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: Lingling Chen

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

POSITION TITLE: Professor of Molecular and Cellular Biochemistry

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
Xiamen University, China	B.S.	07/1988	Physical Chemistry
Stanford University, CA	Ph.D.	05/1996	Biophysical Chemistry
Yale University, CT	Postdoc.	12/2000	Protein Crystallography

A. Personal Statement

As a structural biologist, I have a lasting and strong track record on mechanistic understandings of the chaperonin system. Starting from my postdoctoral training at Yale University, my work on the *E. coli* chaperonin GroEL-substrate interaction using combinatory biology and X-ray crystallography provides structural basis for how GroEL recognizes substrate proteins. My chaperonin research at IU has been focused on mechanistic investigations on the human mitochondrial mHsp60. As in the proposal, purified mHsp60 is unstable and dissociates to nonfunctional monomers. To overcome this difficulty, in our early research we focused on creating stable, single-ring, and functional chaperonin systems as model systems for detailed molecular investigations on mHsp60-mHsp10. Notably, we created a novel reagent, *groES*^{7}, which concatenates seven copies of *E. coli* cochaperonin GroES genes to express the cochaperonin in a continuous polypeptide. Using *groES*^{7}, we identified several GroES^{7} variants to activate the single-ring inactive GroEL^{SR}. Our work together demonstrates that the chaperonin system can function in a single-ring mechanism, a conclusion directly relevant to the single-ring mHsp60-mHsp10. We also find several molecular properties paralleled between the active GroEL^{SR}-GroES^{7} and mHsp60-mHsp10 systems, highlighting the relevance of the model systems. Lately, we have developed a purification protocol to consistently obtain active, single-ring mHsp60, and have used it to obtain a 3.4 Å cryo-EM structure of mHsp60 (ref. 56). Finally, I recently completed the intensive immersion TP1 training at National Center for Cryo-EM Access and Training (NCCAT). During the training, I spent more than three weeks at NCCAT to learn the essential of cryoEM techniques including preparing sample grids via Vitrobot and processing data via cryoSPARC. With our extensive experience in chaperonin, I believe that we are in a unique position to elucidate the molecular mechanism of mHsp60-mHsp10.

My research program has been greatly impacted by a series of challenges including both work and tragic life events. In 2008, my appointment was transferred to the new Molecular and Cellular Biochemistry Department; as one of the four founding members, I have taken on the new department's heaviest teaching load, including designing new *intensive writing* and lab courses for the new undergraduate degree majors. As the department's only female faculty, I have severed in various committees at the departmental, college and university levels. While coping with the decade-long life misfortunes and departmental obligations, I managed to maintain the research activity as much as possible. The recently published paper on cryo-EM structure of mHsp60 speaks for my strong comeback to research. I do expect a high productivity of quality research from my lab.

B. Positions and Honors

Positions and Employment

1996-00 Helen Hay Postdoctoral Fellow, Department of Molecular Biophysics and Biochemistry, Yale University, CT
Advisor: Paul Sigler

2001-07 Assistant Professor, Department of Biology, Indiana University, Bloomington, IN

2008-18 Associate Professor, Dept. of Molecular and Cellular Biochemistry, Indiana Univ., Bloomington, IN
2019- Professor, Dept. of Molecular and Cellular Biochemistry, Indiana Univ., Bloomington, IN

Other Experience and Professional Memberships

2003- Member, American Crystallographic Association
2003- Member, American Society for Microbiology
2006 Panelist (Ad-hoc Member), NSF Signal Transduction Spring Panel
2005, 08,14-16: NSF Ad-hoc Member
2017-19 Oversea Review Panelist, National Science Foundation of China
2017- Reviewing Editorial Board Member, *Cell Stress & Chaperones*
2018- Editorial Board Member, *Scientific Reports*

