BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
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NAME: Cheng-Guo Wu

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

POSITION TITLE: Graduate Student Research Assistant

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
National Yang-Ming University, Taipei, Taiwan	BS	06/2012	Biology
National Taiwan University, Taipei, Taiwan	MS	06/2014	Biochemistry
University of Wisconsin, Madison, WI	PHD		Biophysics

A. Personal Statement

I was trained as a structural biologist in my early stage of research career by Dr. Chi-Yuan Chou when I was an undergraduate student at Yang-Ming University. To investigate protein functions with atomic-level information from protein structures was so fascinating and always intrigued me to dig out the mechanism of biological events. From then on, my research interest has been to reveal the key molecular mechanism of proteins that involves in key cellular processes and in human diseases. Besides to what I've learned from structure biology labs, my research experience has provided me with a profound background in cell biology, biochemistry, biophysics and structural biology. While in my college, I was fortunate enough to be awarded a research fellowship from the National Science Council to conduct my research projects which eventually led to two first-author publications during three years I worked in the lab. My research results provided important structural insights into the drug discovery for anti-SARS-CoV (severe acute respiratory syndrome coronavirus) drugs which gave me a strong sense of achievement because of what I had contributed to this world. Encouraged by this experience, I joined Dr. Chun-Hung Lin's lab in Academia Sinica for my master's study. Dr. Lin's lab is known to combine biological and chemical strategies to develop new drugs for human diseases, especially diseases caused by bacterial infections. During the time I was in the lab, I combined knowledge in biology and chemistry to my projects which broadened my horizon in how to use interdisciplinary approaches to answer biological questions with broader perspectives and strategies. This training allowed me to successfully characterize an important protein target (FUCA2) that plays an important role in bacterial infection. Equipped with tool kits that learned from my first two labs, I decided to pursue my PhD degree in the Biophysics Program in the University of Wisconsin under Dr. Yongna Xing's lab. Working in Dr. Xing's lab has offered me a chance to work on an important human protein (PP2A) which involves in a broad range of cellular functions and human diseases, including cancer and neurological disease. In Dr. Xing's lab, I can not only use my previous expertise on my projects but also learn a lot of new techniques that I didn't have touched before. Especially, I have been learning cryo-EM in the past two years and have already been able to handle most of the key experiments independently. The training here has allowed me to reveal key mechanisms related to PP2A biogenesis and substrate binding. The resulting publications have benefited the field to discover new cellular functions and regulation of PP2A. Currently, I'm working on a project aiming to decipher the structural mechanism of a neurological disease called Jordan's Syndrome using cryo-EM as the major approach. With

plenty of training, I have received since my undergraduate study, I'm ready to contribute myself to society by translating my scientific skills into research results that benefit and impact the world.

B. Positions and Honors

Positions and Employment

2009-2012 Undergraduate Student Research Assistant, National Yang-Ming University
2012-2014 Graduate Student Research Assistant, National Taiwan University
2015- Graduate Student Research Assistant, University of Wisconsin-Madison

Honors

2011 Outstanding Award, Thesis Competition, National Yang-Ming University
2011 Outstanding Award, Poster Presentation Competition, National Yang-Ming University
2011 College Student Research Scholarship (from National Science Council), National Yang-Ming University
2014 Outstanding performance, Oral Presentation, National Taiwan University
2014 Outstanding performance, Poster Presentation Competition, National Taiwan University
2017 Best Junior Student Poster Presentation, Biophysics Colloquium, University of Wisconsin-Madison

C. Contributions to Science

1. Undergraduate Research: I joined Dr. Chi-Yuan Chou's lab since my sophomore year at National Yang-Ming university until I graduated from college. Dr. Chou's laboratory studies important biological topics using structural biology and enzyme kinetics as main approaches. During my time in his lab, my first main contribution was to determine the crystal structure of an attractive protein target for developing an anti-SARS-CoV drug. My research eventually revealed structural insight into the mechanism for controlling the maturation of SARS coronavirus's main protease, benefiting the drug discovery for SARS-CoV. Moreover, I determined the structure of S-crystallin, the lenses protein of cephalopod, to delineate the mechanisms of how has cephalopod S-crystallin evolved from the ancient glutathione S-transferase. My contributions to these works were included in two publications.

