

Karen A. Kirby, Ph.D.

Assistant Professor

Department of Pediatrics, Laboratory of Biochemical Pharmacology

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Education

B.S. Chemistry, University of Minnesota, May 2001

Ph.D. Chemistry, University of Missouri, Dec 2007

Small Molecule Crystallography/Inorganic Chemistry

Positions

Postdoctoral Fellow, University of Missouri School of Medicine, Jan 2008 – Nov 2012

Research Scientist, University of Missouri School of Medicine, Dec 2012 – May 2016

Assistant Research Professor, University of Missouri School of Medicine, June 2016 – Oct 2017

Assistant Professor, Laboratory of Biochemical Pharmacology, Department of Pediatrics, Emory University School of Medicine, Nov 2017 – present

Biomolecular Crystallography, Mentor: Dr. Stefan Sarafianos

I am the senior crystallographer and structural biologist in the Sarafianos laboratory.

I established and managed the high-throughput crystallization setup used by the crystallographic community at the University of Missouri and am currently managing the same setup for the Sarafianos Lab at Emory University. My structural projects are primarily focused on protein crystallography, but also include biomolecular NMR and more recently cryo-electron microscopy (cryo-EM). I have crystallized and solved the crystal structure of various biomedically-important macromolecules, including various drug-resistant mutants and inhibitor complexes of HIV Reverse Transcriptase, HIV RNase H, anti-HIV antibody fragments, HIV capsid, and Xenotropic Murine Leukemia Virus-Related Virus (XMRV) proteins. I have also been involved in structure-based drug design projects, and am currently the senior crystallographer in a multi-site drug discovery team that includes researchers from Emory University, University of Missouri, University of Pittsburgh, and University of Minnesota. I have also more recently become involved in our lab's cryo-EM efforts, including analysis of HBV capsids in complex with novel antiviral compounds.

Grant Applications

Awarded

- 00077678 (PI: Kirby) 07/01/18 to 06/30/19 1.6 calendar mos.
Pediatric Research Alliance/Center for Childhood Infections and Vaccines

\$50,000 Total Costs (\$50,000 Total Direct Costs)

“Targeting Novel Inhibition of the Enterovirus 71 RNA-dependent RNA Polymerase”

This pilot grant in collaboration with Co-I Stefan Sarafianos will validate the antiviral mechanism of action of two lead compounds against Enterovirus 71 (EV71) and screen for novel inhibitors of the RNA-dependent RNA polymerase (RdRp) of EV71, a picornavirus which causes Hand, Foot, and Mouth Disease in children.

- DAA3-17-62988-1 (PI: **Kirby**) **03/14/17 to 03/13/18** **1.0 calendar mo.**
U.S. Civilian Research & Development Foundation (CRDF Global, OISE-17-62937-1) and NSF (OISE-9531011) **\$15,000 Total Costs (\$13,636 Total Direct Costs)**
“Molecular mechanisms by which HIV-1 acquires resistance to second-generation integrase strand transfer inhibitors”
This grant in collaboration with Dr. Atsuko Hachiya at Nagoya Medical Center, Japan, will evaluate the role of novel mutations identified in a patient who failed a raltegravir-based regimen in resistance to HIV-1. This award is part of the Infectious Disease and Immunology Research: U.S.-Japan Cooperative Medical Sciences Program (USJCMSP) Collaborative Award Initiative.
- Excellence in Electron Microscopy Award (PI: **Kirby**) **05/12/17 to 09/01/17, \$2,500 Total Costs**
This is an award to learn cryo-EM techniques at the MU Electron Microscopy Core by preparing samples of assembled HBV capsids in the presence of lead compounds that have been discovered in the Sarafianos lab to affect capsid assembly and block HBV replication. Upon successful preparation of cryo-EM samples at the MU EMC, high resolution data collection is planned on the Titan Krios at Purdue University.
- Advanced Photon Source (APS) General User Proposal GUP-41918, entitled "Crystal structures of HIV-1 proteins in complex with novel inhibitors" by Dr. Karen A. Kirby was selected for Runs 2015-1, 2015-2, 2015-3, 2016-1, and 2016-2 with time allocated at GM/CA beamlines 23-ID-B and 23-ID-D (score of **2.225** on a scale of 1 to 5, 1 is highest).
- APS General User Proposal GUP-51455, entitled "Crystal structures of viral proteins in complex with novel inhibitors" by Dr. Karen A. Kirby was selected for Runs 2017-1, 2017-2, and 2018-1 with time allocated at GM/CA beamlines 23-ID-B and 23-ID-D (score of **1.73** on a scale of 1 to 5, 1 is highest).
- I have played an active role in writing grants in the Sarafianos Lab during the last 11 years. I have assisted in providing intellectual contributions, writing, assembling, and submission of 6 NIH R01 (4 multi-PI), 2 NIH R21, 1 NIH P50/U54, and 1 University of Missouri HIV-related proposals and 3 NIH graduate student diversity and 3 instrumentation supplements which have been funded or received fundable scores (see below), in addition to being involved in many more proposal submissions (>25 total). Additionally, I have helped to coordinate and manage very complex grants such as an NIH P50/U54 award, and grants from international universities and companies. I also assist the PI Dr. Stefan Sarafianos in financial management of awarded grants and am responsible for completing all progress reports.
 - Awarded proposals (primary PI of all proposals is Dr. Stefan Sarafianos).
Total Support (Sarafianos): **\$17,451,814**; Direct costs (Sarafianos): **\$14,133,288**
 - NIH R21 AI094715 “Structure-Based Expansion of Neutralization Ability of KD-247, An Anti-V3 mAb”, 09/01/2011-08/31/2013, Total Support: **\$416,625** (Direct Costs: **\$275,000**).
 - NIH R01 AI100890 “Novel antivirals targeting the RNase H activity of HIV reverse transcriptase” (multi-PI), 07/01/2012-06/30/2017. Total Support: **\$3,456,187** (Direct Costs: **\$3,019,537**).
 - NIH R21 AI112417 “Capsid-Targeting Small Molecules Blocking HIV through Novel Mechanism of Action”, 02/06/2014-01/31/2016. Total Support: **\$413,950** (Direct Costs: **\$275,000**).
 - NIH R01 AI076119 “Ultrapotent inhibitors of HIV-1 reverse transcriptase” (competitive renewal), 05/01/2014-04/30/2019. Total Support: **\$3,415,099** (Direct Costs: **\$2,983,380**).