Honor

1984-88 University Fellowship, Xiamen University, China 1985 Zhong Xue Scholarship, Department of Chemistry, Xiamen University, China
1988 Presidential Award: Chen Jia-Geng Fellowship, Xiamen University, China
1989 Lu Jia-Xi & Cai Qi-Rui Scholarship, Graduate School, Xiamen University, China
1990 Guang-Hua Scholarship, Graduate School, Xiamen University, China
1996-97 Howard Hughes Medical Institute Associate, Yale University 1997-00 Helen Hay Whitney Postdoctoral Fellowship, Yale University
2003 Faculty Summer Fellowship, Indiana University
2010-19 Minjian Fellow, Xiamen University, China
2016 Indiana University Institute for Advance Study Residential Fellow

C. Contributions to Science

1. Mechanism of chaperonins in protein folding

The double-ring chaperonin Hsp60, GroEL in *E. coli*, assists folding of numerous proteins involved in fundamental cellular processes. How GroEL recognizes and interacts with such diverse substrate proteins has been central to the GroEL field. To reveal the structural basis for GroEL-substrate interaction, I used a phage display peptide library to identify a peptide with strong affinity for GroEL, and solved the crystal structure of GroEL/peptide complex. My work provides the first structural evidence indicating that conformational flexibility in the substrate-binding site combined with the nature of non-sequence specific hydrophobic interaction contributes to the substrate promiscuity of GroEL. I also showed that substrate adopts β-sheet conformation while bound to GroEL, supporting that GroEL recognizes and binds the secondary structure of the substrate. I was the primary investigator in this study. I carried on the research on mechanistic study of GroEL as an independent investigator at IU. My lab used nuclear magnetic resonance (NMR) to show that GroEL can bind a peptide in α-helix conformation, strengthening the notion that unlike other chaperone GroEL interact with the secondary structures in the substrates. Recently, my lab has focused on studying the mechanism of single ring variants including human mitochondrial mHsp60 that had not been amenable for biochemical and structural studies until recently. We have developed novel regents to activate a single ring form GroEL^{SR} that is otherwise inactive and nonfunctional. Combining with functional GroEL^{SR} mutants, we identified biochemical determinants that allow chaperonin to function as single ring. Most recently, we developed a purification protocol to obtain active, single-ring mHsp60, enabling us to launch detailed biochemical and structural investigations directly on mHsp60-mHsp10. Our recent reported 3.4 A cryo-EM structure of mHsp60 reveals structural basis for the subunit association dynamics of mHsp60. I directed all these studies.

a. **Lingling Chen** and Paul Sigler (1999), "Crystal Structure of a GroEL/Peptide Complex: Plasticity as a Basis for Substrate Diversity", *Cell*, 99, 757-768. PMID: 10619429
b. Melissa Illingworth, Andrew Ramsey, Zhida Zheng, and **Lingling Chen** (2011), "Stimulating the Substrate Folding Activity of a Single-ring GroEL Variant by Modulating the Cochaperonin GroES", *J. Biol. Chem*. 286: 30401-30408. PMCID: PMC3162399
c. Melissa Illingworth, Holly Ellis and **Lingling Chen** (2017). Creating the Functional Single-Ring GroEL-GroES Chaperonin Systems via Modulating GroEL-GroES Interaction. Sci. Rep., 7:9710, PCMID: PMC5575113
d. Joseph Wang and **Lingling Chen** (2021). Structural Basis for the Structural Dynamics of Human

2. Mechanism of quorum sensing

Quorum sensing (QS) is a well-recognized form of cell-cell communication by which bacteria coordinate their activity in response to population density and diffusivity of their environment**.** In this mechanism, bacteria synthesize specific small molecules that accumulate proportionally to their population density and release them across the bacterial envelope, and once the signal molecule concentration reaches a threshold level, it is perceived via receptor proteins that in turn regulate expression of specific genes. QS-regulated activities include bioluminescence, virulence gene expression, biofilm formation, production of exoenzymes and antibiotics, and in *Agrobacterium tumefaciens* replication and conjugal transfer of tumor-induction (Ti) plasmid. Our biochemical and structural studies have focused on investigating the inhibitory mechanism of the anti-activator TraM on the quorum sensing transcription activator TraR in *A. tumefaciens*. We have solved several crystal structures of TraM and TraR-TraM, and utilized a range of biochemical and biophysical techniques to complement structural studies. One of our most significant findings includes revealing a novel mechanism through which TraM antagonizes TraR through allostery. Association of TraM with TraR induces large structural changes in TraR, preventing it from binding to DNA. I directed all these studies.

