Daniel Kneller, PhD

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2010 Panoramic Way #402, Knoxville, TN, 37932

SUMMARY

- Eager structural biologist with a diverse pre-clinical skillset developed through years of research experience in government, academic, and industry laboratories
- Produced 6 lead-author publications contributing award-winning COVID-19 antiviral crystallography research during inaugural year of postdoctoral experience at ORNL
- Technical skills in molecular modeling, enzyme kinetic assays, and protein crystallization
- Enthusiastic team member with a winning record of successful interdisciplinary projects

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
UT Battelle Research Accomplishment Team Award 2020
Secretary of Energy Honor's Achievement Team Award 2020
Molecular Basis of Disease Fellowship, Georgia State University 2016-2019
Molecular Basis of Disease Fellow Award, Georgia State University 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

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 crystallography efforts 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 as a molecular basis of disease fellow
- 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 abilities with undergraduate mentee and pedagogical successes

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

- Assisted in the development of scalable enzyme production 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 using RNA-Seq 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

Direct Observation of Protonation States Modulation in SARS-CoV-2 Main Protease upon Inhibitor Binding with Neutron Crystallography
Cover: (2021) *Journal of Medicinal Chemistry*. 64(8)4991-5000
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*. 12(4)1513-1527
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.

TECHNICAL SKILLS

Dry Lab: Expert PyMol, Python for structural data science, crystallography software (Phenix, Coot, CCP4, HKL2000, Rigaku homelab), linux command line, BASH scripting, MD simulations (GROMACS, CHARMM ff, CGenFF & ffTK), VIM, Jupyter Notebook, Gaussian, PDB, BLAST & basic bioinformatics, MS Office, Origin, SigmaPlot

Wet Lab: Recombinant protein construct design, expression, & purification, large-volume protein crystallization, protein-ligand co-crystallization and soaking, room-temperature X-ray

crystallography, chromatography, Michalis-Menten and inhibition enzyme kinetics assays, AKTA instruments, basic molecular biology

Organization: Analytical thinker & systematic problem solving, understand operations at a large-scale/budget institution, project management, mentoring and pedagogy, presenting technical data to diverse audiences, ability to prioritize and manage multiple research projects

INVITED PRESENTATIONS

Structure-guided antiviral design of SARS-CoV-2 main protease using X-rays, neutrons, and supercomputers
Southeast Enzymes Conference 11. Atlanta, GA. April 10, 2021

Targeting SARS-CoV-2 main protease using X-rays, neutrons and computation
American Chemical Society Spring 2021. Washington, DC. April 4, 2021

Structure-based inhibitor design and repurposing clinical drugs to target SARS-CoV-2 main protease using X-rays, neutrons, and computation
ASBMB Proteinases and their inhibitors conference. Rockford, ML. Feb 24, 2021

Science as a public servant in the time of coronavirus
Georgia State University undergraduate career seminar, Atlanta, GA. Feb 2, 2021

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, Oak Ridge, TN. 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, Knoxville, TN. April 28, 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

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

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

- Directly trained undergraduate 4 mentees who proceeded to become PhD and MD students
- Supervised a high school student completing a summer research internship

Powerlifting Club founder and coach, *Georgia State University* 2014-2020
Undergraduate Laboratory Teaching Assistant, *Bradley University* 2010-2012
Carlson Leadership Academy, *Chicago, IL* 2011
Resident Advisor, *Bradley University* 2009-2010

POSTER PRESNETATIONS

Room temperature X-ray diffraction reveals structural malleability of SARS-CoV-2 main protease
PDB50. May 5, 2021.
Daniel Kneller, Stephanie Galanie, Gwyn Phillips, Leighton Coates, Andrey Kovalevsky.

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.