Timothy M. Willson, Ph.D.

Curriculum Vitae

PERSONAL

Structural Genomics Consortium
UNC Eshelman School of Pharmacy
The University of North Carolina at Chapel Hill
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EDUCATION

University of Illinois at Urbana-Champaign
Champaign, IL
Postdoctoral fellow, 1986-1988

University of Southampton
Southampton, United Kingdom
Ph.D. Organic Chemistry, 1986

University of Leeds
Leeds, United Kingdom
B.S. in Chemistry, Honors Class 1, 1983

PROFESSIONAL EXPERIENCE

The University of North Carolina at Chapel Hill (2015 – present)
UNC Eshelman School of Pharmacy
Chapel Hill, NC
Research Professor

GlaxoSmithKline (1991 – 2015)
Research Triangle Park, NC
Director of Chemical Biology

Merck Sharp & Dohme Research Laboratories (1989 – 1991)
Harlow, United Kingdom
Research Scientist

Clinical Development Compounds

• Obeticholic acid	FXR agonist for cholestasis (Intercept)	FDA Approved
• Farglitazar	PPARγ agonist for Type 2 diabetes	Phase III (discontinued)
• GW501516	PPARδ agonist for dyslipidemia	Phase II (discontinued)
• GW409544	PPARα/γ agonist for dyslipidemia	Phase I (discontinued)
• GW5638	ER modulator for breast cancer (IOS)	Phase I (discontinued)

HONORS

Listed as one of the world's top 400 living core biomedical researchers in a paper by Boyack, Klavans, Sorensen and Ioannidis. European Journal of Clinical Investigation 2013; 43 (12): 1339-1365

