Daniel Kneller, PhD

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2010 Panoramic Way #402, Knoxville, TN, 37932

SUMMARY

- Eager structural biologist with a diverse skillset developed through 11 years of research experience in government, academic, or industry laboratories
- 1st year of postdoctoral experience at Oak Ridge National Laboratory produced 5 lead-author publications contributing award-winning COVID-19 antiviral research
- Extensive biochemistry skills combined with significant computational chemistry experience
- Enthusiastic team member with track record of delivering interdisciplinary successes

EDUCATION

PhD, Molecular Genetics and Biochemistry 2019
Georgia State University, Atlanta, GA

BS, Cell and Molecular Biology 2012
Bradley University, Peoria, IL

AWARDS AND FELLOWSHIPS

Post-Doc of the Year, Oak Ridge National Lab Neutron Scattering Division 2020
Best Paper, Oak Ridge National Lab Neutron Scattering Division 2020
- "Unusual zwitterionic catalytic site of SARS-CoV-2 main protease revealed by neutron crystallography"

UT Battelle Research Accomplishment Team Award 2020
GSU Molecular Basis of Disease Fellowship 2016-2019
Steven Kudravi Memorial Award, for Outstanding Student Instruction 2019
Travel award, Southeast collaborative access team (SER-CAT) symposium 2019
Bjorklund Research Endowment, $5,000 grant for undergraduate research 2011
David M. Simon Memorial Scholarship, Largest private scholarship at Bradley 2011-2012
Bradley University Dean's List 2009-2012
Interfraternity Council Unsung Hero Award, recognizing campus involvement 2011

Best Presentation Awards
- Virtual talk: "Crystallographic studies of SARS-CoV-2 main protease reveal unexpected structural plasticity of the active site cavity and reactivity of the catalytic cysteine" ORNL Post-doctoral Association symposium. Oak Ridge, TN. 2020
- Poster: "Classifying cancers from RNAseq Data through machine learning" GSU Scientific Computing Day. Atlanta, GA. 2016.
- Poster: "Characterization of the *Tetrahymena thermophila* ART1 fusion gene." Bradley University Student Scholarship Exposition. Peoria, IL. 2010

RESEARCH EXPERIENCE

Postdoctoral Research Associate, *Oak Ridge National Laboratory*, Oak Ridge, TN 2020-
Mentor: Dr. Andrey Kovalevsky, kovalevskyay@ornl.gov
- Contributing to emergency COVID-19 pandemic research efforts

- Structure-guided drug design against SARS-CoV-2 using neutron and X-ray crystallography
- Understanding protein-drug interactions using neutron vibrational spectroscopy of protein
- Developing new molecular dynamics simulation approaches for complex inelastic neutron scattering experiments

PhD Candidate, *Georgia State University*, Atlanta, GA 2013-2019
Advisor: Dr. Irene T. Weber, iweber@gsu.edu

- Structure-guided drug design and molecular mechanisms of HIV drug resistance at an R1 university
- Researched novel inhibitors of HIV-1 protease using high resolution X-ray crystallography
- Spearheaded projects to understand highly-drug resistant mutants using MD simulation & modeling
- Published conference paper of class project using machine learning on cancer transcriptomic data
- Demonstrated leadership and communication abilities by undergraduate mentee and pedagogy successes

Research Intern, *zuChem Inc*, Peoria, IL 2012-2013
Supervisor: Dr. Leila Aminova

- Assisted in the development of scalable production methods for unique carbohydrates

Undergraduate Researcher, *Bradley University*, Peoria, IL 2009-2012
Advisor: Dr. Naomi A. Stover, nstover@bradley.edu

- Awarded the Bjorklund Endowment grant to investigate changes in gene expression in *Tetrahymena thermophila* following anti-parasitic agent treatment
- Explored regulation of gene expression using molecular biology and genomics techniques

PUBLICATIONS

ORCID: https://orcid.org/0000-0002-5416-5789

Inhibitor Binding Modulates Protonation States in the Active Site of SARS-CoV-2 Main Protease

(2021) *Journal of Medicinal Chemistry.* Submitted.
Kneller, DW, Phillips, G, Weiss, KL, Zhang, Q, Coats, L, Kovalevsky, A.

Inhibitor binding influences the protonation states of histidines in SARS-CoV-2 main protease

(2021) *Chemical Science*. Epub ahead of print.
Pavlova, A, Lynch, D, Diadone, I, Zanetti-Polzi, L, Smith, MD, Chipot, C, **Kneller, DW**, Kovalevsky, A, Coates, L, Golosov, A, Dickson, C, Velez-Vega, C, Duca, JS, Pang, YT, Acharya, A, Parks, JM, Smith, JC, Gumbart, JC.

