs with improved properties. To identify the structural determinants of Fdx binding to RNAP, a 3.4 Å cryo-EM structure of a complete *Mtb* RNAP holoenzyme in complex with Fdx was solved. In this structure, the *Actinobacteria*-specific general transcription factor (GTF) RbpA contacts Fdx, explaining its strong effect on *Mtb*. Additional structures define conformational states of *Mtb* RNAP between the free apo-holoenzyme and the promoter-engaged RPo ready for transcription. In particular, conformational dynamics of the clamp module of RNAP play multiple important roles in the transcription cycle. The results establish that Fdx acts like a doorstop to jam the enzyme in an open clamp state, preventing the motions necessary to secure promoter DNA in the active site. The results also establish the molecular details of Fdx interactions with the bacterial RNAP and a mechanism of action for Fdx. Crucially, the essential GTF RbpA plays an important role for the high sensitivity of *Mtb* RNAP to Fdx both *in vitro* and *in vivo*. This work defines the action mechanism of a new antimicrobial that is in clinical use, and provides a complete picture of the molecular interactions important for inhibiting Mtb transcription that will be essential for the development of improved, TB-specific antimicrobials. These structures provide a structural platform for the development of antimicrobials that target the Fdx binding determinant and underscores the need to define structure-activity relationships of drug leads using near-native states, in this case using cryo-EM with the Mtb RNAP initiation complex to guide development of effective Mtb treatments.

a. Boyaci H, Chen J, Lilic M, Palka M, Mooney RA, Landick R, Darst SA, Campbell EA. Fidaxomicin jams Mycobacterium tuberculosis RNA polymerase motions needed for initiation via RbpA contacts. Elife. 2018 Feb 26;7. doi: 10.7554/eLife.34823. PubMed PMID: 29480804; PubMed Central PMCID: PMC5837556.

3. Noncoding RNAs (ncRNAs) play essential roles in the regulation of gene expression from bacteria to humans. Bacterial 6S RNAs globally regulate transcription by binding RNAP and competing with promoter DNA. *Eco* 6S RNA interacts specifically with the *Eco* σ^{70}-holoenzyme ($E\sigma^{70}$) and plays a key role in transcriptional reprogramming upon shifts between exponential and stationary phase. 6S RNAs are widely conserved among bacteria through a common structure that includes transcription bubble mimicry. Inhibition is relieved upon 6S RNA-templated RNA synthesis. How 6S RNA interacts with the DNA-dependent RNAP to outcompete promoter DNA was not elucidated at the structural level. A 3.8 Å resolution structure of a complex between 6S RNA and $E\sigma^{70}$ was determined by single-particle cryo-EM and validated using footprinting and crosslinking approaches. The A-form major groove of RNA duplexes is too deep and narrow for protein side chains to reach the major groove edge of base pairs for sequence-specific readout. In the case of 6S RNA, duplex RNA segments have A-form C3′ endo sugar puckers but have widened major groove widths, giving the RNA an overall architecture that mimics B-form promoter DNA. RNAP interactions with the RNA backbone pry open the major groove, not for the purposes of sequence-specific RNA recognition but in the service of B-form mimicry. The results of this study help explain the specificity of 6S RNA for $E\sigma^{70}$ and show how an ncRNA can mimic B-form DNA to regulate transcription by the DNA-dependent RNAP.

   The cryo-EM structure of the *Eco* 6S RNA/RNAP complex shows how an ncRNA can mimic B-form DNA to directly regulate transcription. Typically, RNA duplexes are restricted to A-form due to C3′ endo sugar puckers. However, our structural analysis shows that extensive protein/RNA interactions can widen the major groove of duplex RNA segments, allowing the overall architecture of the RNA to mimic that of B-form DNA. Direct regulation of RNAP activity by ncRNAs is not limited to the bacterial 6S RNA. Mouse B2 and human Alu ncRNAs both repress mRNA transcription by binding to RNAP II and blocking contacts with promoter DNA. Remarkably, RNAP II can utilize the B2 RNA as both a transcription template and substrate, using an RNA-dependent RNAP activity to extend the 3'-end of the B2 RNA in an internally templated reaction. Extension of the B2 RNA in this way destabilizes the RNA and relieves the RNAP II inhibition. Thus, the functional parallels between the bacterial and eukaryotic ncRNA RNAP inhibitors suggest that the structural principles for 6S RNA binding and inhibition of *Eco* RNAP delineated in this study are also widely applicable.

a. Chen J, Wassarman KM, Feng S, Leon K, Feklistov A, Winkelman JT, Li Z, Walz T, Campbell EA, Darst SA. 6S RNA Mimics B-Form DNA to Regulate Escherichia coli RNA Polymerase. Mol Cell. 2017 Oct 19;68(2):388-397.e6. doi: 10.1016/j.molcel.2017.09.006.
b. Chen J, Noble A, Kang J, Darst S. Eliminating effects of particle adsorption to the air/water interface in single-particle cryo-electron microscopy: Bacterial RNA polymerase and CHAPSO. Journal of Structural Biology: X. 2019/01; 1:100005.

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/1T3wqw6Tprd5g/bibliography/public/

D. Additional Information: Research Support and/or Scholastic Performance
None.

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: Brandon Malone

eRA COMMONS USER NAME (credential, e.g., agency login): BMALONE31

POSITION TITLE: Graduate student

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 College Cork, Cork, Ireland	BPharm	05/2018	Pharmacy & Pharmacology
The Rockefeller University	Ph.D	Ongoing	Molecular Biophysics

A. Personal Statement

The proposed research project will focus on structurally elucidating key steps of the SARs-Cov-2 RNA dependent RNA polymerase lifecycle. As an early stage graduate student, I am well versed in many of the experimental techniques that I will be employing from protein purification to cryo-EM data processing having conducted similar workflows when studying RNA polymerases from both *E.coli* and *M. tuberculosis* under the supervision of Drs. Darst & Campbell.

B. Positions and Honors

2014-2018 – Undergraduate researcher in UCC Cork Cancer Research Centre (Dr Mark Tangney)
2016-2016 Summer undergraduate researcher at the John Innes Centre, Norwich (Dr Tony Maxwell)
2017-2017 Summer undergraduate researcher – Amgen Scholars program, Institut Pasteur (Dr Ludovic Deriano)
2019- Graduate student, Laboratory of Molecular Biophysics (Seth A. Darst), The Rockefeller University, New York, NY

Honors

2014 "All-Ireland Scholarship"-University scholarship based on High school examination results
2014 Pfizer's National High School Seniors (Leaving Certificate) Chemistry Quiz 1st place
2015-2016 Gold medal winner at IGEM 2015 & iGEM 2016
2016 UCC Blackstone Launchpad Entrepreneur of the Year winner 2016, University College Cork, Ireland
2015-2018 Awarded title of "College Scholar", University College Cork, Ireland

C. Contributions to Science

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