a. Guozhou Chen, James Malenkos, Mee-Rye Cha, Clay Fuqua and **Lingling Chen** (2004). "Quorum-sensing antiactivator TraM forms a dimer that dissociates to inhibit TraR", *Mol. Micro.* 52:1641-1651. PMID:15186414
b. Guozhou Chen, Chao Wang, Clay Fuqua, Lian-Hui Zhang and **Lingling Chen** (2006). "The crystal structure and mechanism of TraM2, a second quorum sensing antiactivator of *Agrobacterium tumefaciens* strain A6. *J. Bact.* 188:8244-8251. PCMID: PMC1698194
c. Guozhou Chen, Phillip Jeffery, Clay Fuqua, Yigong Shi and **Lingling Chen** (2007). "Structural basis of TraM anti-activation of quorum sensing transcription factor TraR", *Proc. Natl. Acad. Sci. USA*, 104:16474-16479. PCMID: PMC2034266
d. Mair Churchill and **Lingling Chen** (2011). "Structural Basis of Acyl-homoserine Lactone-Dependent Signaling", *Chem. Rev*. 111: 68-85. PCMID: PMC3494288

3. Coupling activation of T3SS activation with secretion

Many Gram-negative pathogens, including *Pseudomonas aeruginosa,* utilize type III secretion systems (T3SS) to translocate effectors into eukaryotic host cells. Expression of T3SS genes is highly regulated and often coupled to T3SS activity. Transcription of the *P. aeruginosa* T3SS genes is coupled to secretion by a cascade of interacting regulatory proteins (ExsA, ExsD, ExsC, and ExsE). ExsA is an activator of type III gene transcription, ExsD binds ExsA to inhibit transcription, ExsC inhibits ExsD activity, and ExsE inhibits ExsC activity. Transcriptional regulation of T3SS is coupled to T3SS secretion via ExsE, a T3SS secretion substrate. We have shown that although ExsC can form complex with either ExsE or ExsD, it predominately exists as ExsC-ExsE because its binding affinity for ExsE is stronger than for ExsD. We have also shown that the T3SS substrate ExsE is intrinsically disordered and is partially stabilized by interacting with ExsC. Our work supports a model for the efficient activation of T3SS via secretion: secretion of ExsE dissociates ExsE-ExsC complex, allowing ExsC to compete for ExsD from ExsD-ExsA, and the displaced ExsA can bind DNA to activate T3SS genes. The coupling mechanism is immediate, as the intrinsically disordered nature of ExsE allows it to translocate efficiently through the long narrow path of T3SS. I directed all of these studies.

a. Guinivere Lykken, Guozhou Chen, Evan Brutinel, **Lingling Chen**, and Timothy Yahr (2006). "Characterization of ExsC and ExsD self-association and heterocomplex formation", *J. Bact.* 188:6832-6840. PCMID: PMC1595525
b. Zhida Zheng, Guozhou Chen, Evan D. Brutinel, Timothy L. Yahr, and **Lingling Chen** (2007). "Biochemical characterization of a regulatory cascade controlling transcription of the *Pseudomonas aeruginosa* type III secretion system", *J. Biol. Chem.* 282:6136-6142. PMID: 17197437
c. Zhida Zheng, Dejian Ma, Timothy Yahr, and **Lingling Chen** (2012). "The Transiently Ordered Regions in Intrinsically Disordered ExsE Are Correlated with Structural Elements Involved in Chaperone Binding", *Biochem. Biophys. Res. Commun.* 417: 129-134. PMID: 22138394. PMCID: PMC4930836

