Prof. Dr. Xiang Wang

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Education:

B.S.	Chemistry, University of Science & Technology of China Hefei, China	**1999**
Ph.D.	Organic Chemistry, Department of Chemistry Boston University, Boston, MA Advisor: John A. Porco, Jr.	**2005**
Postdoc	Department of Chemistry & Chemical Biology, Harvard University Chemical Biology Program, Broad Institute of Harvard & MIT, Cambridge, MA Advisor: Stuart L. Schreiber	**2008**

Employment:

Assistant Professor	Chemistry & Biochemistry, University of Colorado Boulder	**2008–2016**
Founder and CEO	Recreo Pharmaceuticals	**2013–*present***
Associate Professor	Chemistry, University of Colorado Boulder	**2016–*present***

Honors & Awards:

Sugata Ray Memorial Award, Boston University	**2004**
CRCW Junior Faculty Development Award, University of Colorado	**2009**
Butcher Award, BioFrontiers Institute, University of Colorado	**2010**
Golfers Against Cancer, University of Colorado Comprehensive Cancer Center	**2012**
Bioscience Discovery Evaluation Program Award, State of Colorado	**2014**

Professional Affiliation:

Member	American Chemical Society
Member	American Society for Microbiology
Member	American Association for the Advancement of Science
Member	Colorado Clinical & Translational Sciences Institute
Member	University of Colorado Comprehensive Cancer Center
Member	Network on Antimicrobial Resistance in *Staphylococcus aureus*

Conferences, Invited Lectures, Posters (2008–*present*):

05/2010 NIH Junior Faculty Workshop, Dallas, TX

12/2010 Molecular Oncology Retreat, University of Colorado Cancer Center, Boulder, CO
08/2011 242nd National Meeting of the American Chemical Society, Denver, CO
09/2011 Chemistry Seminar, Hoffmann-La Roche, Nutley, NJ
10/2011 30th Annual High School-University Chemistry Teachers' Conference, Boulder, CO
11/2011 Butcher Symposium, Westminster, CO
05/2012 Chemical Biology Seminar, Shandong University, Jinan, China
07/2012 Gordon Research Conference on Bioorganic Chemistry, Andover, NH
10/2012 Department of Chemistry, University of Toledo, Toledo, OH
03/2013 Chemical Epigenetics and Host Factors in Infectious Disease Symposium, Vienna, Austria
06/2013 Gordon Research Conference on High-throughput Chemistry and Chemical Biology, NH
06/2013 Department of Chemistry, Nanjing University, Nanjing, China
06/2013 Department of Chemistry, Peking University, Shenzhen, China
09/2013 Recent Advances in Modulating the Epigenome Symposia, 246th American Chemical Society National Meeting & Exposition, Indianapolis, IN
03/2014 Gordon Research Conference on New Antibacterial Discovery & Development, CA
04/2014 9th Annual Drug Discovery Chemistry Conference, Cambridge Healthtech Institute, CA
10/2014 Department of Chemistry, University of Denver, Denver, CO
01/2015 Department of Chemistry, Colorado State University, Fort Collins, CO
02/2015 Department of Biochemistry, UT Southwestern Medical Center, Dallas, TX
02/2015 Department of Chemistry, Texas A&M University, College Station, TX
02/2015 Department of Chemistry, Duke University, Durham, NC
02/2015 Department of Chemistry, North Carolina State University, Raleigh, NC
03/2015 Department of Chemistry, Purdue University, West Lafayette, IN
03/2015 Abbvie Symposium, Department of Chemistry, Boston University, Boston, MA
03/2015 Department of Chemistry, Boston College, Newton, MA
04/2015 Structural and Chemical Biology Department, Icahn School of Medicine at Mount Sinai, New York, NY
04/2015 Pharmacology and Oncology Department, Johns Hopkins School of Medicine, Baltimore, MD
05/2015 Department of Chemistry, University of California Santa Barbara, CA
07/2015 School of Chemistry, University of Science & Technology of China, Hefei, China
07/2015 College of Chemistry and Molecular Engineering, Peking University, Beijing, China
09/2015 Department of Chemistry and Biochemistry, University of Colorado, Boulder, CO
12/2015 Gold Catalysis Symposium, Pacifichem, Honolulu, Hawaii
02/2016 Department of Pharmacology, CU Health & Science Center, Aurora, CO
11/2017 PISKL Symposium on Chemical Biology & Drug Discovery, Hong Kong Polytechnic University, Hong Kong
03/2019 Global Summit on Catalysis Research and Applications, Rome, Italy

