

# Xiaoyu Zhang, Ph.D.

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## PROFESSIONAL APPOINTMENT

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<b>Northwestern University</b>	Evanston, IL
Assistant Professor of Chemistry	2022-current
Member of Chemistry of Life Processes Institute (CLP)	2022-current
Member of Robert H. Lurie Comprehensive Cancer Center, Feinberg School of Medicine	2022-current

## EDUCATION AND TRAINING

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<b>The Scripps Research Institute</b>	La Jolla, CA
Postdoctoral associate	2017 – 2021

<b>Cornell University</b>	Ithaca, NY
Ph.D. in Chemistry and Chemical Biology	2012 – 2017

<b>Zhejiang University</b>	Hangzhou, China
M.S. in Pharmaceutical Science	2008 – 2011
B.S. in Pharmaceutical Science	2004 – 2008

## AWARDS AND HONORS

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Damon Runyon-Dale F. Frey Award for Breakthrough Scientists	2021
The NIH Pathway to Independence Award (K99/R00)	2020
Damon Runyon Postdoctoral Fellowship Award	2018 – 2020
Keystone Symposia Future of Science Fund Scholarship	2020
Chinese Government Award for Outstanding Students Abroad	2018
Bayer Teaching Excellence Award of Cornell University	2013
Eli Lilly Asia Outstanding Graduate Thesis Award	2011
Chu Kochen Scholarship of Zhejiang University	2010
Zhejiang Innovation Program and Research Fellowship for Graduate Students	2009 – 2010
First Honor Graduate of Zhejiang Province	2011
First Honor Graduate of Zhejiang University	2011
First-Class Award of Honor for Graduate Students of Zhejiang University	2010
Outstanding Undergraduate Thesis Award of Zhejiang University	2008
First-Class Scholarship for Outstanding Undergraduate Students of Zhejiang University	2006 – 2008

## PUBLICATIONS

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\*equal contribution †co-corresponding authors

1. Kramer LT and **Zhang X**. Expanding the landscape of E3 ligases for targeted protein degradation. *Curr. Res. Chem. Biol.*, 2 (2022) 1-5.
2. Hong JY, Malgapo MIP, Liu Y, Yang M, Zhu C, **Zhang X**, Tolbert P, Linder ME and Lin H. High-Throughput Enzyme Assay for Screening Inhibitors of the ZDHHC3/7/20 Acyltransferases. *ACS Chem. Biol.*, 16 (2021) 1318-1324.
3. Garnar-Wortzel L, Bishop TR, Kitamura S, Milosevich N, Asiaban JN, **Zhang X**, Zheng Q, Chen E, Ramos AR, Ackerman CJ, Hampton EN, Chatterjee AK, Young TS, Hull MV, Sharpless KB, Cravatt BF, Wolan DW and Erb MA. Chemical inhibition of ENL/AF9 YEATS domains in acute leukemia. *ACS Cent. Sci.*, 7 (2021) 815-830.

4. **Zhang X**<sup>†</sup>, Luukkonen LM, Eissler CL, Crowley VM, Yamashita Y, Schafroth MA, Kikuchi S, Weinstein DS, Symons KT, Nordin BE, Rodriguez JL, Wucherpennig TG, Bauer L, Dix MM, Stamos D, Kinsella TM, Simon GM, Baltgalvis KA and Cravatt BF<sup>†</sup>. DCAF11 supports targeted protein degradation by electrophilic proteolysis-targeting chimeras. **J. Am. Chem. Soc.**, 143 (2021) 5141-5149.

Highlight

“Electrophilic Screening Platforms for Identifying Novel Covalent Ligands for E3 Ligases” *Biochemistry*, 2021.

5. **Zhang X**<sup>†</sup>, Thielert M, Li H and Cravatt BF<sup>†</sup>. SPIN4 is a principal endogenous substrate of the E3 ubiquitin ligase DCAF16. **Biochemistry**. 60 (2021) 637-642.

Highlight

“Assembling a Robust Workflow for Characterizing Endogenous E3 Ligase Substrates” *Biochemistry*, 2021.