4. Regulatory mechanism of the IclR transcription family

The IclR transcription factor family controls a wide range of important cellular processes in bacteria, including metabolic pathways, multidrug resistance, aromatic compound degradation, pathogenicity, sporulation, amino acid biosynthesis, and quorum-sensing signal degradation. However, IclR proteins are largely uncharacterized, and molecular understanding of how IclR protein recognizes the promoter DNA and how its DNA-binding activity is regulated is scarce. We have focused on an IclR member, BlcR of *A. tumefaciens*, because it is an experimentally amiable system with a known DNA promoter, a known regulatory ligand, and an in vivo system to confirm the in vitro findings. We have shown that modulating the oligomeric state of BlcR is the mechanism to regulate the DNA-binding function of BlcR. We showed that DNA plays a role in forming the DNA-binding active BlcR tetramer, while the regulatory ligand destabilizes the tetramer leading to dissociation of BlcR from DNA. The BlcR mechanism appears to share among the IclR members, and is drastically different from the only other investigated mechanism adopted by the IclR member TtgV. Our work expands our understanding of the uncharacterized transcription factor family, and our knowledge of how prokaryotes have evolved diverse transcriptional regulators to control transcriptional machinery. I directed all these studies.

a. Yi Pan, Valena Fiscus, Wuyi Meng, Zhida Zheng, Lianhui Zhang, Clay Fuqua, and **Lingling Chen** (2011). "The Agobacterium tumefaciens Transcriptional Factor BlcR Is Regulated via Oligomerization", *J. Biol. Chem.* 286: 20431-20440. PCMID: PMC3121482
b. Yi Pan, Yi Wang, Clay Fuqua, and **Lingling Chen** (2013). "In vivo Analysis of DNA Binding and Ligand Interaction of BlcR, an IclR-type Repressor from *Agrobacterium tumefaciens*". *Microbiology-SGM*, 159:814-822, 2013. PCMID: PMC4083662

5. Small angle X-ray scattering (SAXS) studies of biological systems

SAXS is a powerful technique that reveals structural information of biological molecules in their native, aqueous environment, and is particularly useful to study proteins with flexible conformations or refractory to crystallization. The recent increasing utilization of SAXS owes to technical advances in delivering stable and intense X-ray beam, detector technology, and software for data analysis and modeling. However, in the early 90s, the Hodgson/Doniach group was among the few groups exploring the potentials of applying SAXS to study biological systems. My studies on the Fe protein of nitrogenase and molecular chaperone Hsp70 demonstrate that binding of nucleotide (ATP) induces large conformational change in protein that is otherwise hard to detect using other structural techniques. In particular, my SAXS results on the ATP-induced compaction in Hsp70 have been validated many years later by crystallographic studies. Moreover, my SAXS work on protein folding is among the pioneers in then the new field of time-resolved x-ray scattering. I was the primary investigator of these studies.

a. **Lingling Chen**, Narasaiah Gavini, Hirotsugu Tsuruta, David Eliezer, Barbara K. Burgess, Sebastian Doniach, and Keith O. Hodgson (1994). MgATP-induced conformational changes in the iron protein from *Azotobactor vinelandii*, as studied by small angle x-ray scattering. *J. Bio. Chem*. 269:3290-3294. PMID: 8106367
b. Sigurd M. Wilbanks*, **Lingling Chen***, David B. McKay, Hirotsugu Tsuruta, and Keith O. Hodgson (1995). Solution Small-angle X-ray Scattering Study of A Bovine Heat-Shock Cognate and Its Subfragments. *Biochemistry* 34:12095-12106. (*these two authors contributed equally to this work). PMID: 7547949
c. **Lingling Chen**, Keith O. Hodgson and Sebastian Doniach (1996). A lysozyme folding intermediate revealed by solution x-ray scattering. *J. Mol. Biol.* 261:658-671. PMID: 8800214
d. **Lingling Chen**, Gudrun Wildegger, Thomas Kiefhaber, Keith O. Hodgson and Sebastian Doniach (1998). Kinetics of lysozyme refolding: structural characterization of a non-specifically collapsed state using time-resolved x-ray scattering. *J. Mol. Biol*. 276:225-237. PMID: 9514723

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/lingling.chen.2/bibliography/public/

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
x

NAME: Wang, Che-Yen

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

POSITION TITLE: Assistant 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)	END DATE MM/YYYY	FIELD OF STUDY
Catholic Fu-Jen University, New Taipei City	BS	06/1999	Biology
National Yang-Ming University, Taipei	MS	06/2001	Medical Informatics
National Yang-Ming University, Taipei	PHD	08/2008	Structural Biology
Indiana University, Bloomington, Indiana	Postdoctoral Fellow	06/2013	Structural Biology

