Kenneth H. Pearce, Jr.

CURRICULUM VITAE

University of North Carolina at Chapel Hill
Eshelman School of Pharmacy
Chemical Biology and Medicinal Chemistry
3203 Marsico Hall
125 Mason Farm Road
Chapel Hill, NC 27599-7363

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EDUCATION

Genentech, Inc. South San Francisco, California (1993 -1996)
Postdoctoral Scientist in Department of Protein Engineering
Advisor: Dr. James A. Wells

Research: "Hormone-Receptor Molecular Recognition: Site-Directed Mutagenesis, Phage Display, and Cell-Based Activity Assays for Understanding the Dynamics of Signal Transduction by Receptor Dimerization"

University of North Carolina at Chapel Hill (1989 -1993)
Ph.D. in Chemistry (Biological)
Advisors: Professor Nancy L. Thompson and Professor Richard G. Hiskey

Dissertation: "Characterization of the Binding Mechanism of Prothrombin and its Fragment 1 to Planar Model Membranes Using Laser-Based Total Internal Reflection Fluorescence Microscopy"

University of Richmond, Richmond, Virginia (1985 -1989)
B.S. in Chemistry
Advisor: Professor Richard W. Topham

Undergraduate Research: "The Enzymatic Reduction and Release of Iron from Ferritin"

PROFESSIONAL EXPERIENCE

University of North Carolina at Chapel Hill

Research Professor and Director, Lead Discovery and Characterization
Center for Integrative Chemical Biology and Drug Discovery (2015-present)

Co-Director, Center for Integrative Chemical Biology and Drug Discovery (2021-present)

Appointment, Curriculum in Toxicology (2016-present)

The Graduate School Faculty	(2017-present)
Member, Lineberger Comprehensive Cancer Center Molecular Therapeutics Program	(2018-present)
SmithKline Beecham, GlaxoWellcome, and GlaxoSmithKline	(1996 - 2015)
Group Leader, Biological Sciences	(2013 - 2015)
Senior Research Investigator/Scientific Manager, Biological Reagents and Assay Development	(2003 - 2013)
Research Investigator, Gene Expression and Protein Biochemistry	(2001- 2003)
Research Investigator, Molecular Sciences	(1998 - 2001)
Research Investigator, Anti-Infectives	(1996 - 1998)

HONORS

GlaxoSmithKline
Research Excellence Award for Glucocorticoid Receptor Project (2004)
Silver Award for Proprotein Convertase Program (2014)
Numerous Bronze Awards for Impact on Discovery Programs (2003-2014)

Glaxo Wellcome
Research Excellence Award for Nuclear Receptor Phage Display (2002)

Genentech, Inc.
Outstanding Postdoctoral Conference Presentation (one awarded, 1996)

University of North Carolina
Venable Award (1993) (one awarded)
Hercules Corporation Fellowship (1992)
Dobbins Fellow (1991) (two awarded)
Certificate of Excellence for Outstanding Service from CBMC (2019)

University of Richmond
Blue Key Honor Society (1988)
Sigma Xi and Gamma Sigma Epsilon (Chemistry Honor Society, 1988)
Senior Award for Analytical Chemistry (one awarded, 1989)

PUBLICATIONS

Peer Reviewed Research

1. Topham RW, Goger M, **Pearce KH**, and Schultz P, The Mobilization of Ferritin Iron By Liver Cytosol. A Comparison of Xanthine and NADH as Reducing Substrates. (1989) Biochem. J. 261: 137-143. PMID: 2775199.

2. **Pearce KH**, Hiskey RG, and Thompson NL. Surface Binding Kinetics of Prothrombin Fragment 1 on Planar Membranes Measured by Total Internal Reflection Fluorescence Microscopy. (1992) Biochemistry 31: 5983-5995. PMID: 1627541.

3. Huang Z, **Pearce KH**, and Thompson N.L. Effect of Bovine Prothrombin Fragment 1 on the Translational Diffusion of Phospholipids in Langmuir-Blodgett Monolayers. (1992) Biochim. Biophys. Acta. 1112: 259-265. PMID: 1457457.

4. **Pearce KH**, Hof M, Lentz BR, and Thompson NL. Comparison of the Membrane Binding Kinetics of Bovine Prothrombin and Its Fragment 1. (1993) J. Biol. Chem. 268: 22984-22991. PMID: 8226813.

5. Huang Z, **Pearce KH**, and Thompson NL. Translational Diffusion of Bovine Prothrombin Fragment 1 Weakly Bound to Supported Planar Membranes: Measurement by Total Internal Reflection with Flourescence Pattern Photobleaching Recovery. (1994) Biophys. J. 67: 1754-1766. PMID: 7819508.

6. **Pearce KH**, Ultsch MH, Kelley RF, De Vos AM, and Wells JA. Structural and Mutational Analysis of Affinity-inert Contact Residues at the Growth Hormone-Receptor Interface. (1996) Biochemistry 35: 10300-10307. PMID: 8756685.

7. **Pearce KH**, Potts BJ, Presta LG, Bald LN, Fendly BM, and Wells JA. Mutational Analysis of Thrombopoietin for Identification of Receptor and Neutralizing Antibody Sites. (1997) J. Biol. Chem. 272: 20595-20602. PMID: 9252374.

8. **Pearce KH**, Cunningham BC, Fuh G, Teeri T, and Wells JA. Growth Hormone Binding Affinity for its Receptor Surpasses Requirements for Cellular Activity. (1999) Biochemistry 38: 81-89. PMID: 9890885.

9. Sossong TM, Brigham-Burke MR, Hensley P, and **Pearce KH**. Self-activation of Guanosine Triphosphatase Activity by Oligomerization of the Bacterial Cell Division Protein FtsZ. (1999) Biochemistry 38: 14843-14850. PMID: 10555966.

10. Yan K, **Pearce KH**, and Payne DJ. A Conserved Residue at the Extreme C-terminus of FtsZ is Critical for the FtsA-FtsZ Interaction in Staphylococcus aureus. (2000) Biochem. Biophys. Res. Comm. 270, 387-392. PMID: 10753635.

11. Iannone MA, Consler TG, **Pearce KH**, Stimmel JB, Parks DJ, and Gray JG. Mutliplexed Molecular Interactions of Nuclear Receptors Using Fluorescent Microspheres. (2001) Cytometry 44: 326-337. PMID: 11500849.

12. Bledsoe RK, Montana VG, Stanley TB, Delves CJ, Apolito CJ, McKee DD, Consler TG, Parks DJ, Stewart EL, Willson TM, Lambert MH, Moore JT, **Pearce KH**, and Xu HE. The Crystal Structure of the Glucocorticoid Receptor Ligand Binding Domain Reveals a Novel Mechanism of Receptor Dimerization and Coactivator Recognition. (2002) Cell 110: 93-105. PMID: 12151000. (co-corresponding author)

13. Deng SJ, **Pearce KH**, Dixon EP, Hartley KA, Stanley TB, Lobe DC, Garvey EP, Kost TA, Petty RL, Rocque WJ, Alexander KA, and Underwood M. Identification of Peptides that Inhibit the DNA Binding, Trans-Activator, and DNA Replication Functions of the Human Papillomavirus type 11 E2 Protein. (2004) J. Virol. 78: 2637-2641. PMID: 14963172.