6. **Zhang X**. Chemical Proteomics for Expanding the Druggability of Human Disease. **ChemBioChem**, 21 (2020) 1-3.
7. Vinogradova EV, **Zhang X**, Remillard D, Lazar DC, Suciu RM, Wang Y, Bianco G, Yamashita Y, Crowley VM, Schafroth MA, Yokoyama M, Konrad DB, Lum KM, Simon GM, Kemper EK, Lazear MR, Yin S, Blewett MM, Dix MM, Nguyen N, Shokhirev MN, Chin EN, Lairson LL, Melillo B, Schreiber SL, Forli S, Teijaro JR, Cravatt BF. An Activity-Guided Map of Electrophile-Cysteine Interactions in Primary Human Immune Cells. **Cell**, 182 (2020) 1-18.
8. Kosciuk T, Price IR, **Zhang X**, Zhu C, Johnson KN, Zhang S, Halaby SL, Komaniecki GP, Yang M, DeHart CJ, Thomas PM, Kelleher NL, Fromme JC, Lin H. NMT1 and NMT2 are Lysine Myristoyltransferases Regulating the ARF6 GTPase Cycle. **Nat. Commun.**, 11 (2020) 1-17.
9. Yamashita Y, Vinogradova EV, **Zhang X**, Suciu RM, Cravatt BF. A chemical proteomic probe for the mitochondrial pyruvate carrier complex. **Angew. Chem. Int. Ed. Engl.**, 59 (2019) 1-5.
10. Spiegelman NA, **Zhang X**, Jing H, Cao J, Kotliar IB, Aramsangtienchai P, Wang M, Tong Z, Rosch KM, Lin H. SIRT2 and Lysine Fatty Acylation Regulate the Activity of RalB and Cell Migration. **ACS Chem. Biol.**, 14 (2019) 2014-2023.
11. **Zhang X**<sup>†</sup>, Crowley VM, Wucherpennig TG, Dix MM, Cravatt BF<sup>†</sup>. Electrophilic PROTACs that degrade nuclear proteins by engaging DCAF16. **Nat. Chem. Biol.**, 15 (2019) 737-746.

Highlight

“Stick it to E3s” *Nat. Chem. Biol.*, 15 (2019) 655-656.

“Greatest hits” *Nat. Chem. Biol.*, 16 (2020) 600-603.

“Chemoproteomic-Driven Discovery of Covalent PROTACs” *Biochemistry*, 59 (2020) 128-129.

“PROTACs that Degrade Nuclear Proteins via a Novel E3 Ligase” *The Bench Blog. Synthego*. 25 Sep 2019  
F1000Prime recommendation article. 28 Jun 2019; 10.3410/f.735998607.793561779.

12. Latifkar A, Ling L, Hingorani A, Johansen E, Clement A, **Zhang X**, Hartman J, Fischbach C, Lin H, Cerione RA, Antonyak MA. Loss of Sirtuin 1 Alters the Secretome of Breast Cancer Cells by Impairing Lysosomal Integrity. **Dev. Cell**, 49 (2019) 1-16.
13. Spiegelman NA, Hong JY, Hu J, Jing H, Wang M, Price IR, Cao J, Yang M, **Zhang X**, Lin H. A Small Molecule SIRT2 Inhibitor that Promotes K-Ras4a Lysine Fatty-acylation. **ChemMedChem**, 14 (2019) 744-748.
14. Cao J, Sun L, Aramsangtienchai P, Spiegelman NA, **Zhang X**, Huang W, Seto E, Lin H. HDAC11 regulates type I interferon signaling through defatty-acylation of SHMT2. **Proc. Natl. Acad. Sci.**, 116 (2019) 5487-5492.
15. Hong JY, **Zhang X**, Lin H. HPLC-Based Enzyme Assays for Sirtuins. **Methods Mol. Biol.**, 1813 (2018) 225-234.
16. Spiegelman NA, Price IR, Jing H, Wang M, Yang M, Cao J, Hong JY, **Zhang X**, Aramsangtienchai P, Sadhukhan S, Lin H. Direct Comparison of SIRT2 Inhibitors: Potency, Specificity, Activity-Dependent Inhibition, and On-Target Anticancer Activities. **ChemMedChem**, 13 (2018) 1-6.
17. **Zhang X**, Cao J, Miller SP, Jing H, Lin H. Comparative nucleotide-dependent interactome analysis reveals shared and differential properties of KRas4a and KRas4b. **ACS Cent. Sci.**, 4 (2018) 71-80.

Highlight

“Research probes key protein's role in cancer cell growth.” *Cornell Chronicle*, January 24, 2018.

