BIOGRAPHICAL SKETCH

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

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

POSITION TITLE: Professor and Vice Chair

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 California, Davis, CA	B.S.	1984	Chemistry and Genetics
University of Chicago, Chicago, IL	M.S.	1989	Physical Chemistry
University of Chicago, Chicago, IL	Ph.D.	1989	Chemistry

A. Personal Statement

My laboratory studies the molecular mechanisms of (1) protein post- and co-translational modification with a particular focus on protein acetylation, (2) enzyme signaling in cancer and metabolism, and (3) epigenetic regulation. The laboratory uses a broad range of biochemical, biophysical and structural research tools (X-ray crystallography and cryo-EM) to determine macromolecular structure and mechanism of action. The laboratory also uses high-throughput small molecule screening and structure-based design strategies to develop protein-specific small-molecule probes to interrogate protein function and for preclinical studies.

My laboratory is extremely dedicated to training the next generation of scientist. Over the 25 years of my faculty tenure, 30 graduate students have obtained Ph.D. degrees from my laboratory and 18 postdoctoral fellows have previously worked in my laboratory. In addition, 6 research technicians and 35 undergraduate students have previously worked in my laboratory. Overall, my trainees have either stayed in academics, or taken on leadership positions in universities or industry, including 7 faculty positions, 11 post-doctoral fellowships and 13 industrial positions. My laboratory currently has a highly interactive group of individuals, which includes 4 postdoctoral fellows, 4 predoctoral students, 1 lab manager and 3 undergraduate students. I have also been involved in the recruitment and training of scientists outside my laboratory, including being the PI of training programs in Basic Cancer Research (2007-2013) and the Chemistry-Biology Interface (2005-present), serving as chair or member of 10 faculty recruitment committees and 8 faculty-mentoring committees.

B. Positions and Honors

Positions and Employment:

1994-1998	Assistant Professor, The Wistar Institute, Philadelphia, PA
1994-1998	Wistar Institute Assistant Professor of Chemistry, the Department of Chemistry, University of Pennsylvania
1995-present	Member, Graduate Group in Biophysics and Molecular Biophysics, the University of Pennsylvania School of Medicine
1999-2002	Associate Professor, The Wistar Institute, Philadelphia, PA
1999-2003	Wistar Institute Associate Professor of Chemistry, the Department of Chemistry, University of Pennsylvania
2000-2003	Wistar Institute Associate Professor of Biochemistry & Biophysics, the Department of Biochemistry and Biophysics, University of Pennsylvania School of Medicine
2002-2013	Professor, The Wistar Institute, Philadelphia, PA

2003-2013	Wistar Institute Professor of Biochemistry & Biophysics, the Department of Biochemistry and Biophysics, University of Pennsylvania School of Medicine
2003-2013	Wistar Institute Professor of Chemistry, the Department of Chemistry, University of Pennsylvania
2008-2009	Acting Program Leader, Gene Expression and Regulation Program, The Wistar Institute
2009-2013	Program Leader, Gene Expression and Regulation Program, The Wistar Institute
2010-2013	Hilary Koprowski, M.D. Professor, The Wistar Institute
2013-2017	Professor, Department of Biochemistry & Biophysics, Investigator, Abramson Family Cancer Research Institute, Perelman School of Medicine at the University of Pennsylvania
2016 - 2018	Interim Faculty Director, Electron Microscopy Research Laboratory, Perelman School of Medicine at the University of Pennsylvania
2017 - present	George W. Raiziss Professor and Vice-Chair, Department of Biochemistry and Biophysics, Investigator, Abramson Family Cancer Research Institute, Perelman School of Medicine at the University of Pennsylvania

Other Experience and Professional Memberships:

Intramural Activities (chaired or directed only):