Tan WH*, Cheng SC*, Liu YT*, Wu CG*, Lin MH, Chen CC, Lin CH, Chou CY. (2016) Structure of a highly active cephalopod S-crystallin mutant: new molecular evidence for evolution from an active enzyme into lens-refractive protein. Sci. Rep. 6:31176 (co-first author)

a. Wu CG*, Cheng SC, Chen SC, Li JY, Fang YH, Chen YH, and Chou CY. (2013) Mechanism for controlling the monomer-dimer conversion of SARS coronavirus main protease. Acta Crystallogr. D Biol. Crystallogr. 69, 747-755

2. Graduate Research during master's study: To devoted myself into science, I applied to a master's degree program at National Taiwan University. During two years in my master's study, I joined Dr. Chun-Hung Lin's lab in Academia Sinica to work on a project related to glycobiology. My main project was to characterize human Fucosidase 2 (FUCA2) which is a protein that is over-secreted when the human gastric epithelium is infected by Helicobacter pylori which causes gastritis. My contribution was to prepare recombinant FUCA2 that never been successfully purified before. After successfully prepared FUCA2, I determined the substrate specificity of FUCA2 and unraveled its role in controlling the host-pathogen interaction. Currently, the lab is trying to develop small molecules to target the protein for preventing *H.pylori* infection. During the time in Dr. Lin's lab, I also had a lot of change to work with organic chemists on drug development which incorporated lots of chemical knowledge into my biological projects and expanded my research skillsets. My master's research has been published in my master's thesis.

a. Wu CG, Lin CH (2014) "Characterizations of B. Fragilis GDP-fucose Synthetase and Human alpha-L-Fucosidase 2"

3. Graduate Research: Currently I'm studying my PhD degree instructed by Dr. Yongna Xing at University of Wisconsin. Dr. Xing's lab is a well-established structural biology lab studying the structural basis of human Protein Phosphatase 2A's (PP2A) function and key mechanism involve in PP2A biogenesis. My first research focus was to elucidate the molecular mechanism in disassembly active PP2A into the latent form of PP2A, a

key process to regulate PP2A activity in specific cellular processes. My contribution to this project led to a novel PP2A complex structure that revealed striking mechanisms for disassembly of PP2A holoenzymes. This research provides new insights into PP2A regulation and biogenesis.

a. Wu CG*, Zheng A*, Jiang L, Rowse M, Stanevich V, Chen H, Li Y, Satyshur KA, Johnson B, Gu TJ, Liu Z, Xing Y. (2017) Methylation-regulated decommissioning of multimeric PP2A complexes. Nat Commun. 8: 2272

4. The second direction I worked during my Ph.D. study is to identify interaction motifs for PP2A-B' holoenzymes to reveal the molecular mechanism of substrate recognition for this type of PP2A holoenzymes. In collaboration with Dr. Ylva, we identified consensus motifs that are recognized by PP2A-B' holoenzymes which led us to discover more than 100 new PP2A substrates in the human proteome. Furthermore, we developed a high-throughput strategy to explore and validate PP2A substrates and their cellular functions. Specifically, we identified many proteins at centrosome and midbody have binding motifs for PP2A-B' holoenzymes. Our further studies revealed how these substrates are regulated by the phosphorylation by the interplay between kinases and PP2A to control normal cellular functions during cytokinesis. Discovery of interaction motifs for PP2A-B' holoenzymes has offered significant insights for scientists in the fields and led to the discovery of lots of novel PP2A substrates and cellular functions of PP2A.

a. Wu CG*, Chen H*, Guo F*, Kyaiims V*, Rowse M, Mcilwain SJ, Ong IM, Li Y1 , Gu T, Zheng A, Lee W, Johnson B, Burkard E, Ivarsson Y, Xing Y. PP2A-B' holoenzyme substrate recognition, regulation, and role in cytokinesis. Nature Cell Discovery, (2017) 3, 17027; doi:10.1038.