18. Jiang H\*, **Zhang X\***, Chen X\*, Aramsangtienchai P\*, Tong Z\*, Lin H. Protein lipidation: Occurrence, mechanisms, biological functions, and enabling technologies. **Chem. Rev.**, 118 (2018) 919-988.
19. Jing H\*, **Zhang X\***, Wisner SA, Chen X, Spiegelman NA, Linder ME, Lin H. SIRT2 and lysine fatty acylation regulate the oncogenic activity of K-Ras4a. **eLife**, 6 (2017) e32436.
- Highlight  
 "Research probes key protein's role in cancer cell growth." Cornell Chronicle, January 24, 2018.  
 "Research probes key protein's role in cancer cell growth." The Cornell Daily Sun, March 30, 2018.
20. **Zhang X**, Spiegelman NA, Nelson OD, Jing H, Lin H. SIRT6 regulates Ras-related protein R-Ras2 by lysine defatty-acylation. **eLife**, 6 (2017) e25158.
- Highlight  
 "SIRT6's ability to suppress cancer cell growth is explained." Cornell Chronicle, May 10, 2017.
21. Jin J, He B, **Zhang X**, Lin H, Wang Y. SIRT2 Reverses 4-Oxononanoyl Lysine Modification on Histones. **J. Am. Chem. Soc.**, 138 (2016) 12304-12307.
22. **Zhang X**, Khan S, Jiang H, Antonyak MA, Chen X, Spiegelman NA, Shrimp JH, Cerione RA, Lin H. Identifying the functional contribution of the defatty-acylase activity of SIRT6. **Nat. Chem. Biol.**, 12 (2016) 614-620.
- Highlight  
 "Mutant enzyme study aids in understanding of sirtuin's functions." Cornell Chronicle, Jun 27, 2016.
23. Jiang H\*, **Zhang X\***, Lin H. Lysine fatty acylation promotes lysosomal targeting of TNF- $\alpha$ . **Sci. Rep.**, 6 (2016) 24371.
24. Tong Z, Wang Y, **Zhang X**, Kim DD, Sadhukhan S, Hao Q, Lin H. SIRT7 is activated by DNA and deacetylates histone H3 in the chromatin context. **ACS Chem. Biol.**, 11 (2016) 742-747.
25. He B\*, Hu J\*, **Zhang X\***, Lin H. Thiomyristoyl peptides as cell-permeable Sirt6 inhibitors. **Org. Biomol. Chem.**, 12 (2014) 7498-7502.
26. **Zhang X**, Song Z, Xu J, Ma Z. Improving the NQO1-Inducing Activities of Phenolic Acids from Radix *Salvia miltiorrhiza*: a Methylation Strategy. **Chem. Biol. Drug Des.**, 78 (2011) 558-566.
27. **Zhang X**, Luo L, Ma Z. A deuterium-labelling mass spectrometry–tandem diode-array detector screening method for rapid discovery of naturally occurring electrophiles. **Anal. Bioanal. Chem.**, 400 (2011) 3463-3471.
28. Xu J, Lu J, Sun F, Zhu H, Wang L, **Zhang X**, Ma Z. Terpenoids from *Tripterygium wilfordii*. **Phytochemistry**, 72 (2011) 1482-1487.
29. **Zhang X**, Ma Z. Characterization of bioactive thiophenes from the dichloromethane extract of *Echinops grijsii* as Michael addition acceptors. **Anal. Bioanal. Chem.**, 397 (2010) 1975-1984.
30. **Zhang X**, Zhao X, Ma Z. PYDDT, a novel phase 2 enzymes inducer, activates Keap1-Nrf2 pathway via depleting the cellular level of glutathione. **Toxicol. Lett.**, 199 (2010) 93-101.
31. **Zhang X**, Ma Z. A new fluorescein isothiocyanate-based screening method for the rapid discovery of electrophilic compounds. **Anal. Methods**, 2 (2010) 1472-1478.
32. Shi J\*, **Zhang X\***, Ma Z, Zhang M, Sun F. Characterization of Aromatase Binding Agents from the Dichloromethane Extract of *Corydalis yanhusuo* Using Ultrafiltration and Liquid Chromatography Tandem Mass Spectrometry. **Molecules**, 15 (2010) 3556-3566.
33. Shi J\*, **Zhang X\***, Jiang H. 2-(Penta-1, 3-diynyl)-5-(3, 4-dihydroxybut-1-ynyl) thiophene, a Novel NQO1 Inducing Agent from *Echinops grijsii* Hance. **Molecules**, 15 (2010) 5273-5281.
34. Wang L, Sun F, **Zhang X**, Ma Z, Cheng L. A secoiridoid with quinone reductase inducing activity from *Cortex fraxini*. **Fitoterapia**, 81 (2010) 834-837.
35. Cheng L, **Zhang X**, Zhang M, Zhang P, Song Z, Ma Z, Cheng Y, Qu H. Characterization of chemopreventive agents from the dichloromethane extract of *Eurycorymbus cavaleriei* by liquid chromatography–ion trap mass spectrometry. **J. Chromatogr. A**, 1216 (2009) 4859-4867.
36. Ma Z, **Zhang X**. Seven new benzeneacetic acid derivatives and their quinone reductase activity from *Eurycorymbus cavaleriei*. **Phytochem. Lett.**, 2 (2009) 152-158.