Publications:

35. "A Cell-Free Screen for Bacterial Membrane Disruptors Identifies Mefloquine as A Novel

Antibiotic Adjuvant," Olson, J., Podoll, J. D.; Wang, W.; Wang, X. *under revision.*

34. "One-Pot Synthesis of Polycyclic Isoindolines Using Isoindole Umpolung," Weintraub, R. A.; He, W.; **Wang, X.** *Tetrahedron Lett.,* **2020***, 61*, 152128-152131. [link]

33. "Tryptoline-Based Benzothiazoles Re-sensitize MRSA to β-Lactam Antibiotics," Wang, X.; Chen, J.; Wang, W.; Jaunaraj, A.; **Wang, X.** *Bioorg. & Med. Chem.* **2019**, *27*, 115095–115106. [link]

32. "Identification and Characterization of a Novel Anti-inflammatory Lipid Isolated from *Mycobacterium vaccae*, a Soil-Derived Bacterium with Immunoregulatory and Stress Resilience Properties," Smith, D. G.; Martinelli, R.; Besra, G. S.; Illarionov, P. A.; Szatmari, I.; Brazda, P.; Allen, M. A.; Xu, W.; **Wang, X.**; Nagy, L.; Dowell, R. D.; Rook G. A. W.; Brunet, L. R.; Lowry, C. A. *Phycopharmacology*, **2019**, *236(5),* 1653–1670. [link]

31. "Enantioselective Tandem Cyclization of Alkyne-Tethered Indoles Using Cooperative Silver(I) and Chiral Phosphoric Acid Catalysis," Zhu, Y.; He, W.; Wang, W.; Pitsch, C. E.; Wang, X.; **Wang, X.*** *Angew. Chem. Int. Ed.* **2017**, *40*, 12206–12209. [link]

30. "Diastereoselective Synthesis and Biological Evaluation of Enantiomerically Pure Tricyclic Indolines," He, W.; Griffiths, B. M.; Wang, W.; **Wang, X.*** *Org. Biomol. Chem.* **2017**, *15*, 4241–4245. [link]

29. "Tetracyclic Indolines as a Novel Class of β-Lactam-Selective Resistance Modifying Agent for MRSA," Zhu, Y.; Cleaver, L.; Wang, W.; Podoll, J. D., Walls, S.; Jolly, A.; **Wang, X.*** *Eur. J. Med. Chem.* **2017**, *125*, 130–142. [link]

28. "Bioinspired Discovery of Chemical Reactions and Biological Probes," Griffiths, B. M.; Burl, J. D.; **Wang, X.*** *Synlett* **2016***, 27,* 2039–2042. [link]

27. "Property-Guided Synthesis of Aza-Tricyclic Indolines: Development of Gold Catalysis En Route," Barbour, P. M.; Wang, W.; Chang, L.; Picard, K. L.; Rais, R. Slusher, B. S.; **Wang, X.*** *Adv. Synth. Catal.* **2016**, *358*, 1482–1490. [link]

26. "A Fluorescence Polarization Assay for A *Naegleria* DNA Hydroxylase Tet1," Marholz, L. M.; Wang, W.; **Wang, X.*** *ACS Med. Chem. Lett.* **2016**, *7*, 167–171. [link]

25. "Gold-Catalyzed Cyclization Leads to A Bridged Tetracyclic Indolenine That Represses β-Lactam Resistance," Xu, W., Wang, W., **Wang, X.*** *Angew. Chemie., Int. Ed.* **2015**, *54*, 9546–9549. [link]

