M. Kyle Hadden

University of Connecticut
School of Pharmacy
Department of Pharmaceutical Sciences
Division of Medicinal Chemistry

69 North Eagleville Road, Unit 3092
Storrs, CT 06269-3092
Ph: (860) 486-8446
kyle.hadden@uconn.edu

Employment

Professor of Medicinal Chemistry — 2021-present
University of Connecticut
Department of Pharmaceutical Sciences

Director of Research and Graduate Programs — 2021-present
University of Connecticut School of Pharmacy

Associate Professor of Medicinal Chemistry — 2016-2021
University of Connecticut
Department of Pharmaceutical Sciences

Assistant Professor of Medicinal Chemistry — 2009-2016
University of Connecticut
Department of Pharmaceutical Sciences
Co-Head, UConn High-Throughput Screening Facility

University of Kansas Cancer Center Postdoctoral Fellow — 2007-2008
University of Kansas Postdoctoral Researcher — 2005-2007
Department of Medicinal Chemistry
Advisor: Brian S. J. Blagg, Ph.D.

Postdoctoral Researcher — 2004-2005
University of Wisconsin-Madison
Department of Biochemistry
Advisor: Rebecca I. Montgomery, Ph.D.

Education

Medical University of South Carolina — 2000-2004
Ph.D., Medicinal Chemistry
Department of Pharmaceutical Sciences
Dissertation Advisor: Thomas A. Dix, Ph.D.

Wofford College — 1996-2000
Bachelor of Science, Chemistry

Affiliations

Connecticut Institute for Clinical and Translational Sciences (CICATS)
- Structural Biology Core Interest Group — 2016-present
- New Pathways to Drug Discovery Core Interest Group — 2012-present

Carole and Ray Neag Comprehensive Cancer Center, University of Connecticut Health Center	2009-present
University of Kansas Cancer Center	2007-2008
American Chemical Society	2001-present
ACS Division of Medicinal Chemistry	2007-present

Honors and Awards

UConn Provost's Award - General Education Course Enhancement	2014
American Cancer Society Research Scholar Award	2013
Charles H. Hood Foundation Child Health Research Award	2012
V Foundation for Cancer Research, V Scholar Award	2010
University of Kansas Cancer Center Postdoctoral Fellowship	2007-2008
American Foundation for Pharmaceutical Education Predoctoral Fellowship	2002-2004

Conferences

Invited Speaker:

1. Latest Trends in Organic Synthesis – Ontario, Canada; August 10, 2012.
   "Novel Sterol Probes for Investigating the Hedgehog Signaling Pathway"
2. NERM, American Chemical Society – New Haven, CT; October 23, 2013.
   "Sterol Probes for Investigating the Hedgehog Signaling Pathway"
3. 249th National Meeting of the American Chemical Society – Denver, CO; March 22, 2015.
   "Small Molecule Modulators of Hedgehog Signaling as Therapeutic Agents"
4. 251st National Meeting of the American Chemical Society – San Diego, CA; March 16, 2016.
   "Identification of small molecule translesion synthesis inhibitors that target Rev1 protein-protein interactions."
5. 37th National Medicinal Chemistry Symposium – New York, NY; June 26, 2022.
   "Structural approach to identify leads scaffolds for protein-protein interaction targets."
6. 69th Gordon Conference on Natural Products and Bioactive Compounds – Andover, NH; August 3, 2022.
   "Identification and Early-Stage Development of 8-Hydroxyquinoline Derivatives That Suppress GLI1-Mediated Transcription Through Multiple Mechanisms."

Abstracts:

1. Banerjee, U.; DeBerardinis, A. M.; Sail, V.; Hadden, M. K. Synthesis and evaluation of vitamin D3 analogues as hedgehog pathway inhibitors. 244th ACS National Meeting & Exposition. Philadelphia, PA. August 19-23, 2012. Abstract 299.
2. DeBerardinis, A. M.; Banerjee, U.; Hadden, M. K. Design, synthesis, and evaluation of vitamin D3 analogues as selective hedgehog signaling pathway inhibitors. 244th ACS National Meeting & Exposition. Philadelphia, PA. August 19-23, 2012. Abstract 300.
3. DeBerardinis, A. M.; Banerjee, U.; Hadden, M. K. Development of selective vitamin D3 analogues as hedgehog signaling pathway inhibitors. NERM-ACS, New Haven, CT. October 25, 2013. Oral Presentation 179.
4. Banerjee, U.; DeBerardinis, A. M.; Hadden, M. K. Identification of hedgehog signaling inhibitors based on vitamin D3 scaffold containing modified side chains. NERM-ACS, New Haven, CT. October 25, 2013. Oral Presentation 180.