37. Ma Z, **Zhang X**, Cheng L, Zhang P. Three lignans and one coumarinolignoid with quinone reductase activity from *Eurycorymbus cavaleriei*. *Fitoterapia*, 80 (2009) 320-326.

## **PATENTS**

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1. Cravatt B, Crowley V, **Zhang X**. "Compounds and methods for DCAF-mediated protein degradation" Pub. No. US20200190105A1. *United States Patent and Trademark Office*. 2020.
2. Ma Z, Zhao X, **Zhang X**. "Thiophene compounds as anti-tumor agents" Patent No. 200910099267.X. *State Intellectual Property Office of P.R.C.*, 2009.

## **RESEARCH SUPPORT**

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### ONGOING

#### **DFS-53-22**

03/01/2022 – 02/29/2024

Damon Runyon Cancer Research Foundation

Developing molecular glue degraders as a new drug modality for cancer therapy

ZHANG, XIAOYU (PI)

#### **R00CA248715**

02/01/2022 – 01/31/2025

National Cancer Institute (NCI)

Discovery of small molecule-mediated protein degradation pathways in human cancer

ZHANG, XIAOYU (PI)

### COMPLETED

#### **K99CA248715**

05/01/2020 – 01/07/2022

National Cancer Institute (NCI)

Discovery of small molecule-mediated protein degradation pathways in human cancer

ZHANG, XIAOYU (PI)

#### **DRG-2341-18**

07/01/2018 – 04/30/2020

Damon Runyon Cancer Research Foundation

Discovery of chemical probes that support targeted protein degradation in human cancer

ZHANG, XIAOYU (PI)

#### **YK2009015**

09/01/2009 – 03/31/2011

Education Department of Zhejiang Province

Characterization of naturally occurring electrophiles that modulate KEAP1-NRF2 pathway

ZHANG, XIAOYU (PI)

## **TEACHING AND MENTORSHIP**

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### **Course Instructor**

Spring 2022

Northwestern University, Department of Chemistry

Evanston, IL

- Bioorganic Chemistry/Chemical Biology (CHEM 314/415)

### **Teaching Assistant**

Spring 2013, Spring 2014

Cornell University, Department of Chemistry and Chemical Biology

Ithaca, NY

- Honors Experimental Chemistry (CHEM 3010)

### **Teaching Assistant**

Fall 2012, Fall 2013

Cornell University, Department of Chemistry and Chemical Biology

Ithaca, NY

- Introduction to Experimental Organic Chemistry (CHEM 2510)

### **Research Mentor**

2017 – present

The Scripps Research Institute, Department of Chemistry

La Jolla, CA

- Supervised postdoctoral fellow Yongfeng Tao (09/2020 – present), rotation graduate student Garrett Lindsey (08/2020 – present), visiting master students Marvin Thielert (12/2018 – 12/2019) and Ludwig Bauer (08/2018 – 11/2018), and high school student intern William Murray (06/2019 – 08/2019)

## Research Mentor

Cornell University, Department of Chemistry and Chemical Biology

2013 – 2017

Ithaca, NY

- Supervised graduate students Steve Halaby (03/2014 – 06/2014), Arash Latifkar (03/2015 – 10/2017), Tatsiana Kosciuk (03/2016 – 10/2017) and Seth Miller (10/2016 – 10/2017), master student Patricia Tolbert (01/2017 – 10/2017), and undergraduate student David Kim (11/2015 – 05/2016)

## PROFESSIONAL EXPERIENCE

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Member, American Society for Mass Spectrometry

2021 – present

Guest Editorial Board, PLOS ONE

2019 – present

Manuscript reviewer for

2016 – present

- Cell
- Nature Chemical Biology
- Journal of the American Chemical Society
- Journal of Medicinal Chemistry
- Cell Chemical Biology
- Bioorganic & Medicinal Chemistry (2017 Award for Outstanding Contribution in Reviewing)
- ChemBioChem
- PLOS ONE
- Analytical and Bioanalytical Chemistry
- ACS Omega
- Molecules
- Pharmaceuticals
- Plants
- Antibiotics