Supercomputer-Based Ensemble Docking Drug Discovery Pipeline with Application to Covid-19

Cover: (2020) *Journal of Chemical Information and Modeling.* 60(12)5832-5852
Acharya, A, Agarwal, R, Baker, M, Baudry, J, Bhowmik, D, Boehm, S, Byler, KG, Chen, SY, Coates, L, Cooper, CJ, Demerdash, O, Daidone, I, Eblen, JD, Ellingson, S, Forli, S, Glaser, J, Gumbart, JC, Gunnels, J, Hernandez, O, Irle, S, **Kneller, DW**, Kovalevsky, A, Larkin, J, Lawrence, TJ, Legrand, S, Liu, SH, Mitchell, JC, Park, G, Parks, JM, Pavlova, A, Petridis, L, Poole, D, Pouchard, L, Ramanathan, A, Rogers, D, Santos-Martins, D, Scheinberg, A, Sedova, A, Shen, Y, Smith, JC, Smith, MD, Soto, C, Tsaris, A, Thavappiragasam, M, Tillack, AF, Vermaas, JV, Vuong, VQ, Yin, J, Yoo, S, Zahran, M, Zanetti-Polzi, L

Malleability of the SARS-CoV-2 3CL Mpro active site cavity facilitates binding of clinical antivirals
Featured article: (2020) *Structure.* 28(12)1313-1320.
Kneller, DW, Galanie, S. Phillips, G, O'Neill, HM, Coates, L, Kovalevsky, A.

Unusual zwitterionic catalytic site of SARS-CoV-2 main protease revealed by neutron crystallography
Cover: (2020) *Journal of Biological Chemistry.* 295(50).
Kneller, DW, Phillips, G, Weiss, KL, Pant, S, Zhang, Q, O'Neill, Coates, L, Kovalevsky, A.

Room-temperature X-ray crystallography reveals the oxidation and reactivity of cysteine residues in SARS-CoV-2 3CL Mpro: insights into enzyme mechanism and drug design
(2020) *IUCrJ*. 7(6). November 2020.
Kneller, DW, Phillips, G, O'Neill, HM, Tan, K, Joachimiak, A, Coates, L, Kovalevsky, A.

Room-temperature neutron and X-ray data collection of 3CL Mpro from SARS-CoV-2
(2020) *Acta Crystallogrpahica F*. 76(10)483-487.
Kneller, DW, Phillips, G, Kovalevsky, A, Coates, L.

Structural Plasticity of the SARS-CoV-2 3CL Mpro Active Site Cavity Revealed by Room Temperature X-ray Crystallography
(2020) *Nature Communications.* (11)3202
Kneller, DW, Phillips, G, O'Neill, HM, Jedrzejczak, R, Stols, L, Langan, P, Joachimiak, A, Coates, L, Kovalevsky, A.

Design, Synthesis, and X-ray Studies of Potent HIV-1 Protease Inhibitors with P2-Carboxamide Functionalities
(2020) *ACS Medicinal Chemistry Letters.* 11(10)1965-1972.
Ghosh, AK, Grillo, A, Raghavaiah, J, Kovela, S, Johnson M, **Kneller, DW**, Wang, YF, Hattori, S, Higashi-Kuwata, N, Weber, IT, Mitsuya H.

Highly drug-resistant HIV-1 protease reveals decreased intra-subunit interactions due to coordinated structural changes in clusters of mutations
(2020) *The FEBS Journal*. 287(15)3235-3254.
Kneller, DW, Agniswamy, J, Harrison, RW, Weber, IT.

Potent HIV-1 Protease Inhibitors Containing Carboxylic and Boronic Acids: Effect on Enzyme Inhibition and Antiviral Activity and X-ray Structural Studies of Inhibitor-HIV-1 Protease Complex
(2019) *ChemMedChem.* 14(21)1863-1872.
Ghosh, AK, Xia, Z, Kovela S, Robinson, WL, Johnson, ME, **Kneller, DW,** Wang, YF, Aoki, M, Takamatsu, Y, Weber, IT, Mitsuya, H.

Potent antiviral HIV-1 protease inhibitor combats highly drug resistant mutant PR20
(2019) *Biochemical and Biophysical Research Communications.* 519(1)56-66.

Kneller, DW, Agniswamy, J, Ghosh, A, Weber, IT.

Highly drug-resistant HIV-1 protease mutant PRS17 shows enhanced substrate binding
(2019) *ACS Omega.* 4(5)8707-8719.
Agniswamy, J, **Kneller, DW,** Brothers, R, Wang, YF, Harrison, RW, Weber, IT.

Using guided-inquiry experiments to characterize factors of osmosis and diffusion
(2018) *Principles of Biology Laboratory Manual 4th edition.* 23-34. Hayden-McNeil
Kneller, DW, Gutzler, SJ, Brewer, MW.

