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## Asia 3 Roundtable on Nucleic Acids 2024

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- 2009- Present    PI, State Key Laboratory of Natural and Biomimetic Drugs, School of Pharmaceutical Sciences, Peking University
- 2003-2009        Postdoctoral Researcher, University of Pennsylvania, USA
- 2002 PhD         Technical Institute of Physics and Chemistry, Chinese Academy of Sciences
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#### Research Interests:

Nucleic Acid Chemical Biology, Nucleic Acid Drug Development, Circular oligonucleotides, Gene silencing, Gene editing

#### Selected Publications:

1. Jianfei Xu<sup>†</sup>, Xiaoran Zhao<sup>†</sup>, Xingxing Liang, Dongyang Guo, Jing Wang, Qian Wang\*, **Xinjing Tang\*** Development of miRNA- based PROTACs targeting Lin28 for breast cancer therapy, *Sci. Adv.* **2024**, 10, eadp0334.
2. Yu Zhang, Di Feng, Guanqun Mu, Qian Wang, Jing Wang, Yun Luo, and **Xinjing Tang\***, Light-triggered site-directed RNA editing by endogenous ADAR1 with photolabile guide RNA, *Cell Chem Biol.* **2023** 30, 672–682
3. YingJie Sun, WenDa Chen, Ji Liu, JunJin Li, Yu Zhang, WeiQi Cai, Li Liu, **XinJing Tang\***, Jian Hou\*, Ming Wang\*, and Liang Cheng\*, A Conformational Restriction Strategy for the Control of CRISPR/Cas Gene Editing with Photoactivatable Guide RNAs; *Angew Chem Int Ed.* **2023**, 62, e202212413
4. Xiaoxuan Su, Wenxiao Ma, Boyang Cheng, Qian Wang, Zefeng Guo, Demin Zhou, **Xinjing Tang\*** Efficient Inhibition of SARS-CoV-2 Using Chimeric Antisense Oligonucleotides through RNase L Activation, *Angew Chem Int Ed.* **2021**, 60, 21662–21667
5. Yu Zhang<sup>§</sup>, Xinyu Ling<sup>§</sup>, Xiaoxuan Su, Shilin Zhang, Jing Wang, Pingjing Zhang, Wenjian Feng, York Yuanyuan Zhu, Tao Liu, **Xinjing Tang\*** Optical Control of CRISPR-Cas9 system for gene editing using photolabile crRNA. *Angew Chem Int. Ed.* **2020**, 132, 21081-21085.

## Nucleic acid drugs for targeting RNA and protein degradation

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### Abstract

Nucleic acid drugs have been promising therapeutic agents for targeting different targets. Here we presented a kind of oligonucleotide chimera for targeting RNA and Protein degradation. We first constructed chimeric oligonucleotides comprising antisense oligonucleotide and a 5'-phosphorylated 2'-5' poly(A)<sub>4</sub> (4A2-5) to degrade envelope and spike RNAs of SARS-CoV-2. The oligonucleotide sequence was used for searching and recognizing target viral RNA sequence, and the conjugated 4A2-5 was used for guided RNase L activation to sequence-specifically degrade viral RNAs, indicating a promising antiviral agent based on the nucleic acid-hydrolysis targeting chimera (NATAC) strategy. We also developed a series of miRNA-based Lin28A-miRNA proteolysis-targeting chimeras (Lin28A miRNA-PROTACs) for efficient Lin28A degradation through a ubiquitin- proteasome-dependent mechanism, resulting in up-regulation of mature let-7 family, further exerting inhibitory effects on cancer cell proliferation and migration, and increase its sensitivity to chemotherapy. This study displays an effective miRNA-based PROTACs to degrade Lin28A and inhibit tumor growth, providing a promising therapeutic avenue for cancer treatment with miRNA-based therapy.