Stephen V. Frye

CURRICULUM VITAE

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EDUCATION

University of North Carolina at Chapel Hill, 1983 -1987
Major: Organic Chemistry
Advisor: Prof. Ernest L. Eliel
Dissertation: "*Stereoselective Syntheses Based on Chiral 1,3-Oxathianes: Synthesis of Mevalolactone and Citramalic Acid and Investigation of the Mechanism of Diastereoselection"*
Ph.D. May 1987

Off Campus Graduate Fellow, Institut de Chemie Organique, de Université de Lausanne, Switzerland, March-September 1986

North Carolina State University, 1979-1983
Major: Chemistry Minor: Polymer/Textile Chemistry
B.S. *Summa Cum Laude* with Honors, May 1983

American University, Washington DC, Oct. 1997- Dec. 1998
Graduate certificate in Organizational Change-Leadership

PROFESSIONAL EXPERIENCE

University of North Carolina at Chapel Hill

Fred Eshelman Distinquished Professor, Center for Integrative Chemical Biology and Drug Discovery, Division of Chemical Biology and Medicinal Chemistry, UNC Eshelman School of Pharmacy (March 2022 - present)

Fred Eshelman Distinquished Professor, and Co-Director, Center for Integrative Chemical Biology and Drug Discovery, Division of Chemical Biology and Medicinal Chemistry, UNC Eshelman School of Pharmacy (March 2021 - present)

Fred Eshelman Distinquished Professor, and Director, Center for Integrative Chemical Biology and Drug Discovery, Division of Chemical Biology and Medicinal Chemistry, UNC Eshelman School of Pharmacy (June 2012 – February 2021)

Professor, Division of Medicinal Chemistry, and Director, Center for Integrative Chemical Biology and Drug Discovery, UNC Eshelman School of Pharmacy (November 2011 – May 2012)

Research Professor, Division of Medicinal Chemistry, and
Director, Center for Integrative Chemical Biology and Drug Discovery
UNC Eshelman School of Pharmacy (2007- November 2011)

Co-Leader, Molecular Therapeutics Program, Lineberger Comprehensive Cancer Center (November 2013 – present)

Key Responsibilities – Responsible for vision, creation and productivity of a research center at UNC focused on chromatin chemical biology and oncology drug discovery.

Glaxo, Glaxo-Wellcome and GlaxoSmithKline (1987-2007)

Key Drug Discovery Accomplishments while employed at GSK:

- Project leader and co-inventor of GSK's 5α-reductase inhibitor (Avodart, dutasteride; FDA approved for treatment of benign prostatic hyperplasia; > $1 billion peak world-wide sales).
- Created a global kinase chemistry team that discovered Tykerb (dual erbB2 and EGFR inhibitor, approved for the treatment of metastatic breast cancer) and Pazopanib (VEGF inhibitor approved for the treatment of renal carcinoma).

Scientific, Management and Leadership Roles:

World Wide Vice President, High Throughput Chemistry & Discovery Medicinal Chemistry, Molecular Discovery Research, GSK (July 2000-August 2007)

Key Responsibilities – lead staff of up to 200 internal chemists and >100 external chemists accountable for all hit to lead and prospective compound collection chemistry globally in GSK.

Budget responsibility for $50M operational and $3-5M capital per annum.

Research Unit Head, Chemistry Division, Glaxo Wellcome R&D, Stevenage, UK (overseas assignment, July 1999-July 2000)

Department Head, Medicinal Chemistry, Glaxo Wellcome Inc., RTP (January 1998 – July 1999)

Principal Research Scientist, Glaxo Wellcome Inc., RTP (February 1997 – December 1997)

Department Head, Medicinal Chemistry, Glaxo Wellcome Inc., RTP (July 1995 - February 1997)

Senior Research Investigator II, Chairman of the Cancer Scientific Forum, Glaxo Research Institute, Department of Medicinal Chemistry, RTP (September 1994 - July 1995)

Senior Research Investigator and Project Leader, Glaxo Research Institute, Department of Medicinal Chemistry, RTP (January 1991-September 1994)

Senior Scientist, Glaxo Research Institute, Department of Medicinal Chemistry, RTP (August 1987-January 1991)

Adjunct Assistant Professor, University of North Carolina at Chapel Hill, Department of Chemistry (January 1990-January 1995)

Honors, Fellowships & Awards

CEO's Award 1993, Glaxo Research Institute (Special award for leadership of the 5α-reductase project that led to Avodart)

American Chemical Society, Organic Division Fellowship 1986-1987

University of North Carolina, Off Campus Graduate Fellowship 1986

University of North Carolina, Board of Governor's Fellowship in Science and Technology 1985-1986

University of North Carolina, Department of Chemistry, Dobbins Fellowship 1984

University of North Carolina, Department of Chemistry, Reilley Fellowship 1983

BIBLIOGRAPHY

Publications (*corresponding author)

Peer reviewed commentary and solicited editorial contributions:

1) "Target class drug discovery", Barnash, K. D.; James, L. I.; *Frye, S. V. *Nat Chem Biol* **2017**, *13*, 1053. PMID: 28926557. PMCID: PMC5973815.
2) Cell Voices: "Where is the Future of Drug Discovery for Cancer*:* Drugging the Unprecedented'', *Frye, S. V. *Cell* **2017**, *168*, 564. PMID: 28187277.
3) "Novel Therapeutics Targeting Epigenetics: New Molecules, New Methods", *Frye, S. V.; Jin, J. *ACS Medicinal Chemistry Letters* **2016**, *7*, 123. PMID: 26985299.
4) "Unlocking the potential of chemical probes for methyl-lysine reader proteins", *Frye, S. V., *Future Medicinal Chemistry* **2015**, *7*, 1831. PMID: 26393394.
5) "Tackling reproducibility in academic preclinical drug discovery", *Frye, S. V.; Arkin, M. R.; Arrowsmith, C. H.; Conn, P. J.; Glicksman, M. A.; Hull-Ryde, E. A.; Slusher, B. S., *Nat Rev Drug Discov* **2015**, *14,* 733-4. PMID: 26388229.
6) "The promise and peril of chemical probes", Arrowsmith, C. H. *et al., Nat Chem Bio* **2015**, *11*, 536. PMID: 26196764.
7) "Drug discovery in academic institutions", *Frye, S. V., *ASH Education Program Book* **2013,** 300-305. PMID: 24319195.

8) "Bringing together the academic drug discovery community", *Slusher, B.S.; Conn, P.J.; Frye, S. V.; Glicksman, M.; Arkin, M., Commentary *Nat Rev Drug Discov* **2013**, *12*, 811. PMID: 24172316. PMCID: PMC4076044.
9) "Too many roads not taken", *Edwards, A.; Isserlin, R.; Bader, G.; Frye, S. V.; Willson, T.; Yu, F., Commentary *Nature* **2011,** *470* 163-5. PMID: 21307913.
10) "The art of the chemical probe", *Frye, S. V., Commentary, *Nature Chem Bio*, **2010** *6*, 159-61, (**Cited by Faculty of 1000**). PMID: 20154659.
11) "Epigenetics: tools and technologies", *Janzen, W.; Wigle, T.; Jin, J.; Frye, S. V., *Drug Discovery Today: Technologies* **2010**, *7*, e59-e65. PMID: 21243036. PMCID: PMC3018755.
12) "Inhibitors paradoxically prime kinases", *Frye, S. V.; Johnson, G., News and Views, *Nature Chem. Bio.*, **2009** *5,* 448-9. PMID: 19465930.
13) "Why Academic Drug Discovery?" *Frye, S. V.; Janzen, B., Editorial for *Future Pharma*, August **2009**.