- Mizzou Advantage “Studying HIV-1 Subtype B or C Drug Resistance in Patient Cohorts from Missouri, Cameroon & India”, 05/01/2014-04/30/2016. Total Support: **\$149,945** (Direct Costs: \$149,945).
- NIH Diversity Supplement for R01 AI100890 for graduate student Andrew Huber, 06/01/2014-06/30/2017. Total Support: **\$194,291** (Direct Costs: \$126,573).
- NIH R01 AI120860 “Structural studies of HIV Capsid with host factors and Capsid-targeting antivirals”, 06/15/2015-05/31/2020. Total Support: **\$2,379,497** (Direct Costs: \$1,836,885).
- NIH Diversity Supplement for R01 AI076119 for graduate student Obiaara Ihenacho, 08/25/2015-04/30/2017. Total Support: **\$64,522** (Direct Costs: \$47,520).
- NIH Diversity Supplement for R01 AI120860 for graduate student Mary Casey, 03/16/2016-05/31/2018. Total Support: **\$126,640** (Direct Costs: \$87,792).
- NIH R01 AI121315 “Taking aim at HBV eradication using novel NRTIs and capsid effectors”, 06/14/2016-05/31/2021. Total Support: **\$3,047,249** (Direct costs: \$2,415,784).
- NIH R01 GM118012 “Reverse Transcriptase Multi-Class Drug Resistance and Rilpivirine Susceptibility in Diverse HIV-1 Subtypes”, 07/01/2016-05/31/2016. Total Support: **\$1,423,009** (Direct costs: \$1,141,904).
- NIH Instrumentation Supplement (NanoTemper Monolith NT.115 Microscale Thermophoresis instrument) for R01 GM118012, 07/01/2016-05/31/2017. Total Support: **\$124,050** (Direct costs: \$124,050).
- I played a significant role in putting together both Project 3 and the overall proposal for the successful competitive renewal of the HIVE Center for HIV/AIDS-Related Structural Biology, NIH P50/U54 GM103368 (Dr. Sarafianos is co-Director). 11/01/2017-08/31/2022. Total Support for Center: **\$26,478,479** (Direct costs: \$15,360,000); Total Support for Sarafianos Lab: **\$1,900,272** (Sarafianos Direct costs: \$1,309,440).
- NIH Instrumentation Supplement (Leica Cryo-CLEM microscope) for R01 GM118012, 06/01/2018-05/31/2019. Total Support: **\$79,645** (Direct costs: \$79,645).
- NIH Instrumentation Supplement (super-resolution microscope) for U54 GM103368, 09/01/2018-08/31/2019. Total Support: **\$260,833** (Direct costs: \$260,833).

Editorial Reviewer

- 2015, *Ad hoc reviewer*, PLoS ONE and Journal of Biological Chemistry.
- 2016, *Ad hoc reviewer*, Current HIV Research and Antimicrobial Agents Chemotherapy.
- 2017, *Ad hoc reviewer*, Biochemistry and European Journal of Medicinal Chemistry.
- 2018, *Ad hoc reviewer*, Nature Communications and Journal of Biological Chemistry.

Course Lectures

- Fall 2015, MICROB 4303/7303, Fundamental Virology, Antivirals lecture.
- Fall 2016, MICROB 4303/7303, Fundamental Virology, Antivirals lecture.

Committees

- July-December 2015, Bond Life Sciences Center Committee for Space and Equipment.