A. Personal Statement

I joined Department of Microbiology and Immunology at Penn State University College of Medicine as an assistant professor in 2020. My expertise is single-particle cryo-electron microscopy (cryo-EM). My academic training has focused on structural and functional relationships between biological macromolecules; the emphasis has been on viruses and related macromolecular assemblies. I have published 45 peer-reviewed papers and 18 of them are related to hepatitis B virus structure. I have also mentored 3 pre-doctoral students as a member of their thesis committee.

As a graduate student, I used cryo-EM to design potential vaccine platforms based on the antigenic domain of hepatitis E virus (HEV). My goal was to engineer a multi-valent vaccine by inserting a small peptide into the viral capsid at a position informed by the structure of the capsid protein. In addition, I used cryo-EM to study a novel self-assembling nanoparticle derived from bacteriophage phi29. As a postdoc in Prof. Adam Zlotnick's lab at Indiana University Bloomington, I made seminal contributions to understand hepatitis B virus (HBV) molecular biology. Using single particle cryo-EM, **I was the first to determine how the C-terminal domain (CTD) of the HBV capsid protein affects genome packaging** and how it interacts with host proteins. This work revealed that phosphorylation on the CTD affects capsid structure, which, in turn, affects the RNA genome structure. We also found that the CTD is transiently exposed on the capsid surface, which allows HBV to interact with 2 host proteins, Serine Arginine protein kinase and Importin-β. Furthermore, **I solved the first cryo-EM structure of an authentic HBV intermediate.** A unique doughnut-shaped density in the core was revealed and tentatively identified as the reverse transcriptase. Together, **these studies have provided significant new insights into HBV capsid dynamics and its genome structure.** In addition to performing these experiments and developing novel methods, I trained graduate students in the lab. Together, we described HBV capsid in complex with a therapeutic small molecule at atomic resolution level (3.9Å) using cryo-EM.

As an active educator, I have taught multiple courses during my graduate and post-graduate career. I also mentored seven different undergraduate students on research projects during my Ph.D. training. Prior to join PSU, I have been serving as a co-instructor of two graduate courses for more than 3 years. I very much enjoy teaching these courses, which typically have ~15 students enrolled. After joining PSU, I have started teaching two graduate courses (Concept of Virology and Medical Microbiology) in my first year and now I am also teaching a course (Host Defense and Host Response) for the first-year medical students. I believe the role of a teacher should not be to impress students with his or her knowledge of a given subject. Rather, it should be to make a subject so interesting that it inspires students to become self-motivated in learning about the subject. **My goal is to be a teacher that will inspire students to become engaged in their coursework and become self-motivated, and I will devote my effort in working with students to achieve this goal.**

Presently, my lab focuses on depicting the molecular mechanism of HBV reverse transcription using a combination of cryo-EM, biochemical, and biophysical analyses at different viral intermediate states. Our goal is to obtain the HBV structures at atomic resolution levels. Because there are various HBV particles and genome forms involved in its life cycle, *in depth characterizing the structures and functional roles of these HBV particles will enable us to identify novel targets for interventions.*

Ongoing project that I would like to highlight include:

- R21 AI164119-01 Wang
  Che-Yen (PI)
  06/01/21-07/31/23
  Dissecting Structural Details of Hepadnavirus Subviral Particles

1. Wang JC, Chen L. Structural basis for the structural dynamics of human mitochondrial chaperonin mHsp60. Sci Rep. 2021 Jul 20;11(1):14809. PubMed Central PMCID: PMC8292379.

2. Zhao Z, Wang JC, Zhang M, Lyktey NA, Jarrold MF, Jacobson SC, Zlotnick A. Asymmetrizing an icosahedral virus capsid by hierarchical assembly of subunits with designed asymmetry. Nat Commun. 2021 Jan 26;12(1):589. PubMed Central PMCID: PMC7838286.