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

YEAR	COURSE TITLE	GRADE
	National Yang-Ming University	
2**008**	Principal of Chemistry	A
	Laboratory in Chemistry	B
	Organic Chemistry	A
	Laboratory in Organic Chemistry	A
2009	Life Science II- Biochemistry (1)	A
	Life Science II- Biochemistry (2)	A
	Life Science Laboratory II- Biochemistry	A
	Life Science II - Cell Biology	A
	Life Science II - molecular Biology	A
	Laboratory in molecular Cell Biology	A
2010	Life Science III – Physiology	A
	Life Science III – Developmental Biology	A
	Molecular Enzymology	A
	Tissue Engineering and Regenerative Medicine	A
2011	Instrumental Analysis	A
	Structural Biology (1)	A
	Thermodynamics	A
	Introduction to Clinical Medicine	A
	Molecular Simulation: Concept and Application	A
	National Taiwan University	
2012	Protein Modification Mechanism and Cell Signaling	B
	Structural Biochemistry	A
	DNA Damage Response	A
	The Stories of Great Biochemists	A
	Drug Design and Development	A
2013	Glycobiology	A
	Introduction to Biochemical Laboratory Teaching	A
2014	Protein Structure and Function	A

University of Wisconsin-Madison		
2015	Topic-Macromoleculr/Biophysics	A
	Eukaryotic Molecular Biophysics	B
	Topic-Macromoleculr/ Biophysics	A
2016	Protein&Enzyme Structure&Functtion	A
	Topic-Macromoleculr/ Biophysics	A
2017	Topic-Macromoleculr/ Biophysics	A
2017	Topic-Macromoleculr/ Biophysics	A

BIOGRAPHICAL SKETCH

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NAME: Yitong Li

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

POSITION TITLE: Postdoctoral research associate

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

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
China Agricultural University, Beijing, China	BS	07/2011	Chemistry
Peking University, Beijing, China	PHD	07/2016	Chemical biology
University of Wisconsin-Madison, Madison, WI	Postdoctoral Fellow		Biochemistry and structure biology

A. Personal Statement

I have a broad background in chemistry, biochemistry, chemical biology and biophysics, and have extensive experience in CryoEM technology and DNA damage research in cells. My work has focused on elucidating the molecular, structural and biochemical basis of diverse cell signaling pathways and regulations related to cancer and cytotoxicity, such as phosphatase regulation, aryl hydrocarbon receptor (AHR) signaling, and protein degradation system. My research utilizes diverse multi-disciplinary biophysical and biochemical approaches to gain deep mechanistic understanding and facilitate identification of novel therapeutic targets and strategies.

B. Positions and Honors

Positions

09/2016- Postdoctoral research associate, University of Wisconsin-Madison, Madison, WI

Honors

2008-2010 Merit Student, China Agricultural University, Beijing, China
2008 National Scholarship, China Agricultural University, Beijing, China
2009 National Scholarship for Encouragement, China Agricultural University, Beijing, China
2010 Syngenta Scholarship, China Agricultural University, Beijing, China
2013 Student Award for Social work, Peking University, Beijing, China

C. Contributions to Science

Develop new methods for protein semi-synthesis and modification

Understanding how the posttranslational modifications affect protein intrinsic function, stability, localization, and three-dimensional structure, as well as interactions with other molecules is at the heart of experimental biology. Protein chemical semisynthesis is one of the most powerful methods to generate posttranslationally modified proteins. As a PhD student, I and other colleagues developed a new sortase-mediated hydrazinolysis reaction of proteins, which not only is useful reagents for the hydrazone-type bioconjugation reactions, but also can be used as thioester surrogates for the semichemical synthesis of proteins through native chemical ligation.

1. Yiming Li[+], **Yitong Li[+],** Man Pan, Xiuqi Kong, Yichao Huang, Zhang-Yong Hong, and Lei Liu*, Irreversible Site-Specific Hydrazinolysis of Protein by Use of Sortase. *Angew. Chem. Int. Ed.* **2014***, 53,* 2198. **([+]co-first authors)**
2. Yiming Li, Maiyun Yang, Yichao Huang, **Yitong Li,** Peng R Chen*, and Lei Liu*, Ligation of Expressed Protein α-Hydrazides via Genetic Incorporation of an α-Hydroxy Acid. *ACS Chem. Biol.* **2012**, *7*, 1015.