1996-2001	Chairman, Wistar Institute Seminar Committee
2002-2004	Director, Wistar Institute Summer Undergraduate Research Fellowship Program
2004-2006	Chairman, Graduate Admissions, Biochemistry and Molecular Biophysics Graduate Group, the University of Pennsylvania School of Medicine
2005-2009	Chairman, Wistar Institute Training Committee
2005	Chairman, Wistar Institute Structural Biology Search Committee
2005-present	Director and PI, T32 Wistar/UPenn Chemistry-Biology Interface Training Program
2007-2013	Director and PI, T32 Wistar Basic Cancer Research Training Program
2010	Chairman, Faculty Search Committee, Wistar Institute
2011	Chairman, Faculty Search Committee, Wistar Institute
2012	Chairman, Faculty Search Committee, Wistar Institute
2016 - 2018	Interim Faculty Director, Electron Microscopy Research Laboratory
2017 - present	Vice-Chair, Department of Biochemistry and Biophysics
2017	Co-Chairman, Faculty Search Committee, Department of Biochemistry and Biophysics, University of Pennsylvania
2018	Chairman, Faculty Search Committee, Department of Biochemistry and Biophysics, University of Pennsylvania

Extramural Activities:

1998	Member, NIH Shared Instrumentation Program (NCRR), Special Study Section
1999	Ad Hoc Member, NIH Study Section (ZRG1-AARR3-01)
1999	Ad Hoc Member, NIH Study Section (ZRG1-AARR1-03)
1999	Ad Hoc Member, ACA Study Section (Genetic Mechanism in Cancer)
2000	Ad Hoc Member, ACA Study Section (Genetic Mechanism in Cancer)
2000-2004	Member, ACA Study Section (Genetic Mechanism in Cancer)
2002	Ad Hoc Member, NIH Study Section (BBCA)
2002	Ad Hoc Member, NIH P01review (NCI)
2003	Vice-Chair, ACA Study Section (Genetic Mechanism in Cancer)
2004	Chair, ACS Study Section (Genetic Mechanism in Cancer)
2004	Ad Hoc Member, NIH P01review (GM)
2004	Chair, NIH P01 review (GM)
2005	Ad Hoc Member, NIH Study Section (MSFB)
2005	Ad Hoc Member, NIIH P01 Review (GM)
2006-2010	Member, NIH Study Section - MSFC
2008-2010	Chair, NIH Study Section (MSFC)
2008-2009	Chair, Internal Committee to Review the Genomics and Computational Graduate Group, University of Pennsylvania School of Medicine

2008-2009	Member, Search Committee for the Chair of the Department of Biochemistry and Biophysics, University of Pennsylvania School of Medicine
2011-present	American Federation for Aging Research National Scientific Advisory Council
2011	Site Visit Member, NCI Laboratory of Cell Biology
2011-present	Member, STARR Cancer Consortium Scientific Review Board
2011	Mail-in Reviewer for NSF, Molecular Biophysics Study Section
2012	Mail-in Reviewer for NIH
2014-present	Member, Editorial Board of the Journal of Biological Chemistry
2014	Ad Hoc Member, NIH S10 Study Section (ZRG1 IMST-G)
2014	Ad Hoc Member, NIH Study Section (NCI Omnibus review, ZCA SRB-2)
2014	Ad Hoc Reviewer for Cancer Research UK
2014	Mail-in Reviewer for NSF, Molecular Biophysics Study Section
2014	Mail-n Reviewer for The Wellcome Trust
2014	Mail-in Reviewer for The Medical Research Council
2014	Mail-in Reviewer for The Human Frontier Science Program
2015	Ad Hoc Member, NIH Study Section (NCI Omnibus review, ZCA SRB-2)
2015	Mail-in Reviewer for Research Foundation Flanders
2015	Mail-in Reviewer for NIH Center for Scientific Review Pilot Study
2015	Ad Hoc Member, NIH Study Section (GGG-A(80) AREA)
2016	Ad Hoc Member, NIH Study Section (MSFC)
2016	Member, Innovative Research Grants Committee, Stand Up to Cancer
2016	Ad Hoc Member, NIH NCI P30 Cancer Center Review/Site Visit
2016	Ad Hoc Chair, NIH NCI Special Emphasis Study Section Panel
2017	Ad Hoc Member, NIH MIGMS P30 Synch. Res. Special Emphasis Study Section Panel
2017	Call-in Reviewer, NIH NCI Special Emphasis P01 Study Section Review Panel
2017	Ad Hoc Member, NIH NIGMS MIRA Special Emphasis Study Section Review Panel
2018	Ad Hoc Member, NIH NIGMS MIRA Special Emphasis Study Section Review Panel
2018	Mail-in Reviewer for The Wellcome Trust
2019	Ad Hoc Member, NIH NCI Special Emphasis Panel, Provocative Questions Workshop
2019	Ad Hoc Member, NIH CSR DP5 NIH Director's Early Independence Award Panel