Publications

1. Thallapally PK, **Kirby KA**, and Atwood JL. 2007. "Comparison of porous and nonporous materials for methane storage." *New J. Chem.* **31** (5), 628-630.
2. Michailidis E, Marchand B, Kodama EN, Singh K, Matsuoka M, **Kirby KA**, Ryan EM, Sawani AM, Nagy E, Ashida N, Mitsuya H, Parniak MA, and Sarafianos SG. 2009. "Mechanism of inhibition of HIV-1 Reverse Transcriptase by 4'-Ethylnyl-2-Fluorodeoxyadenosine triphosphate, a Translocation Defective Reverse Transcriptase Inhibitor." *J. Biol. Chem.* **284** (51), 35681-35691. PMID: PMC2790999.
3. Singh K, Marchand B, **Kirby KA**, Michailidis E, and Sarafianos SG. 2010. "Structural Aspects of Drug Resistance and Inhibition of HIV-1 Reverse Transcriptase." *Viruses* **2** (2), 606-638. PMID: PMC2850067.
4. Schuckmann MM, Marchand B, Hachiya A, Kodama EN, **Kirby KA**, Singh K, and Sarafianos SG. 2010. "The N348I Mutation at the Connection Subdomain of HIV-1 Reverse Transcriptase Decreases Binding to Nevirapine." *J. Biol. Chem.* **285** (49), 38700-38709. PMID: PMC2992303.
5. **Kirby KA**, Singh K, Michailidis E, Marchand B, Kodama EN, Ashida N, Mitsuya H, Parniak MA, and Sarafianos SG. 2011. "The Sugar Ring Conformation of 4'-Ethylnyl-2-Fluoro-2'-Deoxyadenosine and its Recognition by the Polymerase Active Site of HIV Reverse Transcriptase." *Cell. Mol. Biol.*, **57** (1), 40-46. PMID: PMC3119259.
6. Hachiya A, Kodama EN, Schuckmann MM, **Kirby KA**, Michailidis E, Sakagami Y, Oka S, Singh K, and Sarafianos SG. 2011. "K70Q Adds High-Level Tenofovir Resistance to "Q151M Complex" HIV Reverse Transcriptase Through the Enhanced Discrimination Mechanism." *PLoS ONE*, **6** (1), e16242. PMID: PMC3020970.
7. Michailidis E, Singh K, **Kirby KA**, Hachiya A, Yoo W, Hong SP, Kim SO, Folk WR, and Sarafianos SG. 2011. "Hepatitis B Virus Genotypic Differences Map Structurally Close to NRTI Resistance Hot Spots." *Inter. J. Curr. Chem.*, **2** (4), 253-260. PMID: PMC3325108.
8. Michailidis E, **Kirby KA**, Hachiya A, Yoo W, Hong SP, Kim SO, Folk WR, and Sarafianos SG. 2012. "Antiviral Therapies: Focus on Hepatitis B Reverse Transcriptase." *Int. J. Biochem. Cell Biol.*, **44** (7), 1060-1071. PMID: PMC3522522. *Invited review*
9. Ndongwe TP, Adedeji AO, Michailidis E, Ong YT, Hachiya A, Marchand B, Ryan EM, Rai DK, **Kirby KA**, Whatley AS, Burke DH, Johnson M, Ding S, Zheng YM, Liu SL, Kodama E, Delviks-Frankenberry KA, Pathak VK, Mitsuya H, Parniak MA, Singh K, and Sarafianos SG. 2012. "Biochemical, Inhibition and Inhibitor Resistance Studies of Xenotropic Murine Leukemia Virus-Related Virus Reverse Transcriptase." *Nucleic Acids Res.* **40** (1), 345-359. PMID: PMC3245923.
10. **Kirby KA**[#], Marchand B[#], Ong YT, Ndongwe TP, Hachiya A, Michailidis E, Leslie MD, Sietsema DV, Fetterly TL, Dorst CA, Singh K, Wang Z, Parniak MA, and Sarafianos SG. 2012. "Structural and Inhibition Studies of the RNase H Function of Xenotropic Murine Leukemia Virus-Related Virus Reverse Transcriptase." *Antimicrob. Agents Chemother.*, **56** (4), 2048-2061. PMID: PMC3318313. [#]equal contribution
11. Hachiya A, Marchand B, **Kirby KA**, Michailidis E, Tu X, Palczewski K, Ong YT, Griffin DT, Schuckmann MM, Tanuma J, Oka S, Singh K, Kodama EN, and Sarafianos SG. 2012. "HIV-1 Reverse Transcriptase (RT) Polymorphism 172K Suppresses the Effect of Clinically Relevant Drug Resistance Mutations to Both Nucleoside and Nonnucleoside RT Inhibitors." *J. Biol. Chem.* **287** (35), 29988-29999. PMID: PMC3436141.
12. Michailidis E, Singh K, Ryan EM, Hachiya A, Ong YT, **Kirby KA**, Marchand B, Kodama EN, Mitsuya H, Parniak MA, and Sarafianos SG. 2012. "Effect of Translocation Defective Reverse Transcriptase Inhibitors on the Activity of N348I, a Connection Subdomain Drug Resistant HIV-1 Reverse Transcriptase Mutant." *Cell. Mol. Biol.* **58** (1), 187-195. PMID: PMC3551986.

13. Ong YT, **Kirby KA**, Hachiya A, Chiang LA, Marchand B, Yoshimura K, Murakami T, Singh K, Matsushita S, and Sarafianos SG. 2012. "Preparation of Biologically Active Single-Chain Variable Antibody Fragments that Target the HIV-1 gp120 V3 Loop." *Cell. Mol. Biol.* 58 (1), 71-79. PMID: PMC3612353.
14. Lee JH, Hachiya A, Shin SK, Lee J, Gatanaga H, Oka S, **Kirby KA**, Ong YT, Sarafianos SG, Folk WR, Yoo W, Hong SP, and Kim SO. 2013. "Restriction Fragment Mass Polymorphism (RFMP) Analysis Based on MALDI-TOF Mass Spectrometry for Detecting Antiretroviral Resistance in HIV-1 Infected Patients." *Clin. Microbiol Infect.* 19 (6), E263-270.
15. Hachiya A[#], Reeve AB[#], Marchand B, Michailidis E, Ong YT, **Kirby KA**, Leslie MD, Oka S, Kodama EN, Rohan LC, Mitsuya H, Parniak MA, and Sarafianos SG. 2013. "Evaluation of Combinations of 4'-Ethyne-2-Fluoro-2'-Deoxyadenosine with Clinically Used Antiretroviral Drugs." *Antimicrob. Agents Chemother.* 57 (9), 4554-4558. PMID: PMC3754316. [#]equal contribution.
16. Michailidis E, Ryan EM, Hachiya A, **Kirby KA**, Marchand B, Leslie MD, Huber AD, Ong YT, Jackson JC, Singh K, Kodama EN, Mitsuya H, Parniak MA, and Sarafianos SG. 2013. "Hypersusceptibility Mechanism of Tenofovir-Resistant HIV to EFdA." *Retrovirology*, 10, 65. PMID: PMC3695782.
17. **Kirby KA**, Michailidis E, Fetterly TL, Steinbach MA, Singh K, Marchand B, Leslie MD, Hagedorn AN, Kodama EN, Marquez VE, Hughes SH, Mitsuya H, Parniak MA, and Sarafianos SG. 2013. "Effects of Substitutions at the 4' and 2 Positions on the Bioactivity of 4'-Ethyne-2-Fluoro-2'-Deoxyadenosine." *Antimicrob. Agents Chemother.* 57 (12), 6254-6264. PMID: PMC3837839.
18. Huber AD, Michailidis E, Schultz ML, Ong YT, Bloch N, Puray-Chavez MN, Leslie MD, Ji J, Lucas AD, **Kirby KA**, Landau NR, and Sarafianos SG. 2014. "SAMHD1 has differential impact on the efficacies of HIV nucleoside reverse transcriptase inhibitors." *Antimicrob. Agents Chemother.* 58 (8), 4915-4919. PMID: PMC4136039.
19. Michailidis E, Huber AD, Ryan EM, Ong YT, Leslie MD, Matzek KB, Singh K, Marchand B, Hagedorn AN, **Kirby KA**, Rohan LC, Kodama EN, Mitsuya H, Parniak MA, and Sarafianos SG. 2014. "4'-ethyne-2-fluoro-2'-deoxyadenosine (EFdA) inhibits HIV-1 reverse transcriptase with multiple mechanisms." *J. Biol. Chem.* 289 (35), 24553-24548. PMID: PMC4148878.
20. Singh K, Flores JA, **Kirby KA**, Neogi U, Sonnerborg A, Hachiya A, Das K, Arnold E, McArthur C, Parniak M, and Sarafianos SG. 2014. "Drug Resistance in Non-B Subtype HIV-1: Impact of HIV-1 Reverse Transcriptase Inhibitors." *Viruses*. 6 (9), 3535-3562. PMID: PMC4189038.
21. **Kirby KA**[#], Ong YT[#], Hachiya A, Laughlin TG, Chiang LA, Pan Y, Moran JL, Marchand B, Singh K, Gallazzi F, Quinn TP, Yoshimura K, Murakami T, Matsushita S, and Sarafianos SG. 2015. "Structural basis of clade-specific HIV-1 neutralization by humanized anti-V3 monoclonal antibody KD-247." *FASEB J.* 29 (1), 70-80. PMID: PMC4285544. [#]equal contribution
22. Vernekar SK, Liu Z, Nagy E, Miller LG, **Kirby KA**, Wilson DJ, Kankanala J, Sarafianos SG, Parniak MA, and Wang Z. 2015. "Design, synthesis, biochemical and antiviral evaluations of C6 benzyl and C6 biaryl methyl substituted 2-hydroxyisoquinoline-1,3-diones: Dual inhibition against HIV reverse transcriptase-associated RNase H and polymerase with antiviral activities." *J. Med. Chem.* 58 (2), 651-664. PMID: PMC4306517.
23. Gres AT, **Kirby KA**, KewalRamani VN, Tanner JJ, Pornillos O, and Sarafianos SG. 2015. "X-ray crystal structures of native HIV-1 capsid protein reveal conformational variability." *Science*. 349 (6243), 99-103. PMID: PMC4584149.
24. Tang J, Liu F, Nagy E, Miller L, **Kirby KA**, Wilson DJ, Wu B, Sarafianos SG, Parniak MA, and Wang Z. 2016. "3-Hydroxypyrimidine-2,4-diones as selective active site inhibitors of HIV reverse transcriptase-associated RNase H: Design, synthesis, and biochemical evaluations." *J. Med. Chem.* 59 (6), 2648-2659. PMID: PMC4871627.

