BIOGRAPHICAL SKETCH

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NAME: Lijia, Jia

eRA COMMONS USER NAME: LIJIA_JIA

POSITION TITLE: Postdoctoral Fellow/Facility Manager

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
The Agricultural University of Hebei, China	B.S.	06/2010	Plant Genetics
China Agricultural University, China	M.S.	3/2013	Plant Genetics and Breeding
University of Chinese Academy of Sciences, China	Ph.D.	07/2017	Structural Biology
Institute of Biophysics, Chinese Academy of Sciences, China	Postdoc	09/2019	Structural Biology; Epigenetics
Florida State University	Postdoc	01/2021	Structural Biology; Biochemistry
UT Health San Antonio (UTHSCSA)	Postdoc/ Facility Manager	01/2021-Ongoing	Structural Biology; Biochemistry

A. Personal Statement

My long-term career goal has been to be a Cryo-EM facility Manager and Research Assistant Professor, with a particular interest in using single particle cryo-EM and eventually cryo-electron tomography to resolve large protein complexes. As an undergraduate and Master's student, I appreciated the value in studying how quantitative methods could inform biology, where I used statistical methods to map out how gene expression could influence mutant phenotypes in wheat production. It is also during this period of training that I became familiar with Maximum Likelihood methods, the main principle behind the popular Cryo-EM software Relion, which help push the resolution revolution in Cryo-EM protein structure determination. This computational background greatly helped me during my postdoctoral training at the Chinese Academy of Sciences to quickly learn the Cryo-EM softwares Relion, Cryosparc, and others and to resolve the structures of large protein complexes.

During my Ph.D., I acquired skillsets in protein biochemistry and structural biology using X-ray crystallography in the Institute of Genetics and Developmental Biology of Chinese Academy of Sciences, the leading research organization in China. During my Ph.D., I developed proficiency in cloning and molecular biology, protein purification, and X-ray crystallography - from crystal growth, data collection, and structure determination, and model building. In addition to experimentally-driven structure determination, I also implemented homology modeling (I-TASSER; Swiss-model; Robetta and Modeller), Molecular dynamics (Gromacs and VMD software), and molecular docking and virtual screening (Autodock and Autodock vina) – all of which helped me broaden my structural biology skills. After I finished my Ph.D. in 2017, I joined Ruiming Xu's group as a postdoctoral fellow, the director of the Institute of Biophysics of the Chinese Academy of Sciences, where we had two Titan Krios and one Talos Arctica for high resolution Cryo-EM structure determination. During this time, I used single particle Cryo-EM to resolve the structure of a chromatin remodeler complex, which allowed me to familiarize myself with various Cryo-EM skillsets, including plunge freezing with a Vitrobot, screening and data collection, and data processing with Relion and Eman2. In 2019, in order to improve my Cryo-EM skills, I started a brief post-doc at Florida State University (FSU), as this institute has a long-standing influence in EM

field. At FSU, I collaborated with Kenneth Taylor's and Scott Stagg's laboratories and gained proficiency in the Cryo-EM data collection software Leginon, as well as reinforced skillsets related to sample preparation, data collection and data processing. During my year at FSU, I was able to biochemically reconstitute a complex related to DNA replication and obtain a medium resolution structure by Cryo-EM.

These experiences have allowed me to move on to UT Health Science Center at San Antonio (UTHSCSA) to now work on developing a cryo-EM infrastructure under the direction of expert structural biologist and biochemists Drs. Shaun Olsen and Patrick Sung. UTHSCSA is in the process of building a state of the art cryo-EM facility with a Glacios cryo-TEM, Falcon 4 direct electron detector, and a Selectris energy filter. This presented me with a unique opportunity to have a large impact on setting up the cryo-EM facility and helping users at the University apply cryo-EM to their research. Since arriving here 6 months ago, I have already set up the Vitrobot, GPU computing, and data processing programs. ***The additional TP2 training at NCCAT will be required for me to perform my duties to independently operate and maintain our new Glacios microscope coming online January 2022, as well as learn other facility management responsibilities, and further strengthen my data processing of single particle data.*** Being able to connect with and learn from the world class staff at NCCAT will allow me to strengthen my skillsets to help the UTHSCSA community learn cryo-EM and eventually obtain high resolution structural information.

B. Positions and Honors

Positions and Employment

2017-2019 Postdoctoral Researcher, Institute of Biophysics, Chinese Academy of Sciences
2019-2020 Postdoctoral Associate, College of Medicine, Florida State University
2020-present Postdoctoral Fellow/Facility Manager, Department of Biochemistry and Structural Biology, UTHSCSA

Experience and Honors

2011 Selected to participate in training for QTL Mapping at the University of Zhejing
2015 Selected to participate in Phenix workshop at Tsinghua University
2017 Selected to participate in the training of Get Acquainted with Cryo-Electron Microscopy: Third Chinese Workshop for Structural Biologists in Tsinghua University
2018 Selected to participate in The 2018 K.H. Kuo CryoEM Tomography workshop & Symposium at the University of Zhejiang

C. Contributions to Science

1. Early career

During my Masters, I mainly focused on using quantitative genetics to map candidate genes controlling wheat yield in the lab of Dr. Qixin Sun, the president of China Agricultural University. These works found that some elite gene sources could be derived from the Tibetan semi-wild wheat. Among them, several QTL-rich regions were mapped on 4 homologous groups. These discoveries expanded our genetic understanding of Tibetan semi-wild wheat, which will expand the repertoire of the genetic diversity of yield-related traits in modern wheat breeding program. Further analysis revealed that wheat Chromosome 4A and 4B harbor very stable genetic loci that control yield-related traits, independent of environmental changes, suggesting that these loci may be manipulated to breed out hardy wheat variants capable of growing well in different environments.

a) Liu G[#], **Jia LJ[#]**, Lu LH, Qin DD, Zhang JP, Guan PF, Ni ZF, Yao YY, Sun QX, Peng HR. (2014) Mapping QTLs of yield-related traits using RIL population derived from common wheat and Tibetan semi-wild wheat. Theor Appl Genet. 127:2415–2432.

b) Guan P[#], Lu L[#], **Jia L[#],** KabirM R, Zhang J, Lan T, Zhao Y, Xin M, Hu Z, Yao Y, Ni Z, Sun Q, Peng H. (2018) Global QTL Analysis Identifies Genomic Regions on Chromosomes 4A and 4B Harboring Stable Loci for Yield Related Traits Across Different Environments in Wheat (Triticum aestivum L.) Front Plant Sci. 9:529.