Peer reviewed publications, chapters and reviews:

Based on research at UNC

14) "AD Informer Set: Chemical tools to facilitate Alzheimer's disease drug discovery", Potjewyd, F.M., Annor-Gyamfi, J.K., Aube, J., Chu, S., Conlon, I.L., Frankowski, K.J., Guduru, S.K.R., Hardy, B.P., Hopkins, M.D., Kinoshita, C., Kireev, D.B., Mason, E.R., Moerk, C.T., Nwogbo, F., Pearce, K.H., Richardson, T.I., Rogers, D.A., Soni, D.M., Stashko, M., Wang, X., Wells, C., Willson, T.M., Frye, S.V., Young, J.E. & Axtman, A.D. *Alzheimers Dement (N Y)* **2022,** *8* (1), e12246. PMID: 35475262. PMCID: PMC9019904.
15) "Use of AD Informer Set compounds to explore validity of novel targets in Alzheimer's disease pathology", Potjewyd, F. M.; Annor-Gyamfi, J. K.; Aubé, J.; Chu, S.; Conlon, I. L.; Frankowski, K. J.; Guduru, S. K. R.; Hardy, B. P.; Hopkins, M. D.; Kinoshita, C.; Kireev, D. B.; Mason, E. R.; Moerk, C. T.; Nwogbo, F.; Pearce, K. H., Jr.; Richardson, T. I.; Rogers, D. A.; Soni, D. M.; Stashko, M.; Wang, X.; Wells, C.; Willson, T. M.; Frye, S. V.; Young, J. E.; Axtman, A. A.-O., **2022, ,** *8* (1), e12253. PMID: 35434254. PMCID: PMC9005681.
16) "Reprogramming CBX8-PRC1 function with a positive allosteric modulator", Suh, J. L.; Bsteh, D.; Hart, B.; Si, Y.; Weaver, T. M.; Pribitzer, C.; Lau, R.; Soni, S.; Ogana, H.; Rectenwald, J. M.; Norris, J. L.; Cholensky, S. H.; Sagum, C.; Umana, J. D.; Li, D.; Hardy, B.; Bedford, M. T.; Mumenthaler, S. M.; Lenz, H. J.; Kim, Y. M.; Wang, G. G.; Pearce, K. H.; James, L. I.; Kireev, D. B.; Musselman, C. A.; *Frye, S. V.; *Bell, O., *Cell Chem Biol* **2022,** *29* (4), 555-571 e11. PMID: 34715055. PMCID: PMC9035045.
17) "Target 2035 – update on the quest for a probe for every protein", *Müller, S.; Ackloo, S.; Al Chawaf, A.; Al-Lazikani, B.; Antolin, A.; Baell, J. B.; Beck, H.; Beedie, S.; Betz, U. A. K.; Bezerra, G. A.; Brennan, P. E.; Brown, D.; Brown, P. J.; Bullock, A. N.; Carter, A. J.; Chaikuad, A.; Chaineau, M.; Ciulli, A.; Collins, I.; Dreher, J.; Drewry, D.; Edfeldt, K.; Edwards, A. M.; Egner, U.; Frye, S. V.; Fuchs, S. M.; Hall, M. D.; Hartung, I. V.; Hillisch, A.; Hitchcock, S. H.; Homan, E.; Kannan, N.; Kiefer, J. R.; Knapp, S.; Kostic, M.; Kubicek, S.; Leach, A. R.; Lindemann, S.; Marsden, B. D.; Matsui, H.; Meier, J. L.; Merk, D.; Michel, M.; Morgan, M. R.; Mueller-Fahrnow, A.; Owen, D. R.; Perry, B. G.; Rosenberg, S. H.; Saikatendu, K. S.; Schapira, M.; Scholten, C.; Sharma, S.; Simeonov, A.; Sundström, M.; Superti-Furga, G.; Todd, M.

H.; Tredup, C.; Vedadi, M.; von Delft, F.; Willson, T. M.; Winter, G. E.; Workman, P.; Arrowsmith, C. H., *RSC Medicinal Chemistry* **2021**, DOI: 10.1039/D1MD00228G.

18) "UNC5293, a potent, orally available and highly MERTK-selective inhibitor", Zheng, H.; Zhao, J.; Li, B.; Zhang, W.; Stashko, M. A.; Minson, K. A.; Huey, M. G.; Zhou, Y.; Earp, H. S.; Kireev, D.; Graham, D. K.; DeRyckere, D.; Frye, S. V.; *Wang, X., *Eur J Med Chem* **2021,** *220*, 113534. PMID: 34038857.
19) "MerTK activity is not necessary for the proliferation of glioblastoma stem cells", Hoque, M.; Wai Wong, S.; Recasens, A.; Abbassi, R.; Nguyen, N.; Zhang, D.; Stashko, M. A.; Wang, X.; Frye, S.; Day, B. W.; Baell, J.; Munoz, L., *Biochemical pharmacology* **2021,** *186*, 114437. PMID: 33571503.
20) "Discovery and Optimization of 2H-1λ2-Pyridin-2-one Inhibitors of Mutant Isocitrate Dehydrogenase 1 for the Treatment of Cancer", Rohde, J. M.; Karavadhi, S.; Pragani, R.; Liu, L.; Fang, Y.; Zhang, W.; McIver, A.; Zheng, H.; Liu, Q.; Davis, M. I.; Urban, D. J.; Lee, T. D.; Cheff, D. M.; Hollingshead, M.; Henderson, M. J.; Martinez, N. J.; Brimacombe, K. R.; Yasgar, A.; Zhao, W.; Klumpp-Thomas, C.; Michael, S.; Covey, J.; Moore, W. J.; Stott, G. M.; Li, Z.; Simeonov, A.; Jadhav, A.; Frye, S.; Hall, M. D.; Shen, M.; Wang, X.; Patnaik, S.; *Boxer, M. B., *J Med Chem* **2021,** *64* (8), 4913-4946. PMID: 33822623.
21) "Discovery of an H3K36me3-Derived Peptidomimetic Ligand with Enhanced Affinity for Plant Homeodomain Finger Protein 1 (PHF1)", Engelberg, I. A.; Liu, J.; Norris-Drouin, J. L.; Cholensky, S. H.; Ottavi, S. A.; Frye, S. V.; Kutateladze, T. G.; *James, L. I., *J Med Chem* **2021,** *64* (12), 8510-8522. PMID: 33999620. PMCID: PMC8225578.
22) "Improved methods for targeting epigenetic reader domains of acetylated and methylated lysine", Engelberg, I. A.; Foley, C. A.; James, L. I.; *Frye, S. V., *Curr Opin Chem Biol* **2021,** *63*, 132-144. PMID: 33852996. PMCID: PMC8384657.
23) "The histone and non-histone methyl-lysine reader activities of the UHRF1 tandem Tudor domain are dispensable for the propagation of aberrant DNA methylation patterning in cancer cells", Vaughan, R. M.; Kupai, A.; Foley, C. A.; Sagum, C. A.; Tibben, B. M.; Eden, H. E.; Tiedemann, R. L.; Berryhill, C. A.; Patel, V.; Shaw, K. M.; Krajewski, K.; Strahl, B. D.; Bedford, M. T.; Frye, S. V.; Dickson, B. M.; *Rothbart, S. B., *Epigenetics Chromatin* **2020,** *13* (1), 44. PMID: 33097091. PMCID: PMC7585203.
24) "Discovery and Characterization of Peptide Inhibitors for Calcium and Integrin Binding Protein 1", Puhl, A. C.; Bogart, J. W.; Haberman, V. A.; Larson, J. E.; Godoy, A. S.; Norris-Drouin, J. L.; Cholensky, S. H.; Leisner, T. M.; Frye, S. V.; Parise, L. V.; *Bowers, A. A.; *Pearce, K. H., *ACS Chem Biol* **2020,** *15* (6), 1505-1516. PMID: 32383857. PMCID: PMC7305997.
25) "Assessing the Cell Permeability of Bivalent Chemical Degraders Using the Chloroalkane Penetration Assay", Foley, C. A.; Potjewyd, F.; Lamb, K. N.; James, L. I.; *Frye, S. V., *ACS Chemical Biology* **2020,** *15* (1), 290-295. PMID: 31846298. PMCID: PMC7010361.
26) "Design and Construction of a Focused DNA-Encoded Library for Multivalent Chromatin Reader Proteins", Rectenwald, J. M.; Guduru, S. K. R.; Dang, Z.; Collins, L. B.; Liao, Y. E.; Norris-Drouin, J. L.; Cholensky, S. H.; Kaufmann, K. W.; Hammond, S. M.; Kireev, D. B.; Frye, S. V.; *Pearce, K. H., *Molecules* **2020,** *25* (4). PMID: 32098353. PMCID: PMC7070942.
27) "MerTK inhibition decreases immune suppressive glioblastoma-associated macrophages and neoangiogenesis in glioblastoma microenvironment", Su, Y. T.; Butler, M.; Zhang, M.; Zhang, W.; Song, H.; Hwang, L.; Tran, A. D.; Bash, R. E.; Schorzman, A. N.; Pang, Y.; Yu, G.; Zamboni, W. C.; Wang, X.; Frye, S. V.; Miller, C.

