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, 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

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)