5. Hadden, M K.; DeBerardinis, A. M.; Banerjee, U.; Pace, J.; Raccuia, D. Probing structural requirements for itraconazole inhibition of hedgehog signaling. Keystone Symposia: Developmental Pathways and Cancer: Wnt, Notch, and Hedgehog. Banff, Alberta, Canada. February 2-7, 2014. Abstract 1033.
6. DeBerardinis, A. M.; Madden, D.; Banerjee, U.; Sail, V.; Hadden, M. K. Design and development of vitamin D3 analogues as selective hedgehog pathway inhibitors. Keystone Symposia: Developmental Pathways and Cancer: Wnt, Notch, and Hedgehog. Banff, Alberta, Canada. February 2-7, 2014. Abstract 1025.
7. Maschinot, C. A.; DeBerardinis, A. M.; Hadden, M. K. Synthesis and biological evaluation of vitamin D3 analogues as selective hedgehog pathway inhibitors. 2015 Annual Meeting of the American Association of Cancer Research, Philadelphia, PA. April 18-22, 2015. Abstract 2771.
8. Pace, J. R. Banerjee, U.; DeBerardinis, A. M.; Hadden, M. K. Synthesis and evaluation of itraconazole analogues for hedgehog pathway inhibition. 2015 Annual Meeting of the American Association of Cancer Research, Philadelphia, PA. April 18-22, 2015. Abstract 1815.
9. DeBerardinis, A. M.; Pace, J. R.; Raccuia, D.; Hadden, M. K. Reconstructing the itraconazole scaffold towards improved specificity for hedgehog signaling inhibition. 2015 Annual Meeting of the American Association of Cancer Research, Philadelphia, PA. April 18-22, 2015. Abstract 1394.
10. Maschinot, C. A.; Hadden, M. K. Vitamin D3 analogues as selective hedgehog pathway inhibitors. 251st ACS National Meeting & Exposition. San Diego, CA. March 13-17, 2016. Abstract MEDI 53.
11. Pace, J. R.; Hadden, M. K. Repurposing itraconazole as an anticancer chemotherapeutic. 251st ACS National Meeting & Exposition. San Diego, CA. March 13-17, 2016. Abstract MEDI 54.
12. Teske, K. A.; Pace, J. R.; Hadden, M. K. Development of azole antifungal analogues to treat cancers dependent on hedgehog signaling. 254th ACS National Meeting & Exposition. Washington, D.C. August 20-24, 2017. Abstract MEDI 52.
13. Ozen, Z.; McCarthy, K. R.; Chow, S.; Chatterjee, N.; Walker, G.; Hadden, M. K. Identification and characterization of small molecule scaffolds as inhibitors of the translesion synthesis pathway. 254th ACS National Meeting & Exposition. Washington, D.C. August 20-24, 2017. Abstract MEDI 60.
14. Maschinot, C. A.; Wen, J.; Hadden, M. K. Selective inhibition of hedgehog signaling by analogues of vitamin D3 and calcitriol. 254th ACS National Meeting & Exposition. Washington, D.C. August 20-24, 2017. Abstract MEDI 65.
15. Zaino, A. M.; Dash, R. C.; Hadden, M. K. Studies towards the identification of small molecule regulators of SWI/SNF chromatin remodeling. 254th ACS National Meeting & Exposition. Washington, D.C. August 20-24, 2017. Abstract MEDI 66.
16. Dash, R. C.; Sail, V.; Hadden, M. K. Design and validation of a peptidomimetic ligand as a translesion synthesis inhibitor. 254th ACS National Meeting & Exposition. Washington, D.C. August 20-24, 2017. Abstract MEDI 100.
17. Pace, J. R.; Hadden, M. K. Synthesis and evaluation of itraconazole analogues for the treatment of medulloblastoma. 254th ACS National Meeting & Exposition. Washington, D.C. August 20-24, 2017. Oral Presentation, Awards Symposium, Abstract MEDI 226.

18. Zaino, A. M.; Dash, R. C.; Hadden, M. K. Studies towards the identification of small molecule regulators of the ADD domain of ATRX. Keystone Symposia: Epigenetics and Human Disease. Banff, Alberta, CA. March 17-22, 2019.
19. Zaino, A. M.; Dash, R. C.; McPherson, K. S.; Korzhnev, D. M.; Hadden, M. K. Identification, design, synthesis, and evaluation of small molecule inhibitors of translesion synthesis. Drug Discovery Chemistry – Virtual Conference, May 18-20, 2021.

Invited Talks

1. University of Kansas – Department of Medicinal Chemistry, September 12, 2013. "Hedgehog Pathway Modulators as Therapeutic Agents"
2. Hunter College – Department of Chemistry, September 12, 2014. "Hedgehog Pathway Inhibitors to Treat Basal Cell Carcinoma and Medulloblastoma"
3. Purdue University – Department of Medicinal Chemistry, January 6, 2015. "Hedgehog Pathway Modulators as Therapeutic Agents"
4. University of North Carolina – Department of Medicinal Chemistry, January 14, 2015. "Hedgehog Pathway Modulators as Therapeutic Agents"
5. St. Jude Children's Research Hospital – Department of Chemical Biology and Experimental Therapeutics, February 2, 2015. "Hedgehog Pathway Modulators as Therapeutic Agents"
6. University of Connecticut Health Center – Department of Molecular Biology and Biophysics, April 2, 2015. "Hedgehog Pathway Modulators as Therapeutic Agents"
7. University of Oklahoma – Department of Chemistry and Biochemistry, September 8, 2017. "Design and Development of Targeted Anti-Cancer Chemotherapeutics"
8. University of Colorado-Denver Anschutz School of Pharmacy, March 29, 2018. "Design and Development of Targeted Anti-Cancer Chemotherapeutics"
9. University of Connecticut – Department of Animal and Nutritional Sciences, September 20, 2019. "Small Molecule Anti-Cancer Drug Development"

Funding

Current

6/1/2019-5/31/2024 Direct Costs - $433,350/yr
NIH/NCI R01CA233959
Title: Inhibition of Translesion Synthesis as a Novel Strategy for Cancer Chemotherapy
Role: PI
The major goal of this project is to develop several promising small molecule scaffolds as translesion synthesis inhibitors for the treatment of lung cancer and lymphoma.

3/1/2020-2/28/25 Direct Costs - $318,588/yr
NIH/NCI R01CA247232
Title: Targeting Replication Stress Avoidance in Cancer
Role: Co-PI (Sharon Cantor, PI)
The major goal of this project is to understand and target cancer cell addictions to stress-tolerance pathways.

Completed

10/1/2019 – 6/30/2021 Direct Costs - $50,000/yr
UConn – Office of the Vice President for Research

Title: Repurposing the FDA Approved Itraconazole and Posaconazole to Treat Picornoviral Diseases
Role: PI (Multi-PI Grant, Simon White)
The major goal of this project is to determine whether itraconazole and posaconazole analogues hold potential as therapeutic treatments for a variety of diseases caused by picornoviruses.

