

Andrew C. Kruse

**Andrew C. Kruse**  
Curriculum Vitae

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**Research interests**

Transmembrane signaling plays a central role in virtually every aspect of human physiology, and membrane proteins are the targets for most therapeutic drugs. My research aims to elucidate the molecular basis for membrane protein signaling through the use of structural and biophysical methods, protein engineering, and molecular pharmacology.

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**Education**

**Stanford University, Stanford, CA**

Ph.D. in Structural Biology (09/2009 – 04/2014; thesis advisor Brian Kobilka, M.D.)

**University of Minnesota Twin Cities, Minneapolis, MN**

B.S. *summa cum laude* and with high distinction; major in Biochemistry, minor in Chemistry (2009)

B.S. Mathematics degree with high distinction (2009)

Certified proficiency in spoken and written Mandarin Chinese and French languages (2007)

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**Academic appointments**

Professor (2020 – present)

Department of Biological Chemistry and Molecular Pharmacology  
Harvard Medical School

Associate Professor (2017 – 2020)

Department of Biological Chemistry and Molecular Pharmacology  
Harvard Medical School

Assistant Professor (2014 – 2017)

Department of Biological Chemistry and Molecular Pharmacology  
Harvard Medical School

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**Selected awards**

Amgen Young Investigator Award (2019)

Sloan Research Fellowship (2017)

Vallee Scholars Award (2016)

Klingenstein-Simons Fellowship Award in Neuroscience (2016)

Forbes 30 under 30 list in healthcare (2016)

Smith Family Award for Excellence in Biomedical Research (2015)

NIH Director's Early Independence Award (2015)

Andrew C. Kruse

National Science Foundation Graduate Research Fellowship (2010 – 2013)

*Phi Beta Kappa* (2009)

Graduation *summa cum laude* and with high distinction, University of Minnesota (2009)

## Teaching

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### Harvard Medical School

Course director

BCMP250: Biophysical and biochemical mechanisms of protein function (Spring 2017 – present)

### Stanford University

Teaching assistant, Methods in Molecular Biophysics (2013)

### University of Minnesota, Twin Cities

Teaching assistant, Department of Biochemistry, Molecular Biology, and Biophysics (2007)

Teaching assistant, Institute of Technology Center for Educational Programs (2005 – 2006)

## Publications

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1. Susa KJ, Rawson S, Kruse AC\*, Blacklow SC\*. Cryo-EM structure of the B cell co-receptor CD19 bound to the tetraspanin CD81. (2021) *Science* 371, 300-305. \*Corresponding authors.
2. Amcheslavsky A, Wallace AL, Ejemel M, Li Q, McMahon CT, Stoppato M, Giuntini S, Schiller ZA, Pondish JR, Toomey JR, Schneider RM, Meisinger J, Heukers R, Kruse AC, Barry EM, Pierce BG, Klempner MS, Cavacini LA, Wang Y. Anti-CfaE nanobodies provide broad cross-protection against major pathogenic enterotoxigenic *Escherichia coli* strains, with implications for vaccine design. (2021) *Sci. Rep.* 11, 2751.
3. Skiba MA, Kruse AC. Autoantibodies as Endogenous Modulators of GPCR Signaling. (2021) *Trends. Pharmacol. Sci.* 42, 135-150.
4. Susa KJ, Seegar TC, Blacklow SC\*, Kruse AC\*. A Dynamic Interaction Between CD19 and the Tetraspanin CD81 Controls B Cell Co-Receptor Trafficking. (2020) *eLife*, 9:e52337. \*Corresponding authors.
5. Greenfield DA, Schmidt HR, Sliz P\*, Kruse AC\*. Virtual screening identifies novel high-affinity sigma-1 receptor ligands. (2020) *A. C. S. Med. Chem. Lett.* 11, 1555-1561. Also preprinted bioRxiv 699793; doi: <https://doi.org/10.1101/699793>. \*Corresponding authors
6. McMahon C, Staus DP, Wingler LM, Wang J, Skiba MA, Elgeti M, Hubbell WL, Rockman HA, Kruse AC\*, Lefkowitz RJ\*. Synthetic nanobodies as angiotensin receptor blockers. (2020) *Proc. Natl. Acad. Sci. U. S. A.* 117, 20284-20291. \*Corresponding authors
7. Sjodt M, Rohs PDA, Gilman MSA, Erlandson SC, Zheng S, Green AGG, Brock KP, Taguchi A, Kahne D, Walker S, Marks DS, Rudner DZ, Bernhardt TG, Kruse AC. Structural coordination of polymerization and crosslinking by a SEDS-bPBP peptidoglycan synthase complex. (2020) *Nat. Microbiol.* 5, 813-820.
8. Suomivuori CM, Latorraca NR, Wingler LM, Eismann S, King MC, Kleinhenz ALW, Skiba MA, Staus DP, Kruse AC, Lefkowitz RJ, Dror RO. Molecular mechanism of biased signaling in a