2. Structural and functional characterization of Plant protein enzymes

During my Ph.D., I utilized my training in plant sciences and computational biology to study the biochemical and structural aspects of Plant UDP-gal epimerase, N-Methyltransferase, vesicle-inducing protein, plastocyanin and salicylic acid biosynthesis regulators. I cloned all the four UDP-Gal epimerase found in the cytosol from Rice, and resolved their crystal structures. Structural comparison shows that the four UDP-Gal epimerases appear to have diverged over evolution. Using homology modeling, we identified key catalytic residues of Arabidopsis N-Methyltransferase, and confirmed biochemically that these sites contribute the enzyme activity and diversity (Li et al. Plant Physiol. 2017). Using homology modeling and molecular dynamics simulations, we identified the residues important for the interaction between plastocyanin and Cu; we confirmed biochemically that mutation of these residues contributes to the differential activtiies found in various plant species (Zhou et al. Plant Sci. 2018). My former research group is at present genetically following up on these observations to determine whether and how these key residues contribute to plant growth and development, discoveries that would allow for the development of more elite genetic resources.

a) Gao F, Chen B, Jiao J, **Jia LJ**, Liu CM. (2017) Two novel vesicle-inducing proteins in plastids 1 genes cloned and characterized in Urartu Triticum. Plos one. 12(1):e0170439.

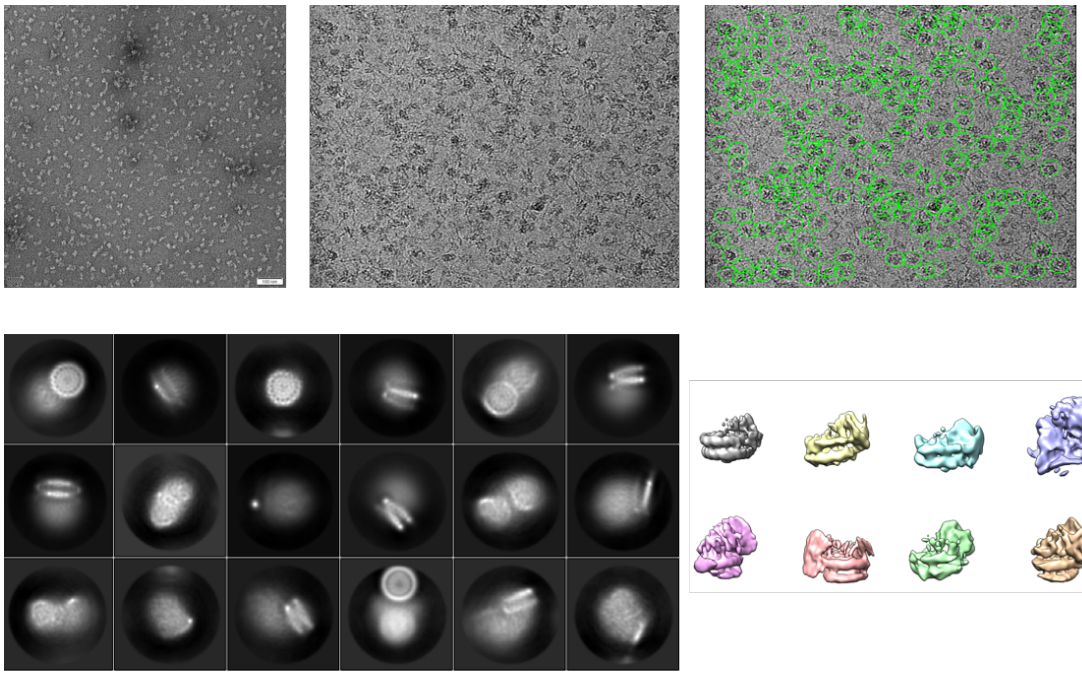
b) Li W, Zhang FX, Wu RR, **Jia LJ**, Li GS, Guo YL, Liu CM, Wang GD. (2017) A novel N-Methyltransferase in Arabidopsis appears to feed a conserved pathway for nicotinate detoxification among land plants and is associated with lignin biosynthesis. Plant Physiol. 174(3):1492-1504.

c) Zhou XT, **Jia LJ**, Wang HY, Zhao P, Wang WY, Liu N, Song SW, Wu Y, Su L, Zhang J, Zhong NQ, Xia GX. (2018) The potato transcription factor StbZIP61 regulates dynamic biosynthesis of salicylic acid in defense against Phytophthora infestans infection. Plant J. 95(6):1055-1068.

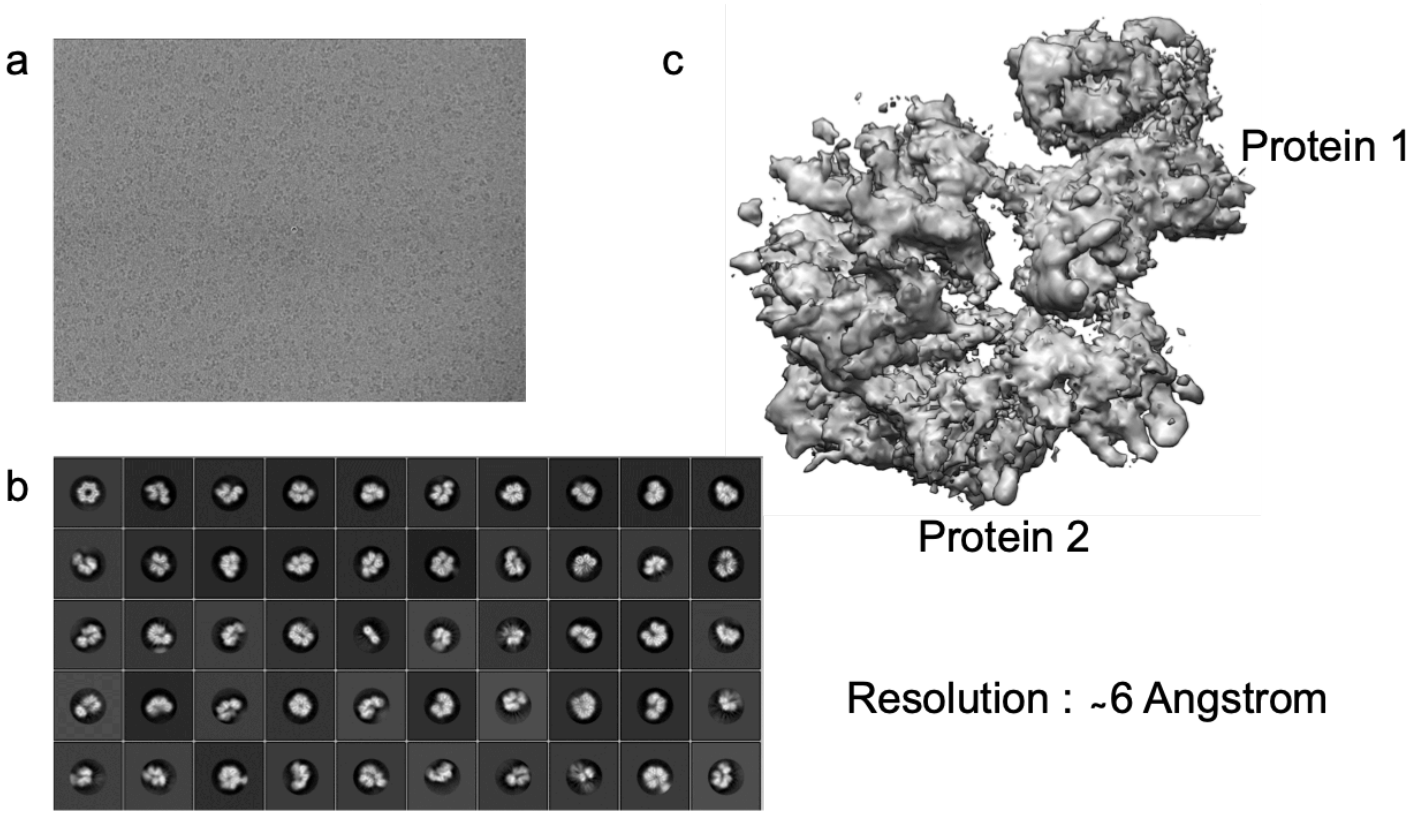
d) Zhou XT, Wang F, Ma YP, **Jia LJ**, Liu N, Wang HY, Zhao P, Xia GX, Zhong NQ. (2018) Ectopic expression of SsPETE2, a plastocyanin from Suaeda salsa, improves plant tolerance to oxidative stress. Plant Sci. 268:1- 10.