12/01/2014-11/30/2020 (NCE) Direct Costs - $237,069/yr
NIH/NCI R01CA190617
Title: Itraconazole Analogues to Treat Medulloblastoma
Role: PI
The major goal of this project is to optimize the potency and drug-like properties of a lead itraconazole analogue synthesized in the Hadden lab as an Hh pathway inhibitor to treat medulloblastoma.

5/1/2017-12/31/20
Program in Innovative Therapeutics for Connecticut's Health (PITCH)
Title: Structure-Activity Relationships for a Novel Small Molecule Scaffold that Inhibits Cellular Translesion Synthesis
Role: Co-PI
This program provides chemistry and biology support for the in vitro and in vivo development of the phenazopyridine scaffold as inhibitors of translesion synthesis.

7/01/2019-9/30/2020 Direct Costs - $25,000/yr
UConn – Office of the Vice President for Research
Title: Development of Gli1 Inhibitors as Anti-Cancer Agents
Role: PI
The major goal of this project is to determine key early stage potency and pharmacokinetic parameters of a small molecule inhibitor of the transcription factor Gli1.

8/01/2015-7/31/2018 Direct Costs - $100,000/yr
NSF – Cellular Dynamics and Function/Chemistry of Life Processes
Title: Novel Biological Activities for the Vitamin D Class of *Seco*-Steroids
Role: PI
The major goal of this project is to utilize a chemical biology approach to explore and identify novel cellular targets of vitamin D3 and calcitriol.

7/1/2013-6/30/2018 Direct Costs - $150,000/yr
American Cancer Society – Research Scholar Award
Title: Vitamin D3 Analogues as Hedgehog Pathway Inhibitors.
Role: PI
The major goal of this project is to continue the early-stage development (in vitro and in vivo) of vitamin D3 analogues as selective Hh pathway inhibitors with anti-cancer potential for the treatment of basal cell carcinoma.

11/1/2016-4/30/2018 Total Direct Costs - $100,000
Gates Foundation – Phase I
Title: A Novel Platform for Screening Non-Hormonal Contraceptives
Role: Key Collaborator

The major goal of this project is to evaluate FDA-approved drugs in a unique screening assay to identify compounds that disrupt follicle rupture and exhibit potential as non-steroidal contraceptives.

7/01/2016-6/30/2017 Direct Costs - $25,000/yr
UConn – Office of the Vice President for Research
Title: Development of Translesion Synthesis Inhibitors as Anti-Cancer Drugs
Role: Co-PI
The major goal of this project is to continue the development of small molecule translesion synthesis inhibitors that target Rev1 as anti-cancer agents.

7/01/2016-6/30/2017 Direct Costs - $25,000/yr
UConn – Office of the Vice President for Research
Title: Developing Small Molecule Probes for the Chromatin Remodeler ATRX
Role: PI
The major goal of this project is to develop and implement screening assays to identify small molecules that inhibit the chromatin remodeling protein ATRX.

7/1/2014-6/30/2016 Direct Costs - $2,500/yr
University of Connecticut Provost's Office - General Education Course Enhancement Award
Title: Molecules in the Media
Role: Co-PI
The goal of this project is to develop and implement a general education science course designed to introduce students to the basic fundamentals of medicinal chemistry and drug discovery through discussions of various small and macromolecules that have received media attention.

9/1/2013-12/31/2015 Total Direct Costs - $25,000
Connecticut Institute for Clinical and Translational Sciences – Pilot Grant Award
Title: Translesion Synthesis DNA Polymerases as Targets for Anti-Cancer Drug Design.
Role: Co-PI
The major goal of this project is to develop new strategies for overcoming cisplatin resistance that exploit selective inhibition of key enzymes of the translesion synthesis (TLS) pathway. The Hadden lab's role in this project is to develop and optimize an FP-based high-throughput assay to identify small molecule inhibitors of protein-protein interactions involving the TLS DNA polymerase Rev1.

5/1/2013-10/31/2015 Direct Costs - $41,538/yr
State of Connecticut Department of Public Health – Biomedical Research Award
Title: Therapeutic Targeting of Vascular Permeability in Cardiovascular Ischemic Disease.
Role: Key Collaborator
The major goal of this project was to demonstrate that novel inhibitors of the phospholipase C-beta 2 (PLC-β2) enzyme can significantly reduce pathological vascular permeability and thus limit cardiac muscle damage and risk of heart failure that occurs after standard of care treatment for cardiac infarction. The Hadden lab's role in this project is to develop and implement a high-throughput screen to identify novel inhibitors of PLC-β2.

7/1/2012-12/30/2014 Direct Costs - $50,000/yr
UCHC/Storrs Regional Campus Incentive Grant Program – UCIG Grant Award
Title: High-Throughput Screen to Identify Therapeutics for Prader-Willi Syndrome.

Role: Co-PI
The major goal of this project was to develop a cell-based assay in human neurons derived from PWS patients and optimize the assay for high-throughput screening.

8/1/2012-7/31/2014 Direct Costs - $67,500/yr
Charles H. Hood Foundation – Child Health Research Award
Title: Vitamin D3 Analogues as Hedgehog Pathway Inhibitors.
Role: PI
The major outcome of this project was the identification of second generation vitamin D3 analogues that selectively target the Hh signaling pathway as potential treatments for medulloblastoma.

7/1/2012-6/30/2013 Total Direct Costs - $20,800
University of Connecticut Research Foundation – Faculty Large Grant Award
Title: Vitamin D3 Analogues as Hedgehog Pathway Inhibitors
Role: PI
The major outcome of this project was the identification of a novel VD3-based scaffold as a potent, selective inhibitor of Hh signaling.

7/1/2011-6/30/2013 Total Direct Costs - $15,000
NIH (NCI) – 1R21CA162470-01A1
Title: HDAC Inhibitors Inspired by Natural Products.
Role: Key Collaborator
The major outcome of this project was the development of a new class of tropolone-based small molecules as inhibitors of histone deacetylase with anti-cancer potential.