25. Kankanala J, **Kirby KA**, Liu F, Miller L, Nagy E, Wilson DJ, Parniak MA, Sarafianos SG, and Wang Z. 2016. "Design, synthesis and biological evaluations of hydroxypyridonecarboxylic acids as inhibitors of HIV reverse transcriptase-associated RNase H." *J. Med. Chem.* 59 (10), 5051-5062. PMID: PMC4882222.
26. Salie ZL, **Kirby KA**, Michailidis E, Marchand B, Singh K, Rohan LC, Kodama EN, Mitsuya H, Parniak MA, and Sarafianos SG. 2016. "Structural basis of HIV inhibition by translocation-defective RT inhibitor 4'-ethynyl-2-fluoro-2'-deoxyadenosine (EFdA)." *Proc. Natl. Acad. Sci. U S A*, 113 (33), 9274-9279. PMID: PMC4995989.
27. Tang J, **Kirby KA**, Huber AD, Casey MC, Ji J, Wilson DJ, Sarafianos SG, and Wang Z. 2017. "6-Cyclohexylmethyl-3-hydroxypyrimidine-2,4-dione as an inhibitor scaffold of HIV reverse transcriptase: Impacts of the 3-OH on inhibiting RNase H and polymerase." *Eur. J. Med. Chem.*, 128, 168-179. PMID: PMC5384110.
28. Huber AD, Michailidis E, Tang J, Puray-Chavez MN, Boftsi M, Wolf JJ, Boschert KN, Sheridan MA, Leslie MD, **Kirby KA**, Singh K, Mitsuya H, Parniak MA, Wang Z, and Sarafianos SG. 2017. "3-hydroxypyrimidine-2,4-diones as novel hepatitis B virus antivirals targeting the viral ribonuclease H." *Antimicrob. Agents Chemother.*, 61 (6), e00245-17. PMID: PMC5444124.
29. Vernekar SKV, Tang J, Wu B, Huber AD, Casey MC, Myshakina NA, Wilson DJ, Kankanala J, **Kirby KA**, Parniak MA, Sarafianos SG, and Wang Z. 2017. "Double-winged 3-hydroxypyrimidine-2,4-diones: Potent and selective inhibition against HIV-1 RNase H with significant antiviral activity." *J. Med. Chem.*, 60 (12), 5045-5056. PMID: PMC5526604.
30. Hachiya A, **Kirby KA**, Ido Y, Shigemi U, Matsuda M, Okazaki R, Imamura J, Sarafianos SG, Yokomaku Y, and Iwatani Y. 2017. "Impact of HIV-1 integrase L74F/V75I mutations from a clinical isolate on resistance to second-generation integrase strand transfer inhibitors." *Antimicrob. Agents Chemother.*, 61 (8), e00315-17. PMID: PMC5527620.
31. **Kirby KA***, Myshakina NA, Christen MT, Chen YL, Schmidt HA, Huber AD, Xi Z, Kim S, Rao RK, Kramer ST, Yang Q, Singh K, Parniak MA, Wang Z, Ishima R, and Sarafianos SG*. 2017. "A 2-hydroxyisoquinoline-1,3-dione active site RNase H inhibitor binds in multiple modes to HIV-1 reverse transcriptase." *Antimicrob. Agents Chemother.*, 61 (10), e01351-17. PMID: PMC5610509. ***co-corresponding author**
32. Kankanala J, **Kirby KA**, Huber AD, Casey MC, Wilson DJ, Sarafianos SG, and Wang Z. 2017. "Design, synthesis and biological evaluations of N-hydroxythienopyrimidine-2,4-diones as inhibitors of HIV reverse transcriptase-associated RNase H." *Eur. J. Med. Chem.* 141, 149-161. PMID: PMC5682218.
33. Huber AD, Wolf JJ, Liu D, Gres AT, Tang J, Boschert KN, Puray-Chavez MN, Pineda DL, Laughlin TG, Coonrod EM, Yang Q, Ji J, **Kirby KA**, Wang Z, and Sarafianos SG. 2018. "The heteroaryldihydropyrimidine Bay 38-7690 induces hepatitis B virus core protein aggregates associated with promyelocytic leukemia nuclear bodies in infected cells." *mSphere*, 3 (2), e00131-18. PMID: PMC5907649.
34. Wang L, Tang J, Huber AD, Casey MC, **Kirby KA**, Wilson DJ, Kankanala J, Xie J, Parniak MA, Sarafianos SG, and Wang Z. 2018. "6-Arylthio-3-hydroxypyrimidine-2,4-diones potently inhibited HIV reverse transcriptase-associated RNase H with antiviral activity." *Eur. J. Med. Chem.* 156, 652-665. PMID: PMC6112573.
35. Wang L, Tang J, Huber AD, Casey MC, **Kirby KA**, Wilson DJ, Kankanala J, Xie J, Parniak MA, Sarafianos SG, and Wang Z. 2018. "6-Biphenylmethyl-3-hydroxypyrimidine-2,4-diones potently and selectively inhibited HIV reverse transcriptase-associated RNase H." *Eur. J. Med. Chem.* 156, 680-691. PMID: PMC6114935.
36. Wu X, Xu G, Li X, Xu W, Li Q, Liu W, **Kirby KA**, Loh ML, Li J, Sarafianos SG, and Qu CK. 2018. "A small molecule inhibitor that stabilizes the autoinhibited conformation of the oncogenic tyrosine phosphatase SHP2." *J. Med. Chem.* Epub Nov. 20.
37. Huber AD, Pineda DL, Liu D, Boschert KN, Gres AT, Wolf JJ, Coonrod EM, Tang J, Laughlin TG, Yang Q, Puray-Chavez M, Ji J, Singh K, **Kirby KA**, Wang Z, and Sarafianos SG. 2018.