3. Postdoctoral career – Using single particle Cryo-EM to resolve protein complexes involved in chromatin biology

During my postdoctoral training, I learned how to recombinantly overexpress proteins for structural determination in insect and mammal cells. I also became familiar with single particle Cryo-EM to expand my structural biology toolkit. My research projects have consistently involved studying complexes involved in chromatin biology – while at the Chinese Academy of Sciences, I studied a chromatin remodeler protein complex, and at FSU and UTHSCSA, I have and am working on DNA lesion and replication complexes. For two of the three projects, I have collected Cryo-EM datasets and have been able to determine medium resolution structures of both these dynamic systems (results below).



Chromatin remodeler complex: top left, negative stain micrograph; top right, cryo-EM micrograph collected on Titan Krios with K2 direct electron detector. Bottom left and right: 2D and 3D classifications, respectively, calculated in Relion.



DNA replication complex: a) cryo-EM micrograph collected on Titan Krios with K3 direct electron detector. b) 2D classification calculated in Cryosparc. c) Refined model determined in Relion to ~6 angstroms after 3D classification.

Complete List of Published Work in MyBibliography:
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BIOGRAPHICAL SKETCH

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NAME: **Sung, Patrick**

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

POSITION TITLE: **Professor, Biochemistry & Structural 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
University of Liverpool	B.Sc.	05/1981	Biochemistry
Oxford University	D/ Phil.	03/1985	Biochemistry
University of Rochester	Postdoctoral	06/1993	Genetics & Biochemistry

A. Personal Statement As a doctoral student at Oxford University, I received training in protein biochemistry and enzymology while focusing on the role of the vitamin K-dependent carboxylase in blood coagulation. My education at Oxford has enabled me to make significant contributions toward delineating the mechanisms of conserved DNA repair pathways in the budding yeast *Saccharomyces cerevisiae* and in human cells. Notably, when I was a postdoctoral fellow at the University of Rochester, I identified the biochemical properties of several key factors that function in nucleotide excision repair (NER), some of which play a dual role in RNA polymerase II transcription. Since establishing my own laboratory in 1993 (at the University of Texas Medical Branch, Galveston), I have maintained a strong commitment toward understanding how yeast and human cells engage homologous recombination (HR) as tool in eliminating DNA breaks and crosslinks. As first defined in *S. cerevisiae,* HR is mediated by genes of the *RAD52* epistasis group. The efficiency of HR catalyzed by the RAD51 recombinase is regulated by the tumor suppressors BRCA1, BARD1, BRCA2, PALB2, and BLM and by components of the Fanconi anemia (FA) pathway of DNA damage response/repair in humans, providing compelling evidence for a key role of HR in cancer avoidance. Our studies have already led to many original findings and provided much-needed conceptual and experimental frameworks for the continual dissection of HR and FA mechanisms. Moreover, our work has direct relevance to understanding aging mechanisms, as DNA repair efficiency and pathway choice are both altered during aging. To date, I have published 282 articles, with 235 of them being original research papers. My *h-index* (according to Scopus) is 78 with >21,150 citations.

I have played a leading role in teaching, advising, and mentoring undergraduate and graduate students at Yale and the University of Texas. Many of my former trainees are now academic faculty in the United States and abroad, and several are already tenured. I am committed to the mentoring of junior faculty colleagues as well. I have been actively involved in peer-reviewing, by serving on various NIH study sections, as a regular reviewer for the NSF, on the editorial board of various journals, as an Editor or Associate Editor of *Molecular & Cellular Biology* (from 2000-2008), *Genes to Cell* (since 2004), and *The Journal of Biological Chemistry* (since 2014), and also as the Co-chair of the 2013 ASBMB Annual Meeting that was held in Boston.

1. Sung P. (1994) Catalysis of ATP-dependent homologous DNA pairing and strand exchange by yeast RAD51 protein. ***Science*** 265:1241-1243.
2. Tarsounas, M and Sung, P. (2020) The antitumorigenic roles of BRCA1-BARD1 in DNA repair and replication. ***Nature Rev. Mol. Cell. Biol.*** doi: 10.1038/s41580-020-0218-z.

B. Appointments

1993-1997 **Assistant Professor**, University of Texas Medical Branch, Galveston.
1997-2001 **Associate Professor**, University of Texas Health Science Center at San Antonio (UTHSCSA).
2001-2003 **Professor**, Department of Molecular Medicine, UTHSCSA.
1997-2001 **Chair**, Graduate Program in Molecular Medicine, UTHSCSA.
2010-2013 **Co-director** (with Alan Tomkinson), NCI-sponsored predoctoral and postdoctoral “Training

Program in DNA Repair".
2001-2003 **Deputy Chair**, Department of Molecular Medicine, UTHSCSA
2002-2003 **Zachry Distinguished Professor of Molecular Medicine**, UTHSCSA
2003-2018 **Professor**, Department of Molecular Biophysics & Biochemistry, Yale University
2006-2012 **Co-leader**, Yale Cancer Center Radiation Biology and Radiotherapy Program
2015- **Instructor in charge**, MB&B/MCDB 105b, "Issues Approach to Biology"; this is introductory biology course with an enrollment of >100 Yale undergraduates.
2007-2009 **Vice Chair**, Department of Molecular Biophysics & Biochemistry, Yale University
2009-2015 **Chair** (two 3-year terms), Department of Molecular Biophysics & Biochemistry, Yale University
2018 (Sept) - **Professor**, Department of Biochemistry & Structural Biology, UTHSCSA
2018 (Sept) - **Robert A. Welch Distinguished Chair in Chemistry**, UTHSCSA
2018 (Sept) - **Scholar of the Cancer Prevention and Research Institute of Texas (CPRIT)**, UTHSCSA
2018 (Sept) - **Co-leader**, Cancer Development and Progression Program, Mays Cancer Center, UTHSCSA
2019 **National Cancer Institute R35 Outstanding Investigator Award**