24. "Novel Scaffolds of Cell-Active Histone Demethylase Inhibitors Identified from High-Throughput Screening," Wang, W.; Marholz, L. J.; **Wang, X.*** *J. Biomol. Screen.* **2015**, *20*, 821–827. [link]

23. "Development of Substrate-Selective Probes for Affinity Pulldown of Histone Demethylases," Marholz, L. J.; Chang, L.; Old, W. M.; **Wang, X.*** *ACS Chem. Biol.* **2015**, *10*, 129–137. [link]

22. "Discovery and Initial Structure-Activity Relationships of *N*-Benzyl Tricyclic Indolines as Antibacterials for Methicillin-Resistant *Staphylococcus Aureus*," Barbour, P. M.; Podoll, J. D.; Marholz, L. J.; **Wang, X.*** *Bioorg. Med. Chem. Lett.* **2014**, *24*, 5602–5605. [link]

21. "A Histone Demethylase Inhibitor, Methylstat, Inhibits Angiogenesis in vitro and in vivo," Cho, Y.; Kim, K. H.; Xu, W.; **Wang, X.**; Kwon, H. J. *RSC Adv.* **2014**, *4*, 38230–38233. [link]

20. "Structure-Activity Relationship Studies of the Tricyclic Indoline Resistance Modifying Agent," Le, C.; Podoll, J. D.; Wang, W.; **Wang, X.*** *J. Med. Chem.* **2014***, 57*, 3803–3817. [link]

19. "Gold Approaches to Polycyclic Indole Alkaloids," Barbour, P. M.; Marholz, L. J.; Chang, L.; Xu, W.; **Wang, X.*** *Chem. Lett.* **2014***, 43*, 572–578. [link]

18. "Bio-Inspired Synthesis Yields A Tricyclic Indoline That Selectively Resensitizes MRSA to β-Lactam Antibiotics," Podoll, J.; Liu, Y.; Chang, L.; Walls, S.; Wang, W.; **Wang, X.*** *Proc. Natl. Acad. Sci. U.S.A.,* **2013**, *110*, 15573–15578. [link] *Highlighted by PNAS; Recommended by Faculty of 1000.*

17. "Quantitative Analysis of Histone Demethylase Probes Using Fluorescence Polarization," Xu, W.; Podoll, J.; Dong, X.; **Wang X.*** *J. Med. Chem.* **2013**, *56*, 5198–5202. [link] *Highlighted in Nature SciBX.*

16. "A One-Pot Three-Component Reaction for the Preparation of Highly Functionalized Tryptamines," Yeo, S. J.; Liu, Y.; **Wang, X.*** *Tetrahedron*. **2012**, *68*, 813–818. [link]

15. "A Selective Inhibitor and Probe of the Cellular Functions of Jumonji C Domain-Containing Histone Demethylases," Luo, X.; Liu, Y.; Kubicek, S.; Myllyharju, J.; Tumber, A.; Ng, S.; Che, K.; Podoll, J.; Heightman, T. D.; Oppermann, U.; Schreiber, S. L.; **Wang, X.*** *J. Am. Chem. Soc.* **2011**, *133*, 9451–9456. [link] *Highlighted in Nature SciBX.*

14. "Selective Gold(I)-Catalyzed Formation of Tetracyclic Indolines: A Single Transition State and Bifurcations Lead to Multiple Products," Noey, E.; **Wang, X.**; Houk, K. *J. Org. Chem.* **2011***, 76,* 3477–3483. [link]

13. "Gold(I)-Catalyzed Tandem Cyclization Approach to Tetracyclic Indolines," Liu, Y.; Xu, W.; **Wang, X.*** *Org. Lett.* **2010**, *12,* 1448–1451. [link]

12. "AAK1 Identified as an Inhibitor of Neuregulin-1/ErbB4-Dependent Neurotrophic Factor Signaling Using Integrative Chemical Genomics and Proteomics," Kuai, L; Ong, S. E.; Madison, J. M.; **Wang, X.**; Duvall, J. R.; Lewis, T. A.; Luce, C. J.; Conner, S. D.; Pearlman, D. A.; Wood, J. L.; Schreiber, S. L.; Carr, S. A.; Scolnick, E. M.; Haggarty, S. J. *Chem & Biol.* **2011**, *18*, 891–906.