R.; Maric, D.; Terabe, M.; Gilbert, M. R.; Earp, H. S.; *Wu, J., *Neurooncol Adv* **2020,** *2* (1), vdaa065. PMID: 32642716. PMCID: PMC7324055.

28) "Discovery and Characterization of a Cellularly Potent Positive Allosteric Modulator of the Polycomb Repressive Complex 1 Chromodomain, CBX7", Lamb, K.N.; Bsteh, D.; Dishman, S.N,; Moussa, H.F.; Fan, H.; Stuckey, J.I.; Norris, J.I.; Cholensky, S.H.; Li, D.; Wang, J.; Sagum, C.; Stanton, B.Z.; Bedford, M.T.; Kenakin, T.P.; Kireev, D.B.; Wang, G.G.; James, L.I.; *Bell, O.; *Frye, S.V. *Cell. Chem. Biol*. **2019**, *26* (10), 1365-1379 e22. PMID: 31422906. PMCID: PMC6800648.
29) "Data-Driven Construction of Antitumor Agents with Controlled Polypharmacology", Da, C.; Zhang, D.; Stashko, M.; Vasileiadi, E.; Parker, R. E.; Minson, K. A.; Huey, M. G.; Huelse, J. M.; Hunter, D.; Gilbert, T. S. K.; Norris-Drouin, J.; Miley, M.; Herring, L. E.; Graves, L. M.; DeRyckere, D.; Earp, H. S.; Graham, D. K.; Frye, S. V.; Wang, X.; *Kireev, D., *J Am Chem Soc* **2019,** *141* (39), 15700-15709. PMID: 31497954. PMCID: PMC6894422.
30) "Kinome profiling of non-Hodgkin lymphoma identifies Tyro3 as a therapeutic target in primary effusion lymphoma", Wong, J. P.; Stuhlmiller, T. J.; Giffin, L. C.; Lin, C.; Bigi, R.; Zhao, J.; Zhang, W.; Bravo Cruz, A. G.; Park, S. I.; Earp, H. S.; Dittmer, D. P.; Frye, S. V.; Wang, X.; Johnson, G. L.; *Damania, B., *Proceedings of the National Academy of Sciences* **2019**, 201903991. PMID: 31346082. PMCID: PMC6697815.
31) "TAM Family Receptor Kinase Inhibition Reverses MDSC-Mediated Suppression and Augments Anti-PD-1 Therapy in Melanoma", Holtzhausen, A.; Harris, W.; Ubil, E.; Hunter, D. M.; Zhao, J.; Zhang, Y.; Zhang, D.; Liu, Q.; Wang, X.; Graham, D. K.; Frye, S. V.; *Earp, H. S., *Cancer Immunol Res* **2019,** *7* (10), 1672-1686. PMID: 31451482. PMCID: PMC6943983.
32) "Application of a MYC degradation screen identifies sensitivity to CDK9 inhibitors in KRAS-mutant pancreatic cancer", Blake, D. R.; Vaseva, A. V.; Hodge, R. G.; Kline, M. P.; Gilbert, T. S. K.; Tyagi, V.; Huang, D.; Whiten, G. C.; Larson, J. E.; Wang, X.; Pearce, K. H.; Herring, L. E.; Graves, L. M.; Frye, S. V.; Emanuele, M. J.; Cox, A. D.; *Der, C. J., *Science Signaling* **2019,** *12* (590), eaav7259. PMID: 31311847. PMCID: PMC6728149.
33) "Discovery of selective activators of PRC2 mutant EED-I363M", Suh, J. L.; Barnash, K. D.; Abramyan, T. M.; Li, F.; The, J.; Engelberg, I. A.; Vedadi, M.; Brown, P. J.; Kireev, D. B.; Arrowsmith, C. H.; James, L. I.; *Frye, S. V., *Scientific Reports* **2019,** *9* (1), 6524. PMID: 31024026. PMCID: PMC6484020.
34) "Inhibition of Inositol Polyphosphate Kinases by Quercetin and Related Flavonoids: A Structure–Activity Analysis", Gu, C.; Stashko, M. A.; Puhl-Rubio, A. C.; Chakraborty, M.; Chakraborty, A.; Frye, S. V.; Pearce, K. H.; Wang, X.; *Shears, S. B.; *Wang, H., *Journal of Medicinal Chemistry* **2019,** *62* (3), 1443-1454. PMID: 30624931 PMCID: PMC6467728.
35) "Canonical PRC1 controls sequence-independent propagation of Polycomb-mediated gene silencing", Moussa, H. F.; Bsteh, D.; Yelagandula, R.; Pribitzer, C.; Stecher, K.; Bartalska, K.; Michetti, L.; Wang, J.; Zepeda-Martinez, J. A.; Elling, U.; Stuckey, J. I.; James, L. I.; Frye, S. V.; *Bell, O., *Nature Communications* **2019,** *10* (1), 1931. PMID: 31036804. PMCID: PMC6488670.
36) "A General TR-FRET Assay Platform for High-Throughput Screening and Characterizing Inhibitors of Methyl-Lysine Reader Proteins", Rectenwald, J. M.; Hardy, P. B.; Norris-Drouin, J. L.; Cholensky, S. H.; James, L. I.; Frye, S. V.; *Pearce, K. H., *SLAS DISCOVERY: Advancing Life Sciences R&D* **2019**, DOI: 10.1177/2472555219844569. PMID: 31017815. PMCID: PMC6586500.
37) "Inhibition of MERTK promotes suppression of tumor growth in BRAF mutant and BRAF wild-type melanoma", Sinik, L.; Minson, K. A.; Tentler, J. J.; Carrico, J.; Bagby,

S. M.; Robinson, W. A.; Karni, R.; Burstyn-Cohen, T.; Eckhardt, S. G.; Wang, X.; Frye, S. V.; Earp, H. S.; DeRyckere, D.; *Graham, D. K. *Molecular Cancer Therapeutics* **2019,** *18* (2), 278. PMID: 30482852.