Professional Activities & Honors:
2000-2008 **Editor**, **"**DNA and Chromosome Dynamics" section, *Molecular & Cellular Biology*
2004- **Associate Editor,** *Genes to Cell*
1998-2000 **Member**, Editorial Board of *Molecular & Cellular Biology.*
2001- **Member**, Editorial Board of *DNA Repair*
2003- **Member**, Editorial Board of *Genes & Development*
2013-2014 **Member**, Editorial Board of *J. Biol. Chem.*
2014- **Associate Editor**, "DNA and Chromosomes" section, *J. Biol. Chem.*
2000-2003 **Charter Member**, NIH Radiation Biology (RAD) Study Section
2003-2004 **Charter Member**, NIH Radiation Therapeutics and Biology (RTB) Study Section
2003-2004 **Member,** NIH Cell Development and Function 2 (CDF2) Special Emphasis Panel
2006-2008 **Charter Member**, NIH Cancer Etiology (CE) Study Section
2008-2010 **Chair**, NIH Cancer Etiology (CE) Study Section
2012- ***Ad hoc* assignments** (as member or chair) on various NIH grant reviewing panels, such as the Cancer Etiology and Molecular Genetics B study sections, and the NCI Outstanding Investigator Award reviewing panel.
1999 **Ray Wu Award in Basic Research**, Society for Chinese Bioscientists in America.
2010 **William H. Bell lectureship**, Oklahoma Medical Research Foundation
2013 **Chair of Nominations Committee**, Society for Chinese Bioscientists in America
American Society for Biochemistry and Molecular Biology, **Co-chair** (with Carol Fierke of the University of Michigan), Annual Meeting of the Society in Boston.
2014 **Distinguished Lecturer**, Cancer Institute of New Jersey
2014 **Elected Member**, The Connecticut Academy of Science and Engineering
2017 **Member**, National Advisory Environmental Health Sciences Council, NIH
2016 **Keynote Speaker**, Annual Graduate Student Symposium, New York Medical College
2018 **Keynote Speaker,** UNIST Symposium on Genome Integrity & Cell Cycle, Bushan, Korea.
2019 **Keynote Speaker,** CINVESTAV Science Days, Irapuato, Mexico
2020 **Keynote Speaker**, Cold Spring Harbor Asia Meeting on DNA Metabolism, Genome Stability , and Human Disease. Suzhou, China.
2018 **Mendel Lecture,** the International Clinical Research Center of St. Anne's University, Brno, the Czech Republic. Supported by the European Union's ICRC-ERA-HumanBridge project.
2018 **Yale Cancer Center Conclave (Basic Science) Award**
2018 **Distinguished Lectureship,** Institute of Biosciences & Biotechnology, Texas A&M Health
1993- **Regular Reviewer** for *Genes & Dev., J. Biol. Chem., PNAS, Science, Cell, Molecular Cell, Cell Rep., Nature*, *Nature Struct. & Mol. Biol., Nature Genetics, Nature Cell Biol., Nature Comm., PLOS Genetics, PLOS Biol., EMBO J, etc.*

C. Contribution to Science. Radiation, chemicals, and obstacles that impede DNA replication induce DNA double-strand breaks (DSBs). Failure to remove these breaks leads to cell death, genetic mutations, gross chromosome rearrangements, and to cell transformation and cancer in mammals. Homologous recombination (HR) represents a major, conserved tool for the elimination of DSBs. Moreover, programmed HR events in meiosis produce chromosome arm crossovers that tie the homologous chromosome pairs, to prepare them for proper disjunction in the first meiotic cell division. HR entails several mechanistically distinct steps, namely, nucleolytic DNA end resection, assembly of a helical recombinase protein filament on ssDNA derived from resection, DNA strand invasion, repair DNA synthesis, and resolution of DNA intermediates to yield

recombinants of distinct types. Moreover, HR is subject to tight control to minimize genome alterations and rearrangements. Below, I document some of the contributions my laboratory has made in understanding the mechanisms of the HR machinery and its regulation in eukaryotic cells since becoming faculty in 1993.

1. DNA End Resection in Homologous Recombination

Starting from a DSB, HR entails the 5' to 3' nucleolytic resection of the DNA ends to yield ssDNA tails, which then serve as the substrate to recruit the Rad51 recombinase and associated factors. The genetic requirement of DNA end resection was first defined in *S. cerevisiae* by the Symington, Ira, and Jackson laboratories. With highly purified *S. cerevisiae* and human factors, we have devised reconstituted systems to examine how end resection is mediated by protein complexes encompassing the DNA helicase Sgs1/BLM, the nuclease Dna2, and the ssDNA binding protein RPA (**a, d**). Moreover, how the yeast Mre11-Rad50-Xrs2 complex and the Top3-Rmi1 (Topo IIIα-RMI in humans) complex influence the efficiency of the resection reaction has been defined (**a, b**). Genetics studies in yeast have revealed that little resection of DSBs occur in G1 cells, and that end resection in the S and G2 phases requires the action of cyclin-dependent kinase (Cdk1). In collaboration with Greg Ira's group at Baylor, we have shown Cdk1-dependent phosphorylation of Dna2 in yeast cells and that this serves to recruit Dna2 to DSBs (**b**). Moreover, we have provided mechanistic evidence to explain the role of the DNA helicase activity of Dna2 in resection (**c**). The experimental systems that we have devised will be invaluable for dissecting the action mechanisms of enzymes and protein ensembles concerned with DNA end resection.

a. Niu, H, Chung, W.H., Zhu, Z., Kwon, Y.H., Zhao, W.X., Chi, P., Prakash, R. Seong, C.H., Liu, D.Q., Lu, L., Ira, G. and Sung, P. (2010) Mechanism of the ATP-dependent DNA Double-stranded Break Resection Machinery from *S. cerevisiae.* ***Nature*** 467:108-11. PMCID: PMC2955862

b. Chen, X.F., Niu, H.Y., Chung, W.H., Zhu, Z., *Sung, P. and Ira, G. (2011) Cell cycle regulation of double-strand break end resection by Cdk1-dependent Dna2 phosphorylation. ***Nature Struct. Mol. Biol***. 18:1015-9. **Sung is a corresponding author.* PMCID: PMC3168961

c. Miller AS, Daley JM, Pham NT, Niu H, Xue X, Ira G, Sung P. (2017) A novel role of the Dna2 translocase function in DNA break resection. ***Genes & Development*** 31:503-510. PMCID: PMC5393064

d. Daley, JM, Tomimatsu, N, Hooks, G, Wang, WB, Miller, AS, Xue, XY, Nguyen, KA, Kaur, H, Williamson, W, B, Mukherjee, B, Hromas, R, Burma, S, and Sung, P. (2020) Specificity of End Resection Pathways for Double-Strand Break Regions Containing Ribonucleotides and Base Lesions. ***Nature Communications*** 11:3088. PMCID: PMC7303207