- prototypical G protein-coupled receptor. (2020) *Science* 367, 881-887.
9. Wingler LM, Skiba MA, McMahon C, Staus DP, Kleinhenz LW, Suomivuori CM, Latorraca NR, Dror RO, Lefkowitz RJ\*, Kruse AC\*. Angiotensin and biased analogs induce structurally distinct active conformations within a GPCR. (2020) *Science* 367, 881-887. \*Corresponding authors.
  10. Pascolutti R, Erlandson SC, Burri DJ, Zheng S, Kruse AC. Mapping and engineering the interaction between adiponectin and T-cadherin. (2020) *J. Biol. Chem.* 295, 2749-4759.
  11. Schmidt HR, Kruse AC. The molecular function of sigma receptors: past, present, and future. (2019) *Trends Pharmacol. Sci.* 40, 636-654.
  12. Chen H, Nwe P, Yang Y, Rosen CE, Bielecka AA, Kuchroo M, Cline GW, Kruse AC, Ring AM, Crawford JM, Palm NW. A forward chemical genetic screen reveals gut microbiota metabolites that modulate host physiology. (2019) *Cell* 177, 1217-1231.
  13. Owens T, Taylor R, Pahil K, Bertani B, Ruiz N\*, Kruse AC\*, Kahne D\*. Structural basis for unidirectional export of lipopolysaccharide to the cell surface. (2019) *Nature* 567, 550-553. \*Corresponding authors
  14. Zheng S, Abreu N, Levitz J, Kruse AC. Structural basis for KCTD-mediated rapid desensitization of GABA<sub>B</sub> signaling. (2019) *Nature* 567, 127-131.
  15. Zheng S, Kruse AC. Solving a specificity mystery (2019) *eLife* e44298. (Invited commentary)
  16. Wingler LM, McMahon C, Staus DP, Lefkowitz RJ\*, Kruse AC\*. Distinctive activation mechanism for angiotensin receptor revealed by a synthetic nanobody. (2019) *Cell* 176, 479-490. \*Corresponding authors
  17. Taguchi A, Welsh MA, Marmont LS, Lee W, Sjodt M, Kruse AC, Kahne D, Bernhardt TG, Walker S. FtsW is a peptidoglycan polymerase that is functional only in complex with its cognate penicillin-binding protein. (2019) *Nat. Microbiol.* 4, 587-594.
  18. Ramírez-Guadiana FH, Rodrigues CDA, Marquis KA, Campo N, Barajas-Ornelas R, Brock K, Marks DS, Kruse AC, Rudner DZ. Evidence that regulation of intramembrane proteolysis is mediated by substrate gating during sporulation in *Bacillus subtilis*. (2018) *PLoS Genet.* 14(11):e1007753.
  19. Rohs PDA, Buss J, Sim SI, Squyres GR, Srisuknimit V, Smith M, Cho H, Sjodt M, Kruse AC, Garner EC, Walker S, Kahne DE, Bernhardt TG. A central role for PBP2 in the activation of peptidoglycan polymerization by the bacterial cell elongation machinery. (2018) *PLoS Genet.* 14(10):e1007726.
  20. Schmidt HR, Betz RM, Dror RO, Kruse AC. Structural basis for  $\sigma_1$  receptor ligand recognition. (2018) *Nat. Struct. Mol. Biol.* 25, 981-987.
  21. Wang X, Hughes AC, Brandão HB, Walker B, Lierz C, Cochran JC, Oakley MG, Kruse AC, Rudner DZ. In vivo evidence for ATPase-dependent DNA translocation by the *Bacillus subtilis* SMC Condensin Complex. (2018) *Mol. Cell* S1097-2765(18)30553-7.
  22. Sham LT, Zheng S, Yakhnina AA, Kruse AC, Bernhardt TG. Loss of specificity variants of WzxC suggest that substrate recognition is coupled with transporter opening in MOP-family flippases. (2018) *Mol. Microbiol.* 109, 633-641.