14. Iannone MA, Simmons CA, Kadwell SH, Svoboda DL, Vanderwall DE, Deng SJ, Consler TG, Shearin J, Gray JG, and **Pearce KH**. Correlation Between in vitro Peptide Binding Profiles and Cellular Activities for Estrogen Receptor-modulating Compounds. (2004) Mol. Endocrinol. 18: 1064-1081. PMID: 14976226. (selected for cover art of issue)

15. Hoekstra WJ, Patel HS, Lian, X, Blanc JB, Heyer DO, Willson TM, Iannone MA, Kadwell SH, Miller LA, **Pearce KH**, Simmons CA, and Shearin, J. Discovery of Novel Quinoline-based Estrogen Receptor Ligands Using Peptide Interaction Profiling. (2005) J. Med. Chem. 48: 2243-2247. PMID: 15771467.

16. Bledsoe RK, Madauss KP, Holt JA, Apolito CJ, Lambert MH, **Pearce KH**, Stanley TB, Stewart EL, Trump RP, Willson TM, and Williams SP. A Ligand-mediated Hydrogen Bond Network Required for the Activation of the Mineralocorticoid Receptor. (2005) J. Biol. Chem. 280: 31283-31293. PMID: 15967794.

17. Trump RP, Cobb JE, Shearer BG, Lambert MH, Nolte RT, Willson TM, Buckholz RG, Zhao SM, Leesnitzer LM, Iannone MA, **Pearce KH**, Billin AN, and Hoekstra WJ. Co-crystal Structure Guided Array Synthesis of PPARgamma Inverse Agonists. (2007) Bioorg. Med. Chem. Lett. 17: 3916-3920. PMID: 17533125.

18. Yin L, Wu N, Curtin JC, Qatanani M, Szwergold NR, Reid RA, Waitt GM, Parks DJ, **Pearce KH**, Wisely GB, and Lazar MA. Rev-erbalpha, a Heme Sensor That Coordinates Metabolic and Circadian Pathways. (2007) Science 318: 1786–1789. PMID: 18006707.

19. Simmons CA, Bledsoe RK, Guex N, and **Pearce KH**. Expression, Purification, and Characterization of Multiple, Multifunctional Human Glucocorticoid Receptor Proteins (2008) Protein Expr. Purif. 62: 29-35. PMID: 18694832.

20. Chao EY, Caravella JA, Watson MA, Campobasso N, Ghisletti S, Billin AN, Galardi C, Wang P, Laffitte BA, Iannone MA, Goodwin BJ, Nichols JA, Parks DJ, Stewart E, Wiethe RW, Williams SP, Smallwood A, **Pearce KH**, Glass CK, Willson TM, Zuercher WJ, and Collins JL. Structure-guided Design of N-phenyl Tertiary Amines as Transrepression-selective Liver X Receptor Modulators with Anti-inflammatory Activity. (2008) J. Med. Chem. 51: 5758-5765. PMID: 18800767.

21. Ishmael FT, Fang X, Houser KR, **Pearce KH**, Abdelmohsen K, Zhan M, Gorospe M, and Stellato C. The Human Glucocorticoid Receptor as an RNA-binding Protein: Global Analysis of Glucocorticoid Receptor-associated Transcripts and Identification of a Target RNA Motif. (2011) J. Immunol. 186: 1189-1198. PMID: 21148795.

22. Wiench M, John S, Baek S, Johnson TA, Sung M, Escobar T, Simmons CA, **Pearce KH**, Biddie SC, Sabo PJ, Thurman RE, Stamatoyannopoulos JA and Hager GJ. DNA Methylation Status Predicts Cell Type-specific Enhancer Activity. (2011) EMBO J. 30: 3028-3039. PMID: 21701563.

23. Gao Y, Mutter-Rottmayer E, Greenwalt AM, Goldfarb D, Yan F, Yang Y, Martinez-Chacin RC, **Pearce KH**, Tateishi S, Major MB, and Vaziri C. A Neomorphic Cancer Cell-specific Role of MAGE-A4 in Trans-lesion Synthesis. (2016) Nat. Commun. 7:12105. PMID: 27377895.

24. Stuckey JI, Simpson C, Norris-Drouin JL, Cholensky SH, Lee J, Pasca R, Cheng N, Dickson BM, **Pearce KH**, Frye SV, and James LI. Structure-Activity Relationships and Kinetic Studies of Peptidic Antagonists of CBX Chromodomains. (2016) J. Med. Chem. 59: 8913-8923. PMID: 27571219.

25. Puhl-Rubio AC, Stashko MA, Wang H, Hardy PB, Tyagi V, Li B, Wang X, Kireev D, Jessen HJ, Frye SV, Shears SB, and **Pearce KH**. Use of Protein Kinase-Focused Compound Libraries for the Discovery of New Inositol Phosphate Kinase Inhibitors. (2018) SLAS Discov. 23: 982-988. PMID: 29842835.

26. Hull-Ryde EA, Porter MA, Fowler KA, Kireev D, Li K, Simpson CD, Sassano MF, Suto MJ, **Pearce KH**, Janzen W, and Coghill JM. Identification of Cosalane as an Inhibitor of Human and Murine CC-Chemokine Receptor 7 Signaling via a High-Throughput Screen. (2018) SLAS Discov. 23: 1083-1091. PMID: 29958052.

27. Vaseva AV, Blake DR, Gilbert TSK, Ng S, Hostetter G, Azam SH, Ozkan-Dagliyan I, Gautam P, Bryant KL, **Pearce KH**, Herring LE, Han H, Graves LM, Witkiewicz AK, Knudsen ES, Pecot CV, Rashid N, Houghton PJ, Wennerberg K, Cox AD, and Der CJ. KRAS Suppression-induced Degradation of MYC Is Antagonized by a MEK5-ERK5 Compensatory Mechanism. (2018) Cancer Cell. 34: 807-822. PMID: 30423298.

28. Gu C, Stashko MA, Puhl-Rubio AC, Chakraborty M, Chakraborty A, Frye SV, **Pearce KH**, Wang X, Shears SB, and Wang H. Inhibition of Inositol Polyphosphate Kinases by Quercetin and Related Flavonoids: A Structure/Activity Analysis. (2019) J. Med. Chem. 62: 1443-1454. PMID: 30624931.

29. **Pearce KH**, Overton LK, Gampe RT, Barrett GB, Taylor JD, McKee DD, Campobasso N, Nolte RT and Reid RA. BacMam Production and Crystal Structure of Non-glycosylated

Apo Human Furin at 1.89 Å Resolution. (2019) Acta Crystallogr. F Struct. Biol. Commun. 75: 239-245. PMID: 30950824.

30. Rectenwald JM, Hardy PB, Norris-Drouin JL, Cholensky SH, James LI, Frye SV, and **Pearce KH**. A General TR-FRET Assay Platform for High-Throughput Screening and Characterizing Inhibitors of Methyl-Lysine Reader Proteins. (2019) SLAS Discov. 24: 693-700. PMID: 31017815.