2. Action Mechanism of the Conserved Recombinases RAD51 and DMC1. During HR, a recombinase enzyme (Rad51 in mitotic cells; Rad51 or Dmc1 in meiotic cells) polymerizes on the ssDNA tails derived from DNA end resection to form a right-handed, helical filament referred to as the "presynaptic filament". The presynaptic filament engages duplex DNA and is responsible for conducting the three-dimensional search process that results in the location of a homologous target in the latter. Once homology is located, DNA strand invasion occurs, to create a nascent heteroduplex DNA joint called the displacement loop, or "D-loop". The ensemble of recombinase filament and the three-stranded DNA structure is called the synaptic complex (see **Section 4**). Our studies have been instrumental in uncovering the recombinase activity in Rad51 and Dmc1 and defining their salient attributes (**a-c**). Moreover, in collaboration with Eric Greene's group at Columbia, single molecule analyses employing nanofabricated DNA curtains coupled with total internal reflection fluorescence microscopy, mechanistic details of the DNA homology search and homologous DNA pairing processes are being elucidated (**d**).

a. Sung P. (1994) Catalysis of ATP-dependent homologous DNA pairing and strand exchange by yeast RAD51 protein. ***Science*** 265:1241-1243.

b. Sung P. and Robberson D. (1995) DNA strand exchange mediated by a RAD51-ssDNA nucleoprotein filament with polarity opposite to that of RecA. ***Cell*** 82:453-461.

c. Sehorn, M.G. Sigurdsson, S., Bussen, W., Unger, V.M. and Sung, P. (2004) The Human Meiotic Recombinase Dmc1 Promotes ATP-dependent Homologous DNA Strand Exchange. ***Nature*** 429:433-37.

d. Lee JY, Terakawa T, Qi Z, Steinfeld JB, Redding S, Kwon Y, Gaines WA, Zhao W, Sung P, and Greene EC. (2015) Base triplet stepping by the Rad51/RecA family of recombinases. ***Science*** 349:977-81. PMCID: PMC4580133

3. Recombination Mediators that Promote Rad51 Presynaptic Filament Assembly.

Owing to its abundance and high affinity for ssDNA, Replication Protein A (RPA) promptly engages the DNA tails stemming from DSB resection. The bound RPA molecules must be displaced to allow for the assembly of the Rad51 presynaptic filament. The handoff from RPA to Rad51 is facilitated by specific "recombination mediators". In *S. cerevisiae*, Rad52 protein functions in conjunction with a group of Rad51-related proteins,

called the Rad51 paralogs, to nucleate Rad51 onto RPA-coated ssDNA to seed the assembly of the presynaptic filament (**a**-**d**). However, RAD52 plays only a subsidiary role in RAD51 presynaptic filament assembly in human cells. Instead, the tumor suppressor BRCA2 has assumed the functional role of yeast Rad52 in presynaptic filament assembly. BRCA2 synergizes with the small acidic protein DSS1 in the mediation of RPA-RAD51 exchange on the ssDNA substrate (**d**), and emerging evidence has implicated the RAD51 paralogs in the BRCA2-dependent pathway of RAD51 presynaptic filament assembly.

a. Sung, P. (1997) Function of yeast Rad52 protein as a mediator between replication protein A and the Rad51 recombinase. ***J. Biol. Chem.*** 272:28194-97.
b. Sung, P. (1997) Yeast Rad55 and Rad57 proteins form a heterodimer that functions with replication protein A to promote DNA strand exchange by Rad51 recombinase. ***Genes & Development*** 11:1111-21.
c. Sigurdsson S, Van Komen S, Bussen W, Schild D, Albala JS, and Sung P. (2001) Mediator function of the human Rad51B-Rad51C complex in Rad51/RPA-catalyzed DNA strand exchange. ***Genes & Development*** 15:3308-18.
d. Zhao WX, Vaithiyalingam S, San Filippo J, Fontenay GV, Kwon YH, Jimenez-Sainz J, Lu, L, Jensen RB, Chazin WJ, Wiese C, Sung P. (2015) Promotion of BRCA2-dependent Homologous Recombination by DSS1 via RPA Targeting and DNA Mimicry. ***Molecular Cell*** 59:176-87. PMCID: PMC4506714 **Our paper is featured on the Journal Cover.*

4. HR Factors that Facilitate DNA Strand Invasion

Work done by us has contributed to the definition of two distinct classes of factors that enhance DNA strand invasion mediated by Rad51 and/or Dmc1. Factors belonging to the first class have a requirement for ATP hydrolysis in their action, and are aptly represented by the *S. cerevisiae RAD54*-encoded protein that geneticists in the field have shown to be indispensable for HR in both mitotic and meiotic cells. Rad54 physically interacts with Rad51 and Dmc1 and, at the expense of ATP hydrolysis, translocate on dsDNA. This DNA translocase activity generates supercoiled domains in the DNA, and the negative supercoils that accumulate can lead to DNA strand opening to facilitate the efficiency of Rad51-mediated DNA strand invasion (**a**). Factors of the second category, e.g. RAD51AP1-UAF1 and the tumor suppressors BRCA1-BARD1 and PALB2, work by physically interacting with the recombinase presynaptic filament, helping capture the incoming duplex DNA, and facilitating the DNA homology search process. We have termed the three-stranded nucleoprotein ensemble harboring the presynaptic filament and these enhancer proteins the "synaptic complex" (**b, c, d**). Our studies provide the experimental framework for defining the functional relation among the aforementioned factors.

a. Petukhova G, Stratton S, and Sung P. (1998) Catalysis of homologous DNA pairing by yeast Rad51 and Rad54 proteins. ***Nature*** 393: 91-94.
b. #Wiese C, #Dray E, Groesser T, San Filippo J, Shi I, Collins DW, Tsai MS, Williams G, Rydberg B, *Sung P, and Schild D. (2007) Promotion of Homologous Recombination and Genomic Stability by RAD51AP1 via RAD51 Recombinase Enhancement. ***Molecular Cell*** 28:482-90. #*Wiese of the Schild group and Dray of the Sung laboratory contributed equally.* **Sung is a corresponding author.* PMCID: PMC2169287
c. Zhao W, Steinfeld JB, Liang FS, Chen XY, Maranon DG, Ma CJ, Kwon YH, Rao T, Wang WB, Sheng C, Song XM, Deng YH, Jimenez-Sainz J, Lu L, Jensen RB, Xiong Y, Kupfer GM, Wiese C, Greene EC, Sung P. (2017) Promotion of RAD51-mediated homologous DNA pairing by BRCA1-BARD1. ***Nature*** 550:360-365.
d. Crickard JB, Moevus CJ, Kwon Y, Sung P, Greene EC. (2020) Rad54 drives ATP hydrolysis dependent sequence alignment during homologous recombination. ***Cell*** 181:1380-1394. PMCID: PMC7418177

5. Helicases that Function in Repair DNA Synthesis or Regulation of Crossover Formation

Our studies have made important contributions toward deciphering the mechanistic underpinnings of the repair DNA synthesis reaction and the mechanisms by which HR-mediated DNA break repair is regulated to favor the formation of non-crossover recombinants to avoid deleterious chromosome rearrangements. Others found that DNA synthesis initiated from the primer end in the Rad51-made D-loop is catalyzed by DNA polymerase d, and our collaborative work with Greg Ira's group led to the identification of the conserved helicase Pif1 in helping drive Pol d-mediated repair synthesis via a migrating D-loop mechanism (**a**). Also in collaboration with the Ira group, we have discovered a remarkable attribute of the Mph1 helicase in dissociating D-loops made by Rad51, thus providing a satisfactory explanation for the anti-crossover role of this conserved helicase (**b**). Our collaborative studies with the Klein group and Guangbin Luo's laboratory (Case Western Reserve University) have shed mechanistic light on the anti-recombinase activity of the Srs2 and the human RECQ5 helicases, by revealing their ability to dismantle the presynaptic filament (**c, d**).