1995-present Manuscript reviews for *Acta Crystallog., Analytical Biochemistry, Biochemistry, Biochemisty Biophysics Acta. Cell, Chembiochem, Chemistry & Biology, Drug Discovery Today, EMBO J., EMBO Reports, Genes & Develop., J. Biol. Chem., J. Leukocyte Biol.*, *J. Med. Chem.*, *J. Mol. Biol., J. Med. Chem. Comm., Mol. Cell, Mol. Cell. Biol., Nature, Nature Communications, Nature Struc. Mol. Biol., PLoS Biology, PLoS ONE, Proc. Natl. Acad. Sci. USA, Proteins, Science, Structure, Traffic, Trends in Biochemical Sciences*

C. Contributions to Science

1. My laboratory has pioneered the structure-function analysis of histone acetyltransferases (HATs) and continues to make seminal contributions in this area. Specifically, my laboratory determined the first crystal structure of a type A HAT and characterized its mechanism of catalysis, and the first to describe the mode of histone substrate binding by a HAT. My laboratory has extended our studies to the broader family of N-acetlyltransferases including the non-histone lysine acetyltrasnferases (KATs) and the N-amino acetyltransferases (NATs). We have uncovered important molecular signatures that distinguish HATs, KATs and NATs. My laboratory has also contributed to the development of acetyltransferase inhibitors. The vast majority of the human proteome is acetylated in a functionally important manner and alterations occur in human diseases. This suggests that protein acetylation may rival protein phosphorylation as a biologically important protein modification and that KATs and NATs represent important therapeutic targets.

a. Lasko, L.M., Jakob, C.G., Edalji, R.P., Qiu W., Montgomery D., Digiammarino .EL., Hansen T.M., Risi R.M., Frey R., Manaves V., Shaw B., Algire M., Hessler P., Lam L.T., Uziel T., Faivre E., Ferguson D., Buchanan F.G., Martin R.L., Torrent M., Chiang G.G., Karukurichi K., Langston J.W., Weinert B.T., Choudhary C., de Vries P., Van Drie J.H., McElligott D., Kesicki E., Marmorstein R., Sun C., Cole P.A., Rosenberg SH, Michaelides M.R., Lai A., Bromberg K.D. Discovery of a selective catalytic p300/CBP inhibitor that targets lineage-specific tumours. (2017) *Nature*, 550:128-132. Epub 2017 Sep. 27.

c. Goris, M., Magin, R.S., Foyn, H., Myklebust, L.M., Varland, S., Ree, R., Drazic, A., Bhambra, P. Støve, S.I., Baumann, M., Haug, B.E., *Marmorstein, R., *Arnesen, T. Structural determinants and cellular environment

define processed actin as the sole substrate of the N-terminal acetyltransferase Naa80. (2018) *Proc. Natl. Acad. Sci.* PMID: 29581307. (* - shared corresponding author)

d. Gottlieb, L. and Marmorstein, R. Structure of human NatA and its regulation by the Huntingtin interacting protein HYPK. (2018) Structure 26:925-935. PMID: 29754825: PMCID: PMC6031454

d. Deng, S., Magin, R.S., Wei, X., Pan, B., Petersson, E.J. and Marmorstein, R., Structure and mechanism of acetylation by the N-terminal dual enzyme NatA/Naa50 complex. (2019) *Structure*, 27: 1057-1070. PMID:31155310; PMCID:6610660

2. My laboratory is studying the molecular basis for how chromatin is assembled and maintain by histone chaperone complexes. We have focused on the binding and histone deposition of H3/H4 complexes by the ASF1 and VPS75 proteins and the multisubunit HIRA complex, which specifically deposits the histone H3 variant, H3.3, in a replication independent manner. Histone H3.3 is deposited at active genes, after DNA repair and in certain forms of heterochromatin in non-proliferating senescent cells, and recurrent H3.3 mutations are found in pediatric glioblastoma and misregulation of H3.3-specific activities in tumor growth and leukemia exemplifies the necessity for proper regulation of H3.3-specific deposition pathways. Together with the Peter Adams laboratory we have pioneered a molecular understanding of the HIRA complex highlighting the particular importance of the HIRA and Ubn1 subunits of H3.3-specific activities.