31. Blake DR, Vaseva AV, Hodge RG, Kline MP, Gilbert TSK, Tyagi V, Huang D, Whiten GC, Larson JE, Wang X, **Pearce KH**, Herring LE, Graves LM, Frye SV, Emanuele MJ, Cox AD, and Der CJ. Application of a MYC Degradation Screen in KRAS-mutant Pancreatic Cancer. (2019) Science Signaling, Jul 16;12(590). pii: eaav7259. doi: 10.1126/scisignal.aav7259. PMID: 31311847.

32. Lamb KN, Bsteh D, Dishman SN, Moussa HF, Fan H, Stuckey JI, Norris JL, Cholensky SH, Li D, Wang J, Sagum C, Stanton BZ, Bedford MT, **Pearce KH**, Kenakin TP, Kireev DB, Wang GG, James LI, Bell O, Frye SV. Discovery and Characterization of a Cellular Potent Positive Allosteric Modulator of the Polycomb Repressive Complex 1 Chromodomain, CBX7. (2019) Cell Chem Biol. Oct 17;26(10):1365-1379.e22. doi: 10.1016/j.chembiol.2019.07.013. Epub 2019 Aug 15. PMID: 31422906.

33. Ervin SM, Hanley RP, Lim L, Walton WG, **Pearce KH**, Bhatt AP, James LI, Redinbo MR. Targeting Regorafenib-Induced Toxicity through Inhibition of Gut Microbial β-Glucuronidases. (2019) ACS Chem Biol. 2019 Dec 20;14(12):2737-2744. doi: 10.1021/acschembio.9b00663. Epub 2019 Nov 12. PMID: 31663730.

34. Potjewyd F, Turner AW, Beri J, Rectenwald JM, Norris-Drouin JL, Cholensky SH, Margolis DM, **Pearce KH**, Herring LE, James LI. Degradation of Polycomb Repressive Complex 2 with an EED-Targeted Bivalent Chemical Degrader. (2019) Cell Chem Biol. 2019 Dec 5. pii: S2451-9456(19)30364-2. doi: 10.1016/j.chembiol.2019.11.006. PMID: 31831267.

35. Atkins SL, Motaib S, Wiser LC, Hopcraft SE, Hardy PB, Shackelford J, Foote P, Wade AH, Damania B, Pagano JS, **Pearce KH**, Whitehurst CB. Small molecule screening identifies inhibitors of the Epstein-Barr virus deubiquitinating enzyme, BPLF1. (2020) Antiviral Res. Jan;173:104649. doi: 10.1016/j.antiviral.2019.104649. Epub 2019 Nov 8. PMID: 31711927.

36. Rectenwald JM, Guduru SKR, Dang Z, Collins LB, Liao Y, Norris-Drouin JL, Cholensky SH, Kaufmann KW, Hammond SM, Kireev DB, Frye SV, **Pearce KH**. Design and Construction of a Focused DNA-Encoded Library for Multivalent Chromatin Reader Proteins. (2020) Molecules. Feb 22;25(4). pii: E979. doi: 10.3390/molecules25040979. PMID: 32098353. (co-corresponding author)

37. Puhl AC, Bogart JW, Haberman VA, Larson JE, Godoy AS, Norris-Drouin JL, Cholensky SH, Leisner TM, Frye SV, Parise LV, Bowers AA, **Pearce KH**. Discovery and Characterization of Peptide Inhibitors for Calcium and Integrin Binding Protein 1. (2020) ACS Chem Biol. Jun 19;15(6):1505-1516. doi: 10.1021/acschembio.0c00144. Epub 2020 May 26. PMID: 32383857.

38. Horton M, Su G, Yi L, Wang Z, Xu Y, Pagadala V, Zhang F, Zaharoff DA, **Pearce K**, Linhardt RJ, Liu J. Construction of heparan sulfate microarray for investigating the binding of specific saccharide sequences to proteins. (2020) Glycobiology. 2020 Jul 16:cwaa068. doi: 10.1093/glycob/cwaa068. PMID: 32681173.

39. Huang W, Carr AJ, Hajicek N, Sokolovski M, Siraliev-Perez E, Hardy PB, **Pearce KH**, Sondek J, Zhang Q. A High-Throughput Assay to Identify Allosteric Inhibitors of the PLC-γ Isozymes Operating at Membranes. (2020) Biochemistry. Oct 20;59(41):4029-4038. doi: 10.1021/acs.biochem.0c00511. PMID: 33028071.

40. Puhl AC, Fritch EJ, Lane TR, Tse LV, Yount BL, Sacramento CQ, Tavella TA, Costa FTM, Weston S, Logue J, Frieman M, Premkumar L, **Pearce KH**, Hurst BL, Andrade CH, Levi JA, Johnson NJ, Kisthardt SC, Scholle F, Souza TML, Moorman NJ, Baric RS, Madrid P, Ekins S. Repurposing the Ebola and Marburg Virus Inhibitors Tilorone, Quinacrine and Pyronaridine: In vitro Activity Against SARS-CoV-2 and Potential Mechanisms. (2021) ACS Omega. Mar 10;6(11):7454-7468. doi: 10.1021/acsomega.0c05996. eCollection 2021 Mar 23. PMID: 33778258.

41. Waybright JM, Clinkscales SE, Barnash KD, Budziszewski GR, Rectenwald JM, Chiarella AM, Norris-Drouin JL, Cholensky SH, **Pearce KH**, Herring LE, McGinty RK, Hathaway NA, James LI. A Peptidomimetic Ligand Targeting the Chromodomain of MPP8 Reveals HRP2's Association with the HUSH Complex. (2021) ACS Chem Biol. 2021 Sep 17;16(9):1721-1736. doi: 10.1021/acschembio.1c00429. Epub 2021 Aug 20. PMID: 34415726.

42. Suh JL, Bsteh D, Hart B, Si Y, Weaver TM, Pribitzer C, Lau R, Soni S, Ogana H, Rectenwald JM, Norris JL, Cholensky SH, Sagum C, Umana JD, Li D, Hardy B, Bedford MT, Mumenthaler SM, Lenz HJ, Kim YM, Wang GG, **Pearce KH**, James LI, Kireev DB, Musselman CA, Frye SV, Bell O. Reprogramming CBX8-PRC1 function with a positive allosteric modulator. (2021) Cell Chem Biol. Oct 26:S2451-9456(21)00437-2. doi: 10.1016/j.chembiol.2021.10.003. PMID: 34715055.

43. Haberman VA, Fleming SR, Leisner TM, Puhl AC, Feng E, Xie L, Chen X, Goto Y, Suga H, Parise LV, Kireev D, **Pearce KH**, Bowers AA. Discovery and Development of Cyclic Peptide Inhibitors of CIB1. (2021) ACS Med Chem Lett. Oct 27;12(11):1832-1839. doi: 10.1021/acsmedchemlett.1c00438. eCollection 2021 Nov 11. PMID: 34795874.