a. #Wilson MA, #Kwon Y, Xu Y, Chung WH, Chi P, Niu H, Mayle R, Chen X, Malkova A, *Sung P, Ira G. Pif1 helicase and Polδ promote recombination-coupled DNA synthesis via bubble migration. (2013) ***Nature***, 502:393-6. *#Wilson of the Ira group and Kwon of the Sung laboratory contributed equally. *Sung is a corresponding author.* PMCID: PMC3915060
b. Prakash R, Satory D, Dray E, Papusha A, Scheller J, Kramer W, Krejci L, Klein H, Haber JE, *Sung P, Ira G. (2009) Yeast Mph1 helicase dissociates Rad51-made D-loops: implications for crossover control in mitotic recombination. ***Genes & Develop.*** 2367-79. ****Sung is a corresponding author.*** PMCID: PMC2632165
c. Krejci L, Van Komen S, Li Y, Villemain J, Reddy MS, Klein H, Ellenberger T, Sung P. (2003) DNA helicase Srs2 disrupts the Rad51 presynaptic filament. ***Nature***, 423:305-9.
d. #Hu Y, #Raynard S, Sehorn MG, Lu X, Bussen W, Zheng L, Stark JM, Barnes EL, Chi P, Janscak P, Jasin M, Vogel H, *Sung P, Luo G. (2007) RECQL5/Recql5 helicase regulates homologous recombination and suppresses tumor formation via disruption of Rad51 presynaptic filaments. ***Genes & Develop.*** 21:3073-84. *#Hu of the Luo group and Raynard of the Sung laboratory contributed equally. *Sung is a corresponding author.* PMCID: PMC2081974

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http://www.ncbi.nlm.nih.gov/sites/myncbi/patrick.sung.1/bibliography/40712342/public/?sort=date&direction=ascending

D. Research Support

Ongoing

5RO1 ES007061-28 Sung (PI) 07/01/2016-6/30/2021
DNA Repair Genes and Proteins of the *RAD52* Group
We will continue to define the hierarchy of physical and functional interactions among the RAD51 recombinase and RAD51 paralogs of the homologous recombination machinery in the budding yeast *Saccharomyces cerevisiae.*

5RO1 CA168635-09 (MPI) Sung & Kupfer (PIs) 03/01/2017-02/28/2022
Mechanistic Dissection of the Fanconi Anemia Pathway of DNA Damage Response
Role in Project: Contact PI
We will use a combination of genetics and biochemistry to delineate the functional significance of the FANCI-FANCD2 complex in the Fanconi anemia pathway of DNA damage response and repair.

5R35 CA241801-02 Sung (PI) 09/01/2019-08/31/2026
Chromosome Damage Repair via the BRCA1/2 Axis
In this NCI Outstanding Investigator Project, a combination of biochemistry, cell-based approaches, biophysics and structural biology will be applied to continue dissecting the mechanisms of BRCA1/2-dependent chromosome damage repair that is mediated by the RAD51 recombinase and its cohort of accessory factors including nucleases, DNA helicases, and DNA polymerases. We will apply knowledge gained for isolating lead chemical compounds to use as chemical biology tools and for preclinical studies.

5PO1 CA92584-20 John Tainer (PI) 09/01/2016-08/31/2021
Structural Cell Biology of DNA Repair Machine
Role in Project: Leader of Project 3
Project 3 of this program project will employ structural (SAXS, X-ray crystallography, and NMR) approaches to address the mechanism of action of protein complexes in homologous recombination reactions in human cells, with a specific focus on the BRCA2-associated acidic protein DSS1 and on the multi-functional DNA repair protein XPG.

5R01CA221858-02 PI: Eric Greene (PI) 02/01/2020-01/31/2025
Defining the contributions of BRCA1, BRCA2 and RAD52 to genome stability
Role in Project: Subcontract PI
The Sung laboratory will construct fluorescently tagged HDR proteins, such as BRCA1, BARD1 and BRCA2, test them for biological activity and in in vitro systems of HDR. Then, the Greene laboratory at Columbia will study these tagged HDR factors for their ability to promote the assembly of RAD51 presynaptic filaments on ssDNA, to help maintain presynaptic filament stability, and to protect the presynaptic filaments against the disruptive action of anti-recombinases such as RECQ5 and FBH1.

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: ***Olsen, Shaun K***.

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

POSITION TITLE: ***Associate Professor***

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

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Rutgers University, New Brunswick, NJ	B.A.	05/2000	Biology
New York University, New York, NY	Ph.D.	05/2006	Biophysics/Biochemistry
Sloan-Kettering Institute, New York, NY	Postdoctoral	07/2013	Biophysics/Biochemistry

A. Personal Statement

In broad terms, the research in my laboratory focuses on mechanisms of molecular recognition in protein-protein interactions and on the structural enzymology of proteins essential for cellular function. The majority of our efforts are focused on understanding how enzymes in the ubiquitin (Ub) conjugation cascade (E1, E2, and E3) function together to conjugate Ub to cellular proteins. Post-translational modification of proteins by Ub is a means of regulating fundamental cellular processes including cell cycle control, DNA repair, signal transduction, and immunity. The importance of understanding how the Ub system works is underscored by the fact that dysregulation of Ub signaling is implicated in a number of human disorders and that the pathway is a validated target for therapeutic intervention in cancer. To achieve our goals, we employ a multidisciplinary approach that includes X-ray crystallography, enzymology, and a variety of biochemical and biophysical techniques. When appropriate, we use yeast genetics and eukaryotic cell-based functional assays to assess the biological importance of our structural, biochemical, and biophysical findings.