“Novel Hepatitis B Virus Capsid-Targeting Antiviral that Aggregates Core Particles and Inhibits Nuclear Entry of Viral Cores.” *ACS Infect. Dis.*, Epub Dec 24.

38. Craveur P, Gres AT, **Kirby KA**, Liu D, Hammond JA, Deng Y, Forli S, Goodsell DS, Williamson JR, Sarafianos SG, and Olson AJ. 2018. “Intersubunit interactions in HIV-1 capsid cores: a target for inhibitor design.” *mBio*, Accepted.

Selected Research Presentations (coauthor of more than 50 presentations):

- **Oral Presentation:** “Crystal Structure of the Fab Fragment of KD-247, a Humanized Anti-V3 Monoclonal Antibody that Inhibits HIV-1 Entry.” *Retroviruses Conference, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, United States, May 19-24, 2008.*
- **Poster:** “Structural Determinants of EFdA that Affect Antiviral Potency and Resistance to Degradation by Adenosine Deaminase.” **Kirby KA**, Steinbach MA, Michailidis E, Marchand B, Singh K, Kodama EN, Matsuoka M, Ashida N, Nagy E, Mitsuya H, Parniak MA, and Sarafianos SG. *Retroviruses Conference, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, United States, May 18-23, 2009.*
- **Poster:** “Functional and Structural Studies of the Ribonuclease H Domain of Xenotropic Murine Leukemia Virus-Related Virus (XMRV) Reverse Transcriptase.” **Kirby KA**, Marchand B, Ong YT, Ndongwe T, Hachiya A, Sietsema DV, Leslie MD, Fetterly TL, Dorst CA, Singh K, Parniak MA, and Sarafianos SG. *American Society of Microbiology Conference on Viral Genome Replication, Banff Centre for Conferences, Banff, Alberta, Canada, February 6-9, 2011.*
- **Poster:** “Structure-Based Drug Design of Novel HIV-1 RNase H Inhibitors.” **Schmidt HA**, **Kirby KA**, Yang Q, Tang J, Iliina T, Wang Z, Parniak MA, and Sarafianos SG. *2014 Annual Institute of Biological Engineering Conference, Lexington, Kentucky, March 6-8, 2014. 2nd place undergraduate poster award*
- **Poster:** “Structure-Based Drug Design of Novel Active Site and Allosteric HIV-1 RNase H Inhibitors.” **Kirby KA**, Schmidt HA, Iliina T, Tang J, Yang Q, Wang Z, Parniak MA, and Sarafianos SG. *27th International Conference on Antiviral Research, Raleigh, North Carolina, May 12-16, 2014.*
- **Poster:** “3-Hydroxypyrimidine-2,4-diones as Novel HIV-1 RNase H Inhibitors.” **Kirby KA**, Tang J, Vernekar SKV, Wu B, Huber AD, Casey MC, Ji J, Nagy E, Miller L, Yang Q, Parniak MA, Wang Z, and Sarafianos SG. *2016 NIGMS Structural Biology Related to HIV/AIDS Meeting, Bethesda, MD, June 23-24, 2016.*
- **Invited Seminar:** “Molecular Mechanisms of Viral Inhibition.” *Clinical Research Center, National Hospital Organization, Nagoya Medical Center, Nagoya, Japan, September 2, 2016.*
- **Oral Presentation:** “3-Hydroxypyrimidine-2,4-diones as Novel HIV-1 RNase H Inhibitors.” **Kirby KA**, Tang J, Vernekar SKV, Wu B, Huber AD, Casey MC, Ji J, Nagy E, Miller L, Yang Q, Parniak MA, Wang Z, and Sarafianos SG. *14th International RNase H Meeting, Kyoto, Japan, September 6-9, 2016.*
- **Oral Presentation:** “Thermal shift assays as a tool for screening SuFEx compounds targeting viral capsids.” *Biannual HIVE Face-to-Face Meeting, The Scripps Research Institute, La Jolla, CA, January 12-13, 2017.*
- **Oral and Poster Presentation:** “2-Hydroxyisoquinoline-1,3-diones and 3-Hydroxypyrimidine-2,4-diones as Novel HIV-1 RNase H Inhibitors.” **Kirby KA**, Huber AD, Casey MC, Hachiya A, Tang J, Vernekar SKV, Wu B, Myshakina NA, Christen MT, Chen YL, Wilson D, Yang Q, Parniak MA, Ishima R, Wang Z, and Sarafianos SG. *Retroviruses Conference, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, United States, May 22-27, 2017.*
- **Oral Presentation:** “Thermal shift assays as a tool for screening SuFEx compounds targeting viral capsids.” *Biannual HIVE Face-to-Face Meeting, Bethesda, MD, June 28, 2017.*