44. Puhl AC, Gomes GF, Damasceno S, Fritch EJ, Levi JA, Johnson NJ, Scholle F, Premkumar L, Hurst BL, LeeMontiel F, Veras FP, Batah SS, Fabro AT, Moorman NJ, Yount BL, Dickmander R, Baric R, **Pearce KH**, Cunha FQ, Alves-Filho JC, Cunha TM, Ekins S. Vandetanib Reduces Inflammatory Cytokines and Ameliorates COVID-19 in

Infected Mice. (2021) bioRxiv. Dec 20:2021.12.16.472155. doi: 10.1101/2021.12.16.472155. Preprint. PMID: 34981062.

45. Lamb KN, Dishman SN, Waybright JM, Engelberg IA, Rectenwald JM, Norris-Drouin JL, Cholensky SH, **Pearce KH**, James LI, Frye SV. Discovery of Potent Peptidomimetic Antagonists for Heterochromatin Protein 1 Family Proteins. (2021) ACS Omega. 2021 Dec 22;7(1):716-732. doi: 10.1021/acsomega.1c05381. eCollection 2022 Jan 11. PMID: 35036738.

Peer Reviewed Book Chapters and Review Articles

1. Thompson NL, **Pearce KH**, and Hsieh HV. Total Internal Reflection Fluorescence Microscopy: Application to Substrate-Supported Planar Membranes. (1993) Eur. Biophys. J. 22: 367-378. PMID: 8112222.

2. **Pearce KH**, and Wells JA. Activation of the Human Growth Hormone Receptor: Structure and Function of the Ligand-Receptor Complex. (2000) book chapter in Human Growth Hormone: Basic and Clinical Research, Humana Press. Ed. Smith RG, Thorner MO. pp. 131-143.

3. Bledsoe RK, Stewart EL, and **Pearce KH**. Structure and Function of the Glucocorticoid Receptor Ligand Binding Domain. (2004) book chapter in Vitamins and Hormones: Nuclear Receptor Coregulators, Vol. 68, Elsevier. Ed. Litwack G. pp. 49-91. PMID: 15193451.

4. **Pearce KH**, Iannone MA, Simmons CA, and Gray JG. Discovery of Novel Nuclear Receptor Modulating Ligands: an integral role for peptide interaction profiling. (2004) Drug Discov. Today. 9: 741-751. PMID: 15450240.

5. Williams SP, Kuyper LF, and **Pearce KH**. Recent Applications of Protein Crystallography and Structure-guided Drug Design. (2005) Curr. Opin. Chem. Biol. 9: 371-380. PMID: 16006182. (selected for cover art of issue)

6. Moore JT, Collins JL, and **Pearce KH**. The Nuclear Receptor Superfamily and Drug Discovery. (2006) ChemMedChem 1: 504-523. PMID: 16892386.

7. Moore JT, Collins JL, and **Pearce KH**. The Nuclear Receptor Superfamily and Drug Discovery (2007) book chapter in Chemical Biology - From Small Molecules to Systems Biology and Drug Design, Wiley-VCH, Weinheim. Ed. Schreiber SL, Kapoor T, Wess G. pp 891-932.

Complete List of Published Work in MyBibliography:
https://pubmed.ncbi.nlm.nih.gov/?term=%28%28%28pearce+kh%5BAuthor%5D%29+OR+%28pearce+k%5BAuthor%5D+AND+topham%5BAuthor%5D%29%29+OR+%28pearce+k%5BAuthor%5D+AND+ishmael%5BAuthor%5D%29%29+OR+%28pearce+k%5BAuthor%5D+AND+Liu%5BAuthor%5D%29&sort=date

TEACHING University of North Carolina

ACTIVITIES

Teaching Assistant for General Chemistry Laboratory, Fall 1989
Teaching Assistant for Honors General Chemistry Laboratory, Spring 1990
Ad hoc Lectures for Biophysical Chemistry Graduate Class, 1992/93
Lectures in CBMC 804a: Biochemical Foundations of Chemical Biology, Spring 2016, 2017, 2018, 2019, 2020, 2021
Lecture in PHRS 801 Foundations in Pharmaceutical Sciences, Fall 2016, 2017, 2018
Lecture in TOXC/ENVR 442, Fall 2016, 2017, 2018, 2019, 2020, 2021
Lecture in Physician's Garden Class, undergraduate Fall 2016, 2017, 2018
Lecture for BBSP first year subgroup Fall 2016, 2017, 2018, 2019
Guest faculty advisor for several classes in PHCO 737: Target-Based Drug Discovery and Cancer Treatment, 2020
Lectures and CICBDD tours for BBSP first year sub-group, 2016, 2017, 2018, 2019
Lectures and CICBDD tours for prospective UNC MD/PhD recruits, 2016, 2017, 2018, 2019, 2020
Lectures and CICBDD tours for visiting Chinese undergraduates in Pharmaceutical Sciences, Summer 2019
CBMC cumulative exam, Fall 2017
Seminar for Biophysical Society Summer Program, 2016, 2017
Mentor for Biophysical Society Summer Program, Alex Dieguez (Summar 2017)
Mentor for Chem/Biol 395, Amy Lee (Fall 2015), David Lindars (Spring 2016), Kaelin Amaya (Fall 2016), Brittany Castellanos (Spring 2017), Kevin Rhash (Fall 2017), Meenakshi Immaneni (Spring 2018), Andrew Reiter (Spring 2019)
Mentor for Eshelman Institute for Innovation Young Investigator Program, Meenakshi Immaneni (Summer 2016), Elijah Whitfield (Summer 2017), Seth Kodikara (Summer 2018), Nicole Bell (Summer 2019), Enoch Sanchez (Summer 2021)
Mentor/Committee for Toxicology Professional Science Master's Student, Allen Kapherr (Fall 2016, Spring 2017)
Mentor for Global Outreach UNC-UCL Program Student, Christopher Launchberry (University College of London, Fall 2019)
Mentor for UNC Undergraduate Research (volunteer), Amy Lee (Summer 2015), David Lindars (Fall 2016), Kaelin Amaya (Spring 2016), Brittany Castellanos (Spring/Fall 2016), Kevin Rhash (Spring, Summer 2017), Meenakshi Immaneni (Spring/Fall 2017), Andrew Reiter (Spring/Fall 2018, Spring 2019), Morgan Sawyer (Fall 2018, Spring 2019), Vinay Kathard (Summer 2018), Pavani Katamreddy (Spring/Summer 2020)
Supervised postdoctoral fellows, Ana Puhl (2016-2018), Zhao Dang (2017-2018), Shiva Guduru (2018-present), Felix Nwogbo (2020-present), Arunima Sikdar (2021-present)
Supervised graduate students, Justin Rectenwald (co-PI with Stephen Frye, 2015-2020), Jacob Larson (2017-present), Devan Shell (2020-present), Eric Merten (2021-present), Jiwoong Lim (2021-present)
Supervised graduate student rotations, Justin Rectenwald (2015), Raquel Martinez (2016), Jacob Larson (2017), Steve Yan (2017), Alex Woodall (2018), Morgan Gibbs (2018), Dre Dobson (2019), Deepika Jayaprakash (2018), Devan Shell

(2019), Alejandro Lopez (2019), Yogitha Chareddy (2019), Jarrett Pelton (2019), Yien Liao (2019), Jiwoong Lim (2020), Ivanna Zhilinskaya (2021)