B. Positions, Scientific Appointments, and Honors

Positions

2006-2008 Research Associate, Protein Research Group, RIKEN Genomic Sciences Center, Yokohama, Kanagawa, Japan

2008-2010 Adjunct Assistant Professor, Department of Chemistry & Biochemistry, Queens College (City University of New York, New York, NY

2008-2013 Postdoctoral Fellow, Structural Biology Program, Sloan-Kettering Institute, New York, NY

2013-2019 Assistant Professor, Department of Biochemistry & Molecular Biology, Medical University of South Carolina, Charleston, SC

2020 Associate Professor, Department of Biochemistry & Molecular Biology, Medical University of South Carolina, Charleston, SC

2020 Associate Professor (tenured), Department of Biochemistry & Structural Biology, University of Texas Health at San Antonio, San Antonio, TX

Honors

1999 Phi Beta Kappa inductee

2000 Degree with Honors in the Liberal Arts, Rutgers University
2010-2012 Charles H. Revson Fellow, Sloan Kettering Institute
2010 Memorial Sloan Kettering Postdoctoral Researcher Award
2011 Blavatnik Award for Young Scientists (Finalist)
2017 MUSC High Impact Publication Award
2017 MUSC College of Graduate Studies Teacher of the Year Award
2018 MUSC College of Graduate Studies Teacher of the Year Award
2019 MUSC Developing Scholar Award
2020 Cancer Prevention & Research Institute of Texas- Rising Star Award
2021 UT STARs Faculty Award

C. Contributions to Science

Post-translational modification of proteins by ubiquitin, Nedd8, and SUMO (collectively termed Ubls) is a means of regulating fundamental cellular processes such as cell cycle control, signal transduction, and differentiation. Ubls are conjugated to proteins through the activity of an enzymatic cascade comprised of an E1 activating enzyme, an E2 conjugating enzyme, and in most instances, an E3 ligase. E1s function as gatekeepers of the conjugation cascades by specifically activating their cognate Ubl in two half-reactions involving adenylation and thioester bond formation. Despite a wealth of biochemical and structural information representing decades of research on E1s, the molecular mechanisms of E1-catalyzed adenylation and thioesterification of Ubls were unknown when I began working in this field, partially due to the unstable nature of key intermediates generated during catalysis. To solve this problem, I was involved in the development and application of semisynthetic protein-based inhibitors of Ubl E1s that enabled us to trap and determine structures of unstable intermediates formed in the two half-reactions catalyzed by E1s. These studies revealed that SUMO E1 has a single active site that is reconfigured for catalysis of adenylation or thioester bond formation via a series of complementary conformational changes in several regions of the E1. After adenylation, contacts to ATP/Mg are released, facilitating a dramatic 130 degree rotation of the E1 Cys domain and remodeling of several other structural elements that comprise the catalytic machinery of the adenylation active site. As a result, more than half of the residues that promote adenylation are replaced with residues that promote thioester bond formation, thereby toggling the catalytic competency of the active site. More recently, we obtained the first crystallographic snapshot of Ub E1 in which domain alternation and active site remodeling were observed. This study suggests that domain alternation and active site remodeling are intrinsic and interconnected structural features of Ub E1 and that the salient features of adenylation and thioester bond formation by Ub E1 is conserved across canonical Ubl E1s.

a. **Olsen SK,** Capili AD, Lu X, Tan DS, Lima CD. Active site remodeling accompanies thioester bond formation in SUMO E1. *Nature* 2010 Feb 18;463(7283):906-12 *[PMCID: 2866016]*

b. Lv Z, Yuan L, Atkison JH, Aldana-Masangkay G, Chen Y, **Olsen SK**. Domain Alternation and Active Site Remodeling Are Conserved Structural Features of Ubiquitin E1. *J. Biol. Chem*. 2017 Jul 21;292(29):12089-12099 *[PMCID: 5519361]*

c. Lv Z, Yuan L, Atkison JH, Williams KM, Vega R, Sessions EH, Divlianska DB, Davies C, Chen Y, **Olsen SK**. Molecular mechanism of a covalent allosteric inhibitor of SUMO E1 activating enzyme. *Nature Communications* 2018 Dec 4;9(1) *[PMCID: 6279746]*

d. Lv Z, Williams KM, Yuan L, Atkison JH, **Olsen SK**. Crystal structure of a human ubiquitin E1-ubiquitin complex reveals conserved functional elements essential for activity. *J. Biol. Chem*. 2018 Nov 23;293(47): 18337-18352 *[PMCID: 6254350]*

II. Once the E1~Ubl thioester intermediate has been generated, the next step in the Ubl conjugation cascade involves recruitment of an E2 enzyme followed by transfer of the Ubl from the E1 catalytic cysteine to the E2 catalytic cysteine. Although the structure of Nedd8 E1 in complex with its E2 had been determined prior to my entering this area of research, the E1 and E2 active sites were situated more than 20 Å away from each other

and thus the conformational changes and contacts involved in bringing the E1and E2 active sites were unknown. Another unresolved issue was the basis by which a particular Ubl E1 achieves selectivity for its cognate E2(s) as opposed to E2s from other Ubl pathways. To gain insights into this process I developed a strategy for trapping E1 and E2 in a catalytically relevant conformation by specifically cross-linking their catalytic cysteine residues, a breakthrough that led to the first crystal structure of a Ub E1-E2 complex. The structure revealed a combinatorial mechanism for Ub E2 recruitment to Ub E1 that involves E2 contacts to two distinct domains of the E1 as well as conformational changes within the E1 that are required for the E1 and E2 active sites to come together during thioester transfer. More recently, we uncovered a new E1 binding mode for the E2 Ubc15 and determined that the intrinsically low level of E1-E2 thioester transfer activity of Ubc15 largely results from the presence of an acidic residue at its N-terminus that electrostatically clashes with an acidic patch on E1. Notably, the N-termini of many other Ub E2s are serine/threonine rich and we demonstrated that phosphorylation of these sites could serve as novel regulatory mechanism of Ub E2 activity.

a) **Olsen SK,** Lima CD. Structure of a ubiquitin E1-E2 complex: insights to E1-E2 thioester transfer. *Mol Cell.* 2013 Mar 7;49(5):884-96 *[PMCID:* 3625138*]*

b) Lv Z, Rickman KA, Yuan L, Williams K, Selvam SP, Woosley AN, Howe, PH, Ogretmen B, Smogorzewska A, **Olsen SK**. *S. pombe* Uba1-Ubc15 structure reveals a novel regulatory mechanism of ubiquitin E2 activity. *Mol Cell.* 2017 Feb 16;65(4):699-714 *[PMCID: 5319395]*

c) Williams KM, Que S, Atkison JH, Salazar-Arango S, Diehl JA, **Olsen SK**. Structural insights into E1 recognition and the ubiquitin-conjugating activity of the E2 enzyme Cdc34. *Nat. Commun.* 2019 Jul 24;10(1):3296 *[PMCID: 6656757]*

d) Yuan L, Lv Z, Adams MJ, **Olsen SK**. Crystal structures of an E1-E2-ubiquitin thioester mimetic reveal molecular mechanisms of transthioesterification. *Nat. Commun. 2021* Apr 22;12(1):2370