23. Zheng S, Sham LT, Rubino FA, Brock KP, Robins WP, Mekalanos JJ, Marks DS, Bernhardt TG, Kruse AC. Structure and mutagenic analysis of the lipid II flippase MurJ from *Escherichia coli*. (2018) *Proc. Natl. Acad. Sci. U.S.A.* 115, 6709-6714.
24. Huang P, Zheng S, Wierbowski BM, Kim Y, Nedelcu D, Aravena L, Liu J, Kruse AC, Salic A. Structural Basis of Smoothed Activation in Hedgehog Signaling. (2018) *Cell* 174, 312-324.
25. Linkens K, Schmidt HR, Sahn JJ, Kruse AC, Martin SF. Investigating isoindoline, tetrahydroisoquinoline, and tetrahydrobenzazepine scaffolds for their sigma receptor binding properties. (2018) *Eur. J. Med. Chem.* 151, 557-567.
26. Sjodt M, Brock K, Dobihal G, Rohs PDA, Green AG, Hopf TA, Meeske AJ, Srisuknimit V, Kahne D, Walker S, Marks DS, Bernhardt TG, Rudner DZ, Kruse AC. Structure of the peptidoglycan polymerase RodA resolved by evolutionary coupling analysis. (2018) *Nature* 556, 118-121.
27. Staus DP, Wingler LM, Choi M, Pani B, Manglik A, Kruse AC, Lefkowitz RJ. Sortase ligation enables homogeneous GPCR phosphorylation to reveal diversity in  $\beta$ -arrestin coupling. (2018) *Proc. Natl. Acad. Sci. U.S.A.* 115, 3834-3839.
28. Erlandson SC, McMahon C, Kruse AC. Structural Basis for G Protein-Coupled Receptor Signaling. (2018) *Annu. Rev. Biophys.* Epub ahead of print.
29. Korczynska M, Clark MJ, Valant C, Xu J, Moo EV, Albold S, Weiss DR, Torosyan H, Huang W, Kruse AC, Lyda BR, May LT, Baltos JA, Sexton PM, Kobilka BK, Christopoulos A, Shoichet BK, Sunahara RK. Structure-based discovery of selective positive allosteric modulators of antagonists for the M2 muscarinic acetylcholine receptor. (2018) *Proc. Natl. Acad. Sci. U.S.A.* 6;115(10):E2419-E2428.
30. McMahon C, Baier AS, Pascolutti R, Wegrecki M, Zheng S, Ong JX, Erlandson SC, Hilger D, Rasmussen SGF, Ring AM, Manglik A\*, Kruse AC\*. Yeast surface display platform for rapid discovery of conformationally selective nanobodies. (2018) *Nat. Struct. Mol. Biol.* 25(3):289-296. \*Corresponding authors
31. Seegar TCM, Killingsworth LB, Saha N, Meyer PA, Patra D, Zimmerman B, Janes PW, Rubinstein E, Nikolov DB, Skiniotis G, Kruse AC, Blacklow SC. Structural basis for regulated proteolysis by the  $\alpha$ -secretase ADAM10. (2017) *Cell* 171, 1638-1648.
32. Manglik A\*, Kruse AC\*. Structural basis for G protein-coupled receptor activation. (2017) *Biochemistry* 56, 5628-5634. \*Corresponding authors.
33. Ramírez-Guadiana FH, Meeske AJ, Rodrigues CDA, Barajas-Ornelas RDC, Kruse AC, Rudner DZ. A two-step transport pathway allows the mother cell to nurture the developing spore in *Bacillus subtilis*. (2017) *PLoS Genet.* 13, e1007015.
34. Alon A, Schmidt HR, Wood MD, Sahn JJ, Martin SF, Kruse AC. Identification of the gene that codes for the sigma-2 receptor. (2017) *Proc. Natl. Acad. Sci. U.S.A.* 114, 7160-7165.
35. Sguazzini E, Schmidt HR, Iyer KA, Kruse AC, Dukat M. Reevaluation of fenpropimorph as a sigma receptor ligand: Structure-affinity relationship studies at human sigma-1 receptors. (2017) *Bioorg. Med. Chem. Lett.* 27, 2912-2919.
36. Paek J, Kalocsay M, Staus DP, Wingler L, Pascolutti R, Paulo JA, Gygi SP, Kruse AC. Multidimensional tracking of GPCR signaling via peroxidase-catalyzed proximity labeling. (2017) *Cell* 169, 338-349.

