

Yiwu Yao

Current Position: Senior Research Fellow, Department of Pathology, Michigan Medicine, University of Michigan

Phone: (+1)734-926-7567

Email: yiwuyao@gmail.com

Web: <https://yiwuyao.github.io/> <https://www.linkedin.com/in/yiwuyao/>

Work Address: 1150 West Medical Center Dr., MSRB 1, room 4522, Ann Arbor, MI 48109

EDUCATION

Guangzhou Institutes of Biomedicine and Health, Chinese Jun. 2016

Academy of Sciences, Guangzhou, Guangdong, China

Ph.D., Medicinal Chemistry

China Pharmaceutical University, Nanjing, Jiangsu, China **Jun. 2012**

M.S., Medicinal Chemistry

China Pharmaceutical University, Nanjing, Jiangsu, China **Jun. 2009**

B.S., Pharmacy

EXPERIENCE

Grembecka/Cierpicki Lab Senior Research Fellow, Aug. 2019 - Present

Research Fellow, Aug. 2016 - Jul. 2019

- My project in Grembecka/Cierpicki lab is the development of small molecule inhibitor targeting PRC1 core component Bmi1-Ring1b E3 ligase.

In this challenging project:

1. We developed a series of first-in-class Bmi1-Ring1b E3 ligase inhibitors

using fragment based drug discovery. The lead compound induces differentiation of leukemia cells.

2. I developed a convergent and divergent pharmacophore-oriented synthesis route which facilitated the SAR study, over 180 compounds were synthesized.
3. The Bmi1-Ring1b protein with bound inhibitor co-crystal structures were obtained using a more soluble, more potent inhibitor. With the insight of the detailed binding mode, I optimized the inhibitors from micromolar to nanomolar binding affinity.
4. I synthesized a few biotin-labeled compounds to develop AlphaLISA assay for the potency evaluation and pull-down assay for target engagement validation.
5. Extensive cell-based studies are ongoing.

Sheng Jiang Lab

PhD, Sep. 2013 – Jun. 2016

Assistant Investigator, Aug. 2012 – Aug. 2013

M.S., Oct. 2010 – Jun. 2012

- I played a key role in the project of the development of novel cyclic depsipeptides and small molecules HDAC inhibitors.
1. We designed a series of cyclic depsipeptides HDAC inhibitor based on nature product romidepsin (FK228) and largazole. The resulting compounds show improved selectivity and reduced toxicity. **The lead compound entered preclinical studies.**
 2. I modified the total synthesis route so that divergent analogues (40+) and gram-scale synthesis is feasible.
 3. I also synthesized a series of small molecular HDAC inhibitors using click chemistry, followed by scaffold-hopping lead to compounds demonstrating class I and IIb subtype selectivity.

- I involved in the total synthesis of biologically active nature products (-)-norsecurinine, (-)-niruroidine and (-)-flueggine A.
- I designed and synthesized two series of dual inhibitors, EGFR/NAMPT and MTH1/NAMPT.
- I developed the practical synthesis of prostaglandin E1.

Hequan Yao Lab**M.S., Jul. 2010 – Sep. 2010**

- I initialed the total synthesis of hyrtiocarboline.

Hongbin Sun Lab**B.S. Intern, Feb. 2009 – May 2009**

- I synthesized the 5HT_{2A} inhibitor naftidrofuryl and its stereoisomers.

EXPERTISE & SKILLS

Expertise Medicinal Chemistry, Hit/Lead Optimization, Fragment-Based Drug Discovery, Structure-Based Drug Design, Protein-Protein Interaction, Total Synthesis

Laboratory NMR, LC-MS, Agilent Q-TOF (HRMS), SFC

Software Maestro (Schrodinger), Pymol, Coot, SeeSAR

PUBLICATIONS

1. Shirish Shukla*, Weijiang Ying*, Felicia Gray*, **Yiwu Yao***, ..., Jolanta Grembecka, Tomasz Cierpicki. First-in-class small molecule inhibitors of Polycomb Repressive Complex 1 (PRC1) RING domain. **Nat. Chem. Bio. In Revision. (*equal contribution)**
2. **Yiwu Yao**, Weijiang Ying, ..., Jolanta Grembecka, Tomasz Cierpicki. First-in-Class Polycomb repressive complex 1 (PRC1) Inhibitors: Fragment-Based Lead Discovery and Structure–Activity Relationship Study. **J. Med. Chem. In Preparation. Expected 2021.**