III. The E2~Ub intermediate resulting from E1-E2 thioester transfer interacts with members of three different families of Ub E3 ligases (RING, HECT, and RING-in-between-RING (RBR)) that catalyze Ub conjugation to target proteins by distinct mechanisms. RBR E3s are a distinct class of Ub E3 ligases that function through a RING/HECT hybrid mechanism in which the RBR RING1 domain initially recruits the E2~Ub thioester intermediate, similar to canonical RING E3s. However, rather than facilitating Ub discharge from E2~Ub onto target protein lysine residues directly like a canonical RING E3, E2~Ub binding to the RING1 domain of RBR E2s is followed by thioester transfer of Ub to a catalytic cysteine residue in the RING2 domain similar to HECT E3s. A fundamental question that arises from these observations is how RBRs prevent Ub discharge to lysine residues upon E2~Ub to the RING1 domain, despite RING1 strongly resembling a canonical RING E3. We recently determined the crystal structure of the RBR E3, HHARI, in complex with a UbcH7~Ub thioester mimetic. The structure revealed mechanistically important UbcH7~Ub-induced conformational changes in the RING1 and UBA-like domains of HHARI that play a key role in determining the specificity of this E2/E3 pair, as well as in promoting recruitment of UbcH7~Ub in the 'open' conformation. Overall, our structural and biochemical studies indicate that HHARI ensures transfer of Ub from E2 to the RING2 catalytic cysteine as opposed to discharge from E2 directly to lysine residues upon RING1 binding in at least three ways: 1) by evolving a mechanism to specifically recruit an E2 that solely performs transthiolation (UbcH7), 2) by harboring a loop insertion in the RING1 domain (unique to RBR E3s) that is involved in determining specificity of HHARI for UbcH7 and is incompatible with the UbcH7~Ub binding in the 'closed' conformation primed for Ub discharge to lysine residues, and 3) contacts between Ub and the UBA-like domain that promote recruitment of UbcH7~Ub in the inactive 'open' conformation.

a) Yuan L, Lv Z, Atkison JH, **Olsen SK**. Structural insights into the mechanism and E2 specificity of the RBR E3 ubiquitin ligase HHARI. *Nat. Commun.* 2017 Aug 8; 8:211 *[PMCID: 5548887]*

IV. Spider dragline silk is a natural polymer harboring unique physical and biochemical properties that make it an ideal biomaterial. Artificial silk production requires an understanding of the *in vivo* mechanisms spiders use to convert soluble proteins, called spidroins, into insoluble fibers. Controlled dimerization of the spidroin N-

terminal domain (NTD) is crucial to this process. A more complete understanding of the molecular mechanisms governing pH-dependent dimerization of the NTD during silk fiber formation *in vivo* could facilitate artificial production of spider silk for use as a biomaterial. Further, silks produced from different spider species vary significantly in physical properties such as flexibility and tensile strength. While currently unknown, the molecular basis underlying these differing properties could prove useful for generation of silks optimized for different applications. To gain insights into these processes, we determined the crystal structure of the *Nephila clavipes* NTD (^{Nc}NTD) to 2.02 Å resolution. Surprisingly, despite having high sequence identity, our structural analysis revealed a distinct asymmetry at the ^{Nc}NTD dimer interface relative to its *E. australis* ortholog. Our analysis revealed a series of novel intra- and intermolecular interactions that play a role in NTD dimer formation and uncovered an additional layer of complexity to the pH-sensitive relay mechanism for NTD dimerization. Based on our findings, we propose that plasticity at the NTD dimer interface plays a role in the pH-dependent transition of the NTD from a loosely to stably associated dimer as the spidroin progresses through the spider's silk extrusion duct and this will be an active area of investigation.

a) Atkison JH, Parnham S, Marcotte WR Jr, **Olsen SK**. Crystal Structure of the *Nephila clavipes* Major Ampullate Spidroin 1A N-terminal Domain Reveals Plasticity at the Dimer Interface. *J. Biol. Chem*. 2016 Sep 2;291(36):19006-17 *[PMCID: 5009272]*

V. Fibroblast growth factors play an essential role in human biology as regulators of embryonic development, homeostasis and regenerative processes. The twenty-two mammalian FGFs elicit their distinct biological effects by binding to and activating a unique subset of FGF receptor tyrosine kinases (FGFR1-4) at the cell surface. Alternative splicing of FGFs and FGFRs generates an additional level of sequence diversity, which in turn ultimately determines specificity in the FGF-FGFR system. A tissue-specific alternative splicing event in Ig domain 3 of FGFR1-3 results in the expression of epithelial FGFRb isoforms and mesenchymal FGFRc isoforms, and allows for directional epithelial-mesenchymal signaling which is required for organogenesis. To better understand the basis for molecular recognition in FGF-FGFR interactions and how alternative splicing governs specificity in these interactions, I structurally and biochemically characterized a selected set of FGF-FGFR pairs. The results of these studies revealed the basis by which FGF8 achieves exquisite specificity for the 'c' isoforms of FGFR and for how alternative splicing at the N-terminus of FGF8 regulates the organizing potential of this protein in the brain. I also determined the molecular basis by which FGF1 functions as a 'pan' FGFR ligand due to its ability to activate all FGFRs. These studies revealed that FGF1 exhibits a remarkable degree of structural plasticity that equips this protein with the adaptability required to engage in contacts with the distinct interaction surfaces presented to it by the repertoire of FGFRs present in cells. Together, this work answered a number of longstanding questions in the FGF field and contributed to the transformation of FGF signaling into one of the foremost structurally understood ligand-receptor systems among receptor tyrosine kinases.

a. **Olsen SK**, Bromleigh C, Ibrahimi OA, Eliseenkova AV, Zhang F, Linhardt RJ, Joyner AL, Mohammadi, M. Structural Basis By Which Alternative Splicing Modulates the Biological Activity of FGF8 in the Brain. Genes Dev. 2006 Jan 15;20(2):185-98. *[PMCID: 1356110]*

b. **Olsen SK**, Ibrahimi OA, Raucci A, Zhang F, Eliseenkova AV, Yayon A, Basilico C, Linhardt RJ, Schlessinger J, Mohammadi M. Insights into the molecular basis for fibroblast growth factor receptor autoinhibition and ligand-binding promiscuity. Proc. Natl. Acad. Sci. U S A. 2004 Jan 27;101(4):935-40 *[PMCID:* 327120*]*

c. **Olsen SK**, Garbi M, Zampieri N, Eliseenkova AV, Ornitz DM, Goldfarb M, Mohammadi, M. Fibroblast growth factor (FGF) homologous factors share structural but not functional homology with FGFs. J. Biol. Chem. 2003 Sep 5;278(36):34226-36 *[PMCID:12815063]*

Complete List of Published Work in My Bibliography:

https://www.ncbi.nlm.nih.gov/myncbi/shaun.olsen.1/bibliography/public/

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

Ongoing

1R01GM115568 09/01/2020 – 08/31/2024 Olsen (PI)

Structural Biology of the Ubiquitin Conjugation System- The research in this proposal aims to establish the rules governing molecular recognition and promiscuity across Ub E1-E2 and E2-RING-in-between-RING E3 ligase interactions.

Role: PI

1R01GM128731 04/15/2019 – 02/28/2023 Olsen (PI)

Structure and function of the essential cell cycle regulator Cdc34- The goal of this project is to elucidate the molecular mechanisms by which the three enzymes E1, Cdc34, and SCF E3 function together as essential regulators of the cell cycle by specifically assembling Lys48 polyubiquitin chains on target proteins.

Role: PI

RR200030 09/01/2020 – 08/31/2025 Olsen (PI)

Recruitment of Rising Stars Investigator- This faculty recruitment award is a startup package that provides general support to the Olsen laboratory over a 5-year period, including salaries for laboratory personnel, supplies, equipment purchase, equipment maintenance and repair, facility renovations, secretarial support, core facility access fees, and travel.

Role: PI