1/1/2011-12/31/2011 Total Direct Costs - $22,000
University of Connecticut Research Foundation – Faculty Large Grant Award
Title: Development of Cell-Based Dual-Luciferase Assays to Identify Modulators of Human Cellular Signaling Pathways.
Role: Co-PI
The major outcome of this project was the development and implementation of a cell-based assay to identify regulators of Hes1 gene expression as potential anti-cancer compounds.

11/01/2010-10/31/2012 Total Direct Costs - $200,000
V Foundation for Cancer Research – V Scholar Award
Title: A Chemical Biology Approach to Understanding the Anti-Cancer Effects of Vitamin D3.
Role: PI
The major outcomes for this project were the identification of vitamin D3 as a non-selective inhibitor of Hh signaling and the determination of a pharmacophore for vitamin D3-mediated inhibition of Hh activity.

11/01/2010-6/30/2011 Total Direct Costs - $221,530
Vice President for Research – University of Connecticut
Title: An Array of Equipment to Establish the University of Connecticut High-Throughput Screening Facility.
Role: PI
The major outcome of this project was the creation of the UConn High-Throughput Screening Facility as a core bioservices facility at the University of Connecticut.

Publications

Peer-Reviewed Research Articles:

1. Dusek, C. O.; Dash, R. C.; McPherson, K. S.; Calhoun, J. T.; Bezsonova, I.; Korzhnev, D. M.; Hadden, M. K. DNA sequence specificity reveals a role of the HLTF HIRAN domain in the recognition of trinucleotide repeats. *Biochemistry* **2022**, *61*, 992-1004.
2. Stanzione, M.; Zhong, J.; Wong, E.; Lasalle, T. J.; Wise, J. F.; Simoneau, A.; Myers, D. T.; Phat, S.; Sade-Feldman, M.; Lawrence, M. S.; Hadden, M. K.; Zou, L.; Farago, S.; Dyson, N. J.; Drapkin, B. J. Translesion DNA synthesis mediates acquired resistance to olaparib plus temozolomide in small cell lung cancer. *Sci. Adv.* **2022**, *8*, eabn1229.
3. Wen, J.; Hadden, M. K. Affinity-based protein profiling identifies vitamin D3 as a heat shock protein 70 antagonist that regulates hedgehog transduction in murine basal cell carcinoma. *Euro. J. Med. Chem.* **2022**, *228*, 114005.
4. Ikeh, K. E.; Lamkin, E. N.; Crompton, A.; Deutsch, J.; Fisher, K. J.; Gray, M.; Argyle, D. J.; Lim, W. Y.; Korzhnev, D. M.; Hadden, M. K.; Hong, J.; Zhou, P.; Chatterjee, N. REV1 inhibition enhances radioresistance and autophagy. *Cancers* **2021**, *13*, 5290.
5. Jiang, K.; Zhang, J.; Huang, Y.; Xiao, S.; Hadden, M. K.; Woodruff, T.; Sun, J. A novel platform utilizing Drosophila ovulation for non-hormonal contraceptive screening. *Proc. Natl. Acad. Sci. USA* **2021**, *118*, e2026403118.
6. McPherson, K. S.; Zaino, A. M.; Dash, R. C.; Rizzo, A. A.; Li, Y.; Hao, B.; Bezsonona, I.; Hadden, M. K.; Korzhnev, D. M. Structure-based drug design of phenazopyridine derivatives as inhibitors of Rev1 interactions in translesion synthesis. *ChemMedChem* **2021**, *16*, 1126-1132.
7. Dash, R. C.; Wen, J.; Zaino, A. M.; Morel, S. R.; Chau, L. Q.; Wechsler-Reya, R. J.; Hadden, M. K. Structure-based virtual screening identifies the 8-hydroxyquinoline scaffold as a new class of GLI1 inhibitors. *Mol. Ther. Oncolytics* **2021**, *20*, 265-276.
8. Chen, C.; Bosko, C.; McGeough, C.; McLean, R.; Zaino, A. M.; Hadden, M. K.; Peczuh, M. W. Exploring the physicochemical and antiproliferative properties of biaryl-linked [13]-macrodilactones. *Bioorg. Med. Chem.* **2020**, *28*, 115671.
9. Huang, C.; Bernard, D.; Zhu, J.; Dash, R. C.; Chu, A.; Knupp, A.; Hakey, A.; Hadden, M. K.; Garmendia, A.; Tang, Y. Small molecules block the interaction between porcine reproductive and respiratory syndrome virus and CD163 receptor and the infection of pig cells. *Virol. J.* **2020**, *17*, 116.
10. Bai, G.; Kermi, C.; Story, H.; Schiltz, C.; Bacal, J.; Zaino, A. M.; Hadden, M. K.; Eichman, B.; Lopes, M.; Cimprich, K. A. HLTF promotes fork reversal, limiting replication stress resistance and preventing multiple mechanisms of unrestrained DNA synthesis. *Mol. Cell* **2020**, *78*, 1237-1251.
11. Hadden, M. K.; Zaino, A. M. Introduction to medicinal chemistry: A five-day course for high school students. *J. Chem. Ed.* **2020**, *97*, 1543-1548.
12. Nayak, S.; Calvo, J. A.; Cong, K.; Peng, M.; Berthiaume, E.; Jackson, J.; Zaino, A. M.; Vindigni, A.; Hadden, M. K.; Cantor, S. B. Inhibition of the translesion synthesis polymerase Rev1 exploits replication gaps as a cancer vulnerability. *Sci. Adv.* **2020**, *6*, eaaz7808.
13. Zaino, A. M.; Dash, R. C.; Hadden, M. K. Probing the protein-protein interaction between the $ATRX_{ADD}$ domain and the Histone H3 tail. *Molecules* **2020**, *25*, 1500.
14. Wen, J.; Teske, K. A.; Hadden, M. K. Inhibition of hedgehog signaling by stereochemically defined *des*-triazole itraconazole analogues. *Bioorg. Med. Chem. Lett.* **2020**, *30*, 126794.