- **Poster Presentation:** “2-Hydroxyisoquinoline-1,3-diones and 3-Hydroxypyrimidine-2,4-diones as Novel HIV-1 RNase H Inhibitors.” **Kirby KA**, Huber AD, Casey MC, Hachiya A, Tang J, Vernekar SKV, Wu B, Myshakina NA, Christen MT, Chen YL, Wilson D, Yang Q, Parniak MA, Ishima R, Wang Z, and Sarafianos SG. *2017 NIGMS Structural Biology Related to HIV/AIDS Meeting, Bethesda, MD, June 29-30, 2017.*
- **Poster Presentation:** “A Novel Bis(Sulfonyl Fluoride) Compound Covalently Binds to the HIV-1 Capsid Protein.” Casey MC, **Kirby KA**, Bare G, Wang H, Torbett BE, Olson AJ, Sharpless KB, and Sarafianos SG. *2018 NIGMS Structural Biology Related to HIV/AIDS Meeting, Bethesda, MD, June 28-29, 2018.*

Crystal Structures Deposited in Protein Data Bank

1. **Kirby KA**, Sarafianos SG. **3NTC**, Crystal Structure of KD-247 Fab, an Anti-V3 Antibody that Inhibits HIV-1 Entry, 1.55 Å resolution, released 08/25/2010.
2. **Kirby KA**, Sarafianos SG. **3P1G**, Crystal Structure of the Xenotropic Murine Leukemia Virus-Related Virus (XMRV) RNase H Domain, 1.50 Å resolution, released 10/13/2010.
3. Tu X, **Kirby KA**, Marchand B, Sarafianos SG. **4DG1**, Crystal Structure of HIV-1 Reverse Transcriptase (RT) with Polymorphism Mutation K172A and K173A, 2.15 Å resolution, released 06/20/2012.
4. Gres AT, **Kirby KA**, Sarafianos SG. **4XFX**, Structure of the native full-length HIV-1 capsid protein, 2.43 Å resolution, released 06/10/2015.
5. Gres AT, **Kirby KA**, Sarafianos SG. **4XFY**, Structure of the native full-length dehydrated HIV-1 capsid protein, 2.8 Å resolution, released 06/10/2015.
6. Gres AT, **Kirby KA**, Sarafianos SG. **4XFZ**, Structure of the native full-length HIV-1 capsid protein in complex with PF-3450074 (PF74), 2.7 Å resolution, released 06/10/2015.
7. **Kirby KA**, Sarafianos SG. **5HBM**, Crystal Structure of a Dihydroxycoumarin RNase H Active-Site Inhibitor in Complex with HIV-1 Reverse Transcriptase, 3.0 Å resolution, released 02/24/2016.
8. **Kirby KA**, Sarafianos SG. **5J1E**, Crystal Structure of a Hydroxypyridone Carboxylic Acid Active-Site RNase H Inhibitor in Complex with HIV Reverse Transcriptase, 2.9 Å resolution, released 06/15/2016.
9. Li Z, **Kirby KA**, Sarafianos SG. **5J2M**. HIV-1 reverse transcriptase in complex with DNA and EFdA-triphosphate, a translocation-defective RT inhibitor, 2.4 Å resolution, released 08/03/2016.
10. Li Z, **Kirby KA**, Sarafianos SG. **5J2N**. HIV-1 reverse transcriptase in complex with DNA that has incorporated EFdA-MP at the P-(post-translocation) site and dTMP at the N-(pre-translocation) site, 2.9 Å resolution, released 08/03/2016.
11. Li Z, **Kirby KA**, Sarafianos SG. **5J2P**. HIV-1 reverse transcriptase in complex with DNA that has incorporated EFdA-MP at the P-(post-translocation) site and a second EFdA-MP at the N-(pre-translocation) site, 2.5 Å resolution, released 08/03/2016.
12. Li Z, **Kirby KA**, Sarafianos SG. **5J2Q**. HIV-1 reverse transcriptase in complex with DNA that has incorporated a mismatched EFdA-MP at the N-(pre-translocation) site, 2.8 Å resolution, released 08/03/2016.
13. **Kirby KA**, Sarafianos SG. **5TUQ**. Crystal Structure of a 6-Cyclohexylmethyl-3-hydroxypyrimidine-2,4-dione Inhibitor in Complex with HIV Reverse Transcriptase, 2.7 Å resolution, released 6/28/2016.
14. **Kirby KA**, Sarafianos SG. **5UV5**. Crystal Structure of a 2-Hydroxyisoquinoline-1,3-dione RNase H Active Site Inhibitor with Multiple Binding Modes to HIV Reverse Transcriptase, 3.0 Å resolution, released 08/16/2017.
15. Gres AT, **Kirby KA**, Sarafianos SG. **5W4O**. Structure of the R18A mutant of the HIV-1 capsid protein, 2.1 Å resolution, released 6/20/2018.