Associate Faculty Member, Faculty of 1000

2013 – 2016

Editorial Board, Current Metabolomics and Systems Biology

2020 – 2021

## PRESENTATIONS

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1. Discovery of small molecule-mediated protein degradation pathways. *Dana Farber Targeted Protein Degradation Webinar. July 2021, webinar. [invited speaker]*
2. Electrophilic PROTACs that degrade nuclear proteins by engaging DCAF16. *Translational Chemical Biology Conference. October 2020, virtual conference. [invited speaker]*
3. Electrophilic PROTACs that degrade nuclear proteins by engaging DCAF16. *Keystone Symposia on Proteomics in Cell Biology and Disease. September 2020, virtual conference. [invited speaker]*
4. Electrophilic PROTACs that degrade nuclear proteins by engaging DCAF16. *Broad Institute Next Generation in Biomedicine Symposium. September 2019, Cambridge, MA, US. [invited speaker]*
5. Discovery of small molecule-mediated protein degradation pathways. *San Diego Researchers Association Seminar. September 2019, San Diego, CA, US. [invited speaker]*
6. SIRT6 regulates protein secretion and exosome biogenesis by lysine defatty-acylation. *Membrane Signaling Group Seminar, Cornell University, April 2016, Ithaca NY, US. [invited speaker]*
7. The defatty-acylase activity of SIRT6 in tumor suppression. *Keck Biomembrane Retreat, Cornell University and Weill Cornell Medical College, June 2015, Ithaca NY, US. [invited speaker]*
8. A simple on-line screening method for rapid discovery of Michael addition acceptors from natural products. *Westlake International Medical Conference-Translational Medicine, June 2010, Hangzhou, China. [invited speaker]*
9. PYDDT, a novel Nrf2 activator. *The 6<sup>th</sup> Chinese Conference on Oncology & 9<sup>th</sup> Cross-Strait Academic Conference on Oncology, May 2010, Shanghai, China. [invited speaker]*

10. Zhang X, Crowley VM, Wucherpfennig TG, Dix MM, Cravatt BF. Electrophilic PROTACs that degrade nuclear proteins by engaging DCAF16. *Keystone Symposia on Proteomics in Cell Biology and Disease*. September 2020, virtual conference. [poster]
11. Zhang X, Crowley VM, Wucherpfennig TG, Dix MM, Cravatt BF. Degradation of nuclear proteins by electrophilic probes via engaging a Cullin-RING E3 ubiquitin ligase. *Damon Runyon Cancer Research Foundation Annual Fellows' Retreat*. September 2018, Beverly MA, US. [poster]
12. Zhang X, Khan S, Jiang H, Antonyak MA, Chen X, Spiegelman NA, Shrimp JH, Cerione RA, Lin H. Identifying the functional contribution of the defatty-acylase activity of SIRT6. *Emerging Paradigms in Drug Discovery & Chemical Biology, The New York Academy of Sciences*, October 2016, New York City NY, US. [poster]
13. Zhang X, Khan S, Jiang H, Antonyak MA, Chen X, Spiegelman NA, Shrimp JH, Cerione RA, Lin H. Identifying the functional contribution of the defatty-acylase activity of SIRT6. *Gordon Research Conference-Bioorganic Chemistry*, June 2016, Andover NH, US. [poster]
14. Zhang X, Antonyak MA, Cerione RA, Lin H. Functional dissection of SIRT6 enzymatic activities. *Cornell Chemistry Biology Interface Symposium, Cornell University*, April 2016, Ithaca NY, US. [poster]
15. Zhang X, Lin H. Investigating the function of protein lysine fatty-acylation. *Cornell Chemistry Biology Interface Symposium*, May 2015, Ithaca NY, US. [poster]
16. Zhang X, Ma Z. Discovery and functional study of novel naturally occurring electrophiles. *Lilly China Innovation Symposium and Award Ceremony*, June 2011, Shanghai, China. [poster]
17. Zhang X, Ma Z. Depleting cellular glutathione and subsequently S-glutathionylation of Keap1 by electrophilic agents activates Keap1-Nrf2 pathway. *AACR 101<sup>st</sup> Annual Meeting*, April 2010, Washington DC, US. [poster]