15. Pace, J. R.; Jog, R.; Burgess, D. J.; Hadden, M. K. Formulation and evaluation of itraconazole liposomes for hedgehog pathway inhibition. *J. Liposome Res.* **2020**, *30*, 305-311.
16. Wen J.; Chennamadhavuni, D.; Morel, S. R.; Hadden, M. K. Truncated itraconazole analogues exhibiting potent anti-hedgehog activity and improved drug-like properties. *ACS Med. Chem. Lett.* **2019**, *10*, 1290-1295.
17. Dash, R. C.; Ozen, Z.; McCarthy, K. R.; Chatterjee, N.; Harris, C. A.; Rizzo, A. A.; Walker, G. C.; Lorzhnev, D. M.; Hadden, M. K. Virtual pharmacophore screening identifies small-molecule inhibitors of the Rev1-CT/RIR protein-protein interaction. *ChemMedChem* **2019**, *14*, 1610-1617.
18. Pace, J. R.; Teske, K. A.; Chau, L. Q.; Dash, R. C.; Zaino, A. M.; Wechsler-Reya, R. J.; Hadden, M. K. Structure-activity relationships for itraconazole-based triazolone analogues as hedgehog pathway inhibitors. *J. Med. Chem.* **2019**, *62*, 3873-3885.
19. Ozen, Z.; Dash, R. C.; McCarthy, K. R.; Chow, S. A.; Rizzo, A. A.; Korzhnev, D. M.; Hadden, M. K. Small molecule scaffolds that disrupt the Rev1-CT/RIR protein-protein interaction. *Bioorg. Med. Chem.* **2018**, *26*, 4301-4309.
20. Teske, K. A.; Dash, R. C.; Morel, S. R.; Chau, L. Q.; Wechsler-Reya, R. J.; Hadden, M. K. Development of posaconazole-based analogues as hedgehog signaling pathway inhibitors. *Euro. J. Med. Chem.* **2019**, *163*, 320-332.
21. Maschinot C. A.; Chau, L. Q.; Wechsler-Reya, R. J.; Hadden, M. K. Synthesis and evaluation of third generation vitamin D3 analogues as inhibitors of hedgehog signaling. *Euro. J. Med. Chem.* **2019**, *162*, 495-506.
22. Thompson, E. N.; Sail, V.; Raccuia, D. S.; Hadden, M. K. Probing *seco*-steroid inhibition of the hedgehog signaling pathway. *Mol. Cell. Biochem.* **2019**, *450*, 75-85.
23. Dash, R. C.; Ozen, Z.; Rizzo, A. A.; Lim, S.; Korzhnev, D. M.; Hadden, M. K. Structural approach to identify a lead scaffold that targets the translesion synthesis polymerase Rev1. *J. Chem. Inf. Model.* **2018**, *58*, 2266-2277.
24. Dash, R. C.; Zaino, A. M.; Hadden, M. K. A metadynamics approach to understanding the recognition mechanism of the histone H3 tail with the $ATRX_{ADD}$ domain. *BBA Gene Regul. Mech.* **2018**, *1861*, 594-602.
25. Wen, J. and Hadden, M. K. Structure-activity relationship studies of vitamin D3 analogues containing an ether or thioether linker as hedgehog pathway inhibitors. *ChemMedChem*, **2018**, *13*, 748-753.
26. Maschinot, C. A.; Hadden, M. K. Synthesis and evaluation of vitamin D3 analogues with C-ring modifications as inhibitors of hedgehog signaling. *Bioorg. Med. Chem. Lett.* **2017**, *27*, 4011-4014.
27. Sail, V.; Rizzo, A. A.; Chatterjee, N.; Dash, R. C.; Ozen, Z.; Walker, G. C.; Korzhnev, D. M.; Hadden, M. K. Identification of small molecule translesion synthesis inhibitors that target the Rev1-CT/RIR protein-protein interaction. *ACS Chem. Biol.* **2017**, 12, 1903-1912.
28. Dash, R. C.; Maschinot, C. R.; Hadden, M. K. A molecular dynamics approach to identify an oxysterol-based hedgehog pathway inhibitor. *Biochim. Biophys. Acta* **2017**, *1861*, 168-177.
29. Pace, J. R.; DeBerardinis, A. M.; Sail, V.; Tacheva-Grigorova, S. K.; Chan, K.; Tran, R.; Raccuia, D. S.; Wechsler-Reya, R. J.; Hadden, M. K. Repurposing the clinically efficacious anti-fungal agent itraconazole as an anti-cancer chemotherapeutic. *J. Med. Chem.* **2016**, *59*, 3635-3649.