37. Alon A, Schmidt HR, Zheng S, Kruse AC. Structural Perspectives on sigma-1 receptor function. (2017) in Sylvia Smith *et al.* (Eds.), *Sigma Receptors: Their Role in Disease and as Therapeutic Targets. Adv. Exp. Med. Biol.*, Vol. 964.
38. Kruse AC. Structural insights into sigma-1 function. (2017) *Handb. Exp. Pharmacol.* 244, 13-25.
39. Zimmerman B, Kelly B, McMillan BJ, Seegar TCM, Dror RO, Kruse AC\*, Blacklow SC\*. Crystal structure of a full-length human tetraspanin reveals a cholesterol binding pocket. (2016) *Cell* 167, 1041-1051. \*Corresponding authors
40. Pascolutti R, Sun X, Kao J, Maute RL, Ring AM, Bowman GR, Kruse AC. Structure and dynamics of PD-L1 and an ultra high-affinity PD-1 receptor mutant. (2016) *Structure* 24, 1719-1728.
41. Meeske AJ, Riley EP, Robins WP, Uehara T, Mekalanos JJ, Kahne D, Walker S, Kruse AC, Bernhardt TG, Rudner DZ. SEDS proteins are a widespread family of bacterial cell wall polymerases. (2016) *Nature* 537, 634-638.
42. Staus DP, Strachan RT, Manglik A, Pani B, Kahsai AW, Kim TH, Wingler LM, Ahn S, Chatterjee A, Masoudi A, Kruse AC, Pardon E, Steyaert J, Weis WI, Prosser RS, Kobilka BK, Costa T, Lefkowitz RJ. Allosteric nanobodies reveal the dynamic range and diverse mechanisms of G-protein-coupled receptor activation. (2016) *Nature* 535, 448-452.
43. Schmidt HR, Zheng S, Gurpinar E, Koehl A, Manglik A, Kruse AC. Crystal structure of the human sigma-1 receptor (2016) *Nature* 532, 527-530.
44. Meyer PA, Socias S, Key J, Ransey E, Tjon EC, Buschiazzi A, Lei M, Botka C, Withrow J, Neau D, Rajashankar K, Anderson KS, Baxter RH, Blacklow SC, Boggon TJ, Bonvin AM, Borek D, Brett TJ, Cafilisch A, Chang CI, Chazin WJ, Corbett KD, Cosgrove MS, Crosson S, Dhe-Paganon S, Di Cera E, Drennan CL, Eck MJ, Eichman BF, Fan QR, Ferré-D'Amaré AR, Christopher Fromme J, Garcia KC, Gaudet R, Gong P, Harrison SC, Heldwein EE, Jia Z, Keenan RJ, Kruse AC, Kvensakul M, McLellan JS, Modis Y, Nam Y, Otwinowski Z, Pai EF, Pereira PJ, Petosa C, Raman CS, Rapoport TA, Roll-Mecak A, Rosen MK, Rudenko G, Schlessinger J, Schwartz TU, Shamoo Y, Sondermann H, Tao YJ, Tolia NH, Tsodikov OV, Westover KD, Wu H, Foster I, Fraser JS, Maia FR, Gonen T, Kirchhausen T, Diederichs K, Crosas M, Sliz P. Data publication with the structural biology data grid supports live analysis. (2016) *Nat. Commun.* 7, 10882
45. Baxter EL, Aguila L, Alonso-Mori R, Barnes CO, Bonagura CA, Brehmer W, Brunger AT, Calero G, Caradoc-Davies TT, Chatterjee R, Degrado WF, Fraser JS, Ibrahim M, Kern J, Kobilka BK, Kruse AC, Larsson KM, Lemke HT, Lyubimov AY, Manglik A, McPhillips SE, Norgren E, Pang SS, Soltis SM, Song J, Thomaston J, Tsai Y, Weis WI, Woldeyes RA, Yachandra V, Yano J, Zouni A, Cohen AE. High-density grids for efficient data collection from multiple crystals. (2016) *Acta Crystallogr. D* 72, 2-11.
46. Li Q, Tachie-Baffour Y, Liu Z, Baldwin MW, Kruse AC, Liberles SD. Non-classical amine recognition evolved in a large clade of olfactory receptors. (2015) *eLife*, 4:e10441.
47. Maute RL, Gordon SR, Mayer AT, McCracken MN, Natarajan A, Ring NG, Kimura R, Tsai JM, Manglik A, Kruse AC, Gambhir SS, Weissman IL, Ring AM. Engineering high-affinity PD-1 variants for optimized immunotherapy and immune-PET imaging. (2015) *Proc. Natl. Acad. Sci. U.S.A.*, 112, E6506-E6514.
48. Kruse AC. Structural insights into activation and allosteric modulation of G protein-coupled