3. Wang JC, Nickens DG, Lentz TB, Loeb DD, Zlotnick A. Encapsidated hepatitis B virus reverse transcriptase is poised on an ordered RNA lattice. Proc Natl Acad Sci U S A. 2014 Aug 5;111(31):11329-34. PubMed Central PMCID: PMC4128116.

4. Wang JC, Dhason MS, Zlotnick A. Structural organization of pregenomic RNA and the carboxy-terminal domain of the capsid protein of hepatitis B virus. PLoS Pathog. 2012 Sep;8(9):e1002919. PubMed Central PMCID: PMC3447754.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2020 -	Assistant Professor, Department of Microbiology and Immunology, Pennsylvania State University College of Medicine, Hershey, PA
2015 - 2020	Staff Scientist, Electron Microscopy Center, Indiana University, Bloomington, IN
2013 - 2020	Research Assistant Professor, Molecular and Cellular Biochemistry Department , Indiana University, Bloomington, IN
2010 - 2013	Postdoctoral Researcher, Molecular and Cellular Biochemistry Department, Indiana University, Bloomington, IN
2009 - 2010	Visiting Scholar, Department of Biosciences and Nutrition, Karolinska Institutet, Huddinge
2005 - 2008	Junior Specialist, Department of Molecular and Cellular Biology, University of California, Davis, CA
2003 - 2005	Exchange PhD Student, Department of Biosciences and Nutrition, Karolinska Institutet, Huddinge
1998 - 2000	Research Assistant, National Research Institute of Chinese Medicine , Taipei

Honors

2021	Dean's Award for Excellence in Teaching, Penn State College of Medicine
2016	Travel Grant, 2016 International Meeting on Molecular Biology of Hepatitis B Viruses
2013	Travel Grant, International Meeting on Molecular Biology of Hepatitis B Viruses
2011	Research Panel, Gordon-Kenan Research Seminar on Physical Virology
2005	Award of Graduate Students Study Abroad Grant, Ministry of Science and Technology, Taipei, Taiwan
2003	Award of Enhancing International Competitiveness Grant, National Yang-Ming University, Taipei, Taiwan

C. Contribution to Science

1. **Dynamics of the HBV capsid proteins and interactions between the protein and nucleic acid.** Since I was a postdoc, my focus has been structural and functional characterization of hepatitis B virus (HBV). We determined some of the features of protein-protein and protein-nucleic acid interactions that are responsible for viral capsid formation, using the HBV core protein as a model. We were the first to deliver vital information regarding the structures of the carboxyl-terminal domain, polymerase and its packaged RNA of the hepatitis B virus.

    a. Zhao Z, Wang JC, Zhang M, Lyktey NA, Jarrold MF, Jacobson SC, Zlotnick A. Asymmetrizing an icosahedral virus capsid by hierarchical assembly of subunits with designed asymmetry. Nat Commun. 2021 Jan 26;12(1):589. PubMed Central PMCID: PMC7838286.

    b. Chen C, Wang JC, Pierson EE, Keifer DZ, Delaleau M, Gallucci L, Cazenave C, Kann M, Jarrold MF, Zlotnick A. Importin β Can Bind Hepatitis B Virus Core Protein and Empty Core-Like Particles and Induce Structural Changes. PLoS Pathog. 2016 Aug;12(8):e1005802. PubMed Central PMCID: PMC4982637.

    c. Wang JC, Nickens DG, Lentz TB, Loeb DD, Zlotnick A. Encapsidated hepatitis B virus reverse transcriptase is poised on an ordered RNA lattice. Proc Natl Acad Sci U S A. 2014 Aug 5;111(31):11329-34. PubMed Central PMCID: PMC4128116.

    d. Wang JC, Dhason MS, Zlotnick A. Structural organization of pregenomic RNA and the carboxy-terminal domain of the capsid protein of hepatitis B virus. PLoS Pathog. 2012 Sep;8(9):e1002919. PubMed Central PMCID: PMC3447754.