30. *Maschinot, C. A.; Corman, A. R.; DeBerardinis, A. M.; Hadden, M. K. Synthesis and evaluation of osteogenic oxysterols as hedgehog pathway activators. *ChemMedChem*, **2016**, 11, 679-686.
    *Front Cover Featured Article
31. DeBerardinis, A. M.; Raccuia, D. S.; Maschinot, C. A.; Thompson, E.; Hadden, M. K. Vitamin D3 analogues that contain modified A- and seco-B-rings as hedgehog pathway inhibitors. *Euro. J. Med. Chem.* **2015**, *93*, 156-171.
32. Banerjee, U.; DeBerardinis, A. M.; Hadden, M. K. Design, synthesis, and evaluation of hybrid vitamin D3 side chain analogues as hedgehog pathway inhibitors. *Bioorg. Med. Chem.* **2015**, *23*, 548-555.
33. DeBerardinis, A. M.; Madden, D.; Banerjee, U.; Sail, V.; De Carlo, D.; Lemieux, S. M.; Meares, A.; Hadden, M. K. Structure-activity relationships for vitamin D3-based aromatic A-ring analogues as hedgehog pathway inhibitors. *J. Med. Chem.* **2014**, *57*, 3724-3736.
34. DeBerardinis, A. M.; Lemieux, S.; Hadden, M. K. Analogues of the Inhoffen-Lythgoe diol with anti-proliferative activity. *Bioorg. Med. Chem. Lett.* **2013**, *23*, 5367-5370.
35. DeBerardinis, A. M.; Banerjee, U.; Hadden, M. K. Identification of vitamin D3-based hedgehog pathway inhibitors that incorporate an aromatic A-ring isostere. *ACS Med. Chem. Lett.* **2013**, *4*, 590-595.
36. Sail, V.; Hadden, M. K. Identification of small molecule Hes1 modulators as potential anti-cancer chemotherapeutics. *Chem. Biol. Drug Des.* **2013**, *81*, 334-342.
37. Viswanathan, K.; Ononye, S. N.; Cooper, H. D.; Hadden, M. K.; Anderson, A. C.; Wright, D. L. Viridin analogs derived from steroidal building blocks. *Bioorg. Med. Chem. Lett.* **2012**, *22*, 6919-6922.
38. Oblak, E. Z.; Bolstad, E. S. D.; Ononye, S. N.; Priestley, N. D.; Hadden, M. K.; Wright, D. L. The furan route to tropolones: probing the antiproliferative effects of β-thujaplicin analogs. *Org. Biomol. Chem.* **2012**, *10*, 8597-8604.
39. Corman, A.; DeBerardinis, A. M.; Hadden, M. K. Structure-activity relationships for side chain oxysterol agonists of hedgehog signaling. *ACS Med. Chem. Lett.* **2012**, *3*, 828-833.
40. DeBerardinis, A. M.; Banerjee, U.; Miller, M.; Lemieux, S.; Hadden, M. K. Probing the structural requirements for vitamin D3 inhibition of hedgehog signaling. *Bioorg. Med. Chem. Lett.* **2012**, *22*, 4859-4863.
41. Banerjee, U.; Ghosh, M.; Hadden, M. K. Evaluation of vitamin D3 A-ring analogues as hedgehog pathway inhibitors. *Bioorg. Med. Chem. Lett.* **2012**, *22*, 1330-1334.
42. Hadden, M. K. and Blagg, B. S. J. Synthesis and evaluation of radamide analogues, a chimera of radicicol and geldanamycin. *J. Org. Chem.* **2009**, *74*, 4697-4704.
43. Hadden, M. K.; Hill, S.; Davenport, J.; Matts, R. L.; Blagg, B. S. J. Synthesis and evaluation of Hsp90 inhibitors that contain the 1,4-naphthoquinone scaffold. *Bioorg. Med. Chem.* **2009**, *17*, 634-640.
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48. Hadden, M. K.; Blagg, B. S. J. Cytotoxic small molecule dimers and their inhibitory activity against human breast cancer cells. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 5063-5067.
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51. Avila, C.; Hadden, M. K.; Ma, Z.; Kornilayev, B. A.; Ye, Q. Z.; Blagg, B. S. J. High-throughput screening for Hsp90 ATPase inhibitors. *Bioorg. Med. Chem. Lett*. **2006**, *16*, 3005-3008.
52. Hadden, M. K.; Orwig, K. S.; Kokko, K. P.; Mazella, J.; Dix, T. A. Design, synthesis, and evaluation of the antipsychotic potential of orally bioavailable neurotensin(8-13) analogues containing non-natural arginine and lysine residues. *Neuropharmacology.* **2005**, *49*, 1149-1159.
53. Hadden, M. K.; Kokko, K. P.; Dix, T. A. Asymmetric synthesis of w-bromo-2(S)-methyl acids as precursors for novel arginine, lysine, and mercapto residues. *Syn. Comm.* **2005**, *35*, 1675-1680.
54. Hadden, M. K.; Walle, T.; Dix, T. A. Cellular uptake of a radiolabelled analogue of neurotensin in the caco-2 cell model. *J. Pharm. and Pharmacol.* **2005**, *57*, 327-333.
55. Kokko, K. P.; Hadden, M. K.; Price, K. L.; Orwig, K. S.; See, R. E.; Dix, T. A. Behavioral effects of stable, receptor-selective neurotensin[8-13] analogues that cross the blood-brain barrier. *Neuropharmacology*. **2003**, *48*, 417-425.
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<u>Peer-Reviewed Review Articles:</u>

1. Dash, R. C.; Hadden, M. K. Protein-protein interactions in translesion synthesis. *Molecules*, **2021**, *26*, 5544.
2. Wen, J.; Hadden, M. K. Medulloblastoma drugs in development: Current leads, trials and drawbacks. *Euro. J. Med. Chem.* **2021**, *215*, 113268.
3. Dusek, C.; Hadden, M. K. Targeting the GLI family of transcription factors for the development of anti-cancer drugs. Invited Review. *Expert Opin. Drug Discov.* **2021**, *16*, 289-302.
4. Patel, S.; Dash, R. C.; Hadden, M. K. Translesion synthesis inhibitors as a new class of cancer chemotherapeutics. Invited Review. *Expert Opin. Inv. Drugs.* **2021**, *30*, 13-24.
5. Teske, K. A.; Hadden, M. K. Methyllysine binding domains: Structural insight and small molecule probe development. Invited Review. *Euro. J. Med. Chem.* **2017**, *136*, 14-35.
6. Korzhnev, D. M.; Hadden, M. K. Targeting the translesion synthesis pathway for the development of anti-cancer chemotherapeutics. Invited Review *J. Med. Chem.* **2016**, *59*, 9321-9336.