11. "Chemical Genetics Identifies Small-Molecule Modulators of Neuritogenesis Involving Neuregulin-1/ErbB4 Signaling," Kuai, L.; **Wang, X.**; Madison, J. M.; Schreiber, S. L.; Scolnick, E. M.; Haggarty, S. J. *ACS Chem. Neurosci.* **2010**, *1*, 325–342.

10. "Syntheses of Aminoalcohol-Derived Macrocycles Leading to a Small-Molecule Binder to and Inhibitor of Sonic Hedgehog," Peng, L.F.; Stanton, B. Z.; Maloof, N.; **Wang, X**.; Schreiber, S. L. *Bioorg. Med. Chem. Lett.* **2009**, *19,* 6319–6325.

9. "Identifying the Proteins to Which Small-Molecule Probes and Drugs Bind in Cells," Ong, S.-E.; Schenone, M.; Margolin, A.; Li, X.; Do, K.; Doud, M.; Mani, D.; Kuai, L.; **Wang, X**.; Wood, J.; Tolliday, N.; Koehler, A.; Marcaurelle, L.; Golub, T.; Gould, R.; Schreiber, S. L.; Carr, S. *Proc. Natl. Acad. Sci. U. S. A.* **2009**, *106,* 4617–4622.

8. "A Small Molecule that Binds Hedgehog and Blocks its Signaling in Human Cells," Stanton, B.; Peng, L. F.; Maloof, N.; Nakai, K.; **Wang, X**.; Duffner, J. L.; Taveras, K. M.; Hyman, J. M.; Lee, S. W.; Koehler, A. N.; Chen, J. K.; Fox, J. L.; Mandinova, A.; Schreiber; S. L. *Nature Chem. Biol.* **2009**, *5*, 154–156.

7. "Diversity Synthesis of Complex Pyridines Yields a Probe of a Neurotrophic Signaling Pathway," Gray, B. L.; **Wang, X**.; Schreiber, S. L. *Org. Lett*. **2008**, *10*, 2621–2624.

6. "Small-Molecule Reagents for Cellular Pull-down Experiments," **Wang, X.**; Imber, B. S.;

Schreiber, S. L. *Bioconjug. Chem.* **2008**, *19*, 585–587.

5. "Synthesis of the Tetracyclic Core of the Tetrapetalones *via* Transannular Oxidative [4+3] Cyclization," **Wang, X**.; Porco, J. A., Jr. *Angew. Chem., Int. Ed.* **2005**, *44*, 3067–3071; **2006**, *45*, 6607.
4. "Total Synthesis of the Salicylate Enamide Macrolide Oximidine III: Application of Relay Ring-Closing Metathesis," **Wang, X**.; Bowman, E. J.; Bowman, B. J.; Porco, J. A., Jr. *Angew. Chem., Int. Ed.* **2004**, *43*, 3601–3605.
3. "Total Synthesis of the Salicylate Enamide Macrolide Oximidine II," **Wang, X.**; Porco, J. A., Jr. *J. Am. Chem. Soc*. **2003**, *125*, 6040–6041.
2. "Modification of *C*-Terminal Peptides to Form Peptide Enamides: Synthesis of Chondriamides A and C," **Wang, X.**; Porco, J. A., Jr. *J. Org. Chem.* **2001**, *66*, 8215–8221.
1. "Parallel Synthesis and Purification Using Anthracene-Tagged Substrates," **Wang, X**.; Parlow, J. J.; Porco, J. A., Jr. *Org. Lett*. **2000**, *2*, 3509–3512.

