Yiwu Yao

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

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EDUCATION

Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Sciences (GIBH, CAS), Guangzhou, Guangdong, China — **Jun. 2016**
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

RESEARCH EXPERIENCES

Grembecka/Cierpicki Lab — **Aug. 2016 - Present**
Postdoc Research

- My project in Cierpicki/Grembecka lab is development of First-In-Class small molecule inhibitor targeting PRC1 core component Ring1B-Bmi1 E3 ligase using fragment-based drug discovery. In this challenging project:
  1. I improved the inhibitor binding affinity from micromolar to nanomolar.
  2. I developed a convergent and divergent pharmacophore oriented synthesis route which facilitated the SAR study.
  3. Co-crystal structure was obtained using a more soluble and potent inhibitor.
  4. Extensive cell based study is ongoing.

Sheng Jiang Lab — **Oct. 2010 – Jun.2016**
Graduate Research, M.S. & PhD

- Design synthesis, and biological evaluation of cyclic depsipeptides and small molecules as anticancer agents selectively targeting Class I HDAC. **This project entered**

preclinical studies.

- Total synthesis of biologically active nature products (-)-norsecurinine, (-)-niruroidine and (-)-flueggine A.
- Design, synthesis and antitumor activity evaluation of EGFR/NAMPT dual inhibitors.
- Practical synthesis of bio-active nature products. (>10 steps)

Hequan Yao Lab **Jul. 2010 – Sep.2010**

Graduate Research, M.S.

- Total synthesis of hyrtiocarboline.

Hongbin Sun Lab **Feb. 2009 – May 2009**

Undergraduate Research

- Synthesis of naftidrofuryl and its stereoisomers.

EXPERTISE & SKILLS

Expertise	Medicinal Chemistry, Hit/Lead Optimization, FBDD & SBDD, Protein-Protein Interaction, Total Synthesis, Structure Biology, Cancer Biology
Laboratory	NMR, LC-MS, Combi-Flash, Lyophilizer, Agilent Q-TOF (HRMS), SFC
Software	ChemOffice, MestReNova, Maestro (Schrodinger), Pymol, Coot, SeeSAR, GOLD, CSD-CrossMiner,

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*, (2019) ([*]**equal contribution**)
8. 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).
9. 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).
10. 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).
11. 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).
12. 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).
13. 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).
14. 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 & HONOURS

- 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

CONFERENCES

- 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)