38) "Highly Selective MERTK Inhibitors Achieved by a Single Methyl Group", Zhao, J.; Zhang, D.; Zhang, W.; Stashko, M. A.; DeRyckere, D.; Vasileiadi, E.; Parker, R. E.; Hunter, D.; Liu, Q.; Zhang, Y.; Norris-Drouin, J.; Li, B.; Drewry, D. H.; Kireev, D.; Graham, D. K.; Earp, H. S.; Frye, S. V.; *Wang, X. *J Med Chem* **2018,** *61* (22), 10242-10254. PMID: 30347155.
39) "MERTK Promotes Resistance to Irreversible EGFR Tyrosine Kinase Inhibitors in Non-small Cell Lung Cancers Expressing Wild-type EGFR Family Members", Yan, D.; Parker, R. E.; Wang, X.; Frye, S. V.; *Earp, H. S., 3rd; DeRyckere, D.; Graham, D. K. *Clin Cancer Res* **2018**, DOI: 10.1158/1078-0432.CCR-18-0040. PMID: 30194074.
40) "MERTK Mediates Intrinsic and Adaptive Resistance to AXL-targeting Agents", McDaniel, N. K.; Cummings, C. T.; Iida, M.; Hulse, J.; Pearson, H. E.; Vasileiadi, E.; Parker, R. E.; Orbuch, R. A.; Ondracek, O. J.; Welke, N. B.; Kang, G. H.; Davies, K. D.; Wang, X.; Frye, S. V.; Earp, H. S.; Harari, P. M.; Kimple, R. J.; DeRyckere, D.; Graham, D. K.; *Wheeler, D. L. *Mol Cancer Ther* **2018**, *17*, 2297. PMID: 30093568. PMCID: PMC6215511.
41) "MERTK inhibition alters the PD-1 axis and promotes anti-leukemia immunity", Lee-Sherick, A. B.; Jacobsen, K. M.; Henry, C. J.; Huey, M. G.; Parker, R. E.; Page, L. S.; Hill, A. A.; Wang, X.; Frye, S. V.; Earp, H. S.; Jordan, C. T.; DeRyckere, D.; *Graham, D. K. *JCI Insight* **2018**, *3*. PMID: 30385715. PMCID: PMC6215511.
42) "Chromatin remodeling controls Kaposi's sarcoma-associated herpesvirus reactivation from latency", Hopcraft, S. E.; Pattenden, S. G.; James, L. I.; Frye, S.; Dittmer, D. P.; *Damania, B. *PLOS Pathogens* **2018**, *14*, e1007267. PMID: 30212584. PMCID: PMC6136816.
43) "Use of Protein Kinase-Focused Compound Libraries for the Discovery of New Inositol Phosphate Kinase Inhibitors", Puhl-Rubio, A. C.; Stashko, M. A.; Wang, H.; Hardy, P. B.; Tyagi, V.; Li, B.; Wang, X.; Kireev, D.; Jessen, H. J.; Frye, S. V.; *Shears, S. B.; *Pearce, K. H. *SLAS Discov* **2018**, *23*, 982. PMID: 29842835. PMCID: PMC6148399.
44) "Donated chemical probes for open science", Müller, S.; Ackloo, S.; Arrowsmith, C. H.; Bauser, M.; Baryza, J. L.; Blagg, J.; Böttcher, J.; Bountra, C.; Brown, P. J.; Bunnage, M. E.; Carter, A. J.; Damerell, D.; Dötsch, V.; Drewry, D. H.; Edwards, A. M.; Edwards, J.; Elkins, J. M.; Fischer, C.; Frye, S. V.; Gollner, A.; Grimshaw, C. E.; Ijzerman, A.; Hanke, T.; Hartung, I. V.; Hitchcock, S.; Howe, T.; Hughes, T. V.; Laufer, S.; Li, V. M. J.; Liras, S.; Marsden, B. D.; Matsui, H.; Mathias, J.; O'Hagan, R. C.; Owen, D. R.; Pande, V.; Rauh, D.; Rosenberg, S. H.; Roth, B. L.; Schneider, N. S.; Scholten, C.; Singh Saikatendu, K.; Simeonov, A.; Takizawa, M.; Tse, C.; Thompson, P. R.; Treiber, D. K.; Viana, A. Y. I.; Wells, C. I.; Willson, T. M.; Zuercher, W. J.; Knapp, S.; Mueller-Fahrnow, A. *eLife* **2018**, *7*, e34311. PMID: 29676732.
45) "Quantitative Characterization of Bivalent Probes for a Dual Bromodomain Protein, Transcription Initiation Factor TFIID Subunit 1", Suh, J. L.; Watts, B.; Stuckey, J. I.; Norris-Drouin, J. L.; Cholensky, S. H.; Dickson, B. M.; An, Y.; Mathea, S.; Salah, E.; Knapp, S.; Khan, A.; Adams, A. T.; Strahl, B. D.; Sagum, C. A.; Bedford, M. T.; James, L. I.; *Kireev, D. B.; *Frye, S. V. *Biochemistry* **2018**, *57*, 2140. PMID: 29558110. PMCID: PMC5937704.
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Frye, S. V.; Ewend, M. G.; Sulman, E. P.; Gilbert, M. R.; Earp, H. S.; *Miller, C. R. *Neuro Oncol* **2018***, 20, 92*. PMID: 28605477. PMCID: PMC5761530.

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9) "Pyrrolopyrimidine compounds for the treatment of cancer", Wang, X.; Liu, J.; Zhang, W.; Frye, S.V.; Kireev, D. PCT/US2012/058298, WO2013052417 A1, US2013/641729, US 9273056 (Issued on March 1, 2016), ZL2012800568254 (Issued on Dec 12, 2016).
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28) "17-β-Acyl-6-Azaandrost-4,6-Diazo-4-ene-3-ones", Frye, S. V.; Middlemiss, D.; Fang, F., U. S. Patent 5,457,098.
29) "Heterocyclic Inhibitors of 5-Alpha-Testosterone Reductase", Frye, S. V.; Middlemiss, D.; Fang, R., U. S. Patent 5,302,589.
30) "Substituted 6-Azaandrostenones", Andrews, R.; Cribbs, C.; Frye, S. V.; Haffner, C.; Maloney, P., U. S. Patent 5,708,001
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32) "Cobalt Porphyrins", Johnson, M.; Frye, S. V., U. S. Patent 5,192,757.
33) "Cobalt Porphyrin Pharmaceutical Compositions", Johnson, M.; Frye, S. V., U. S. Patent 5,149,697.
34) "Synthesis of 2-Aminobenzophenones", Johnson, M.; Frye, S. V., U. S. Patent 5,136,085.
35) "Synthesis of 2-Aminobenzophenones", Johnson, M.; Frye, S. V., U. S. Patent 5,053,543.

Selected Presentations & Meetings

1) Keynote Speaker "Allosteric modulators of methyl-lysine reader domain interactions with DNA/RNA", 3rd Dana-Farber Chemical Biology Symposium, September 23, 2021.
2) Seminar Speaker "Allosteric modulators of methyl-lysine reader domain interactions with DNA/RNA", Memorial Sloan Kettering, April 6, 2021.
3) Seminar Speaker "Allosteric antagonists of methyl-lysine reader domain interactions with DNA/RNA", NIEHS Epigenetics and Stem Cell Biology Seminar Series, December 10, 2020.
4) Seminar Speaker "Allosteric antagonists of methyl-lysine reader domain interactions with DNA/RNA", Scripps Chemistry Bicoastal Seminar Series, November 16, 2020.
5) Invited Speaker "Allosteric antagonists of methyl-lysine reader domain interactions with DNA/RNA", Transcription Therapy Symposium, St. Jude, September 25, 2020.
6) Keynote Presentation "Science and Structure: Molecular Therapeutics at UNC Lineberger", Emory/Winship Cancer Center 2020 Discovery and Developmental Therapeutics Virtual Retreat on Friday, August 14, 2020.
7) Seminar Speaker "Academic Drug Discovery and Chemical Biology", Oregon Health Sciences University, Portland, May 2019.
8) Seminar Speaker "Academic Drug Discovery and Chemical Biology", University of New Mexico Comprehensive Cancer Center, Albuquerque, April 2019.
9) Invited Speaker "Academic Drug Discovery and Chemical Biology", Naff Symposium, University of Kentucky, Lexington, April 2019.

10) Seminar Speaker "Academic Drug Discovery and Chemical Biology**"**, University of Utah, Salt Lake City, March 2019.

11) Seminar Speaker "Academic Drug Discovery and Chemical Biology**"**, Northeastern University, Boston, November 2018.

12) Distinguished Seminar Series in Therapeutics Discovery "Academic Drug Discovery and Chemical Biology**"**, Mount Sinai University, September 2018.

13) Seminar Speaker "Academic Drug Discovery and Chemical Biology**"**, University of Wisconsin, Madison, September 2018.

14) Invited Speaker "MRX-2843, a dual MERTK/FLT3 inhibitor enabled by the NCI Chemical Biology Consortium (CBC) entering Phase 1 clinical trials (MEDI 303)", ACS National Meeting, Boston, August 2018.

15) Invited Speaker "Academic Drug Discovery and Chemical Biology**",** Guangzhou High-tech Park, PRC, June 2018.

16) Alexander R. Matzuk Lecture "Academic Drug Discovery and Chemical Biology", Baylor University, Houston, May 2018.

17) Invited Speaker "Oncology target validation with chemical probes: Exploring polycomb repressive complex 1 function in cancer", AACR Annual Meeting, Chicago, April 2018.

18) Invited Speaker "Chemical Biology of Chromatin Regulation and Drug Discovery", ASPET Annual Meeting at Experimental Biology 2017, Chicago, April 2017.

19) Invited Speaker "Chemical Probes of Chromatin Regulation: Case Histories", From Chemistry to the Clinic, AACR National Meeting, Washington DC, March 2017.

20) Seminar Speaker "Chemical Biology of Chromatin Regulation", University of Georgia, March 2017.

21) Seminar Speaker "Academic Drug Discovery and Chemical Biology, a tale of two targets", Notre Dame University, January 2017.

22) Invited Speaker "Chemical Biology of Polycomb Methyl Lysine Readers", Drugging Transcription Conference, Whitehead Institute, Cambridge, MA, November 2016.

23) Seminar Speaker "Chemical Biology of Methyl-Lysine Readers", Purdue University, October 2016.

24) Invited Speaker "Chemical Biology of Methyl-Lysine", Gordon Research Conference: Natural Products, Andover, NH, July 2016.

25) Keynote Speaker "Chemical Biology of Chromatin Regulation", Philadelphia Drug Discovery Symposium, Wistar Institute, Philadelphia, June 2016.