University of Richmond
Assistant for Introduction to Biochemistry Laboratory (Fall, 1988)

SELECTED INVITED SEMINARS

UNC University Research Week (UNC URW), ID@UNC Creativity Hub and READDI - 2021
Duke University, BioCoRE Program - 2017
University of North Carolina, Toxicology - 2016
Shaw University, Natural Sciences and Mathematics - 2016
University of North Carolina, Pathology and Lab Medicine, Grand Rounds - 2015
Gordon Conference – Proprotein Processing and Regulation - 2014
(postdoc career discussion panel and scientific poster presentation)
University of Richmond, Powell Lectureship - 2010
(http://chemistry.richmond.edu/resources/powell/index.html)
National Institute of Environmental Health Sciences - 2009
University of Pennsylvania, Department of Biochemistry - 2008
National Institute of Environmental Health Sciences - 2007
Inflammation Research Association NY - 2003
Presentations at several GSK key opinion leader meetings in US - 2002-2004
University of North Carolina, Department Chemistry - 2000
Ursinus College, Departments of Chemistry and Biology - 1998
University of Kentucky, Department of Biochemistry - 1996

FORMER GSK-SUPPORTED RESEARCH AGREEMENTS

Dr. Gordon Hager – National Institute of Health/National Cancer Institute
Prof. Matt Redinbo – University of North Carolina (MTA only)
Dr. Faoud Ishmael – Johns Hopkins/Hershey Penn State Medical Center
Prof. Mitch Lazar – University of Pennsylvania
Prof. Nancy Thompson – University of North Carolina
Prof. Richard Losick – Harvard University
Prof. Masayori Inouye – Rutgers University
Dr. Anastasia Kralli – Scripps Research Institute

EDITORIAL BOARD AND REVIEWER

ACS Omega
ACS Pharmacology & Translational Science
Bioorganic & Medicinal Chemistry
Biochemistry
Cancer Cell
Cell
Cell Chemical Biology

ChemMedChem
Current Drug Discovery Technologies
Current Opinion on Drug Discovery
Drug Discovery Today
Expert Review of Molecular Diagnostics
Letters in Drug Design and Discovery
Molecular and Cellular Endocrinology
Nature Communications
PLoS Biology

CURRENT RESEARCH SUPPORT

R01 ES029079-02 (Vaziri/Pearce) 02/01/2019-11/30/2023
NIH/NIEHS $2,327,700
Pathological Reprogramming of DNA Damage Signaling in Neoplastic Cells
The goal of this project is to define the molecular mechanisms by which Cancer Testes Antigens (CTAs) pathologically reprogram genome maintenance pathways to stimulate mutagenesis and carcinogenesis in response to environmental genotoxic exposures.
Role: MPI

5R01 CA223495-02 (Rossman) 09/13/2018-08/31/2022
NIH $1,622,712
A HTS Approach to Discover Guanine Nucleotide-Competitive Inhibitors of Oncogenic KRAS
The goal of this proposal is to utilize HTS assays with diverse small molecule libraries, and virtual screens that leverage our recently solved x-ray structures of KRAS mutants to discover mutation-selective inhibitors of KRAS oncoproteins.
Role: Investigator

R01 CA229530-02 (Vaziri/Pearce) 04/02/2019-03/31/2024
NIH-NCI $2,022,089
Establishing MAGE-A4/RAD18 as a novel cancer-specific chemotherapeutic target
The goals of this project are to validate the MAGEA4-RAD18 DNA repair pathway as a therapeutic target using pre-clinical mouse models and to generate small molecule inhibitors of the MAGEA4-RAD18 complex that sensitize cancer cells to DNA-damaging therapies.
Role: MPI

U54AG065187-01 (Levey) 09/30/2019-08/31/2024
NIH/Emory University $10,169,709
Open Drug Discovery Center for Alzheimer's Disease
The overarching goal of this program is to develop and openly distribute the experimental tools necessary for the academic research community to test a wide range of therapeutic hypotheses for Alzheimer's disease (AD). Targets will be nominated from across the research field and prioritized by our team of experts who will inform prioritization through a combined expertise in AD biology, clinical translational studies, neuropathology, genetics, and bioinformatics. Open drug discovery will be performed through the international Structural Genomics Consortium (SGC) under the direction of Co-PI Stephen Frye (University of North Carolina).

Role: Investigator

1 R01 GM135218-01 (Redinbo) 9/20/2019 – 6/30/2023
NIH $1,458,332
Structural Basis for Hormone and Neurotransmitter Processing by Gut Microbial Enzymes
We will test several hypotheses by completing three aims focused on the endobiotic-glucuronide conjugates of thyroid hormones, estrogens, and neurotransmitters. The results we obtain will crucially advance our basic understanding of the chemical crosstalk between human tissues and the microbiota and may lead to novel approaches for the treatment of hormone imbalances, cancer, gut health, cardiovascular disease, and even psychological disorders.
Role: Investigator

R35 CA232113-01 (Der) 09/01/2018-08/31/2025
NIH/NCI $6,426,706 (**0.6 cal months in future years TBD; no support to Pearce for 2022)
Targeting Undruggable RAS for Cancer Treatment
This broad proposal involves numerous approaches to study the role of KRAS and MYC in cancer signaling and pancreatic cancer. The Pearce lab will work with Der lab personnel to establish and perform the GPS-MYC/KRAS chemical library screens for the larger project. We will also complete the protein kinase profiling analyses of hits with recombinant proteins and biochemical assays.
Role: Investigator

1 R01 CA249190-01 (Wang) 04/01/2020 – 03/31/2025
NIH $2,530,339
MERTK/AXL dual inhibitors provide novel treatment for cancer by targeting tumor cells and activating anti-tumor immunity
The goal of this project is to deliver a dual MERTK/AXL-selective inhibitor suitable for advancement to GLP toxicity studies in multiple species, all of the preclinical validation studies to support an IND application describing this compound, and a viable method for large-scale synthesis of the compound
Role: Investigator

1 R03 CA252796-01 (Jarstfer) 7/2/2020 – 6/30/2022
NIH $77,750
Targeting ALT-Cancer
The long-term goal of the proposed project is to identify the first chemical probes and potential clinical candidates targeting the alternative lengthening of telomeres (ALT) mechanism present in a subset of cancer cells.
Role: Investigator

No number (Zhang/Pearce/Sondek) 03/2021-02/2023
Cure Alzheimer's Fund $345,000
Small molecule activators of PLC-γ2 as novel therapeutics for Alzheimer's disease
This project seeks to develop selective activators of PLC-γ2 that will likely replicate the protective effects of the gain-of-function variant PLC-γ2 (P522R) to attenuate neuroinflammation and slow AD progression.
Role: MPI Zhang Q, Pearce K, Sondek J

1 R01 CA259077-01 (Wang) 04/01/2021-03/31/2023
NIH/NCI $1,629,277
Novel TYRO3 inhibitors for treatment of cancer
Major Goals: TYRO3 is a member of the TAM (TYRO3, AXL, MERTK) family of receptor tyrosine kinases and is a potential therapeutic target in a wide variety of human tumors. Here, we propose to develop novel, potent, and selective TYRO3 inhibitors and validate their biochemical and functional activities in TYRO3-dependent tumor xenograft models and immune-competent syngeneic cancer models.
Role: Investigator