a. Ricketts, M.D., Frederick, B., Hoff. H., Tang, Y., Schultz, D.C. Rai, T.S., Vizioli, M.G. Adams, P.D. and Marmorstein, R. Ubinuclein-1 confers histone H3.3-specific binding specificity by the HIRA histone chaperone complex. (2015) *Nature Communications*. 6:7711-. PMID: 26159857: PMCID: PMC4509171

b. Haigney, A., Ricketts, M. D. and Marmorstein, R. Dissecting the Molecular Roles of Histone Chaperones in Histone Acetylation by Type B Histone Acetyltransferases (HAT-B), (2015) *J. Biol. Chem*., 290:30648-30657. PMID: 26522166

c. Ray-Gallet, D., Ricketts, M.D., Sato, Y., Gupta, K., Boyarchuk, E., Senda, T., Marmorstein, R., and Almouzni, G. Functional activity of the H3.3 histone chaperone complex HIRA requires trimerization of the HIRA subunit. (2018) *Nat. Commun*. 9:3103. PMID:30082790: PMCID:PMC6078998

d. Ricketts, M.D., Dasgupta, N., Fan, J., Han, J., Gerace, M., Tang, Y., Black, B.E., Adams, P.D. and Marmorstein, R. The HIRA histone chaperone complex subunit UBN1 harbors H3/H4 and DNA binding activity. (2019) *J. Biol. Chem.*, 294: 9239-9259. PMID:31040182; PMCID:PMC6556585

3. My laboratory has leveraged out expertise in biochemistry and X-ray crystallography with small molecule screening for the structure-based Inhibitor development for therapy of melanoma and other cancers. There is a particular interest in melanoma and the laboratory had developed inhibitors to several important oncogenic kinases in melanoma including BRAF, PI3K, PAK1 and S6K1. The laboratory has also targeted the oncoproteins E7 and E6 from human papillomavirus (HPV). HPV is known to be the causative agent of a number of epithelial cancers, most notably cervical cancer, and has also been implicated to have a causative role in about 20% of head and neck cancers as well as several other cancers. We have recently reported on the development of potent and selective HPV-E7 and HPV-E6 inhibitors. These studies have important implications for therapy.

a. Qin, J., Rajaratnam, R., Feng, L., Salami, J., Barber-Rotenberg, J.S., Domsic, J., Reyes-Uribe, P., Liu, H., Dang, W., Berger, S.L., Villanueva, J., Meggers, E. and Marmorstein, R. Development of organometallic S6K1 inhibitors. (2015) *J. Med. Chem*. 58:305-314. PMID: 25356520; PMCID:PMC4289024

b. Grasso, M., Estrada, M.A., Ventocilla, C., Samanta, M., Maksimoska, J., Villanueva, J., Winkler, J.D. and Marmorstein, R. Chemically linked vemurafenib inhibitors promote an inactive BRAFV600E conformation. (2016) *ACS Chem. Biol.* 11: 2876-2888. PMID: 27571413: PMCID:PMC5108658

c. Emtage, R.P., Schoeberger, M.J. Fergusion, K.M., and Marmorstein, R. Intramolecular autoinhibition of Checkpoint Kinase 1 is mediated by conserved basic motifs of the C-terminal Kinase Associated-1 domain. (2017) *J. Biol. Chem*. Pii: jbc.M117.811265. [Epub ahead of print]

d. Grasso, M., Estrada, M.A., Berrios, K.N., Winkler, J.D. and Marmorstein, R. N-(7-Cyano-6-(4-fluro-3-(2-(3-(trifluoromethyl)phenyl)acetamido)phenoxy)benzo[d]thiazol-2-yl)cyclopropanecarboxamide (TAK632) promotes inhibition of BRAF through the induction of inhibited dimers. (2018) J. Med. Chem. 61:5034-5046. PMID: 29727562

4. My laboratory has more recently studied the connection between metabolism with cancer signaling and chromatin regulation with a particular focus on the acetyl-CoA metabolism and metabolite acylation enzymes such as ATP citrate lyase (ACLY). Our studies uncovered the molecular mechanism ACLY and provided a

molecular scaffold for the structure-based development of ACLY inhibitors for therapy of cancer and metabolic and cardiovascular disorders.