26) Seminar Speaker "Chemical Biology of Methyl-Lysine", The Department of Epigenetics and Molecular Carcinogenesis, MD Anderson, Smithville, April 2016.

27) Seminar Speaker "Chemical Biology of Methyl-Lysine", Department of Pharmacology and Toxicology, Michigan State University, East Lansing, April 2016.

28) Seminar Speaker "Chemical Biology of Chromatin Regulation", Pharmaceutical Sciences & UCSF-Stanford Center of Excellence in Regulatory Science and Innovation, UCSF, February 2016.

29) Invited Speaker "Academic drug discovery and chemical biology: A tale of two targets", Academic Drug Discovery Session, Pacifichem, Honolulu, December 2015.

30) Invited Speaker "Progress towards chemical probes for methyl-lysine readers", Small Molecule Epigenetic Modulators Session, Pacifichem, Honolulu, December 2015.

31) Invited Speaker "Targeting Chromatin Regulation for Cancer Therapy: Progress Towards Chemical Probes for Methyl-Lysine Readers", Chapel Hill Pharmaceutical Sciences Conference, Chapel Hill, October 2015.

32) Seminar Speaker "Academic Drug Discovery and Chemical Biology", Seminar in the Duke Cancer Institute Speaker Series, Duke University, Durham, September 2015.

33) Seminar Speaker "Targeting Chromatin Regulation: Progress Towards Chemical Probes for Methyl-Lysine Readers", Seminar in the Department of Biochemistry & Molecular Biophysics, Washington University, St. Louis, September 2015.

34) Invited Speaker "Targeting Chromatin Regulation for Cancer Therapy: Progress Towards Chemical Probes for Methyl-Lysine Readers", International Symposium, Molecular Targets in Cancer Genomics, University of Montreal, May 2015.

35) Invited Speaker "Academic Drug Discovery: Progress Towards High-quality Chemical Probes of Methyl-Lysine Readers for Target Validation", Academic Drug Discovery Workshop, Cambridge, UK, May 2015.

36) Invited Speaker "Chemical Probes for Methyl-lysine Reader Domains", Armenise Symposium on the Chemistry:Biology Interface, Harvard Medical School, Cambridge, MA, November 2014.

37) Invited Speaker "The Unexplored Kinome: Mer Kinase's Role in Cancer and Viral Infection", Kinase Symposium, Gilead Sciences, Foster City, CA, October 2014.

38) Invited Speaker and Co-organizer "Academic Drug Discovery: Where the Rubber Meets the Road", Addressing Irreproducibility in Target Validation Symposium, Academic Drug Discovery Consortium, Novartis Institute, Cambridge, MA, October 2014.

39) Seminar Speaker "Academic Drug Discovery: Something Old and Something New", Institute for Cancer Research, Sutton, UK, October 2014.

40) Seminar Speaker "Academic Drug Discovery and Chemical Biology of Chromatin Regulation", Seminar in the Department of Chemical Biology and Therapeutics, St. Jude Children's Hospital, Memphis, October 2014.

41) Invited Speaker "Targeting Epigenetics for Cancer Therapy: Progress Towards Chemical Probes for Methyl-Lysine Readers", SGC/DiscoveRx Epigenetics Symposium, Cambridge, MA, June 2014.

42) Invited Speaker "Oncology Drug Discovery and Target Validation in Academic Institutions", American Society of Hematology Annual Meeting, New Orleans, LA, 7th and 9th, December 2013.

43) Seminar Speaker "Chemical Biology in Oncology Drug Discovery and Target Validation", Cincinnati Children's Hospital, November 2013.

44) Keynote Speaker "Academic Drug Discovery and Chemical Biology: A Tale of Two Targets", Northwestern Drug Discovery Symposium, Chicago, November 2013.

45) Invited Speaker "Structural Biology in Cancer: Target Validation and Drug Discovery", Northeastern Structure Symposium, U. Conn., October 2013.

46) Invited Speaker "Chemical Biology of Methyl-Lysine: Discovery of a chemical probe for L3MBTL3", American Chemical Society National Meeting, Indianapolis, IN, September 2013.

47) Invited Speaker "Academic Drug Discovery: A Call to Arms", Molecular Therapeutics of Cancer Research Conference, Boulder CO, July 2013.

48) Invited Speaker "Chemical Biology of Methyl-Lysine", Clinical Translation of Epigenetics in Cancer Therapy, 6th Biennial Workshop, Asheville, NC, January 2013.

49) Seminar Speaker "Chemical Biology of Methyl-Lysine", Harvard Medical School, December 2012.

50) Invited Speaker "Chemical Biology of Methyl-Lysine", Southeastern Regional Meeting (SERMACS 2012), Raleigh, NC, November 2012.

51) Seminar Speaker "Chemical Biology of Methyl-Lysine", University of Minnesota, October 2012.

52) Seminar Speaker "Chemical Biology of Methyl-Lysine", University of Michigan, October 2012.

53) Keynote Speaker "Chemical Biology of Methyl-Lysine", SBNet 2012, Swedish Structural Biology Network, Tällberg, June 2012.

54) Co-chair, 36th Lineberger Symposium, "Chemical Biology and Cancer Drug Discovery", April 2012.

55) Werblow Lecture "Chemical Biology of Methyl-Lysine", Weill Cornell Medical College, May 2012.

56) Invited Speaker "Chemical Biology of Methyl-Lysine", Transcription and Cancer Meeting, Banbury Center, Cold Spring Harbor, April 2012.

57) Seminar Speaker "Chemical Biology of Methyl-Lysine", Drug Development and Pharmacogenomics Academy, Emory University, April 2012.

58) Co-chair "Addressing the Challenges of Drug Discovery – Novel Targets, New Chemical Space and Emerging Approaches", Keystone Symposia, Tahoe City, March 2012.

59) Seminar Speaker "Chemical Biology of Methyl-Lysine", John Hopkins Department of Pharmacology, Baltimore, October 2011.

60) Invited Speaker "Building Academic Drug Discovery Centers", Drug Discovery in Academia, Baltimore, October 2011.

61) Invited Speaker "The Role of Academic Drug Discovery and Chemical Biology of Chromatin Regulation", Frontiers in Chemical Biology and Drug Discovery, Stony Brook SUNY, October 2011.

62) Invited Speaker "Chemical Biology of Methyl-Lysine", Vertex, Cambridge, October 2011.

63) Invited Speaker "Chemical Biology of Methyl-Lysine", Eli Lilly, Indianapolis, September 2011.

64) Invited Speaker "Academic Drug Discovery: US Perspective and Examples", NCI Translational Science Meeting, Washington DC, July 2011.

65) Invited Speaker "Kinase Chemical Probes – Why?" Structural Genomics Consortium Annual Retreat, Barbados, May 2011.

66) Seminar Speaker "Promoting Illiteracy in Epigenetics: Antagonists of the Readers and Writers of the Histone Code", Department Cellular and Molecular Pharmacology, UCSF, April 2011.

67) Invited Speaker "Promoting Illiteracy in Epigenetics: Antagonists of the Readers and Writers of the Histone Code", Genentech, San Francisco, April 2011.

68) Seminar Speaker "Promoting Illiteracy in Epigenetics: Antagonists of the Readers and Writers of the Histone Code", Division of Chemical Biology, Walter & Eliza Hall Institute of Medical Research, Melbourne, Australia, March 2011.

69) Invited Speaker "Promoting Illiteracy in Epigenetics: Antagonists of the Readers and Writers of the Histone Code", Structural Biology and Drug Discovery Conference, Cancun, December 2010.

70) Invited Speaker "Chemical Biology Consortium – Overview of Funded Projects", American Association of Cancer Institutes, Chicago, October 2010.

71) Invited Speaker & Session Chair, "Why Academic Drug Discovery Makes Sense", SBS Symposium, Research Triangle Park, October 2010.

72) Invited Speaker, "Promoting Illiteracy in Epigenetics: Antagonists of the Readers of the Epigenetic Code", Jilin University Chemical Biology and Drug Discovery Symposium, Changchun China, May, 2010.

73) Keynote Speaker, "Chemical Biology of Epigenetics: Antagonists of the Readers and Writers of the Histone Code", Alabama Drug Discovery Alliance Symposium, Birmingham, May 2010.

74) Invited Speaker, "Promoting Illiteracy in Epigenetics: Antagonists of the Readers and Writers of the Epigenetic Code", American Chemical Society National Meeting, San Francisco, March 2010.