1 R01 CA258993-01 (Zhang/Pearce/Sondek) 05/01/2021-04/30/2025
NIH $1,803,151
A high-throughput platform to identify selective allosteric inhibitors of the PLC-γ isozymes
We propose to develop and implement a high-throughput platform to identify efficacious and selective inhibitors of the PLC-γ isozymes. These compounds will be essential as chemical probes to dissect cellular functions of PLC-γ isozymes and will also serve as leads for the development of drugs to treat human diseases promoted by aberrantly active PLC-γ isozymes.
Role: MPI Zhang Q, Pearce K, Sondek J
Source of Support: NIH

NC State Reference No: 123766 (Simpson) 01/01/2022-12/312023
Lineberger Comprehensive Cancer Center $200,000
Development of selective inhibitors to a novel target in progression of castration resistant prostate cancer
We propose two aims: 1) Determine the efficacy of kinase:UDP-glucose dehydrogenase (UGDH) combined inhibition in the control of tumor cell androgen dependence and therapeutic response. We will use a peptide inhibitor of UGDH identified through phage display as proof of concept to demonstrate anti-proliferative effects of pharmacological UGDH targeting in vitro. 2) Use a high throughput approach to identify small molecule lead compounds for selective inhibition of UGDH. The UGDH-binding peptide will be used as a probe to inform small molecule inhibitor discovery by computational and biochemical screening methods. Manipulation of UGDH activity in combination with inhibition of its putative regulatory kinase will support use of the kinase-UGDH “axis” as a selective therapeutic target.
Role: Investigator

PENDING RESEARCH SUPPORT

U19 AI171292 (Baric/Willson) 05/2022-04/2027
NIH/NIAID $108,858,068
Rapidly Emerging Antiviral Drug Development Initiative-AViDD Center (READDI-AC)
READDI-AC is a public-private partnership designed to identify and develop oral, broadly active drugs that control the diseases caused by contemporary and new emerging RNA viruses from the coronavirus, alphavirus, flavivirus and filovirus families, including many dangerous zoonotic viruses that threaten the health of global populations.
Role: Investigator and Co-Core Lead

1 R01 AT076902-01 (Zhang/Pearce/Sondek) 07/01/2022-06/30/2026
NIH $3,074,639
Discovery of allosteric activators of phospholipase C-gamma2 to treat Alzheimer's disease
Current drugs used to treat Alzheimer's disease ameliorate the symptoms of the disease but do not slow or reverse disease progression. We propose to discover small molecules that selectively activate PLC-γ2 to reproduce the highly robust neuroprotective effects of PLC-γ2 (P522R). These compounds will be unique tools to dissect the roles of PLC-γ2 in neuroprotection and serve as the initial leads for further work to develop novel therapeutics to treat Alzheimer's disease.
Role: MPI Zhang Q, Pearce K, Sondek, J

NIH PPG 3/1/2021 – 2/28/2026
(Moorman) $9,997,308

Defining cell signaling networks controlling viral pathogenesis
The goal of this program project is to define how disparate virus families manipulate cellular signaling pathways to favor virus replication. These findings will not only enhance our basic understanding of how viruses manipulate the cell to promote their replication, but also reveal how virus-induced signaling changes contribute to viral pathogenesis. As such, our results are likely to identify cellular targets for new virus-specific antiviral drugs, as well as new targets for broad-spectrum antivirals useful against a wide range of human viral pathogens.
Role: Co-Investigator

TBD (Simpson, NC State) 07/2022-06/2024
NIH R21 $93,300
Improving prostate cancer therapeutic response by targeting a novel regulatory mechanism
We will assist with aspects of aims 2 and 3 involving the validation, development, and mechanistic characterization of UGDH peptide and small molecule inhibitors. These contributions include 1) development of a peptide tracer TR-FRET assay, 2) small molecule screening with the UGDH assay using the UNC 50,000 compound library, 3) validation of top small molecule hits by ITC and 4) application of computational methods for clustering hits, creating docking models, and virtual screening.
Role: Investigator

R01 HL165786 (Taylor) 07/2022-06/2026
NIH/NHLBI $3,046,032
Atheroprotection by smooth muscle selective RhoGAPs
The goals of this proposal are to identify mechanisms that contribute to the development of hypertension and vascular stiffening, to better understand how these parameters promote atherosclerotic disease, and to generate novel therapeutics for these prevalent conditions.
Role: Investigator

TBA (RFA W81XWH-21-PRMRP-IIRA) 01/2022-12/2025
DOD (Duke, Scaglione) $400,000
Development of small-molecule activators of the neuroprotective E3 ligase CHIP

We will use our CHIP assays in collaboration with the Center for Integrative Chemical Biology and Drug Discovery at UNC-CH to screen the 100,000 diversity compound library, in parallel with complementary screens at two other institutions, to identify small molecules that increase CHIP's ubiquitin ligase activity. Lead compounds will be tested in secondary screens, both in vitro and in cells. We will then use structural activity relationships to optimize compounds, validate in cells, and ultimately in preclinical models of neurological disease.
Role: Investigator

R01 CA271080 (Rossman) 04/2022-03/2027
NIH/NCI $1,916,131
Defining the Molecular Basis of Inhibitor Specificity for the RAS Switch II pocket
Major Goals: Using the tools of protein structure, biochemistry and cell biology, we will investigate the ability of KRAS G12C covalent inhibitors to target the NRAS and HRAS isoforms, determine their mode of binding to the RAS SIIP, and compare them to the mechanisms utilized by KRpep-2d and UNC34. The ultimate goal is to achieve an understanding of the molecular basis for high affinity binding to the SIIP's of KRAS, NRAS and HRAS to guide the future development of non-covalent inhibitors of nucleotide exchange.
Role: Investigator

NC – State Funding (Moorman/Baric) TBD; $345,000
READDI COVID-19 drug discovery and development.
We will develop assays, perform high throughput screening (HTS), and conduct medicinal chemistry to optimize the pharmacological properties of existing hit compounds for novel anti-viral targets including SARS-CoV-2 main protease (Mpro) and the SARS-CoV-2 papain-like protease (PLpro), and chikungunya nsp2 protease and other emerging essential targets that are genetically validated by the UNC virology team and others in the literature.
Role: Lead of Chemical Biology Core (Co with Willson/Wang)

COMPLETED RESEARCH SUPPORT

Eshelman Institute for Innovation Frye/Pearce (Co-PI) 7/1/17-6/30/20
Development of DNA-encoded Chemical Library Technology for Enhancement of CICBDD High Throughput Screening Capabilities.
We propose establishing a transformational technology in the CICBDD to utilize DNA-encoded libraries (DELs) where diverse compounds are selected as hits in binding assays versus targets of interest.

RX03912106 (Pearce) 06/01/19-05/31/20
Eshelman Institute for Innovation
Development of SETDB1 Inhibitors for Treatment of Hepatocellular Carcinoma
The objective of this proposal is to initiate a drug discovery effort using a novel label-free screening technology for finding small molecules that inhibit SETDB1 methyltransferase activity. Our hypothesis is that this effort will lay the foundation toward novel therapeutic agents for liver cancer and may have a broader impact with other cancers including kidney, lung, prostate, and skin. Moreover, validated small molecule inhibitors will also provide key chemical probes to shed new light on the mechanism by which SETDB1 contributes to tumorigenesis and metastasis.