a. Bazilevsky, G.A., Affronti, H.C., Wei, X., Campbell, S.L., Wellen, K.E. and Marmorstein. R. ATP-citrate lyase multimerization is required for coenzyme-A substrate binding and catalysis, (2019) J. Biol. Chem. 294:7529-7268. PMID:30877197; PMCID:PMC6509486

b. Wie, X., Schultz, K., Bazilevsky, G.A., Vogt, A. and Marmorstein R. Molecular basis of acetyl-CoA production by ATP-citrate lyase. (2019) *Nature Structural & Molecular Biology*, in press

Complete bibliography is available at: http://www.ncbi.nlm.nih.gov/pubmed/?term=Marmorstein+R
(>195 manuscripts; Scopus H-index=66; Google Scholars H-index=77)

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

NIH P01 AG 031862 (Dr. S. Berger) 07/01/2008-6/31/2023
Epigenetics of Aging and Age-Associated Diseases
Project 1: Molecular basis for epigenome homeostasis by histone chaperone and acetyltransferase complexes (Dr. R. Marmorstein, Project Leader)
Project 1 covers our work on studying the structure/function of the HUCA histone chaperone complex and molecular events associated with H4K16 acetylation

NIH R35 GM118090 (Dr. R. Marmorstein) 07/01/2016-06/31/2021
Molecular Mechanisms and inhibition of Protein Acetyltransferases
The overall goal of this proposal is to understand the molecular mechanisms of protein acetylation by HATs, non-histone KATs and NATs.

Beckman Foundation N/A (Dr. R. Marmorstein) 06/01/2017-05/31/2022
Creation of an Arnold and Mabel Beckman Center for Cryo-Electron Microscopy
The goal of this proposal is to purchase state-of the art Cryo-EM instrumentation and peripherals, including as its key components, a FEI Titan Krios G2 300 kV FEG TEM and a Gatan K3 Summit direct electron detector camera.

NIH R01 CA226888 (Drs. R. Marmorstein and J. Winkler) 12/03/2018-11/30/2023
Development of BRAF Dimer Inhibitors to Treat Drug Resistant Melanoma
The overall goal of this proposal is to use the RAS-RAF-MEK-ERK (MAPK/ERK) signaling pathway as a model to develop small molecule inhibitors that specifically target kinase dimers as lead compounds for therapeutic development

NIH R35 GM118090-04S1 (Marmorstein) 7/01/2019-06/31/2020
Molecular Mechanisms and inhibition of Protein Acetyltransferases - Supplement
This is an Administrative Supplement for Equipment Purchase to R35 GM118090 for a 16 GPU Cluster for single particle cryo-electron microscopy reconstruction.

NIH R01 CA226888-01-A1S1 (Marmorstein/Winkler) 09/01/2019-08/31/2022
Development of BRAF Dimer Inhibitors to Treat Drug Resistant Melanoma - Supplement
This is an Administrative Diversity Supplement to R01 CA226888 to fund an underrepresented minority postdoctoral fellow, Andrea Acevedo, to develop peptide-based inhibitors of $BRAF^{V600E}$ dimerization with RAF and MEK to treat melanoma.

N/A (Wellen/Asangani/Marmorstein) 12/01/2019-11/31/2020
University of Pennsylvania Pilot Grant - AFCRI
Probing the Metabolism-Epigenetics Link as a Therapeutic Target in Prostate Cancer
The goal in the Marmorstein lab is the structure-based development of ATP citrate lyase inhibitors.

Sanofi iAward (Marmorstein) 1/01/2020-12/31/2021
Structure-Based Development of bivalent BRAF-MEK Inhibitors
The goal of this proposal is the structure-based development of BRAF-MEK inhibitors.