- receptors. (2015) in G. Scapin *et al.* (Eds.), *Multifaceted Roles of Crystallography in Modern Drug Discovery*, NATO Science for Peace and Security Series A: Chemistry and Biology.
49. Cohen AE, Soltis SM, González A, Aguila L, Alonso-Mori R, Barnes CO, Baxter EL, Brehmer W, Brewster AS, Brunger AT, Calero G, Chang JF, Chollet M, Ehrensberger P, Eriksson TL, Feng Y, Hattne J, Hedman B, Hollenbeck M, Holton JM, Keable S, Kobilka BK, Kovaleva EG, Kruse AC, Lemke HT, Lin G, Lyubimov AY, Manglik A, Mathews II, McPhillips SE, Nelson S, Peters JW, Sauter NK, Smith CA, Song J, Stevenson HP, Tsai Y, Uervirojnangkoorn M, Vinetsky V, Wakatsuki S, Weis WI, Zadvornyy OA, Zeldin OB, Zhu D, Hodgson KO. Goniometer-based femtosecond crystallography with X-ray free electron lasers. (2014) *Proc. Natl. Acad. Sci. U.S.A.*, 111, 17122-17127.
  50. Kruse AC, Kobilka BK, Gautam D, Sexton PM, Christopoulos A, Wess J. Muscarinic acetylcholine receptors: novel opportunities for drug development. (2014) *Nat. Rev. Drug Discov.*, 13, 549-560.
  51. Kruse AC\*, Hu J, Kobilka BK, Wess J\*. Muscarinic acetylcholine receptor X-ray structures: potential implications for drug development. (2014) *Curr. Opin. Pharmacol.* 16C, 24-30.  
\*Corresponding authors
  52. Weichert D, Kruse AC, Manglik A, Hiller C, Zhang C, Hübner H, Kobilka BK, Gmeiner P. Covalent neurotransmitter surrogates for the structural investigation of aminergic G protein-coupled receptors. (2014) *Proc. Natl. Acad. Sci. U.S.A.* 111, 10744-10748.
  53. Kruse AC\*, Ring AM\*, Manglik A, Hu J, Hu K, Eitel K, Hübner H, Pardon E, Valant C, Sexton PM, Christopoulos A, Felder CC, Gmeiner P, Steyaert J, Weis WI, Garcia KC, Wess J, Kobilka BK. Activation and allosteric modulation of a muscarinic acetylcholine receptor. (2013) *Nature* 504, 101-106. \*Equal contributors
  54. Kruse AC, Li J, Hu J, Kobilka BK, Wess J. Novel insights into M<sub>3</sub> muscarinic acetylcholine receptor physiology and structure. (2013) *J. Mol. Neurosci.* 53, 316 - 323.
  55. Kruse AC, Manglik A, Kobilka BK, Weis WI. Applications of molecular replacement to G protein-coupled receptors. (2013) *Acta Crystallogr.* D69, 2287-2292.
  56. Kruse AC\*, Weiss DR\*, Rossi M, Hu J, Hu K, Eitel K, Gmeiner P, Wess J, Kobilka BK, Shoichet BK. Muscarinic receptors as model targets and antitargets for structure-based ligand discovery. (2013) *Mol. Pharm.* 84, 528-540. \*Equal contributors
  57. Ring AM\*, Manglik A\*, Kruse AC\*, Enos MD, Weis WI, Garcia KC, Kobilka BK. Adrenaline-activated structure of the  $\beta_2$ -adrenoceptor stabilized by an engineered nanobody. (2013) *Nature* 502, 575-579. \*Equal contributors
  58. Chae PS, Kruse AC, Gotfryd K, Rana RR, Cho KH, Rasmussen SG, Bae HE, Chandra R, Gether U, Guan L, Kobilka BK, Loland CJ, Byrne B, Gellman SH. Novel Tripod Amphiphiles for Membrane Protein Analysis. *Chem. Eur. J.* 19, 15645-15651.
  59. Shukla AK\*, Manglik A\*, Kruse AC\*, Xiao K, Reis RI, Tseng WC, Staus DP, Hilger D, Uysal S, Huang LY, Paduch M, Tripathi-Shukla P, Koide A, Koide S, Weis WI, Kossiakoff AA, Kobilka BK, Lefkowitz RJ. Structure of active  $\beta$ -arrestin-1 bound to a G-protein-coupled receptor phosphopeptide. (2013) *Nature* 497, 137-141. \*Equal contributors
  60. Chae PS, Rana RR, Gotfryd K, Rasmussen SG, Kruse AC, Cho KH, Capaldi S, Carlsson E, Kobilka