Patent:

1. "Histone Demethylase Inhibitors and Methods for Using the Same," Xu, W.; **Wang, X.** US 2013/0137720 A1. (licensed to Sigma-Aldrich and EMD Millipore)
2. "Indoline Alkaloid Compounds," Podoll, J. D.; Chang, L.; **Wang, X.** PCT/US14/32585. (licensed to Recreo Pharmaceuticals)
3. "Polycyclic Indoline and Indolenine Compounds," Barbour, P. M.; **Wang, X.** PCT/US62/154,792. (licensed to Recreo Pharmaceuticals)
4. "1,3,4,9-Tetrahydro-2H-Pyrido[3,4-B]Indole Derivative Compounds and Uses Thereof," Zhang, J.; Podoll, J. D.; **Wang, X.** US 62/719,048.
5. "Tryptoline-Based Benzothiazoles and their use as Antibiotics and Antibiotic Resistance-Modifying Agents," Wang, X.; **Wang, X**. US 62/895,380.

Funding:

Active

R33 AI121581 (NIH/NIAID) Wang (PI) 12/01/2017-11/30/2021
Total: $1,386,000
Development of Novel Resistance-Modifying Agents for MRSA
This project aims to use a medicinal chemistry approach to systematically develop novel resistant-modifying agents that re-sensitize methicillin-resistant *Staphylococcus aureus* (MRSA) to β-lactam antibiotics.
Role: PI

Completed

R33 AI121365 (NIH/NIAID) Detweiler and Wang (PIs) 12/01/2017-11/30/2020
Total Cost: $1,379,609
A Novel Screen for Antibacterials that Are Non-Toxic to Mammals
This project aims to use an image-based high-content screen to identify therapeutics that target nonessential bacterial virulence factors and will be effective against antimicrobial-resistant bacteria.
Role: PI

R01 GM098390 (NIH/NIGMS) Wang (PI) 08/01/2012–07/31/2018
Total: $1,311,132
Specific Chemical Probes for Histone Demethylases
This project will develop a series of specific chemical probes for the studies of the cellular functions and substrate scopes of the JmjC domain-containing histone demethylases.
Role: PI

R21 AI121581 (NIH/NIAID) Wang (PI) 12/01/2015–11/30/2017
Total: $411,061
Development of Novel Resistance-Modifying Agents for MRSA
This project aims to use a medicinal chemistry approach to systematically develop novel resistant-modifying agents that re-sensitize methicillin-resistant *Staphylococcus aureus* (MRSA) to β-lactam antibiotics.
Role: PI

R21 AI121365 (NIH/NIAID) Detweiler and Wang (PIs) 12/01/2015–11/30/2017
Total: $411,140
A Novel Screen for Antibacterials that Are Non-Toxic to Mammals
This project aims to use an image-based high-content screen to identify therapeutics that target nonessential bacterial virulence factors and will be effective against antimicrobial-resistant bacteria.

BDEG (State of Colorado) Wang (PI) 07/01/2014–06/30/2016
Total: $200,000
Development of Novel Resistance-Modifying Agents for the Treatment of MRSA
This project will conduct proof-of-concept studies to developing novel resistant-modifying agents that re-sensitize methicillin-resistant *Staphylococcus aureus* (MRSA) to β-lactam antibiotics.
Role: PI

Golfers Against Cancer Award (UCCC) Taatjes and Wang (PIs) 11/01/2012–10/31/2013
Total: $50,000
Develop Chemical Probes to Define and Control the p53-Mediator Interface
This project aims to develop a systematic screening approach to discover novel transcriptional regulators that selectively interact with transcription factor and Mediator.
Role: Co-PI

Butcher Award (BioFrontiers Institute) Wang and Yi (PIs) 05/01/2010–04/30/2012
Total: $100,000
A Chemical Genetics Approach to Study Epigenetic Regulation in Mammalian Skin
The project aims to develop selective histone demethylase inhibitors and use them to study epigenetic regulation in mouse skin development in vivo.
Role: Co-PI