BIOGRAPHICAL SKETCH

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

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

POSITION TITLE: Postdoctoral Researcher

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

INSTITUTION AND LOCATION	DEGREE *(*if applicable*)*	START DATE MM/YYYY	END DATE MM/YYYY	FIELD OF STUDY
Chongqing University, Chongqing, China	BS	09/2006	06/2010	Bioengineering
Institute of Biophysics, Chinese Academy of Sciences, Beijing, China	PHD	09/2010	11/2016	Biophysics
Harvard University, Boston, MA	Postdoctoral	12/2016	10/2017	Cell biology, biochemistry
University of Pennsylvania, Philadelphia, PA	Postdoctoral	10/2017	present	Structural biology, biochemistry

A. Personal Statement

My career goal is to have my own academic research laboratory. I am currently a postdoctoral researcher in the laboratory of Dr. Ronen Marmorstein in the Department of Biochemistry and Biophysics in the Perelman School of Medicine at the University of Pennsylvania. I received my Ph.D. degree (Biophysics; mentor: Dr. Zhenfeng Liu) from the Institute of Biophysics, Chinese Academy of Sciences, one of the best biophysics institutions in China. I have been focusing on protein science and structural biology for 9 years. I was one of the most productive graduate students of my Ph.D. mentor's laboratory. I published 3 peer-reviewed first author manuscripts during my Ph.D. and my Ph.D. thesis was awarded the outstanding Ph.D. thesis of the Chinese Academy of Sciences. From 12/2016 to 10/2017, I carried out postdoctoral work with Dr. Tom A. Rapoport at Harvard Medical School. Dr. Rapoprot is a well-known cell biologist in the field of protein translocation and ER associated protein degradation. I gained extensive training in cell biology in the Rapoport laboratory, but my interest in structural work led me to switch the the laboratory of Dr. Ronen Marmorstein.

B. Positions and Honors

Positions and Employment

12/2016 – 10/2017 Postdoctoral Researcher, Harvard University
10/2017- present Postdoctoral Researcher, University of Pennsylvania

Honors

2015 Excellent Student of University of Chinese Academy of Sciences
2015 National Scholarship
2016 Excellent Student of University of Chinese Academy of Sciences
2018 Award for outstanding doctoral thesis of Chinese Academy of Sciences

C. Contribution to Science

1. **Graduate Career:** My graduate research contributions focused on structural biology aspects of an oxygen evolving complex in higher plant photosynthesis. We determined the structure of a 1.2 Mega Dalton supercomplex higher plant photosystem II at resolution of 3.2 Å. We then improved the resolution to 2.7 Å, which is the highest resolution of a membrane protein solved by cryo-EM single particle analysis. These studies were published at *Nature* in 2016 and *Science* in 2017. These two papers had been cited for 350 times. The photosystem II structure reveals a homodimeric supramolecular system in which each monomer contains 25 protein subunits, 105 chlorophylls, 28 carotenoids and other cofactors. Three extrinsic subunits (PsbO, PsbP and PsbQ), which are essential for optimal oxygen-evolving activity of photosystem II, form a triangular crown that shields the Mn4CaO5-binding domains of CP43 and D1. By analyzing the closely connected interfacial chlorophylls, we obtained detailed insights into the energy-transfer pathways between the antenna and core complexes.
    a. **Wei X**, Guo J, Li M, Liu Z. Structural mechanism underlying the specific recognition
    between the Arabidopsis state-transition phosphatase TAP38/PPH1 and phosphorylated lightharvesting complex protein Lhcb1. ***The Plant Cell.*** **2015**; **27**(4): 1113-27
    b. **Wei X**, Su X, Cao P, Liu X, Chang W, Li M, et al. Structure of spinach photosystem II–LHCII supercomplex at 3.2 Å resolution. ***Nature***. **2016**; **534**(7605): 69
    c. Su X, Ma J, **Wei X**[#], Cao P, Zhu D, Chang W, et al. Structure and assembly mechanism of plant C2S2M2-type PSII-LHCII supercomplex. ***Science***. **2017**; **357**(6353): 815-20. **(#equal contribution)**
2. **Postdoctoral Career:** As a postdoctoral fellow with Dr. Ronen Marmorstein, my research has provided a comprehensive understanding of human ATP citrate lyase dynamics as a function of bound substrates or products. We determined ACLY structures in its apo, substrate bound and product bound states. In our studies, 5 distinct conformational states were captured by cryo-EM single particle reconstruction. We identified the substrate binding sites and catalytic sites in the EM structure. These substrate binding and catalytic sites were further validated using biochemical studies. Our studies challenged a previously proposed catalytic mechanism of ACLY. We had reported the finding in these studies in a manuscript, which is accepted in *Nature Structural & Molecular Biology*. As ATP citrate lyase is an emerging target for pharmacotherapy, we are will determine structures of ACLY in complex with inhibitors, and more specific inhibitors will be developed based on these studies. These additional ACLY studies will also be published in near future.