3. **Yao, Y.**, Tu, Z., Liao, C., Wang, Z., Li, S., Yao, H., Li, Z. & Jiang, S. Discovery of Novel Class I Histone Deacetylase Inhibitors with Promising in Vitro and in Vivo Antitumor Activities. **J. Med. Chem.** 58, 7672-7680, (2015).
4. Ma, N. *, **Yao, Y. ***, Zhao, B.-X., Wang, Y., Ye, W.-C. & Jiang, S. Total synthesis of securinega alkaloids (-)-norsecurinine, (-)-niruroidine and (-)-flueggine A. **Chem. Commun.** 50, 9284-9287, (2014). (*equal contribution)
5. **Yao, Y.**, Li, Z., Qiu, Y., Bai, J., Su, J., Zhang, D. & Jiang, S. Unprecedented reactions: from epichlorohydrin to epoxyglycidyl substituted divinyl ether and its conversion into epoxyglycidyl propargyl ether. **Sci. Rep.** 5, 14231pp., (2015).
6. **Yao, Y.**, Liao, C., Li, Z., Wang, Z., Sun, Q., Liu, C., Yang, Y., Tu, Z. & Jiang, S. Design, synthesis, and biological evaluation of 1, 3-disubstituted-pyrazole derivatives as new class I and IIb histone deacetylase inhibitors. **Eur. J. Med. Chem.** 86, 639-652, (2014).
7. Zhang, K. *, **Yao, Y. ***, Qiu, Y., Chen, D., Jiang, S., Tu, Z., Wang, Z., Liao, C., Hamilton, D. J. & Li, Z. Discovery of class I histone deacetylase inhibitors based on romidpesin with promising selectivity for cancer cells. **Future Med. Chem.** 12, 311-323. (2020) (*equal contribution)
8. Zhang, W. *, Zhang, K. *, **Yao, Y. ***, Liu, Y. *, Ni, Y., Liao, C., Tu, Z., Qiu, Y., Wang, D., Chen, D., Qiang, L., Li, Z. & Jiang, S. Dual nicotinamide phosphoribosyltransferase and epidermal growth factor receptor inhibitors for the treatment of cancer. **Eur. J. Med. Chem.** 113022. (2020) (*equal contribution)
9. Jin, Y., **Yao, Y.**, Chen, L., Zhu, X., Jin, B., Shen, Y., Li, J., Du, X., Lu, Y., Jiang, S. & Pan, J. Depletion of γ -catenin by histone deacetylase inhibition confers elimination of CML stem cells in combination with imatinib. **Theranostics** 6, 1947-1962, (2016).

10. Sun, Q., **Yao, Y.**, Liu, C., Li, H., Yao, H., Xue, X., Liu, J., Tu, Z. & Jiang, S. Design, synthesis, and biological evaluation of novel histone deacetylase 1 inhibitors through click chemistry. *Bioorg. Med. Chem. Lett.* 23, 3295-3299, (2013).
11. Zhu, X., Chen, L., Jiang, S., Chen, C., **Yao, Y.**, Chen, D., Xue, H. & Pan, J. PQJS380: a novel lead compound to induce apoptosis in acute lymphoblastic leukemia cells. *Cancer Biol. Ther.* 15, 119-127, (2014).
12. Su, J., Qiu, Y., Ma, K., **Yao, Y.**, Wang, Z., Li, X., Zhang, D., Tu, Z. & Jiang, S. Design, synthesis, and biological evaluation of largazole derivatives: alteration of the zinc-binding domain. *Tetrahedron* 70, 7763-7769, (2014).
13. Li, X., Tu, Z., Li, H., Liu, C., Li, Z., Sun, Q., **Yao, Y.**, Liu, J. & Jiang, S. Biological evaluation of new largazole analogues: Alteration of macrocyclic scaffold with Click chemistry. *ACS Med. Chem. Lett.* 4, 132-136, (2013).
14. Su, K., Qiu, Y., **Yao, Y.**, Zhang, D. & Jiang, S. 8-hydroxyquinoline-N-oxide-promoted copper-catalyzed C-S cross-coupling of thiols with aryl iodides. *Synlett* 23, 2853-2857, (2012).
15. Hao, J., Chen, B., **Yao, Y.**, Hossain, M., Nagatomo, T., Yao, H., Kong, L. & Sun, H. Practical access to four stereoisomers of naftidrofuryl and their binding affinity towards 5-hydroxytryptamine 2A receptor. *Bioorg. Med. Chem. Lett.* 22, 3441-3444, (2012).