Role: PI

RXALL17005 (James/Headey) 01/02/18-12/31/19
PharmAlliance
Discovery of Inhibitors for SETDB1 for Cancer Therapy using a Fragment-Based Screening Approach
The objective of this proposal is to employ fragment-based screening and follow up medicinal chemistry strategies to arrive at lead inhibitors of the tudor domain of SETDB1 for future development as high quality chemical probes.
Role: Investigator

NC TraCS Institute (Bowers/Pearce/Vaziri) 10/1/17 - 9/30/18
Developing Therapeutic Peptides Against Chemoresistant Cancer
This is a pilot project to establish Melanoma Antigen A4 (MAGE-A4, a Cancer/Testes Antigen) as a new and tractable target for cancer therapy. Our central hypothesis is MAGE-A4 promotes chemoresistance via activation of the DNA repair protein RAD18.
Role: MPI

PharmAlliance (James/Headey) 1/18/16 - 12/22/17
Discovery of Inhibitors for the Methyl-Lysine Reader Protein, 53BP1, Using Fragment-Based Screening
The focus of this study was to use fragment-based screening with NMR and SPR to discover hits for 53PB1 suitable for initiation of a medicinal chemistry optimization effort.
Role: Investigator

UNC UCRF Tier 2 (Pearce) 1/1/16 - 12/31/17
A Cellular Screen Utilizing the Global Protein Stability Method to Identify Chemical Probes that Expedite the Myc-degradation Pathway
The focus of this study is to employ an engineered pancreatic cancer cell assay to screen focused kinase inhibitor libraries and identify small molecules that cause rapid loss of Myc protein.
Role: PI

2016-IDG-1015 (Pearce) 4/15/16 - 4/14/17
North Carolina Biotechnology Center
High Content Cell Imager for Enabling Cellular and Phenotypic Assay Drug Discovery Screens
The focus of this application is to enhance high content imaging capabilities for phenotypic screens and secondary assay mode-of-action studies. This funding enables the purchase of a GE IN Cell Analyzer 2200 instrument to be housed in the Center for Integrative Chemical Biology and Drug Discovery. Purchase of the instrument includes matching funds from the School of Pharmacy and the School of Medicine
Role: PI

R01 DK101645 (Pearce) 7/1/15 - 4/30/18
National Institutes of Health (NIH)

High Throughput Screening Assay for IP7K Inositol Pyrophosphate Kinases
The focus of this application is to develop and validate assay methods applicable to high throughput screening, with accompanying orthogonal and in-cell assays, to screen chemical libraries with the aim of discovering novel, cell-permeable inhibitors of IP7K activity.
Role: PI

Eshelman Institute for Innovation (Hull-Ryde) 10/1/15 - 9/30/16
Controlling the Mucus that Kills Pulmonary Patients: IRE1β Inhibitors
The goal of this proposal is initiate a program to discover 'first-in-class' drugs to treat life-threatening pulmonary mucus overproduction by inhibiting the IRE1β kinase. IRE1β is activated during inflammation and upregulates mucin production and secretion. IRE1β contains serine/threonine kinase and endonuclease (RNase) activities, and is localized to mucin producing cells in the airways and GI track. This proposal provides a path toward a drug that is highly first to target IRE1β and will be the first to treat airway mucus overproduction for treating severe asthma, chronic obstructive pulmonary disease (COPD), and cystic fibrosis (CF).
Role: Investigator

NC Policy Collaboratory (Pearce) 5/4/20-12/30/20
North Carolina General Assembly (NCGA)
Rapidly Emerging Antiviral Drug Discovery Initiative (READDI)
The Pearce lab, as part of the Center for Integrative Chemical Biology and Drug Discovery (CICBDD), will optimize the pharmacological properties of existing hit compounds with the goal of delivering a clinical candidate through the READDI drug development effort. The Pearce lab, in coordination with the Willson lab, will also generate new hit compounds based on validated SARS2 targets.
Role: PI

(Sondek/Pearce/Zhang) 07/01/19-06/30/21
Leukemia and Lymphoma Society
Screen to Lead Program
PLC-γ isozymes: unexploited drug targets for the treatment of leukemias and lymphomas
We propose to use novel fluorescent substrates to develop assays for high-throughput screens that will identify compounds that selectively inhibit the two human PLC-γ isozymes. Validated inhibitors will serve as hit compounds for subsequent development of drug candidate molecules for potential treatment of lymphomas and leukemias driven by constitutively active forms of the PLC-γ isozymes. Our drug discovery effort will benefit enormously from our success in determining the first atomic-resolution structure of a full-length PLC-γ isozyme.
Role: MPI

RX03912117 (Pearce) 06/01/19-05/31/20
Eshelman Institute for Innovation
Sugar-Based Chemistry in the Gut Microbiota
The major goal of this pilot project is focused on the immunosuppressant mycophenolate and the alleviation of its microbiome-initiated GI toxicity.
Role: PI (no salary support)

UNC Creativity Hub (Moorman/Pearce) 07/01/19-06/30/21
UNC-Chapel Hill

ID3@UNC: the Infectious Disease Drug Discovery program at UNC

Viral infection is a leading cause of morbidity and mortality worldwide, accounting for billions of dollars in direct medical and economic costs annually. Most antiviral drugs target viral proteins needed for virus replication. Such drugs are useful, but limited by viral genetic diversity and drug resistance. Here, we propose an alternative by targeting cellular components viruses need for replication. Since viruses cannot replicate on their own, they must redirect cells to generate energy and metabolites required for replication by altering cellular signaling, usually by activating specific protein kinases. Targeting virus-induced kinase changes has the potential to potently suppress a wide variety of viral infections, with little risk of drug resistance, and holds enormous promise as a therapeutic strategy. The Infectious Disease Drug Discovery program at UNC (ID3@UNC) merges UNC expertise in virology, proteomics, bioinformatics, chemical biology, and drug discovery to develop novel kinase inhibitors for use as new broad-spectrum antiviral drugs. In doing so, the ID3@UNC will address a critical unmet public health need by providing new antiviral therapeutics useful for treating multiple human viral diseases.
Role: MPI (no salary support)

PROFESSIONAL SERVICE

Affiliations

American Association for the Advancement of Science (1992 – present)
Endocrine Society (2006 - 2015)
Protein Society (1998 - 2005)
Biophysical Society (1990 - 1995)
American Chemical Society (1987 - 1992)

Symposia and Meetings

Session lead, PharmAlliance Research Symposium – Drug Discovery 2016

Presentation to potential ESOP investors, partners – Charles River 2018, Deerfield 2018, NIH NCATS 2019, 5AM Ventures 2019, NIH NCATS 2019, AstraZeneca 2019, BASF 2020