75) Invited Speaker, "Promoting Illiteracy in Epigenetics: Antagonists of the Readers and Writers of the Epigenetic Code", Epigenetic Mechanisms in Health and Disease, Toronto, Canada, October 2009.

76) Invited Speaker, "Target Identification and Validation in the Context of Gene Families, a Chemical Biology Perspective" Medicinal Biochemistry Symposium, UNC-Greensboro, April 2009.

77) Invited Speaker, "Target Identification and Validation in the Context of Gene Families, a Chemical Biology Perspective", Karolinska Structural Genomics Consortium Symposium, Stockholm, Sweden, March 2009.

78) Invited Speaker, "Drug Discovery and Intellectual Property Strategy in Academia", Society for Biomolecular Screening, Valley Forge, PA, October 2008.

79) Invited Speaker, "Translational Medicine: Role of Academic Drug Discovery", BioPharm America, Atlanta, GA, September 2008.

80) Invited Speaker, "Mechanistic Understanding in Organic Chemistry and Drug Discovery", Reaction Mechanisms Conference, Chapel Hill, NC, June 2008.

81) Chair: 2008 Chapel Hill Drug Conference, Chapel Hill, NC, May 16-17.

82) Invited Speaker: "Target Validation and Drug Discovery in the Context of Gene Families", European Symposium on Bio-Organic Chemistry, Gregynog, Wales, May 2007.

83) Invited Speaker: "Target Identification and Validation in the Context of Gene Families", Therapeutic Applications of Computational Chemistry and Biology, Wellcome Trust Conference Center, Hinxton, UK, March 2007.

84) Invited Speaker: "Target-Class Focused High Throughput Chemistry", Combinatorial Chemistry Gordon Research Conference, Oxford, UK, August 2006.

85) "Structure Activity Relationship And Homology (SARAH): A Genomic Approach to Protein Kinase Drug Discovery", American Association of Cancer Research, New Orleans LA, March 2001.

86) Co-chair: 2000 Bioorganic Gordon Research Conference, Proctor Academy, Andover NH, June 18-23.

87) Invited Speaker: "Kinase Systems Based Research: Target Class Science for Drug Discovery", University of California at San Francisco & Berkeley, March, 2000.

88) Invited Speaker: "Discovery and Development of GG745, A Potent Inhibitor of Both Isozymes of 5α-Reductase", Symposium on Urogenital Disease, American Chemical Society National Meeting, Boston, MA, August, 1998

89) Invited Speaker: "Characterization of a Microsomal Metalloendopeptidase That Processes Tumor Necrosis Factor", Gordon Research Conference: Bioorganic Chemistry, Plymouth State College, NH 1996.

90) "6-Azasteroids: Potent Dual Inhibitors of Human Type 1 and 2 Steroid 5α-Reductase", American Chemical Society National Meeting, San Diego, CA, March, 1994.

91) Invited Speaker: "Are Chelates Truly Intermediates in Cram's Chelate Rule?", Gordon Research Conference: Stereochemistry, Salve Regina College, Newport, RI, 1992.

92) "One-Pot Halogen-Lithium Exchange, *N*-Methoxy-*N*-Methylamide Route to 2-Aminobenzophenones", Poster Sesson, French-American Chemical Society, Captiva Island, Florida, 1991.

93) "Rapid Injection Nuclear Magnetic Resonance Investigation of the Reactivity of α- and β-Alkoxyketones with Dimethylmagnesium. Kinetic Evidence for Chelation", American Chemical Society National Meeting, Denver, Colorado, 1987.

94) "Prevention of Chelation by an Oxygen Function Through Protection with a Triisopropylsilyl Group", American Chemical Society Southeastern Regional Meeting, Louisville, Kentucky, 1986.

95) "Asymmetric Synthesis of *(R)*- and *(S)*-Mevalolactone and *(R)*- and *(S)*-Citramalic Acid in High Enantiomeric Purity", American Chemical Society National Meeting, Chicago, Illinois, 1985.

RESEARCH SUPPORT

ACTIVE or AWARDED

R35 GM139514-01 (PI: Frye) 04/01/21-03/31/26 3.978 mos.
NIH $290,132
Probing Allostery in Methyl Lysine Reader Domains

Allosteric interactions in chromatin regulatory complexes are critically important phenomena that create unique opportunities for pharmacologic intervention. We will focus our future endeavors on this exciting frontier in the Kme reader family.

1R01CA218392-02 (PI: Frye) 4/1/18-3/31/21 (now in NCE) 2.4 calendar months
NIH $504,942 $198,028 d.c. Frye Lab
Discovery of in vivo chemical probes for Polycomb CBX domains
The overarching objective of this program is to develop an in vivo chemical probe of the CBX reader domains of Polycomb repressive complex 1 (PRC1). The deliverable from this effort will be a high-quality in vivo chemical probe, freely available to the academic community, with confirmed activity and well characterized mechanism versus the CBX readers of PRC1 to catalyze progression of this target toward new therapeutic discoveries in oncology and, potentially, other diseases.

U54 (Levey; Role: MPI) 9/30/19-8/31/24 3 calendar months
NIH/Emory University $1,126,560 annual direct costs to UNC
TREAT-AD 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 UNC Structural Genomics Consortium (UNC-SGC) and the CICBDD based at UNC Chapel Hill. Dr. Frye is the PI of the Medicinal Chemistry Core within TREAT-AD.

UL1TR002489-02 (PI: Buse) 3/30/18 – 02/28/23 0.6 calendar months
NIH salary support only
UNC Clinical and Translational Science Award
Major Goals: A national consortium of medical research institutions, funded through Clinical and Translational Science Awards, is working together and shares a common vision: to improve the way biomedical research is conducted across the country, reduce the time it takes for laboratory discoveries to become treatments for patients, engage communities in clinical research efforts, and train the next generation of clinical and translational researchers.
Dr. Frye serves as a peer reviewer on the UNC CTSA study section.

P30-CA016086-43 (PI: Earp) 12/1/15-11/30/21 (ongoing) 0.6 calendar months
NCI $36,814
Cancer Center Core Support Grant – Molecular Therapeutics Research Program
The major goal of this project is to provide leadership of the Lineberger Comprehensive Cancer Center's continued scientific and intellectual development and strategic planning, including program priorities, recruitment, core facilities and use of development funds; develop and promote individual and collaborative research projects, especially translational research; serve as senior scientific advisory and mentor to program members.
Dr. Frye co-leads the Molecular Therapeutics program.

MCR012BRT1 7/0/2020 – 6/30/2021 (ongoing) 0.0 calendar months
UNC Lineberger Comp. Cancer Res. Fund (PI: Frye) $625,500
University Cancer Research Fund
State funds that are used to support the Center for Integrative Chemical Biology and Drug Discovery (CICBDD) operational expenses related to cancer drug discovery pilot projects that are not externally funded.

Dr. Frye is Director of the CICBDD.

COMPLETED

R01CA2059398-01A1 (Lead PI: Earp) 12/1/16-11/30/21 0.0 calendar months
NIH/NCI; Role: Other Significant Contributor $221,887
MerTK and the Immune Response to Melanoma
Our overall hypothesis is that MerTK, Axl and Tyro 3 are in part responsible for the counterproductive, immunosuppressive immune infiltrate in melanoma (and other tumor types) through their innate immune cell action. We will use wild type and knockout mice with preclinical syngeneic and genetically-engineered mouse melanomas as our models. Dr. Frye serves in a consulting role on the project and attends periodic project meetings as needed. There is no fixed or measurable commitment of time or effort on the project. No salary support is provided.

R01GM100919-07 (PI: Frye) 8/1/16-7/31/20 1.68 calendar months
NIH $416,687 $249,973 d.c. Frye lab
Discovery of Chemical Probes for Chromatin Readers
The overarching objectives of this program are to develop chemical probes of chromatin reader domains that exploit three distinct mechanisms of molecular recognition: 1) reader domains that function as dimers; 2) reader domains that operate via a dynamic, induced-fit recognition mechanism; and 3) multivalent reader domains.

R01GM100919-07S1 (PI: Frye) 8/1/18-7/31/20 0 calendar months
NIH $90,000 Frye lab
Supplement: Discovery of Chemical Probes for Chromatin Readers
This supplement provides for the purchase of a Liquid Chromatography/Mass Selective Detector for the parent project.