The regulatory mechanism study of post-translationally modified Autophagy Regulation Proteins via protein semi-synthesis

Autophagy is a catabolic process for the degradation of cellular contents. More than 40 autophagy related proteins are charged for the tight control of autophagic functions. There are multiple post-translational modifications to regulate Autophagy. However, it is difficult to obtain pure site-specific modified protein to perform research. To synthesize LC3-II, we developed a new method to use a light-activatable solubilizing side chain to assist the ligation of the lipopeptides. Next, I semi-synthesized double acetylated Atg3 using expressed protein ligation. We found that acetylation of Atg3 significantly enhanced the binding between Atg3 and liposome containing physiological level of PE. Our work provided new insights into regulation of Autophgy.

1. **Yitong Li,** Cong Yi, Huan Lan, Man Pan, Shao-Jin Zhang, Yi-Chao Huang, Yiming Li*, Li Yu*, and Lei Liu*, Protein Acetylation Enhances Membrane Binding: A Semisynthetic Study on Autophagy Regulation Protein Atg3. *Nat. Commun.* **2017**, *8,* 14846.
2. Yichao Huang, Yiming Li, Yang Chen, Man Pan, **Yitong Li,** Li Yu, Qingxiang Guo, and Lei Liu*, Synthesis of Autophagosomal Marker Protein LC3-II under Detergent-Free Conditions. *Angew. Chem. Int. Ed.* **2013**, *52*, 4858

New semi-synthesis method to generate fluorogenic substrate for deubiquitinating enzymes

Ubiquitination is a reversible post-translational modification process that plays an important role in cell biology. The removal of Ub (ubiquitin) from a modified protein is regulated by the deubiquitinating enzymes (DUBs). Increasing evidences have revealed the involvement of malfunctioning DUBs in some human diseases. To monitor the activity of DUBs and to screen small molecule inhibitors against DUBs, we developed a new method to synthesize various biochemical tools such as the C-terminal conjugates of Ub with fluorophores such as 7-amino-4-methylcoumarin (AMC) and 7-amino-4-carbamoylmethyl-coumarin (ACC).

1. **Yitong Li,** Yichao Huang, Yang Xu, Man Pan, Yiming Li*, Ubiquitin 7-amino-4-carbamoylmethylcoumarin as an improved fluorogenic substrate for deubiquitinating enzymes. *Tetrahedron*. **2016**, *72*, 4085.
2. **Yitong Li,** Jun Liang, Jiabin Li, Gemin Fang, Yong Huang, and Lei Liu*, New semi-synthesis of ubiquitin C-terminal conjugate with 7-amin-4-methylcoumarin. *J. Pept. Sci.* **2014**, *20*, 102.

Structural biology and molecular mechanism study of the protein phosphatase 2A (PP2A) regulation

My current research is focused on deciphering the biogenesis and regulatory mechanism of PP2A holoenzyme by combination of biochemistry, cryoEM and cell biology methods. We recently found that PME-1 interacts with various PP2A holoenzymes and directly catalyzes the demethylation besides core enzyme. The interaction between PME-1 and PP2A holoenzyme hinders substrate recognition of the holoenzymes.