Participant, UNC and RTI International Collaboration Meeting, 2019

Committees

Served on doctoral committee for Liz Mutter-RottMayer (Toxicology, 2015-2018), Justin Rectenwald (Biochem. Biophys., 2016-2020), Devon Blake (Pharmacology, 2018-2019), Kelly Bird (CBMC, 2016-2020), Caleb Vogt (CBMC, 2016-2021), Maurice Horton (CBMC, chair, 2017-2021), Isabelle Engelberg (CBMC; 2018-2021), Jacob Larson (CBMC, 2018-present), Matt Fleming (CBMC, 2018-present), Rodney Park (Biochem. Biophys., 2019-present), Drew Thieme (CBMC, chair, 2019-present), Sabrina Iskandar

(CBMC; 2020-present), Deepika Jayaprakash (Oral and Craniofacial Biomedicine; 2019-present), Lilly Chiou (Gen. and Mol. Biol., 2020-present), Devan Shell (CBMC, 2020-present)

CBMC Research Faculty Hiring and Promotion Committee, 2017-2019

CBMC PhD recruiting video redesign, 2019

Curriculum in Toxicology & Environmental Medicine, Doctoral Written Exam Committee, 2017-2019

BBSP SCPS Admissions Committee, 2021-2021

Study Sections

Blueprint Neurotherapeutics Network NIH, November, 2015

UNC Lineberger Developmental Grants review committee, 2016, 2017

Reviewer for Leiden NL-OPENSCREEN proposal, 2017

Reviewer for study section SBIR/STTR NIH - Small Business: Cell and Molecular Biology [IMST (15)], San Francisco, November, 2017, Bethesda, MD, March, 2018, San Francisco, November 2018

Reviewer for study section R21 and R03 NIH/NCI Omnibus, Bethesda, November 2018, March 2019

Internal reviewer for Mary Kay Foundation pre-proposals, January 2019, January 2020

Reviewer for Eshelman Institute for Innovation Student Proposals, December 2019, December 2020

ERC Synergy Grant Mechanism, May 2020

Reviewer for study section SBIR/STTR ZRG1 OTC-T (10) B Cancer Therapeutics, February 2020, June 2020

PAR Panel: High Throughput Screening ZRG1 BST-F (55), March 2021

Eshelman Institute for Innovation, full proposals, April 2021

Department of Pharmaceutical Sciences, Irma Lerma Rangel College of Pharmacy, Texas A&M University, tenure review panel, June 2021

EU ERC-2021-STG NeuRoPROBE, external reviewer, August 2021

Search Committees
Director, CICBDD – 2018, 2019
Assistant Director, Eshelman Institute for Innovation – 2019
Project Director, Pinnacle Hill – 2019

Research Statement Narrative

Introduction

Drug discovery is an immensely complex endeavor and requires a unique combination of knowledge, perseverance, teamwork, and passion. There is never one formula for success. Additionally, even if efforts fail to deliver new medicines, discovery of quality tool molecules is an important side product from programs to help mode-of-action and target validation efforts. The purpose of this statement is to convey:

1) my background and experiences in drug and tool discovery
2) my research interests
3) my passion for drug discovery science and future aspirations

Brief Summary of Past Research (prior to UNC)

My fundamental research skills are in protein biochemistry, biophysics, assay design, compound screening, hit qualification, and cellular assay development. Within GlaxoSmithKline, I have gained experience for a wide variety of therapeutic areas including: antibacterials, antivirals, metabolic diseases, cancer, inflammatory diseases, and tissue fibrosis. I have led multidisciplined teams for both early and late stage drug discovery programs.

Two specific research areas where I will cite some highlights of my accomplishments are:
1) signal transduction
2) protein processing and regulation

Signal Transduction

My interest in receptor signaling began as a postdoctoral scientist in the lab of Dr. James Wells at Genentech. Using biophysical, structural, and cellular methods, I investigated the hormone-receptor interface and the two site nature of human growth hormone and thrombopoeitin. The goal was to aid discovery of peptide mimetics and more effective biopharmaceuticals. This work stimulated my interest in discovering new therapeutics.

At GlaxoSmithKline, a significant body of my research focused on nuclear receptor signaling. The primary goal of this work was to discover novel nuclear receptor (NR)-modulating small molecules. I contributed to numerous NR projects and provide below particular highlights for work conducted on the glucocorticoid receptor (GR), estrogen receptor (ER), and estrogen-related receptor alpha (ERRα).

- Initiated and led a team to express, purify and characterize GR protein and solve the first reported crystal structure. This work helped drive a non-steroidal GR agonist program and was essential for characterization of a current marketed drug, Veramyst (fluticasone furoate).
- Led a team to profile ER modulators using a multiplexed peptide binding assay and profile clustering methods. Data was used to select a novel lead molecule and resulted in first time in human clinical studies. This profiling method was also used to drive multiple NR modulator programs.

• Initiated and led a team to discover a novel ERRα ligand through assay design, screening, lead optimization, phenotypic assays, and a diseased animal model study.

Proprotein Convertases and Protein Regulation

My interest in proteases also originated from my time in Dr. Wells' lab which studied the bacterial proprotein convertase, subtilisin. At GlaxoSmithKline, I headed numerous protease programs including leading a drug discovery team for the proprotein convertase subtilisin/kexin family of enzymes. These enzymes are attractive drug targets for cancer and anti-infectives, but historically they have been chemically intractable. Some highlights of my contributions are:

• Led the effort to identify novel inhibitors for this difficult family of enzymes using high-throughput, combinatorial, DNA-encoded library affinity-selection, and fragment-based screens.
• Applied fluorescence, isothermal titration calorimetry, crystallography, and enzymology methods to discover and validate several first in the world types of inhibitors. This work provided the foundation for a lead optimization and candidate selection program.
• Developed numerous novel cellular and disease-relevant phenotypic assays to characterize compounds and allow selection of tools for animal models of human disease.

Outlook and Future Perspectives

My background in pharmaceutical research has given me valuable experiences, both with target-based methods and more recently phenotypic-based methods for tool and drug discovery. I have had the good fortune to work with extremely talented and inspirational discovery scientists and I have gained important scientific and leadership capabilities necessary for future success. At this point in my career, I remain steadfastly committed to initiate, enable, and drive efforts for new medicine and tool compound discovery research. The collaborative approach is essential for successful drug discovery programs. I have the desire, experience, and ability to build and lead biology teams and foster the very important chemistry – biology interface. I look forward to joining a research center where members share the same interests: high quality science and innovation, continual learning and applied knowledge, and a sincere passion for research that may benefit patients.

Teaching Statement

My philosophy on teaching the biological and chemical sciences, including my primary expertise of assay development, compound screening, hit validation and characterization for chemical probes and drug leads, is to create excitement for learning the fundamentals. One way to do this is to teach students why learning the basics can empower one to be a better health care professional/ research scientist and also generate new ideas and invention. It is imperative that students understand the importance of broad learning and understanding basic concepts for them to be successful in their chosen field or profession founded on science. Including real life and literature examples of discoveries is also important to encourage learning, rather than simply memorizing facts. Additionally, there is no better way to get science education than hands on experience, exposure to research, and collaborative science. I have experienced this with my undergraduate, graduate and post graduate training and I fully realize the importance and value of a constructive hands-on approach to teaching.