
Asia 3 Roundtable on Nucleic Acids 2024

Caiguang Yang, Professor

Center for Chemical Biology,
Shanghai Institute of Materia Medica, Shanghai
201203, China.
Tel: +86-21-xxxxxxx
Email: yangcg@simm.ac.cn



2008- Present Professor, Shanghai Institute of Materia Medica
2002-2008 Postdoctoral Researcher, The University of Chicago, USA
2002 PhD Shanghai Institute of Organic Chemistry
1997 BS Huazhong University of Science and Technology

Research Interests:

RNA Epigenetics, Chemical Probes, Target Validation, Drug Discovery

Selected Publications:

1. Lu Liu, Yuanlai Qiu, Yuying Suo, Siyao Tong, Yiqing Wang, Xi Zhang, Liang Chen, Yue Huang, Huchen Zhou, Hu Zhou*, Ze Dong*, **Cai-Guang Yang***. Discovery of a potent PROTAC degrader for RNA demethylase FTO as antileukemic therapy, *Acta Pharm Sin B*, 2024, <https://doi.org/10.1016/j.apsb.2024.07.016>.
2. Yue Huang, Wenyang Xia, Ze Dong, **Cai-Guang Yang***. Chemical inhibitors targeting the oncogenic m⁶A modifying proteins, *Acc Chem Res*, 2023, *56*, 3010-3022.
3. Lin-Lin Zhou, Tao Zhang, Yun Xue, Chuan Yue, Yihui Pan, Pengyu Wang, Teng Yang, Meixia Li, Hu Zhou, Kan Ding, Jianhua Gan, Hongbin Ji*, **Cai-Guang Yang***, Selective activator of human ClpP triggers cell cycle arrest to inhibit lung squamous cell carcinoma, *Nat Commun*, 2023, *14*:7069.
4. Yi Liu, Guanghao Liang, Hongjiao Xu, Wenxin Dong, Ze Dong, Zhiwei Qiu, Zhihao Zhang, Fangle Li, Yue Huang, Yilin Li, Jun Wu, Shenyi Yin, Yawei Zhang, Peijin Guo, Jun Liu, Jianzhong Jeff Xi, Peng Jiang, Dali Han*, **Cai-Guang Yang***, Meng Michelle Xu*. Tumors exploit FTO-mediated regulation of glycolytic metabolism to evade immune surveillance. *Cell Metab*, 2021, *33*, 1221-1233.
5. Yue Huang, Rui Su, Yue Sheng, Lei Dong, Ze Dong, Hongjiao Xu, Tengfeng Ni, Zijie Scott Zhang, Tao Zhang, Chenying Li, Li Han, Zhenyun Zhu, Fulin Lian, Jiangbo Wei, Qiangqiang Deng, Yungui Wang, Mark Wunderlich, Zhiwei Gao, Guoyu Pan, Dafang Zhong, Hu Zhou, Naixia Zhang, Jianhua Gan, Hualiang Jiang, James C. Mulloy, Zhijian Qian*, Jianjun Chen*, **Cai-Guang Yang***. Small-molecule Targeting of Oncogenic FTO Demethylase in Acute Myeloid Leukemia, *Cancer Cell*, 2019, *35*, 677-691.

Chemical Targeting RNA Epigenetic Proteins

Caiguang Yang

State Key Laboratory of Drug Research, Center for Chemical Biology, Shanghai
Institute of Materia Medica, Chinese Academy of Sciences, Shanghai 201203, China

Abstract

Epigenetics comes to RNA, introducing a new dimension to gene expression regulation. The *N*⁶-methyladenosine (m⁶A) is an abundant internal modification on eukaryote mRNA, while the significance of m⁶A in mRNA had been long neglected until the fat mass and obesity-associated (FTO) enzyme was identified as the first m⁶A demethylase. The m⁶A modification influences nearly every step of RNA metabolism and thus broadly affects gene expression at multiple levels, playing a critical role in many biological processes, including cancer progression, metastasis, and immune evasion. It is essential to develop chemical probes and lead compounds for an indepth investigation into m⁶A biology and the translational discovery of anticancer drugs targeting m⁶A modifying oncogenic proteins. I would like to review the recent developments of chemical inhibitors to regulate m⁶A in mRNA by targeting the FTO demethylase, and elucidate the mode of action (*Acc Chem Res* **2023**, *56*, 3010-3022). Towards the end, I would like to talk our discovery on the first FTO PROTAC degrader with potent *in vivo* antileukemic effects (*Acta Pharm Sin B*, 2024, <https://doi.org/10.1016/j.apsb.2024.07.016>). Collectively, these small-molecule modulators that selectively target RNA epigenetic proteins will promote indepth studies on the regulation of gene expression and potentially accelerate anticancer target discovery.

1. Yue Huang, Wenyang Xia, Ze Dong, **Cai-Guang Yang***. Chemical inhibitors targeting the oncogenic m⁶A modifying proteins, *Acc Chem Res*, 2023, *56*, 3010-3022.
2. Lu Liu, Yuanlai Qiu, Yuying Suo, Siyao Tong, Yiqing Wang, Xi Zhang, Liang Chen, Yue Huang, Huchen Zhou, Hu Zhou*, Ze Dong*, **Cai-Guang Yang***. Discovery of a potent PROTAC degrader for RNA demethylase FTO as antileukemic therapy, *Acta Pharm Sin B*, 2024, <https://doi.org/10.1016/j.apsb.2024.07.016>.