1. **Yitong Li,** Michael Rowse, Cheng-Guo Wu, Seunghyeon Seok, Anastasia Phoebe Bravos, Mohammed Jeffri, Yongna Xing* Dual roles of PME-1 in demethylation and inhibition of PP2A holoenzymes.*2020***,** in preparation.
2. Ryan M De Palma, Stuart R Parnham, **Yitong Li,** Joshua J Oaks, Yuri K Peterson, Zdzislaw M Szulc, Braden M Roth, Yongna Xing and Besim Ogretmen* The NMR-based characterization of the FTY720-SET complex reveals an alternative mechanism for the attenuation of the inhibitory SET-PP2A interaction. *The FASEB Journal* **2019,** *33,* 7647.
3. Cheng-Guo Wu, Aiping Zheng, Li Jiang, Michael Rowse, Vitali Stanevich, Hui Chen, **Yitong Li,** Kenneth A Satyshur, Benjamin Johnson, Ting-Jia Gu, Zuojia Liu, Yongna Xing* Methylation-regulated decommissioning of multimeric PP2A complexes. *Nat. Commun.* **2017**, *8,* 2272.
4. Cheng-Guo Wu, Hui Chen, Feng Guo, Vikash K Yadav, Sean J Mcilwain, Michael Rowse, Alka Choudhary, Ziqing Lin, **Yitong Li,** Tingjia Gu, Aiping Zheng, Qingge Xu, Woojong Lee, Eduard Resch, Benjamin Johnson, Jenny Day, Ying Ge, Irene M Ong, Mark E Burkard, Ylva Ivarsson*, and Yongna Xing*, PP2A-B′ holoenzyme substrate recognition, regulation and role in cytokinesis. *Cell Disc.* **2017**, *3*, 17027.

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

Active
Proposal 51297 03/2020-03/2022
Pacific Northwest Center for Cryo-EM
Structural study of PP2A-B'δ holoenzyme
Completed
Proposal 50743
Pacific Northwest Center for Cryo-EM 05/2019-02/2020
Decommissioning of protein phosphatase 2A holoenzymes

BIOGRAPHICAL SKETCH

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NAME: Ramya, Sundaresan

eRA COMMONS USER NAME (credential, e.g., agency login): ramya_s (created in previous institution)

POSITION TITLE: Post-doctoral Research Associate

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

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Madras, India	B.Sc	04/2005	Microbiology
University of Madras, India	M.Sc	04/2007	Biotechnology
University of Madras, India	Ph.D.	09/2015	Biotechnology-Crystallogaphy and Biophysics

A. Personal Statement

I have a broad background in Microbiology, Biotechnology with specific training and expertise in protein purification, protein biochemistry and structural biology. My doctoral studies under Prof. P. Karthe, mainly focused on protein purification, biophysical characterization, crystallization and structural studies of bacterial surface adhesive proteins. My doctoral work also comprised structural analysis of two arginine biosynthesis pathway enzymes (TtNAGK and TtOTC) from thermophilic organisms. I believe my transition from being a micro-biologist as an under-graduate to protein-biochemist/ structural biologist during my doctoral studies had taught me several skillsets and enabled me to venture new arenas and challenges. My first post-doctoral experience in Dr. Rakhi Rajan's lab, gave me wide scope to explore the protein-RNA/DNA biochemical aspects. I was exposed to the world of RNA during this time and gained experience in understanding the intricacies involved in in-vitro RNA transcription and RNA bulk production for both biochemical and structural characterization of a protein-RNA complex. I had the wonderful opportunity to learn the basics of Cryo-EM with hands on experience (Cryo-EM-workshop in ASU, Phoenix) in negative staining sample preparation and cryo-plunging. In my current second post-doctoral studies in Dr. Yongna Xing's lab, University of Wiscondin-Madison, I had the wonderful opportunity to explore PP2A biology and acquire several new skillsets including insect-cell based protein production and cryo-EM techniques with respect to PP2A B'delta holoenzyme. I have acquired the necessary training in insect cell-based protein preparation and also strengthening my cryo-EM techniques. With my research experience in protein biochemistry and with the current possibilities of excellent cryo-EM facilities to achieve high resolution structures I believe I can contribute in understanding the cross talk between PP2A cell and also identify their key regulatory components and thereby enabling designs for cancer therapeutics

a) **Sundaresan, R.**, Parameshwaran, H. P., Yogesha, S. D., Keilbarth, M. W., & Rajan, R. (2017). RNA-Independent DNA Cleavage Activities of Cas9 and Cas12a. Cell Rep, 21(13), 3728-3739. doi:10.1016/j.celrep.2017.11.100
b) **Sundaresan, R.**, Samen, U., & Ponnuraj, K. (2015). Structure of KRT4 binding domain of Srr-1 from Streptococcus agalactiae reveals a novel beta-sheet complementation. Int J Biol Macromol, 75, 97-105. doi:10.1016/j.ijbiomac.2014.12.048

c) **Sundaresan, R.**, Ragunathan, P., Kuramitsu, S., Yokoyama, S., Kumarevel, T., & Ponnuraj, K. (2012). The structure of putative N-acetyl glutamate kinase from Thermus thermophilus reveals an intermediate active site conformation of the enzyme. Biochem Biophys Res Commun, 420(3), 692-697. doi:10.1016/j.bbrc.2012.03.072