Highly resistant HIV-1 proteases and strategies for their inhibition
(2015) *Future Medicinal Chemistry.* 7(8)1023-38.
Weber, IT, **Kneller, DW,** Wong-Sam, AE.

Classifying Cancers from RNAseq Data through Machine Learning
Proceedings of the International Symposium on Bioinformatics Research and Applications (ISBRA), Norfolk, VA, June 7-10, 2015.
Klimov, S, **Kneller, DW,** Stone, RD, Mandric, I, Artsiomenka, A, Weber, IT, Harrison, RW, Zelikovsky, A, Aneja, R, Jiang, Y.

LIST OF TECHNICAL SKILLS

Dry Lab: Python for structural data science, expert PyMol, crystallography software (Phenix, Coot, CCP4, HKL2000, Rigaku homelab), linux command line, MD simulations (GROMACS, CHARMM ff, CGenFF & ffTK), MatPlotLib, basic shell/BASH scripting, VIM, Jupyter Notebook, Gaussian, PDB, BLAST & basic genomics, MS Office, Origin, SigmaPlot
Wet Lab: Recombinant protein construct design, expression, & purification, large-volume protein crystallization, protein-ligand co-crystallization and soaking, Chromatography, Michalis-Menten and inhibition enzyme kinetics assays, Akta instruments, basic molecular biology, TLC
Organization: Analytical thinker & systematic problem solving, understand operations at a large-scale/budget institution, time-management, mentoring and pedagogy, presenting technical data to diverse audiences, ability to prioritize and manage multiple research projects

INVITED PRESENTATIONS

Race for the neutron crystal structure of SARS-CoV-2 main protease reveals insights for drug design
ORNL Neutron Scattering Division COVID-19 research update, Dec 4, 2020.

Room-temperature X-ray and neutron crystallography of SARS-CoV-2 main protease at Oak Ridge National Lab
Florida Institute of Technology graduate seminar, Melbourne, FL. Nov 5, 2020.

Crystallographic studies of SARS-CoV-2 main protease reveal unexpected structural plasticity of the active site cavity and reactivity of the catalytic cysteine
People's Choice Award winner at Oak Ridge Postdoctoral Association annual symposium, Oak Ridge, TN, June 22, 2020

Neutron Structural Studies of COVID-19 proteins essential for viral replication
East Tennessee STEM hub event, virtual, April 28th, 2020

Potent antiviral HIV-1 protease inhibitor developed through structure-guided drug design combats highly-resistant mutant PR20
MBD Fellowship Retreat, Atlanta, GA. September 9, 2019

Highly drug-resistant HIV-1 protease shows coordinated structural changes from distal mutation clusters
MBD Fellows seminar, Atlanta, GA. April 11, 2019

Hydrogens and deuteriums in high resolution X-ray crystal structures of HIV-1 Protease
MDB Fellows seminar, Atlanta, GA. Dec 7, 2017

Infusing inquiry-based teaching methods in an undergraduate Biology laboratory course.
GSU Center for Excellence in Teaching and Learning Conference, Atlanta, GA. May 12, 2017.
With Stephanie Gutzler and Adani Pujada

Gene expression comparison between the synergistic anti-parasitic agents malachite green and formaldehyde in *Tetrahymena thermophila*.
Bradley University Bjorklund Endowment Presentation, Peoria, IL. 2011

TEACHING AND LEADERSHIP EXPERIENCE

Graduate Teaching Assistant, *Georgia State University* 2015-2019

- Awarded the Steven Kudravi Memorial award for excellence in introductory education
- Instructed 1-2 sections of an introductory laboratory course for 24 undergraduate biology and chemistry majors per semester
- Assisted in instruction of graduate level Bioinformatics courses
- Initialized update of a passive didactic learning module to an active inquiry-based exercise
- Demonstrated effective communication skills to a diverse audience of students

Undergraduate Research Mentor, *Georgia State University* 2013-2018

- Directly trained undergraduate mentees who have gone on to become PhD and MD students
- Supervised a high school student completing a summer research internship

Undergraduate Laboratory Teaching Assistant, *Bradley University* 2010-2012
Carlson Leadership Academy, *Bradley University* 2011
Resident Advisor, *Bradley University* 2009-2010

POSTER PRESNETATIONS

Crystallography of SARS-CoV-2 main protease at ORNL
SLAC Users meeting. Oct. 9, 2020.
Daniel Kneller, Gwyn Phillips, Leighton Coates, Andrey Kovalevsky.

HIV-1 Protease inhibitor developed through structure-guided drug design combats highly drug resistant mutant PR20
Pittsburgh Diffraction Conference, Oak Ridge National Lab, TN, Oct. 25, 2019.
Daniel Kneller, Johnson Agniswamy, Arun Ghosh, Irene Weber.