7. Maschinot, C. A.; Pace, J. R.; Hadden, M. K. Synthetic small molecule inhibitors of Hh signaling as anti-cancer chemotherapeutics. Invited Review *Curr. Med. Chem.* **2015**, 22, 4033-4057.
8. Hadden, M. K. Targeting GLI proteins in human cancer by small molecules (WO2014116651 A1): a patent evaluation. Invited Evaluation. *Expert Opin. Ther. Patents* **2015**, *25*, 613-617.
9. Banerjee, U.; Hadden, M. K. Recent advances in the design of hedgehog pathway inhibitors for the treatment of malignancies. Invited Review. *Expert Opin. Drug Discov.* **2014**, *9*, 751-771.
10. Hadden, M. K. Hedgehog pathway agonism: Therapeutic potential and small molecule development. *ChemMedChem* **2014**, *9*, 27-37.
11. Lemieux, S.; Hadden, M. K. Targeting the fibroblast growth factor receptors for the treatment of cancer. *Anti-Cancer Agents Med. Chem.* **2013**, *13*, 748-761.
12. Hadden, M. K. Hedgehog pathway inhibitors: a patent review (2009-present). Invited Review. *Expert Opin. Ther. Patents* **2013**, *23*, 345-361.
13. Sail, V.; Hadden, M. K. Notch pathway modulators as anticancer chemotherapeutics. Annual Reports in Medicinal Chemistry. Ed. Manoj Desai. Vol. 47, ARMC, UK: Academic Press, 2012, 267-280.
14. DeCarlo, D.; Hadden, M. K. Oncoepigenomics: Making histone-lysine methylation count. *Eur. J. Med. Chem.* **2012**, *56*, 179-194.
15. Hadden, M. K.; Blagg, B. S. J. Dimeric approaches to anti-cancer chemotherapeutics. *Anti-Cancer Agents Med. Chem.* **2008**, *8*, 807-816.
16. Hadden, M. K.; Lubbers, D. J.; Blagg, B. S. J. Geldanamycin, radicicol, and chimeric inhibitors of the Hsp90 N-terminal ATP binding site. *Curr. Top. Med. Chem*. **2006**, *6*, 1173-1182.

Book Chapters:

1. Blagg, B. S. J.; Hadden, M. K. "Hsp90 Inhibitors." Burger's Medicinal Chemistry, Drug Discovery and Development. Eds. Donald Abraham and David Rotella, 7th ed. Vol 6. 2010.
2. Hadden, M. K. "Hedgehog and Vitamin D Signaling Pathways in Development and Disease." Vitamin D Hormone. Vitamins & Hormones. Ed. Gerald Litwack. Elsevier. Volume 100, 2016, 231-253.

Awarded Patents

1. Itraconazole Analogues and Methods of Use Thereof. US Patent No. 9,650,365. Awarded May 16, 2017.
2. Itraconazole Analogues and Methods of Use Thereof. US Patent No. 9,839,636. Awarded December 12, 2017.

Patent Applications

1. Small Molecule Inhibitors of DNA Translesion Synthesis. Provisional Patent Application filed by the University of Connecticut, August 2017.
2. Analogs of Vitamin D3 and Calcitriol and Uses Thereof. Provisional Patent Application filed by the University of Connecticut, August 2017.
3. Azole Analogs and Methods of Use Thereof. Provisional Patent Application filed by the University of Connecticut, August 2017.

Teaching and Mentoring

Teaching Activities:

School of Pharmacy:

PHRX 3002 - Foundations in Bioorganic Chemistry: 2009-present (Coordinator)
PHRX 3012 - Pharmacy Research Seminar: 2011-2013 (Coordinator)
PHRX 3009 – Principles of Drug Action: 2016-2017 (Coordinator)

Graduate Education:

PHAR 5302 – Chemical Biology and Drug Design: 2015-present (Co-coordinator)
PHAR 5393 – Seminar in Medicinal Chemistry 2010-present (Coordinator)
Recurring Guest Lectures: PHAR 5297 – Drug Discovery and Development – 2009-present
PHAR 5471 – Advanced Pharmacology I – 2013-present

Mentoring Activities:

Graduate Students:

1. Upasana Banerjee – 2009-2014 (Ph.D. 2014): ACS Division of Medicinal Chemistry Travel Award, 2012; MEDI-ACSMCL Poster Award, Fall 2012. Graduate Dissertation Fellowship, 2013; Boehringer-Ingelheim Medicinal Chemistry Intern, 2013.
2. Jennifer Pace – 2013-2017 (Ph.D. 2017): ACS Division of Medicinal Chemistry Predoctoral Fellowship (2016-2017).
3. Chad Maschinot – 2013-2018 (Ph.D. 2018).
4. Angela Zaino – 2016-2021 (Ph.D. 2021).
5. Jackson Calhoun – 2021-present.
6. Noah Harrahill – 2021-present.

Postdoctoral Researchers:

1. Albert DeBerardinis – 2011-2015.
2. Kelly Teske – 2015-2018.
3. Divya Chennamadhavuni – 2017-2018.
4. Jiachen Wen – 2016-2021.
5. Radha Charan Dash – 2016-2022.

Undergraduate and Professional Pharmacy Students:

1. Daniel DeCarlo – 2009-2013 (Pharm. D., 2014): UConn Pharm.D. Research Grant Award, 2011.
2. Steven Lemieux – 2009-2013 (Pharm. D., 2014): UConn Pharm.D. Research Grant Award, 2011; UConn School of Pharmacy Student Researcher of the Month, February 2013.
3. Michele Miller – 2010-2013 (Pharm. D., 2014): UConn Presidential Scholar, 2009; UConn School of Pharmacy Student Researcher of the Month, March 2013.
4. Audrey Corman – 2010-present (Pharm. D., anticipated 2015) UConn Pharm.D. Research Grant Award, 2012 and 2014; UConn School of Pharmacy Student Researcher of the Month, November 2012; Life Sciences Honors Thesis Award, 2013.
5. Daniel Madden – 2012-2014 (B.S. Molecular and Cellular Biology, 2014): UConn University Scholar, 2012-2014; Summer Undergraduate Research Fellowship, 2013.
6. Daniel Raccuia – 2013-2016: UConn Pharm. D. Research Grant Award (2014).
7. Evrett Thompson – 2014-2016. UConn University Scholar, 2014-2016.
8. Kelly Chan – 2014-2018. UConn Honors Student; Summer Undergraduate Research Fellowship, 2015; Antipas Family Research Scholarship, 2015; UConn University Scholar,