2. **Study virus assembly using cryo-EM.** Through my PhD to my current career, I have been using cryo-EM to study virus capsid proteins that either threaten human health or damage crop production.

    a. Bond K, Tsvetkova IB, Wang JC, Jarrold MF, Dragnea B. Virus Assembly Pathways: Straying Away but Not Too Far. Small. 2020 Dec;16(51):e2004475. PubMed PMID: 33241653.

    b. Zhao Z, Wang JC, Gonzalez-Gutierrez G, Venkatakrishnan B, Asor R, Khaykelson D, Raviv U, Zlotnick A. Structural Differences between the Woodchuck Hepatitis Virus Core Protein in the Dimer and Capsid States Are Consistent with Entropic and Conformational Regulation of Assembly. J Virol. 2019 Jul 15;93(14) PubMed Central PMCID: PMC6600186.

    c. Snyder AJ, Wang JC, Danthi P. Components of the Reovirus Capsid Differentially Contribute to Stability. J Virol. 2019 Jan 15;93(2) PubMed Central PMCID: PMC6321938.

    d. Wang JC, Chen C, Rayaprolu V, Mukhopadhyay S, Zlotnick A. Self-Assembly of an Alphavirus Core-like Particle Is Distinguished by Strong Intersubunit Association Energy and Structural Defects. ACS Nano. 2015 Sep 22;9(9):8898-906. PubMed Central PMCID: PMC5683390.

3. **Structural characterization of the nano-material assembly.** One of my research interests is to utilize the viral protein as a nano-material to generate functionalized nano-assemblies. We have constructed different lattices, arrays or particles, to mimic the structural complexity of biological structures.

    a. Tsvetkova IB, Anil Sushma A, Wang JC, Schaich WL, Dragnea B. Radiation Brightening from Virus-like Particles. ACS Nano. 2019 Oct 22;13(10):11401-11408. PubMed PMID: 31335115.

    b. Lee LS, Brunk N, Haywood DG, Keifer D, Pierson E, Kondylis P, Wang JC, Jacobson SC, Jarrold MF, Zlotnick A. A molecular breadboard: Removal and replacement of subunits in a hepatitis B virus capsid. Protein Sci. 2017 Nov;26(11):2170-2180. PubMed Central PMCID: PMC5654856.

    c. van Eldijk MB, Wang JC, Minten IJ, Li C, Zlotnick A, Nolte RJ, Cornelissen JJ, van Hest JC. Designing two self-assembly mechanisms into one viral capsid protein. J Am Chem Soc. 2012 Nov 14;134(45):18506-9. PubMed Central PMCID: PMC3510441.

    d. Green DJ, Wang JC, Xiao F, Cai Y, Balhorn R, Guo P, Cheng RH. Self-assembly of heptameric nanoparticles derived from tag-functionalized phi29 connectors. ACS Nano. 2010 Dec 28;4(12):7651-9. PubMed PMID: 21080706.

4. **Structural studies of macromolecules using TEM.** In addition to virus, I have worked with multiple investigators and used TEM to solve and characterize the structures of their research interests.

   a. Wang JC, Chen L. Structural basis for the structural dynamics of human mitochondrial chaperonin mHsp60. Sci Rep. 2021 Jul 20;11(1):14809. PubMed Central PMCID: PMC8292379.

   b. Nero TM, Dalia TN, Wang JC, Kysela DT, Bochman ML, Dalia AB. ComM is a hexameric helicase that promotes branch migration during natural transformation in diverse Gram-negative species. Nucleic Acids Res. 2018 Jul 6;46(12):6099-6111. PubMed Central PMCID: PMC6158740.

   c. Rogers CM, Wang JC, Noguchi H, Imasaki T, Takagi Y, Bochman ML. Yeast Hrq1 shares structural and functional homology with the disease-linked human RecQ4 helicase. Nucleic Acids Res. 2017 May 19;45(9):5217-5230. PubMed Central PMCID: PMC5605238.

   d. Wang JC, Zlotnick A, Mecinović J. Transmission electron microscopy enables the reconstruction of the catenane and ring forms of CS2 hydrolase. Chem Commun (Camb). 2014 Sep 14;50(71):10281-3. PubMed Central PMCID: PMC4159558.

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/myncbi/joseph che-yen.wang.1/bibliography/public/