BIBLIOGRAPHY AND PRODUCTS OF SCHOLARSHIP

Publications

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2. Müller S, Ackloo S, Al Chawaf A, Al-Lazikani B, Antolin A, Baell JB, Beck H, Beedie S, Betz UAK, Bezerra GA, Brennan PE, Brown D, Brown PJ, Bullock AN, Carter AJ, Chaikuad A, Chaineau M, Ciulli A, Collins I, Dreher J, Drewry D, Edfeldt K, Edwards AM, Egner U, Frye SV, Fuchs SM, Hall MD, Hartung IV, Hillisch A, Hitchcock SH, Homan E, Kannan N, Kiefer JR, Knapp S, Kostic M, Kubicek S, Leach AR, Lindemann S, Marsden BD, Matsui H, Meier JL, Merk D, Michel M, Morgan MR, Mueller-Fahrnow A, Owen DR, Perry BG, Rosenberg SH, Saikatendu KS, Schapira M, Scholten C, Sharma S, Simeonov A, Sundström M, Superti-Furga G, Todd MH, Tredup C, Vedadi M, von Delft F, **Willson TM**, Winter GE, Workman P, Arrowsmith CH. Target 2035 – update on the quest for a probe for every protein. RSC Medicinal Chemistry. 2021. doi: 10.1039/D1MD00228G.
3. Eduful BJ, O'Byrne SN, Temme L, Asquith CRM, Liang Y, Picado A, Pilotte JR, Hossain MA, Wells CI, Zuercher WJ, Catta-Preta CMC, Zonzini Ramos P, Santiago AS, Couñago RM, Langendorf CG, Nay K, Oakhill JS, Pulliam TL, Lin C, Awad D, **Willson TM**, Frigo DE, Scott JW, Drewry DH. Hinge Binder Scaffold Hopping Identifies Potent Calcium/Calmodulin-Dependent Protein Kinase Kinase 2 (CAMKK2) Inhibitor Chemotypes. J Med Chem. 2021 Jul 15. doi: 10.1021/acs.jmedchem.0c02274. Epub ahead of print. PMID: 34264658.
4. Cichońska A, Ravikumar B, Allaway RJ, Wan F, Park S, Isayev O, Li S, Mason M, Lamb A, Tanoli Z, Jeon M, Kim S, Popova M, Capuzzi S, Zeng J, Dang K, Koytiger G, Kang J, Wells CI, **Willson TM**; IDG-DREAM Drug-Kinase Binding Prediction Challenge Consortium, Oprea TI, Schlessinger A, Drewry DH, Stolovitzky G, Wennerberg K, Guinney J, Aittokallio T. Crowdsourced mapping of unexplored target space of kinase inhibitors. Nat Commun. 2021 Jun 3;12(1):3307. doi: 10.1038/s41467-021-23165-1. PMID: 34083538; PMCID: PMC817570
5. Wells CI, Al-Ali H, Andrews DM, Asquith CRM, Axtman AD, Dikic I, Ebner D, Ettmayer P, Fischer C, Frederiksen M, Futrell RE, Gray NS, Hatch SB, Knapp S, Lücking U, Michaelides M, Mills CE, Müller S, Owen D, Picado A, Saikatendu KS, Schröder M, Stolz A, Tellechea M, Turunen BJ, Vilar S, Wang J, Zuercher WJ, **Willson TM**, Drewry DH. The Kinase Chemogenomic Set (KCGS): An Open Science Resource for Kinase Vulnerability Identification. Int J Mol Sci 2021 Jan 8;22(2):E566. doi: 10.3390/ijms22020566. PMID: 33429995.
6. Picado A, Chaikuad A, Wells C, Shrestha S, Zuercher W, Pickett JE, Kwarcinski F, Sinha P, de Silva C, Zutshi R, Liu S, Kannan N, Knapp S, Drewry D, **Willson T**. A Chemical Probe for Dark Kinase STK17B Derives its Potency and High Selectivity Through a Unique P-loop Conformation. J Med Chem. 2020 Dec 10;63(23):14626-14646. doi: 10.1021/acs.jmedchem.0c01174. Epub 2020 Nov 20. PMID: 33215924
7. O'Byrne S, Eduful BJ, **Willson TM**, Drewry D. Concise, Gram-Scale Synthesis of Furo[2,3-B]pyridines, with Functional Handles for Chemoselective Cross-Coupling. Tetrahedron Lett. 2020 Sep 17;61(38):152353. doi: 10.1016/j.tetlet.2020.152353. Epub 2020 Aug 16. PMID: 33012852
8. Wells CI, Vasta JD, Corona CR, Wilkinson J, Zimprich CA, Ingold MR, Pickett JE, Drewry DH, Pugh KM, Schwinn MK, Hwang BB, Zegzouti H, Huber KVM, Cong M, Meisenheimer PL, **Willson TM**, Robers MB. Quantifying CDK inhibitor selectivity in live cells. Nat Commun. 2020 Jun 2;11(1):2743. doi: 10.1038/s41467-020-16559-0. PubMed PMID: 32488087.
9. Asquith CRM, Tizzard GJ, Bennett JM, Wells CI, Elkins JM, **Willson TM**, Poso A, Laitinen T. Targeting the water network in cyclin G associated kinase (GAK) with 4-anilino-quin(az)oline

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11. O'Byrne SN, Scott JW, Pilotte JR, Santiago ADS, Langendorf CG, Oakhill JS, Eduful BJ, Wells CI, Zuercher WJ, **Willson TM**, Drewry DH In depth analysis of kinase cross screening data to identify CAMKK2 inhibitory scaffolds. Molecules. 2020 Jan 13;25(2). pii: E325. doi: 10.3390/molecules25020325.
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agonists. **Bioorg. Med. Chem. Lett**. 2008 18 5018-5022.

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Patents and Patent Applications