R21CA216673 (MPI: Frye/Strahl) 12/18/17 – 11/30/19 0.91 calendar months
NIH/NCI $ 151,918 TDC first year $ 72,117 Frye lab
Modulating the DNA methylation program through UHRF1 antagonism
The goal of this research is to discover chemical inhibitors of the epigenetic reader UHRF1, whose deregulation may contribute to cancer initiation and progression. In addition to the potential for UHRF1 inhibitors as cancer therapeutics, these chemical tools will facilitate future study of UHRF1 and the epigenetic program in normal and diseased cells.

1UM1AI126619 - 01 (PI: Margolis) 7/1/16-6/30/19 0.0 calendar months
NIH; Role: Project Lead, Chemical Biology no salary support
Collaboratory of AIDS Researchers for Eradication (CARE)

The overarching objective of this program is to seek eradication of HIV infection by developing and testing therapies that will permanently destroy the persistent viral reservoir in the T cells of HIV patients receiving potent antiretroviral therapy. My role is to consult on the creation of targeted compound sets and to advise on assay development and hit to probe optimization approaches, chemistry plans, and structure activity relationships (SAR) to improve potency, selectivity, and cellular activity.

1R01CA207416-01 (Redinbo) 7/1/16-6/30/19 0.25 calendar months
NIH; Role: Co-Investigator $438,140 first year $15,275 Frye

Microbiome-Targeted Probes to Eliminate Chemotherapy-Induced GI Toxicity
Our overarching hypothesis is that microbial enzymes expressed by the GI microbiome can be inhibited using targeted small molecules to prevent the unwanted reactivation of potent antineoplastic drugs in the intestinal lumen. We have assembled an interdisciplinary team of medicinal chemists, biochemists, structural biologists, and experts in animal models of chemotherapy all at the University of North Carolina at Chapel Hill. We will test this hypothesis using chemical synthesis, *in vitro* characterization, and *in vivo* validation in mouse models of chemotherapy-induced toxicity.

Basic Ordering Agreement 16X125 4/1/16-11/12/19 up to 3.0 calendar months
Leidos Biomedical Research, Inc. (PI/Site Head: Frye) no current support
North Carolina Comprehensive Chemical Biology Center (NC-CCBC) under NCI Experimental Therapeutics (NExT) Program
The UNC-CH has been selected as a Specialized Center under RFP 16-001 from NCI NExT Program Chemical Biology Consortium. Projects will be funded under individual task orders to be negotiated.

R01DK101645 (Pearce) 7/1/15-4/30/18 0.6 calendar months
NIH $225,000 first year $11,456 Frye
Role: Co-Investigator (formerly interim PI)
High Throughput Screening Assay for IP7K inositol pyrophosphate kinases
This application proposes a collaboration between UNC Chapel Hill and Dr. Stephen Shears at the National Institute of Environmental Health Sciences. The specific aims are: 1. Develop primary HTS assay for IP7K activity; 2. Application of secondary assays to determine the specificity of hits from the high throughput screen; 3. A pilot screen of 5000 kinase focused compounds, and a novel in-cell assay of specific “hits”; 4. Develop a strategy for virtual screening and computer-assisted design of IP7K inhibitors.

Qura Therapeutics, LLC (Margolis PI/PD) 10/1/15-12/31/16 0.12 calendar months
Role: Project Lead for Project 5a $134,691 5a TDC first year $110,088 Frye lab
Epigenome/Kinome pilot studies in HIV latency. The goal of this project is to explore the potential of combinations of chromatin regulatory probes and protein kinase inhibitors to synergistically reverse latency in HIV patient cells.

R41 TR001330 (Juliano/Frye, MPI)
08/15/15-08/14/16
NCATS-STTR
Development of Small Molecules that Enhance the Delivery and the Pharmacological Effects of Oligonucleotides
A key impediment to oligonucleotide-based therapeutics is the difficulty in delivering these large, highly polar molecules to their sites of action in the cytosol or nucleus of tissue cells. While chemical modification of oligonucleotides and the utilization of various nanotechnology-based delivery approaches have been helpful, the delivery problem remains largely unresolved. We have taken an orthogonal approach to this problem and have developed small molecule compounds that enhance the functional delivery and pharmacological effectiveness of oligonucleotides by manipulating their intracellular trafficking. Here we propose to optimize compounds as in vivo probes; it seems likely that this effort will have a major impact on the entire field of oligonucleotide therapeutics.

R41 CA200189 (Parise/Frye, MPI)

09/01/15-08/31/16
NCI-STTR
Developing therapeutic inhibitors of CIB1 for breast cancer
Breast cancer (BC) is the largest cause of cancer related deaths in women worldwide. Triple negative breast cancer (TNBC) is an especially alarming form of breast cancer due to its resistance to hormone therapy and HER2-directed agents. In fact, no targeted therapy exists for TNBC. The intracellular protein, CIB1 appears to be an outstanding potential therapeutic target for several types of breast and other cancers, including TNBC. This proposal seeks to accelerate hit-to-lead optimization of small molecule inhibitors of CIB1 for preclinical testing in this disease.

R21AI111667 (Multiple PI: Braunstein/Frye)
3/1/2014 – 2/28/2016
NIH
Targeting SecA1 of Mycobacterium tuberculosis for Novel Drug Development
With the rise in drug resistant *Mycobacterium tuberculosis* (*Mtb*) strains, the need to develop new drugs for tuberculosis is greater than ever. The research in this proposal will assess the potential of targeting a novel pathway for *Mtb* drug development: the *Mtb* Sec export pathway. More specifically, we will investigate the potential of targeting the SecA1 component of the pathway. Because SecA proteins are conserved throughout bacteria, the results of this study may also aid efforts to develop new drugs for other bacterial pathogens.

R01 NS067688 (Zylka)
10/1/2009-9/30/2014
NIH Role: Investigator
Harnessing Ectonucleotidases to Treat Chronic Pain
In this application we propose to discover and develop novel pro-drugs targeting prostatic acid phosphatase for treating chronic pain.

R01GM98894 (Zhang)
7/1/2011-6/30/2014
NIH Role: Investigator
High-throughput Screens to Identify Modulators of Phospholipase C Isozymes
The focus of this proposal is to develop a fluorescent assay and integrate it with a series of secondary assays for a complete set of high-throughput screening protocols to identify modulators of PLC activity.

BOA 29XS126 (Frye, Lead PI)
7/22/2010-4/30/2014
NCI/SAIC-Frederick, Inc. (Task Order 07)
Developing Small Molecule Mer Inhibitor Candidates for Novel Treatment of Acute Lymphoblastic Leukemia.
This contract funds specific tasks and milestones to develop Mer-selective small molecules as drug candidates to treat ALL and as tool compounds to uncover the mechanism whereby Mer activation sustains the survival and perhaps contributes to the maturity and niche adaptation of lymphoid malignancies and selected carcinomas that overexpress Mer as defined in the Statement of Work.

RC1 GM090732 (Frye)
9/30/2009-8/31/2011

NIH Challenge Grant
Discovery of Small Molecule MBT Domain Antagonists
We propose to develop potent antagonists of methyl-lysine recognition by human and *Drosophila* MBT domain containing proteins in order to permit exploration of the biological consequences of blocking this recognition in cell based and in vivo models with relevance to normal and disease biology. Specifically, we propose to 1) develop biological assays for human and *Drosophila* MBT containing proteins; 2) use focused and diversity based screening, virtual screening, and structure-based design to identify potential antagonists of methyl-lysine recognition; and 3) optimize hits via iterative design, synthesis, and biological assessment.

HRSA-09-163 (Frye)
09/01/2009-6/30/2010
DHHS HRSA
Automated Compound Storage System for the Center for Integrative Chemical Biology and Drug Discovery at the University of North Carolina at Chapel Hill
The award provides partial funding for the acquisition of an automated compound storage and retrieval system for storing liquid aliquots of the Center's collection of small molecules for use in drug discovery and as tool compounds. Samples will be stored to facilitate cherry-picking compounds or sets of compounds and arraying them in user specific formats. No salary support is included.

BOA 29XS126 (Frye, Lead PI)
9/1/2009-12/29/2009
NCI/SAIC-Frederick, Inc. (Task Order 01)
For participation in a network collaborative effort to develop a shared curation filter for a pooled compound file library consisting of the curated libraries of each CBC member organization using standard criteria agreed upon by all members.