a. Bazilevsky, G.A., Affronti, H.C., **Wei, X.**, Campbell, S.L., Wellen, K.E. and Marmorstein. R. ATP-citrate lyase multimerization is required for coenzyme-A substrate binding and catalysis, (2019) *J. Biol. Chem.* 294:7529-7268.
b. Deng, S., Magin, R.S., **Wei, X.**, Pan, B., Petersson, E.J. and Marmorstein, R., Structure and mechanism of acetylation by the N-terminal dual enzyme NatA/Naa50 complex. (2019) *Structure*, 27:1057-1070.
c. **Wei, X.**, Schultz, K., and Marmorstein. R. Molecular basis of acetyl-CoA production by ATP-citrate-lyase. (2019) *Nature structural & Molecular biology (in press)*

Complete List of Published Work in My google scholar profile:
https://scholar.google.com/citations?user=VRlzCL8AAAAJ&hl=en

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

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: Schultz, Kollin

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

POSITION TITLE: Graduate Student

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

INSTITUTION AND LOCATION	DEGREE *(*if applicable*)*	START DATE MM/YYYY	END DATE MM/YYYY	FIELD OF STUDY
Utica College	BA	08/2014	05/2018	Biochemistry
University of Pennsylvania	PHD	06/2018		Biochemistry & Biophysics

A. Personal Statement

My goals for my Ph.D., are to develop a strong skillset of biochemical, biophysical, and structural biology techniques, and use them to further our understanding of acetyl-CoA metabolism. As an undergraduate student at Utica College, I completed a diverse set of coursework in biology, chemistry, math, and physics that has uniquely prepared me to join a lab like Dr. Ronen Marmorstein's that uses a wide array of techniques to answer complex biological questions. When I first arrived at the University of Pennsylvania, I completed a lab rotation in Dr. Kathryn Wellen's lab where I was involved in investigating the role of acetyl-CoA metabolism in the development of pancreatic cancer, and the potential of targeting it as a novel therapy. My work there contributed to Dr. Wellen's publication in *Cancer Discovery*. Following my time in Dr. Wellen's lab, I completed a second lab rotation in Dr. Marmorstein's lab where I worked on the protein ATP-citrate lyase (ACLY) which is the main acetyl-CoA producing enzyme in the cytoplasm. We were able to resolve the structure of recombinantly expressed ACLY with single particle cryo-EM and validate the structure and catalytic mechanism with site-directed mutagenesis and other biochemical and biophysical techniques. This work resulted in a recent publication in *Nature Structural and Molecular Biology*. For my thesis work, I plan to build on these projects in collaboration with Dr. Wellen's lab to further understand the interplay between acetyl-CoA producing enzymes, like ACLY, and downstream acetyl-CoA consuming enzymes. I believe that I am particularly qualified to take on this project because of my background and experiences in both Dr. Wellen's and Dr. Marmorstein's labs.

1. Alessandro Carrer, Sophie Trefely, Steven Zhao, Sydney Campbell, Robert J Norgard, **Kollin C Schultz**, Simone Sidoli, Joshua L.D. Parris, Hayley C Affronti, Sharanya Sivanand, Shaun Egolf, Yogev Sela, Marco Trizzino, Alessandro Gardini, Benjamin A Garcia, Nathaniel W Snyder, Ben Z. Stanger and Kathryn Wellen. Acetyl-CoA metabolism supports multi-step pancreatic tumorigenesis. *Cancer Discov* (2019) DOI: 10.1158/2159-8290.CD-18-0567

2. Xuepeng Wei, **Kollin Schultz**, Gleb Bazilevsky, Austin Vogt, and Ronen Marmorstein. Molecular Basis for Acetyl-CoA Production by ATP-Citrate Lyase. *Nature Structural and Molecular Biology* (2019), in press