US 8221991 Orphan nuclear receptor (PXR)
US 698712 Composition and methods for hepatoprotection and treatment of cholestasis
US 6984650 Use of FXR ligands
US 6710063 Activators of PPAR delta.
WO 2004009091 Purine derivatives as liver x receptor agonists.
US 20030203939 Compositions and methods for hepatoprotection and treatment of cholestasis.
WO 02/94865 Nonhuman pregnane x receptor sequences for use in comparative pharmacology.
WO 02/70011 Treatment regimes (use of PPAR delta agonists)
WO 02/61089 Crystallized HNF4γ ligand binding domain polypeptide and screening methods.
WO 02/24632 Chemical compounds (LXR agonists).
WO 01/97856 Orphan nuclear receptor binding CYP3A4 promoter for drug screening.
WO 01/00603 Thiazole and oxazole derivatives and their pharmaceutical use.
WO 00/55118 Novel nitroaryl amides as nuclear receptor arylating compounds.
WO 00/37077 Assays for ligands for nuclear receptors using peptide sequences.
WO 00/27832 Preparation of 4-oxothiazole-5-acetamides as PPARγ receptor antagonists.
WO 00/23407 Chemical compounds as selective activators of PPAR alpha.
WO 00/08002 Substituted oxazoles and thiazoles derivatives as hPPAR gamma and hPPAR alpha activators.
GB 2335597 Stereoisomers of troglitazone in the treatment of diabetes
WO 99/48915 Orphan nuclear receptor binding CYP promoter for drug screening.
US 5902726 Activators of the nuclear orphan receptor peroxisome proliferator-activated receptor gamma for treatment of diabetes and cardiovascular disorders.
WO 99/07668 Preparation of non-steroidal ligands as estrogen agonists.
US 5795887 Method of inducing cholecystokinin agonist activity using 1,4 benzodiazepine compounds.
US 5681835 Non-steroidal ligands for the estrogen receptor.
WO 97/36579 Use of agonists of the peroxisome proliferator activated receptor alpha for treating obesity.
WO 97/31907 Substituted 4-hydroxy-phenylalcanoic acid derivatives with agonist activity to PPAR-

gamma.

WO 96/11940	Preparation of (acylamino)acetamide derivatives with agonist activity for CCK-A receptors.
WO 95/28391	CCK or gastrin modulating 1,5-benzodiazepine derivatives.
WO 95/28399	A method of inducing cholecystokinin agonist activity using 1,4-benzodiaepine compounds.
US 5346906	Substituted pyridines, their preparation, formulations, and use in dementia.
EP 412798	Preparation of substituted pyridylquinuclidines and their analogs, formulations, and use in treatment of dementia.

GRANTS

Ongoing Support

NC Policy COVID-19 Collaboratory Award (PI: Willson) 7/1/20 – 12/30/20
Rapidly Emerging Antiviral Drug Discovery Initiative (READDI)
Development of orally active CSNK2 inhibitors as a potential host directed therapy for treatment of COVID-19. CSNK2 inhibitors will be optimized for potency as inhibitors of viral replication and to improve pharmacokinetic properties to enable administration on animal models of COVID-19.

Agora Open Science Foundation (PI: Willson) 7/1/20 – 12/30/20
Chemical Probes of the WDR41-C9ORF72-SMARC8 complex to enable discovery of therapies for Frontotemporal Dementia
Identification of a small molecule ligands for WDR41 and development of chemical biology reagents to probe the role of WDR41 in neurodegeneration.

Takeda COVID-19 grant (PI: Willson) 7/1/20 – 6/30/22
Identification of kinase inhibitors as therapies for SARS CoV 2 and future pandemic viruses
The project will create a tool box of host-acting kinase inhibitors that target cellular mechanisms essential for the replication or pathogenesis of coronavirus clades, and that can be “pulled off the shelf” not only for SARS-CoV-2, but also for the next potential pandemic caused by a related coronavirus.

1U24DK116204-01 (PI: Johnson) 09/15/17 – 08/31/23
Illuminating Function of the Understudied Druggable Kinome
A multi-PI grant to fund a Kinase Data and Resource Generation Center that will generate small molecule inhibitors and cell-based assays for 160 poorly studied dark kinases.
Role: Co-I

W81XWH810064 (PI: McDonnell) 06/15/18 – 06/14/22
Cancer cell intrinsic and extrinsic actions of steroid hormones in breast tumors
Subaward 3130816 of a DOD Innovator’s Award to Dr. McDonnell. The goal of the project is to identify new estrogen receptor antagonists for breast cancer that do not disrupt the immune system.
Role: Co-I