16. Gres AT, **Kirby KA**, Sarafianos SG. **5W4P**. Structure of the E28A mutant of the HIV-1 capsid protein, 2.2 Å resolution, released 6/20/2018.
17. Gres AT, **Kirby KA**, Sarafianos SG. **5W4Q**. Structure of the R18A/E28A mutant of the HIV-1 capsid protein, 2.3 Å resolution, released 6/20/2018.
18. **Kirby KA**, Sarafianos SG. **6AOC**. Crystal Structure of an N-Hydroxythienopyrimidine-2,4-dione RNase H Active Site Inhibitor with Multiple Binding Modes to HIV Reverse Transcriptase, 1.8 Å resolution, released 08/08/2018.
19. Gres AT, **Kirby KA**, Sarafianos SG. **6AXR**. Structure of the P122A mutant of the HIV-1 capsid protein, 2.3 Å resolution, deposited 09/07/2017.
20. Gres AT, **Kirby KA**, Sarafianos SG. **6AXS**. Structure of the V111/T58A/P122A mutant of the HIV-1 capsid protein, 2.4 Å resolution, deposited 09/07/2017.
21. Gres AT, **Kirby KA**, Sarafianos SG. **6AXT**. Structure of the T58S/T107I/P122A mutant of the HIV-1 capsid protein, 2.4 Å resolution, deposited 09/07/2017.
22. Gres AT, **Kirby KA**, Sarafianos SG. **6AXV**. Structure of the T58S/T107I/P122A mutant of the HIV-1 capsid protein in complex with PF-3450074 (PF74), 2.77 Å resolution, deposited 09/07/2017.
23. Gres AT, **Kirby KA**, Sarafianos SG. **6AXW**. Structure of the I124A mutant of the HIV-1 capsid protein, 2.4 Å resolution, deposited 09/07/2017.
24. Gres AT, **Kirby KA**, Sarafianos SG. **6AXX**. Structure of the T58A/I124A mutant of the HIV-1 capsid protein, 2.6 Å resolution, deposited 09/07/2017.
25. Gres AT, **Kirby KA**, Sarafianos SG. **6AXY**. Structure of the V111/T58A/I124A mutant of the HIV-1 capsid protein, 2.78 Å resolution, deposited 09/07/2017.
26. Gres AT, **Kirby KA**, Sarafianos SG. **6AY9**. Structure of the native full-length HIV-1 capsid protein in complex with CPSF6 peptide, 2.5 Å resolution, deposited 09/07/2017.
27. Gres AT, **Kirby KA**, Sarafianos SG. **6AYA**. Structure of the native full-length HIV-1 capsid protein in complex with Nup153 peptide, 2.4 Å resolution, deposited 09/07/2017.
28. Gres AT, **Kirby KA**, Sarafianos SG. **6B2G**. P38A mutant of the HIV-1 capsid protein, 2.4 Å resolution, deposited 09/20/2017.
29. Gres AT, **Kirby KA**, Sarafianos SG. **6B2H**. P38A/T216I mutant of the HIV-1 capsid protein, 2.6 Å resolution, deposited 09/20/2017.
30. Gres AT, **Kirby KA**, Sarafianos SG. **6B2I**. E45A mutant of the HIV-1 capsid protein, 2.5 Å resolution, deposited 09/20/2017.
31. Gres AT, **Kirby KA**, Sarafianos SG. **6B2J**. E45A mutant of the HIV-1 capsid protein (other crystal form), 2.21 Å resolution, deposited 09/20/2017.
32. Gres AT, **Kirby KA**, Sarafianos SG. **6B2K**. E45A/R132T mutant of the HIV-1 capsid protein, 2.0 Å resolution, deposited 09/20/2017.
33. **Kirby KA**, Sarafianos SG. **6ECL**. Crystal Structure of a 1,2,4-Triazole Allosteric RNase H Inhibitor in Complex with HIV Reverse Transcriptase, 2.38 Å resolution, submitted 08/08/2018.

Workshops/Courses Completed

- CCP4 School: From data processing to structure refinement and beyond. Argonne National Laboratory, Chicago, IL, May 23 – May 28, 2008.
- Programming for Everybody (Getting Started with Python) by University of Michigan on Coursera. Certificate earned on July 30, 2017.
- EMAN2.2 Image Processing Workshop. University of Missouri, Columbia, MO, August 3-4, 2017.
- 3-D Reconstruction with SerialEM and IMOD Short Course. 2017 Microscopy & Microanalysis Meeting, St. Louis, MO, August 6, 2017.

- Next Generation Sequencing Training (sample and library preparation, MiSeq, and analysis) with Dr. Atsuko Hachiya, Clinical Research Center, Laboratory Infectious Diseases, National Hospital Organization, Nagoya Medical Center, Nagoya, Aichi, Japan, September 25-29, 2017.
- HIVE Center Trainee Retreat on Molecular Docking, Virtual Screening, Molecular Dynamics, Mesoscale Modeling, and Bioinformatics, The Scripps Research Institute, La Jolla, CA, January 10, 2018.
- Light Scattering University, Wyatt Technologies, Santa Barbara, CA, March 20-22, 2018.
- Dynamic Light Scattering University, Wyatt Technologies, Santa Barbara, CA, March 22-23, 2018.
- SerialEM for Data Acquisition Short Course. 2018 Microscopy & Microanalysis Meeting, Baltimore, MD, August 5, 2018.