Highly drug-resistant HIV-1 protease uses distal mutation clusters for coordinated structural changes
Southeast Regional Collaborative Access Team meeting. Birmingham, AL. Mar. 15, 2019.
Daniel Kneller, Johnson Agniswamy, Robert Harrison, Irene Weber.

Detecting Hydrogens and Deuteriums in high resolution X-Ray crystal structures of HIV-1 protease
Southeast Enzyme Conference. Atlanta, GA. April 7, 2018.
Daniel Kneller, Andrey Kovalevsky, Yuan-Fang Wang, Robert Harrison, Irene Weber.

Detecting Hydrogens and Deuteriums in high resolution X-Ray crystal structures of HIV-1 protease
Brains and Behavior Retreat. Atlanta, GA. May 5, 2018.
Daniel Kneller, Andrey Kovalevsky, Yuan-Fang Wang, Robert Harrison, Irene Weber.

Detecting Hydrogens and Deuteriums in high resolution X-Ray crystal structures of HIV-1 protease
Southeast Enzyme Conference. Atlanta, GA. April 4, 2017.
Daniel Kneller, Andrey Kovalevsky, Yuan-Fang Wang, Robert Harrison, Irene Weber.

Classifying cancers from RNAseq Data through machine learning
Scientific Computing Day. Atlanta, GA. Sept 30, 2016.
Daniel Kneller, Sergey Klimov, Robert D. Stone Ritu Aneja, Yi Jiang, Irene Weber, Robert Harrison.

Highly Resistant HIV Proteases and Strategies for Inhibition
Tim Bartness Memorial Biotech symposium. Atlanta, GA. Sept 23-24, 2016.
Daniel Kneller, Andres E. Wong-Sam, Johnson Agniswamy, Yuan-Fang Wang, Irene Weber.

Detecting Hydrogens and Deuteriums in high resolution X-Ray crystal structures of HIV-1 protease
Southeast Enzyme Conference. April 16, 2016.
Daniel Kneller, Andrey Kovalevsky, Yuan-Fang Wang, Robert Harrison, IreneWeber.

Detecting Hydrogens and Deuteriums in high resolution X-Ray crystal structures of HIV-1 protease
Southeast Regional Collaborative Access Team meeting. Decatur, GA. Mar 18, 2015.
Daniel Kneller, Andrey Kovalevsky, Yuan-Fang Wang, Robert Harrison, Irene Weber.

Highly Resistant HIV Proteases
Center for Diagnostics and Therapeutics Retreat. Atlanta, GA. Nov. 31, 2015.
Daniel Kneller, Andres E. Wong-Sam, Johnson Agniswamy, Yuan-Fang Wang, Irene Weber.
Highly Resistant HIV Protease.

Classifying cancers from RNAseq Data through machine learning
Scientific Computing Day. Atlanta, GA. Sept. 18, 2015.
Daniel Kneller, Sergey Klimov, Robert D. Stone, Ritu Aneja, Yi Jiang, Irene Weber, Robert Harrison.

Classifying cancer from RNAseq data through machine learning
The Society for Math Biology Meeting. Atlanta, GA, 2015.
Sergey Klimov, **Daniel Kneller**, Robert D. Stone.

Highly Resistant HIV Proteases
Brains and Behavior Retreat. Atlanta, GA. Apr. 24. 2015
Daniel Kneller, Andres Wong, Chen-Hsiang Shen, Irene T. Weber.

Highly Resistant HIV Proteases
Center for Diagnostics and Therapeutics Conference. Atlanta, GA. Apr. 2, 2015
Daniel Kneller, Andres Wong, Chen-Hsiang Shen, Irene T. Weber.

Highly Resistant HIV Proteases
Southeast Enzyme Conference. Atlanta, GA. Apr. 11, 2015
Daniel Kneller, Andres Wong, Chen-Hsiang Shen, Irene T. Weber.

Gene expression comparison between the synergistic anti-parasitic agents malachite green and formaldehyde in *Tetrahymena thermophila*
Bradley University Student Scholarship Exposition. Peoria, IL. 2011
Daniel Kneller and Naomi Stover.

Gene expression comparison between the synergistic anti-parasitic agents malachite green and formaldehyde in *Tetrahymena thermophila*
Midwest Protozoology Conference. Peoria, IL, 2011
Daniel Kneller and Naomi Stover.

Characterization of the *Tetrahymena thermophila* ART1 fusion gene
Bradley University Student Scholarship Exposition. Peoria, IL. 2010.
Peter Shanine, **Daniel Kneller**, Gavin Coyle, Naomi Stover.

Characterization of the *Tetrahymena thermophila* ART1 fusion gene
Midwest Protozoology Conference. Peoria, IL. 2010.
Peter Shanine, **Daniel Kneller**, Gavin Coyle, Naomi Stover.