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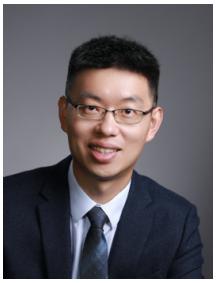

2015- Present	Professor, Nanjing University
2013-2015	Postdoctoral Researcher, Yale University, USA
2013 PhD	Arizona State University, USA
2007 BS	Peking University

Research Interests:
chemically modified nucleic acid, xeno-nucleic acid, DNAzyme, aptamer

Selected Publications:

1. Ze Zhang, Wanqing Wei, Siqi Chen, Jintao Yang, Dongfan Song, Yinghan Chen, Zerun Zhao, Jiawen Chen, Fulong Wang, Jiahuan Wang, Zhe Li, Yong Liang* and **Hanyang Yu***, Chemoenzymatic installation of site-specific chemical groups on DNA enhances catalytic activity, ***J. Am. Chem. Soc.***, 146, 7052-7062 (2024)

2. Bohe Qin, Qi Wang, Yuang Wang, Feng Han, Haiyan Wang, Shuoxing Jiang* and **Hanyang Yu***, Enzymatic synthesis of TNA protects DNA nanostructures, ***Angew. Chem. Int. Ed.***, 63, e202317334 (2024)

3. Xintong Li, Ze Zhang, Fangyan Gao, Yuxuan Ma, Dongying Wei, Zhangwei Lu, Siqi Chen, Mengqi Wang, Yueyao Wang, Kun Xu, Runtian Wang, Feng Xu, Jia-Yu Chen, Chengjun Zhu, Zhe Li, **Hanyang Yu***, and Xiaoxiang Guan*, c-Myc-targeting PROTAC based on a TNA-DNA bivalent binder for combination therapy of triple-negative breast cancer, ***J. Am. Chem. Soc.***, 145, 9334-9342 (2023)

4. Yueyao Wang, Yao Wang, Dongfan Song, Xin Sun, Zhe Li*, Jia-Yu Chen and **Hanyang Yu***, An RNA-cleaving threose nucleic acid enzyme capable of single point mutation discrimination, ***Nat. Chem.***, 14, 350-359 (2022)

5. Yao Wang, Yueyao Wang, Dongfan Song, Xin Sun, Ze Zhang, Xintong Li, Zhe Li and **Hanyang Yu***, A threose nucleic acid enzyme with RNA ligase activity, ***J. Am. Chem. Soc.***, 143, 8154-8163 (2021)

Chemical Biology of Xeno-Nucleic Acids

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Abstract

Nucleic acids can fold into distinct tertiary structures with binding affinities and catalytic activities, and thus offer versatile molecular tools to chemistry and biomedicine. However, functional DNAs and RNAs are inherently constrained due to the susceptibility to nuclease degradation and a limited repertoire of chemical functionality. Xeno-nucleic acids (XNAs) are synthetic genetic polymers with superior biological stability and enriched chemical diversity, and provide promising modalities for various biomedical applications.

We primarily focus on threose nucleic acid (TNA), which contains a noncanonical tetrose moiety and is thus refractory to nuclease digestion. We leverage *in vitro* selection to identify TNA aptamers towards therapeutic target proteins, and catalytic TNAs (TNAzymes) with RNA endonuclease and RNA ligase activities. Specifically, an RNA-cleaving TNAzyme discriminates single point mutation within the substrate, and induces allele-specific gene silencing in living cells. An RNA ligase TNAzyme introduces a noncanonical 2'-5' phosphodiester linkage in the product, and can thus modulate RNA function. An *in vitro* selected c-Myc-binding TNA aptamer can be assembled into a heterobifunctional PROTAC to mediate targeted protein degradation. We also develop a chemoenzymatic method to install various chemical groups site-specifically onto DNA, and identify chemically modified DNAzyme variants that exhibit substantially enhanced catalytic activities and reduced metal ion dependence. These results underscore the importance of chemical modification in delivering functional nucleic acids with appealing properties.