2015-2017; UConn School of Pharmacy Student Researcher of the Month, March 2016.
9. Raymond Tran – 2015-2018. UConn Honors Student.
10. Kaitlyn McCarthy – 2016-present. UConn Honors Student; UConn School of Pharmacy Student Researcher of the Month, December 2016.
11. Shana Morel – 2017-2019. UConn Summer Undergraduate Research Fellowship, 2018.
12. Kimberly Snow – 2017-2020.
13. Samantha Chow – 2017-2019.
14. Seema Patel – 2019-2022. UConn Summer Undergraduate Research Fellowship, 2020. Goldwater Scholarship, 2021.
15. Matthew Russolillo – 2020-2021.
16. Gabriella Mendoza – 2022-present.
17. Jordan Bernard – 2022-present.

Service

UConn School of Pharmacy Committees and Advising:
Medicinal Chemistry Hiring Committee – 2009-2011
School of Pharmacy Mentoring Committee – 2009-2012
Medicinal Chemistry Division Coordinator – 2012-2019
Graduate Advisory Council – 2012-2019
School of Pharmacy Student Advising – 2012-present
Department of Pharmaceutical Sciences PTR Committee – 2016-2019 (Chair, 2017-2019)
Pharmaceutical Sciences Department Head Search Committee, Chair – 2018-2020
Department of Pharmaceutical Sciences Administrative Assistant Search Committee – 2020
Medicinal Chemistry Faculty Search Committee, Chair – 2020-2021
Medicinal Chemistry Faculty Search Committee, Chair – 2021-2022
UConn SOP Director of Research and Graduate Programs – 2021-present
UConn SOP Dean's Executive Committee – 2021-present
Boehringer-Ingelheim Endowed Chair Search Committee, Chair – 2021-present

University of Connecticut Committees
Graduate Faculty Council – 2012-2013
Graduate Advisory Council – 2012-2019
UConn Service Center and Cost Recovery Committee – 2016-present
Department of Chemistry Faculty Search Committee – 2016-2017
University of Connecticut, Research Advisory Council – 2018-2019
University of Connecticut, Internal Competition Advisory Board – 2020-present
University of Connecticut NMR Facility Advising Committee – 2016-present
University of Connecticut Research Deans Council – 2021-present
Biomedical and Health Sciences Industry Team – 2021-present
UConn Research Space Committee – 2021-present

National and International Service:
Executive Board Member at Large – Connecticut Valley Section of the American Chemical Society. 2015-2016.
Editorial Board – Molecules, Bioorganic Chemistry Section. 2019-present.
Guest Editor – "Probing New and Underexplored Protein-Protein Interactions."

Guest Editor – "Protein-Protein Interactions 2021"

Manuscript Review:
Journal of Medicinal Chemistry, Bioorganic & Medicinal Chemistry, Bioorganic and Medicinal Chemistry Letters, ACS Medicinal Chemistry Letters, Experimental Biology and Medicine, ChemMedChem, Medicinal Chemistry Communications, Molecular Cancer Therapeutics, European Journal of Medicinal Chemistry, Endocrinology, Analytical Chemistry, Cells, ACS Chemical Biology, Nature Communications.

Proposal Review:
University of Connecticut Research Excellence Program Grant Reviewer – 2015, 2017, 2018
University of Connecticut Research Excellence Program Panel Co-Chair – 2019-present
University of Connecticut Program in Accelerated Therapeutics for Healthcare Reviewer - 2019
American Cancer Society Ad Hoc Grant Reviewer, CDD Panel – January 2017
American Cancer Society, Standing Member CDD Panel – 2018-2021. Vice Chair, 2020.
American Cancer Society, Standing Member Experimental Therapeutics Panel – 2021-present. Chair, 2021-present.
National Science Foundation, Panelist – 2017.
National Institutes of Health Ad Hoc Grant Reviewer, DMP Panel – October 2019, June 2020, March 2021.
National Institutes of Health Ad Hoc Grant Reviewer, CDDT Panel – November 2020, March 2021, November 2021.
National Institutes of Health Ad Hoc Grant Reviewers, SBCA Panel – June 2022.
Ad Hoc Proposal Review: Health Research Board (Ireland); V Foundation for Cancer Research; British Lung Foundation; South Dakota Biomedical Research Initiative; Foundation ARSEP – French Multiple Sclerosis Research Society; INSERM – Plan Cancer (France). Children's Cancer and Leukemia Group (UK).

Additional Service:
1. Guest Editor – Current Medicinal Chemistry, 2015, Volume 22, Number 35.
"Recent Advances in Developmental Signaling Pathway Inhibitors for the Treatment of Cancer."

2. Science outreach experiment with students from Woodstock Academy. High school students tour the Hadden lab, learn about drug discovery research at UConn, and perform a biological assay.
Spring 2015 – 1 class, 12 students.
Spring 2016 – 2 classes, 26 students.
Spring 2017 – 2 classes, 23 students.
Fall 2017 – 1 class, 22 students.
Fall 2018 – 1 class, 21 students.

3. Hosted Samantha Chow, a student at Glastonbury High School enrolled in the Advanced Research Mentorship course, for the 2016-2017 academic year. Samantha performed multiple experiments in my lab throughout the year as part of an ongoing project in the group.

4. UConn Pre-College Summer Program – "Pre-Pharmacy: Medicinal Chemistry and Drug Discovery". An intense week long summer course for high school students at UConn.
Summer 2017 – 1 class, 15 students.
Summer 2018 – 1 class, 11 students.

Summer 2019 – 1 class, 12 students.
Summer 2020 – Cancelled by UConn due to COVID-19.
Summer 2021 – Cancelled by UConn due to COVID-19.
Summer 2022 – 1 class, 12 students.