B. Positions and Honors

Positions and Employment

2019-until now Post-doctoral Researcher, University of Wisconsin-Madison, WI
2016-2019 Post-doctoral Fellow, University of Oklahoma, OK

Other Experience and Professional Memberships

2019- Member, National Postdoctoral Association

Honors

2008-2009 Project Fellow awarded by the Department of Biotechnology
2009-2011 Junior Research Fellowship, by University Grants Commission (UGC) under Research Fellowship in Sciences for Meritorious Students (RFSMS) Scheme
2012-2014 Senior Research Fellowship, by University Grants Commission (UGC) under Research Fellowship in Sciences for Meritorious Students (RFSMS) Scheme

C. Contribution to Science

1. My early career contributions were mainly based on my practical applications of my knowledge from Microbiology and Biotechnology. My acquired skill sets along with my passion to explore science fortunately led me to step into the world of proteins and structural biology under the guidance of my mentor Professor P.Karthe. I had the wonderful opportunity to expand my understanding on basic molecular biology practices and purification of bacterial surface proteins. My particular role in the project was to express and purify a small domain of recombinant serine rich repeat protein1 of *Streptococcus agalactiae* for the ultimate goal of obtaining its structure. I had the training on protein purification techniques including chromatography techniques like affinity, ion-exchange and size-exclusion chromatography using AKTA-FPLC. I had also explored the protein structures of the Arginine biosynthesis pathway of thermophilic micro-organisms. My bio-informatics approach and skill sets were expanded and vastly acquired during these structural analysis explorations. I also obtained extensive training on the crystallization techniques and necessary basic structure solving techniques. My key contributions to the scientific field during doctoral studies were obtaining the crystal structure implications of the keratin binding domain of Srr-1 protein from *S.agalactiae* and the structural understanding of N-acetyl glutamate kinase enzymes from thermophilic organisms. A compilation of other contributions related to my work during this period are listed below as publications.
    a) **Sundaresan, R.**, Ebihara, A., Kuramitsu, S., Yokoyama, S., Kumarevel, T., & Ponnuraj, K. (2015). Crystal structure analysis of ornithine transcarbamylase from Thermus thermophilus --HB8 provides insights on the plasticity of the active site. Biochem Biophys Res Commun, 465(2), 174-179. doi:10.1016/j.bbrc.2015.07.096
    b) **Sundaresan, R.**, Samen, U., & Ponnuraj, K. (2015). Structure of KRT4 binding domain of Srr-1 from Streptococcus agalactiae reveals a novel beta-sheet complementation. Int J Biol Macromol, 75, 97-105. doi:10.1016/j.ijbiomac.2014.12.048
    c) **Sundaresan, R.**, Ragunathan, P., Kuramitsu, S., Yokoyama, S., Kumarevel, T., & Ponnuraj, K. (2012). The structure of putative N-acetyl glutamate kinase from Thermus thermophilus reveals an intermediate active site conformation of the enzyme. Biochem Biophys Res Commun, 420(3), 692-697. doi:10.1016/j.bbrc.2012.03.072
    d) **Sundaresan, R.**, Samen, U., & Ponnuraj, K. (2011). Expression, purification, crystallization and preliminary X-ray diffraction studies of the human keratin 4-binding domain of serine-rich repeat

protein 1 from Streptococcus agalactiae. Acta Crystallogr Sect F Struct Biol Cryst Commun, 67(Pt 12), 1582-1585. doi:10.1107/S1744309111040413

2. As a postdoctoral fellow, my initial research experience with protein-RNA/DNA biochemical studies in the field of CRISPR has provided me a whole new perspective of the protein-nucleic acid relationship. Our major work was translated into a publication as "RNA-Independent DNA Cleavage Activities of Cas9 and Cas12a" which highlights the possible effects of metal ions on CRISPR-associated (Cas) protein activities in absence of a guide RNA, thereby cautioning the gene editing applications.