B. Positions and Honors

Positions and Employment

2017 NSF Genomes to Phenomes REU – Neuroscience
2018- Graduate Student University of Pennsylvania

Other Experience and Professional Memberships

2018 Member, New York Academy of Science

Honors

2015 CRC Freshman Chemistry Achievement Award
2016 ACS Undergraduate award in Analytical Chemistry
2017 ACS Undergraduate award in Physical Chemistry
2020 NIH T32- Chemistry-Biology Interface Training Grant

C. Contribution to Science

1. **Graduate Research**: My first lab rotation project as a graduate student focused on the role of acetyl-CoA metabolism in the development of pancreatic cancer, and the potential of targeting downstream fates of acetyl-CoA as a novel treatment method. My work contributed to a publication in Cancer Discovery. As a rotation student and member of my thesis lab, I worked with a postdoc on elucidating the structure and molecular mechanism of ATP-citrate lyase (ACLY). Our work is published in Nature Structural and Molecular Biology. For my thesis work I will be building from these projects on a collaborative project with Dr. Katy Wellen's lab to further elucidate the role of acetyl-CoA metabolism in disease and develop novel therapeutics.
    a. Alessandro Carrer, Sophie Trefely, Steven Zhao, Sydney Campbell, Robert J Norgard, **Kollin C Schultz**, Simone Sidoli, Joshua L.D. Parris, Hayley C Affronti, Sharanya Sivanand, Shaun Egolf, Yogev Sela, Marco Trizzino, Alessandro Gardini, Benjamin A Garcia, Nathaniel W Snyder, Ben Z. Stanger and Kathryn Wellen. Acetyl-CoA metabolism supports multi-step pancreatic tumorigenesis. *Cancer Discov* (2019) DOI: 10.1158/2159-8290.CD-18-0567
    b. Xuepeng Wei, **Kollin Schultz**, Gleb Bazilevsky, Austin Vogt, and Ronen Marmorstein. Molecular Basis for Acetyl-CoA Production by ATP-Citrate Lyase. *Nature Structural and Molecular Biology* (2019), in press

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

Scholastic Performance

YEAR	COURSE TITLE	GRADE
	UTICA COLLEGE	
2014	General Biology I	A
2014	General Chemistry I	A
2014	Written Communication I	A
2014	Advanced Fitness	A
2014	Beginning Spanish II	A
2014	First Year Seminar	A
2015	General Biology II	B+
2015	General Chemistry II	A
2015	Intro to Chem Research Methods	A
2015	Written Communication II	A
2015	Calculus II	A
2015	Genetics	A
2015	Organic Chemistry I	A
2015	Intro to Public Speaking	A
2015	Critical Thinking	A
2015	General Physics I	A-
2016	Cell Biology	A
2016	Organic Chemistry II	A
2016	History of Art I	A
2016	General Physics II	A
2016	Statistics in the Behavior Sci	A
2016	Quantitative Analysis	A
2016	Phys Chem I: Therm & Kinetics	A
2016	Biochemistry	A
2016	Biochemistry Lab	A
2016	Introduction to Psychology	A
2017	Molecular Biology	A
2017	Physical Chemistry II: Struct	A
2017	Physical Chemistry Lab	A
2017	Res Methods: Nanomaterials I	A
2017	Adv Organic Chem Lab	A
2017	Biochemistry II	A
2017	Senior Seminar	A
2017	Native American Culture & Hist	A
2017	Inorganic Chemistry	A
2017	Calculus III	A
2017	Ordinary Differential Equation	B
2017	Physics III	A
2018	Immunology	A

YEAR	COURSE TITLE	GRADE
2018	Res: Explore Mech/Chem Reaction	A
2018	Instrumental Methods	A
2018	Senior Seminar	A
2018	DC and AC Electronics	A
2018	Special Topics in Physics	A
	UNIVERSITY OF PENNSYLVANIA	
2018	Cell Biology	B+
2018	Macromolecular Biophysics: Principles and Methods	A+
2018	Macromolecular Crystallography: Methods and Application	A
2018	Lab Rotation	A
2019	Structural & Mechanistic Biochemistry	A
2019	Data Analysis and Scientific Inference	A+
2019	Lab Rotation	A
2019	Chemical Biology	A-
2019	Structural Biology TG	A
2019	Pre-Dissertation Lab	A
2019	Stress Responses and Metabolism in Cancer	A