- BK, Loland CJ, Gether U, Banerjee S, Byrne B, Lee JK, Gellman SH. Glucose-neopentyl glycol (GNG) amphiphiles for membrane protein study. (2013) *Chem. Commun.* 49, 2287-2289.
61. Kruse AC, Hu J, Pan AC, Arlow DH, Rosenbaum DM, Rosemond E, Green HF, Liu T, Chae PS, Dror RO, Shaw DE, Weis WI, Wess J, Kobilka BK. Structure and dynamics of the M<sub>3</sub> muscarinic acetylcholine receptor. (2012) *Nature* 482, 552-556.
62. Haga K\*, Kruse AC\*, Asada H\*, Yurugi-Kobayashi T, Shiroishi M, Zhang C, Weis WI, Okada T, Kobilka BK, Haga T, Kobayashi T. Structure of the human M<sub>2</sub> muscarinic acetylcholine receptor bound to an antagonist. (2012) *Nature* 482, 547-551. \*Equal contributors
63. Granier S, Manglik A\*, Kruse AC\*, Kobilka TS, Thian FS, Weis WI, Kobilka BK. Crystal structure of the  $\delta$ -opioid receptor bound to naltrindole. (2012) *Nature* 485, 400-404. \*Equal contributors
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65. Chae PS, Rasmussen SG, Rana RR, Gotfryd K, Kruse AC, Manglik A, Cho KH, Nurva S, Gether U, Guan L, Loland CJ, Byrne B, Kobilka BK, Gellman SH. A new class of amphiphiles bearing rigid hydrophobic groups for solubilization and stabilization of membrane proteins. (2012) *Chem. Eur. J.* 18, 9485-9490.
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