A19-0753-001 (PI: Willson) 09/30/18 – 6/30/20
Structural Genomics Consortium Funding Award
Funding to support the operation of the US site of the SGC
Role: PI

No Number (PI: Willson) 09/30/2018 – 8/31/2020

Replenishing supply of Kinase Inhibitors to the Core Kinase Chemogenomic Set (KCGS)
These funds will be used to resynthesize mg quantites of the kinase inhibitors that comprise the Kinase Chemogenomic Set (KCGS). The stocks are used to create the KCGS plates for distribution to the scientific community.
Role: PI

U54AG065187-01 (PI: Levey) 09/01/19 – 08/31/2024
Open Drug Discovery Center for Alzheimer's Disease
The overarching goal of this program is to develop and openly distribute the experimental tools necessary for the academic research community to test a wide range of therapeutic hypotheses for Alzheimer's disease (AD). Open drug discovery medicinal chemistry will be performed collaboratively by the SGC-UNC and the UNC CICBDD.
Role: Co-I

R01 AI152092-01 (PI: Chibale) 04/01/20 – 03/31/2024
Repurposing kinase inhibitor chemotypes as antimalarials
The objective of this subaward is to identify kinase targets with antiplasmodial activity for treatment of malaria.
Role: Co-I

Completed Research Support

Fred Eshelman Gift Trust (PI: Willson) 07/01/17 – 06/30/20
The SGC-UNC: A Center for Open and Collaborative Target Discovery
The goal of this project is to promote innovation in drug discovery through open sharing of research, material, and data for the protein kinases
Role: PI

The UNC Eshelman Institute for Innovation Tier 4 (PI: Willson) 10/01/15 – 9/30/17
The SGC-UNC: A Center for Open and Collaborative Target Discovery
This grant supports the creation of the first SGC site in the US. The primary goal of the SGC-UNC is to promote innovation in drug discovery through open sharing of research tools and data for the understudied protein kinases
Role: PI

Lineberger Comprehensive Cancer Center (PI: Willson) 07/21/15 – 6/30/17
The SGC-UNC: A Center for Open and Collaborative Target Discovery
Start-up grant for the SGC-UNC laboratory to support hiring of personnel to conduct and support research and operating costs.
Role: PI

PharmAlliance Tier 1 Travel Grant (PI: Willson) 07/01/17 – 11/30/17
To support meetings between scientists from the UNC Eshelman School of Pharmacy and the UCL School of Pharmacy, London to identify collaborative opportunities to develop research tools for kinases.
Role: PI

PharmAlliance Tier A (PI: Axtman) 01/04/17 – 01/03/18
Pilot studies to establish a UCL/UNC kinase drug discovery platform
To support screening of kinase inhibitors in human disease-relevant assays
Role: Co-I

NCBC Grant #2018-IDG-1030 (PI: Willson) 03/15/18 – 03/14/19
Kinase Chemical Biology Center at UNC-CH
Funding for purification equipment and a plate reader by the North Carolina Biotechnology Center
Role: PI

RESEARCH STATEMENT

My research focus has been the development of chemical probes and their distribution to the global research community to study the biological function of proteins. My laboratory initially identified chemical probes for the orphan nuclear receptors PPARγ, PPARδ, FXR, LXR, CAR and PXR, leading to the discovery of their roles in human liver and metabolic diseases. I subsequently formed a public-private consortium (coordinated by the Structural Genomics Consortium) to develop small molecule inhibitors of enzyme modifiers and protein readers of histone tails. The consortium partners synthesized and released over 30 chemical probes for lysine demethylases, lysine methyltransferases, bromodomain and methyl reader proteins that have been used to study their role in epigenetic regulation of human disease. My current laboratory at the UNC Eshelman School of Pharmacy is now dedicated to discovering and sharing selective, small molecule inhibitors of protein and lipid kinases. Operating as the first U.S. site of the Structural Genomics Consortium, the SGC-UNC will synthesize and distribute chemical probes for kinases and create a scientific hub for kinase research. The knowledge generated by our laboratory will allow drug researchers to select the right kinase for the right disease and help speed the creation of new medicines for patients.