PROFESSIONAL SERVICE

Pharmaceutical Industry Consulting and SAB Activities *(active)*

Artios Pharmaceuticals (SAB member, consultant)

Astex Inc. (SAB member, consultant)

Cullgen Inc. (SAB member, consultant)

Flare Therapeutics (SAB member, consultant)

Mitokinin (consultant)

Larkspur (consultant)

Meryx Pharmaceuticals Inc. (http://www.meryxpharma.com/home, Founder, former CEO and President (noncompensated)) – transitioned to member of Board in Dec 2021.

Nonprofit Advisory Roles

Chair of the Drug Discovery Committee for Cancer Research UK, London, 2014-2018.

Member of A*STAR Project Review Committee of the Experimental Therapeutics Center, Biomedical Research Council, Singapore, 2014-2018.

Co-Founder of the Academic Drug Discovery Consortium and member of board, 2013 – 2020, Vice-president 2016-2020. (http://www.addconsortium.org).

Member of SAB for the Chemical Biology Consortium of Sweden, 2012 - 2016.

Member of the SGC Chemical Probes Scientific Committee, 2015 – present.

Member of SAB for Baylor University's CPRIT Drug Discovery Program, 2016 - present.

Collaborative Ependymoma Research Network (CERN), SAB Member, 2010-2014.

Advisory Committee to the Canadian Cancer Stem Cell Consortium (CSCC), 2011.

Moffitt Cancer Center P01 External Advisory Board member, January, 2009.

National Academy of Sciences invited participant: "The Chemistry Platform for Pharmaceuticals: A scoping meeting", August, 2008.

Harvard Medical School Therapeutics Strategy Retreat invited speaker, October 2008.

North Carolina Drug Discovery Center of Innovation Steering Group and Scientific Advisory Board, January 2008 – 2010.

Scientific Advisory Committee member of the Structural Genomics Consortium, August 2007 – 2011.

External Advisory Board Member to UNC Department of Chemistry, 2003 – 2007.

Physical and Mathematical Sciences Advisory Board Member, NCSU, 2003 – 2010.

Peer reviewer for funding agencies

Member, Synthetic and Biological Chemistry A (SCBA) NIH study section, October 2018 – June 2022.

Member, NCTracs study section, UNC CTSA, September 2018 – December 2021.

Reviewer for the NCI Intramural Research Program: Lymphoid Malignancies Branch, July 2017.

Chair of the Quinquennial review of the Institute for Cancer Research CRUK Drug Discovery Unit, Sutton, UK, September 2016.

Chair of the Quinquennial review of the Cancer Technology Discovery Laboratories, Cancer Research UK, February, 2013.

Ad-hoc Reviewer for Drug Discovery and Molecular Pharmacology Study Section, NIH, June 2013.

NIH Molecular Libraries Probe Network, Member of Probe Report Review Board, 2010-2011, 2013.

Ad hoc reviewer, Synthetic and Biological Chemistry B (SBCB), October 14-15, 2012.

External Reviewer for MD Anderson Department of Experimental Therapeutics, September 2012.

External reviewer for the Higuchi Biosciences Center at U. Kansas, January 2012.

Cooperative Research Center for Cancer Therapeutics, Australia, Third Year Review Panel Member, March 2011.

St. Jude Children's Hospital, Chemical Biology and Therapeutics Review Group, August, 2010.

University of Dundee Division of Biological Chemistry and Drug Discovery, Quinquennial Review Board member, September, 2009.

Wellcome Trust, Peer Reviewer, 2010-present.

BBSRC UK Research Council, Peer Reviewer, 2011.

Research Corporation for Science Advancement, 2009-2010.

UNC Gillings Innovation Lab Proposals, Reviewer, 2010.

Cancer Research UK, Program Reviewer, 2010.

North Carolina Biotechnology Center, Education Enhancement Grant Reviewer, 2009.

Peer reviewer for scholarly journals

ACS Medicinal Chemistry Letters
ACS Pharmacology and Translational Science (editorial board member)
Biochemistry
Bioorganic and Medicinal Chemistry
Drug Discovery Today
Cell
Cell Chemical Biology (editorial board member)
Journal of Medicinal Chemistry
Journal of Clinical Investigation
Nature
Nature Chemical Biology
Nature Biotechnology
Medicinal Chemistry Communications
Molecular Cancer Therapeutics
Pharmaceutical Research

Proceedings of the National Academy of Sciences
Science
Tetrahedron Letters

Service to UNC-CH

Co-leader (with Gary Johnson) of Molecular Therapeutics Program in LCCC, 2013-March 2022.
Member of Team Science ARPT Committee, Dec. 2017-Dec. 2021.
Member of LCCC Associate Director Search Committee, Chair: Ned Sharpless, 2013.
Member of the Chancellor's Innovation Circle, Chair: Judith Cole, 2009-2010.
Member of Biochemistry and Biophysics Faculty Search Committee, Chair: Leslie Parise, 2007-2010.
Member of the University Cancer Research Fund Therapeutics Theme Team, Chair: Shelley Earp, 2009-2021.

Service to the School of Pharmacy

Member of ESOP Conflict of Interest Committee, 2013 – present.
Member of ESOP Full Professor's Committee, 2010 - present.
Member of Senior Faculty Search Committee, Chair: Jian Liu, 2012.
Member of Senior Faculty Search Committee, Chair: Hal Kohn, 2010-2011.
Chair of Faculty Search Committee for Carolina Partnership CICBDD Recruitment, 2009.
Seminar speakers hosted: Haian Fu (Emory), Mike Pollastri (Northeastern), Kevan Shokat (UCSF), Aled Edwards (U. Toronto), Cheryl Arrowsmith (U. Toronto), Ben Cravatt (Scripps), Jeff Stafford (Quanticel), Tim Willson (GSK), Paul Thompson (Scripps Florida).
Member of Search Committee for ESOP Human Resources Staff Hire, 2008.
Organized and chaired the 2008 Chapel Hill Drug Conference.

PhD Thesis Committees *(Advisor, affiliation)*

Katherine Albanese (Marcey Waters, Department of Chemistry)
Christopher Travis (Marcey Waters, Department of Chemistry)
Han Wee Ong (David Drewry, Chemical Biology and Medicinal Chemistry (CBMC))
Devan Shell (Ken Pearce, Chemical Biology and Medicinal Chemistry (CBMC)
Rebecca Johnson (Lindsey James, CBMC)
Peter Buttery (Lindsey James, CBMC)
Caroline Foley (Stephen Frye and Lindsey James, Department of Chemistry)
Isabelle Engelberg (Stephen Frye and Lindsey James, CBMC)
Caleb Vogt (chair, Jeff Aubé, CBMC)
Tory Haberman (Albert Bowers, CBMC)
Kathryn Headley (Nate Hathaway, Genetics and Molecular Biology)
Kimberly Barnash (Stephen Frye, CBMC)
Kelsey Lamb (Stephen Frye, CBMC)
Junghyun Lee (Stephen Frye, CBMC)
Stephen Capuzzi (chair, Alex Tropsha, CBMC)
Morgan Chapman (Scott Singleton, CBMC)
Anna Chiarella (Nate Hathaway, Genetics and Molecular Biology)
Jon Edwards (Matt Redinbo, Chemistry)
David Grawoig (Kevin Weeks, Chemistry)

Venita Gresham (Howard McLeod, Pharmacotherapy and Experimental Therapeutics)
Paul Himes (chair, Albert Bowers, CBMC)
Jui-Hua Hsien (Alex Tropsha, CBMC)
Amber King (Hal Kohn, CBMC)
Samantha Kistler (Sharon Campbell, Biochemistry)
Kyle Konze (Jian Jin, CBMC)
Man Lou (Alex Tropsha, CBMC)
Pierre Morieux (Hal Kohn, CBMC)
Tim O'Leary (Jian Liu, CBMC)
Nate Oien (David Lawrence, CBMC)
Michael Perfetti (Stephen Frye, CBMC)
Sherket Peterson (Jian Liu, CBMC)
Joe Rittiner (Mark Zylka, Neurosciences)
Jacob Stuckey (Stephen Frye, CBMC)
Wei Sun (Qisheng Zhang, CBMC)
Brett Wallace (Matt Redinbo, Chemistry)
Marty Whittle (Gary Johnson, Pharmacology)
Brittany Wright (Mark Zylka, Neurosciences)