Skills and Techniques

- Protein Crystallography
 - **Crystallization:** Highly skilled in setting trays for crystallization and optimizing crystallization conditions.
 - Hanging and sitting drop trays, streak seeding techniques
 - Also very proficient in cryoprotection of crystals for X-ray diffraction studies.
 - **High-Throughput Crystallization:** Extensive experience in programming and operating an Art Robbins Crystal Gryphon robotic crystallization system and CrysCam microscope. I am in charge of instrument maintenance and coordinating usage of the instrument for all users on the Emory campus. In addition to using the instrument frequently for my own experiments, I assist users in designing and creating programs to meet their crystallization needs and requirements. I also routinely optimize hits obtained from high-throughput screening into 24-well crystallization trays to grow suitable crystals for X-ray diffraction experiments.
 - **Data Collection:** Expert-level data collection experience on R-Axis IV and IV++ and Rigaku SuperNova systems as well as on synchrotron beamlines (Beamline 4.2.2 of the Advanced Light Source, Lawrence Berkeley National Lab; Beamlines 23-ID-B and 23-ID-D of the Advance Photon Source, Argonne National Lab; and Beamline BL9-2 at of the Stanford Synchrotron Radiation Lightsource, Stanford University). I am in charge of spearheading lab efforts for preparing and shipping crystals, scheduling beamline time, and collecting data.
 - **Data Processing:** Highly proficient in using XDS, d*TREK, HKL2000, iMosflm programs for data processing.
 - **Structure Solution and Refinement:** Regular use of programs in the CCP4 suite (including Molrep and Phaser for molecular replacement and DM for density modification), Coot, PHENIX, and REFMAC.
 - **Structure Validation:** Very proficient in using MolProbity and the PDB Validation Server to validate structures.
 - Highly skilled in using the PyMOL molecular graphics system to analyze structures and make publication-quality figures and movies, including an *invited figure and two movies for the Cold Spring Harbor Perspectives in Medicine series book "HIV: From Biology to Prevention and Treatment" 2011, Cold Spring Harbor Laboratory Press.*
- Small Molecule X-ray Crystallography
 - Crystallized, collected data, and solved structures independently for 3+ years in graduate school.
 - Used programs SMART, SAINT, SADABS, XPREP, SHELX, and X-SEED to collect, reduce, and refine data and solve structures.

- Electron Microscopy (SEM, TEM, and cryo-EM)
 - Used cryo-SEM and TEM methods in graduate work to determine the structures of carbon nanotubes in solution and in the solid state.
 - Currently involved in negative stain and cryo-TEM efforts to study the structure of HBV capsid and the effect of new antivirals on the formation of the capsid structure.
- Protein Expression
 - Optimization of protein expression in bacterial systems
- Protein Purification
 - Extensive protein chemistry experience
 - Proficient in purifying proteins with (Strep, His, GST, MBP tags) and without fusion tags.
 - Participated in designing complex purification protocols involving tandemly-connected columns (such as Ni NTA-Heparin) to isolate protein-DNA complexes.
 - Considerable experience in performing various types of anion and cation exchange chromatography and gel filtration/size exclusion techniques.
 - Familiar with various Fast Protein Liquid Chromatography (FPLC) purification systems, particularly AKTA Purifier and Prime Plus instrumentation. I am in charge of keeping up AKTA Purifier and Prime Plus systems, and I help troubleshoot any problems that arise during purification for all lab members.
- Dynamic Light Scattering (DLS)
 - Proficient in using 96-well DynaProII DLS instrument for measuring dynamic light scattering
- Size Exclusion Multi-Angle Light Scattering (SEC-MALS)
 - Proficient in using a Dawn HELEOS instrument coupled to an HPLC to separate protein complexes and analyze them using multi-angle light scattering
- Surface Plasmon Resonance and Microscale Thermophoresis (MST)
 - Have used a Biacore T100 to study the binding of nucleic acid and small molecules to protein (immobilized on SA, NTA, and CM5 sensor chips) and determine kinetic parameters (k_{on} , k_{off} , K_D).
 - I managed a Biacore T100 for the MU campus for two years. I coordinated use, trained users to run kinetic experiments, coordinated billing, and maintained the instrument.
 - Have used a NanoTemper Monolith NT.115 MST instrument to measure protein-protein, protein-DNA, and protein-small molecule interactions (K_D measurements).
- Thermal Shift Assays
 - I have used a real-time PCR machine to perform thermal shift assays to screen for small molecule compounds targeting viral proteins such as HIV capsid, HBV capsid, HIV reverse transcriptase.
- Nuclear Magnetic Resonance (NMR) Spectroscopy
 - Collection of 1D 1H and 2D 1H - 1H COSY and NOESY data of nucleoside reverse transcriptase inhibitors (NRTIs) for determination of 1H - 1H coupling constants. Coupling constants were then used to determine the pseudorotational parameters of the sugar ring puckering (C-3'-endo [North] vs. C-3'-exo [South]), which in turn allowed for the assessment of the effectiveness of these compounds as inhibitors.
- High Pressure Liquid Chromatography (HPLC) for analysis of reaction components
 - Using a C18 column on an Agilent 1100 HPLC, I evaluated the degradation of NRTIs by adenosine deaminase.
- Spectrophotometry
 - Skilled in using various types of spectrophotometric techniques, such as luminescence, absorbance, fluorescence. I have used spectrophotometric techniques to perform biochemical assays, including enzymatic, DNA polymerization/inhibition, RNase H activity/inhibition, order-of-addition, and deamination assays.

- Thermal Analysis (Differential Scanning Calorimetry and Thermogravimetric Analysis)
- Atomic Force Microscopy
 - Learned at the University of Durham, Durham, U.K. for 3 months during Summer 2004

Teaching Experience

- Supervised and trained most of the new lab members of the Sarafianos laboratory, including more than 50 undergraduates, 10-20 graduate students, postdoctoral researchers, and technicians.
- TA for Chem 1310 (1st semester general chemistry) for 2 semesters and Chem 1320 (2nd semester general chemistry) for 9 semesters
 - Extensive TA experience that culminated in a head TA position for more than 5 semesters, overseeing the teaching of several thousand students
 - Held weekly review sessions/office hours
 - Taught lab sections and occasional lectures (for 300+ students per class)

Professional Activities

- Microscopy Society of America, 2017-present
- International Society for Antiviral Research, 2014-present
- American Society for Microbiology, 2010-present
- American Crystallographic Association, 2008-present
- American Chemical Society, 2002-2007
- Alpha Chi Sigma (Professional Chemistry Fraternity), 2002-present
- Phi Eta Sigma Honor Society, 1998-present