    a. **Sundaresan, R.**, Parameshwaran, H. P., Yogesha, S. D., Keilbarth, M. W., & Rajan, R. (2017). RNA-Independent DNA Cleavage Activities of Cas9 and Cas12a. Cell Rep, 21(13), 3728-3739. doi:10.1016/j.celrep.2017.11.100
    b. Murugan, K., Babu, K., **Sundaresan, R.**, Rajan, R., & Sashital, D. G. (2017). The Revolution Continues: Newly Discovered Systems Expand the CRISPR-Cas Toolkit. Mol Cell, 68(1), 15-25. doi:10.1016/j.molcel.2017.09.007

3. In my second post-doctoral research, my current focus in Dr. Xing's lab related to this application is on understanding the complex protein phosphatase (PP2A) and related signaling mechanisms by unravelling the key structural components of PP2A holoenzymes contributing to the PPP2R5D disorder termed "Jordan's syndrome", thereby contributing for cancer therapeutics. With all the necessary training and hand's on experience in protein preparation and Cryo-EM sample preparations obtained within this span in Dr. Xings's lab, I am quite confident and excited to explore the PPP2R5D biology with respect to my contributions in protein preparations and structural implications using Cryo-EM approach.

Complete List of Published Work in MyBibliography:

    a. **Sundaresan, R.**, Parameshwaran, H. P., Yogesha, S. D., Keilbarth, M. W., & Rajan, R. (2017). RNA-Independent DNA Cleavage Activities of Cas9 and Cas12a. Cell Rep, 21(13), 3728-3739. doi:10.1016/j.celrep.2017.11.100
    b. Murugan, K., Babu, K., **Sundaresan, R.**, Rajan, R., & Sashital, D. G. (2017). The Revolution Continues: Newly Discovered Systems Expand the CRISPR-Cas Toolkit. Mol Cell, 68(1), 15-25. doi:10.1016/j.molcel.2017.09.007

    c. **Sundaresan, R.**, Ebihara, A., Kuramitsu, S., Yokoyama, S., Kumarevel, T., & Ponnuraj, K. (2015). Crystal structure analysis of ornithine transcarbamylase from Thermus thermophilus --HB8 provides insights on the plasticity of the active site. Biochem Biophys Res Commun, 465(2), 174-179. doi:10.1016/j.bbrc.2015.07.096
    d. **Sundaresan, R.**, Samen, U., & Ponnuraj, K. (2015). Structure of KRT4 binding domain of Srr-1 from Streptococcus agalactiae reveals a novel beta-sheet complementation. Int J Biol Macromol, 75, 97-105. doi:10.1016/j.ijbiomac.2014.12.048
    e. **Sundaresan, R.**, Ragunathan, P., Kuramitsu, S., Yokoyama, S., Kumarevel, T., & Ponnuraj, K. (2012). The structure of putative N-acetyl glutamate kinase from Thermus thermophilus reveals an intermediate active site conformation of the enzyme. Biochem Biophys Res Commun, 420(3), 692-697. doi:10.1016/j.bbrc.2012.03.072
    f. **Sundaresan, R.**, Samen, U., & Ponnuraj, K. (2011). Expression, purification, crystallization and preliminary X-ray diffraction studies of the human keratin 4-binding domain of serine-rich repeat

protein 1 from Streptococcus agalactiae. Acta Crystallogr Sect F Struct Biol Cryst Commun, 67(Pt 12), 1582-1585. doi:10.1107/S1744309111040413

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

Ongoing Research Support

JGA Dr. Yongna Xing 12/09/2019- until now

The goal of this project is to study the structural implications of PPP2R5D related disorder causing mutants and to contribute in creating personal medicine for these affected patients

Role: Postdoctoral researcher

Completed Research Support

COBRE Grant Dr.Rakhi Rajan (PI) 08/17/2016-12/08/2019

The goal of this project was to assess a community-based strategy for reducing alcohol abuse among older individuals.
Role: Post-doctoral researcher