PATENTS

- 1 Cierpicki, T., Grembecka, J., Ying, W., **Yao, Y.**, Gray, F. & Zhao, Q. Preparation of pyrrole derivatives as PRC1 inhibitors and methods of treatment therewith. WO2019236957A1 (2019).

- 2 Jiang, S., Tu, Z., Hao, H., Yao, H., Qiu, Y., **Yao, Y.** & Chen, D. Preparation of heterocyclic urea compounds as anticancer agents. WO2018133716A1 (2018).
- 3 Jiang, S., Tu, Z., Zheng, D., Qin, D., Bai, J., Qin, X., **Yao, Y.**, Liu, Y., Qiu, Y. & Chen, J. Preparation of 3-(pyridin-3-yl)acrylamide derivatives as nicotinamide phosphoribosyltransferase inhibitors useful for the treatment of cancer. WO2016095581A1 (2016).
- 4 Jiang, S., Yao, Z., **Yao, Y.**, Qiu, Y., Lu, C., Su, K. & Yao, X. Cyclic peptide compound, and preparation method, pharmaceutical composition and use thereof. WO2015027959A1 (2015).
- 5 Jiang, S., Li, S., Yao, Z., **Yao, Y.**, Zhang, F., Chao, Y., Ye, H. & Chen, M. Preparation of cyclopeptides as histone deacetylase inhibitors. WO2013071715A1 (2013).
- 6 10 Chinese Patents. CN107674059A (2018), CN106928192A (2017), CN106866571A (2017), CN104557863A (2015), CN103524598A (2014), CN103601742A (2014), CN103086971A (2013), CN102311398A (2012), CN102391359A (2012), CN102276689A (2011).

AWARDS & HONORS

- National Scholarship, Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Sciences, 2015
- The Third Prize GIBH Scholarship, Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Sciences, 2015
- Merit Student, Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Sciences, 2014&2015

PRESENTATIONS

- Chinese Academy of Sciences Guangzhou Branch Symposium, 2015 (Oral)
- 2011&2015 Chinese Medicinal Chemistry Symposium & 3rd&5th CPA-RSC Symposium on Medicinal Chemistry (Poster)
- 7th CCS National Organic Chemistry Conference 2011(Poster)
- 3rd&4th Lingnan Organic Chemistry Forum 2013&2014 (Poster)

REFERENCES

Tomasz Cierpicki, PhD

Associate Professor, Department of Pathology

University of Michigan

1150 West Medical Center Dr

MSRB 1, room 4510C

Ann Arbor, MI 48109, USA

Phone: +1-734-6159324

Email: tomaszc@umich.edu

Jolanta Grembecka, PhD

Associate Professor, Department of Pathology

University of Michigan

1150 West Medical Center Dr

MSRB I, Room 4510D

Ann Arbor, MI, 48109, USA

Pphone: +1-734-6159319

Email: jolantag@med.umich.edu

Sheng Jiang, Ph.D

Professor of Department of Medicinal Chemistry

China Pharmaceutical University

639 Longmian Avenue

Nanjing, Jiangsu, 210009, P. R. China

Phone: +86-18688888237

Email: jiang_shengg@126.com, jiang_sheng@gibh.ac.cn

Hequan Yao, Ph.D

Professor of Department of Medicinal Chemistry

Director of Office of Science & Technology

China Pharmaceutical University

24 Tongji Xiang

Nanjing, Jiangsu, 210009, P. R. China

Phone: +86-25-83271042 (office), +86-13815420541 (mobile)

Email: hyao@cpu.edu.cn, cpuhyao@126.com