

## Debin Ji

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### EDUCATION

- 2014 06–Present**      **-Department of Chemistry, Stanford University, CA 94305, USA**  
-Postdoc in Chemical biology  
-Supervised by Professor Eric T. Kool
- 2012 06–2014 06**      **-Department of Chemistry, University of California at Riverside, CA 92507, USA**  
-Postdoc in Chemical biology  
-Supervised by Professor Yinsheng Wang
- 2007 09–2012 06**      **-Dalian Institute of Chemical Physics, CAS, Dalian 116023, China**  
-Ph.D. in Organic Chemistry (Chemical Biology)  
-Dissertation Title: Construction of Bioorthogonal Redox Systems  
Supervised by Professor Zongbao Zhao
- 2004 09–2007 09**      **-Hebei University of Science and Technology, Shijiazhuang 050018, China**  
-College of Chemical and Pharmaceutical Engineering,  
-Master in Medicinal Chemistry.  
-Dissertation Title: Synthesis of a series of unnatural amino acids by reduction of oximino esters and biocatalysis resolution  
Supervised by Professor Shouxin Liu
- 2000 09–2004 07**      **-Linyi University, Linyi 276000, China**  
-College of life science  
-Bachelor's degree in Science of Biology.

### LIST OF PUBLICATIONS

1. **Ji DB**, Wang L, Hou SH, Liu WJ, Wang JX, Wang Q, Zhao, ZB. Creation of Bioorthogonal Redox Systems Depending on Nicotinamide Flucytosine Dinucleotide. *J. Am. Chem. Soc.* **2011**, *133*, 20857–20862.
2. **Ji DB**, Wang YS. Facile Enzymatic Synthesis of Base J-Containing Oligodeoxyribonucleotides and an Analysis of the Impact of Base J on DNA Replication in Cells. *Plos. One* **2014**, *9*, e103335.
3. **Ji DB**, Lin K, Song JK, Wang YS. Effects of Tet-induced Oxidation Products of 5-Methylcytosine on Dnmt1-and DNMT3a-mediated Cytosine Methylation. *Mol. Biosyst.* **2014**, *10*, 1749–1752.
4. **Ji DB**, You CJ, Wang PC, Wang YS. Effects of Tet-Induced Oxidation Products of 5-Methylcytosine on DNA Replication in Mammalian Cells. *Chem. Res, Toxicol.* **2014**, *27*, 1304–1309.
5. **Ji DB**, Wang L, Liu WJ, Hou SH, Zhao, ZB. Synthesis of NAD Analogs to Develop Bioorthogonal Redox System. *Science Chin. Chem.* **2013**, *56*, 296–300.

6. **Ji DB**, Wang L, Zhou YJ, Yang W, Wang Q, Zhao, ZB. Oxidative Decarboxylation of L-Malate by Using a Synthetic Bioredox System. *Chin. J. Catal.* **2012**, *33*, 530–535.
7. Xiao YS, **Ji DB**, Guo L, Wang YS. Comprehensive Characterization of (S)GTP-Binding Proteins by Orthogonal Quantitative (S)GTP-Affinity Profiling and (S)GTP/GTP Competition Assays. *Anal. Chem.* **2014**, *86*, 4550–4558.
8. Hou SH, **Ji DB**, Liu WJ, Wang L, Zhao, ZB. Identification of Malic Enzyme Mutants Depending on 1,2,3-Triazole Moiety-containing Nicotinamide Adenine Dinucleotide Analogs. *Bioorg. Med. Chem. Lett.* **2014**, *24*, 1307–1309.
9. Liu S, **Ji DB**, Cliffe L, Sabatini R, Wang YS. Quantitative Mass Spectrometry-Based Analysis of beta-D-Glucosyl-5-Hydroxymethyluracil in Genomic DNA of *Trypanosoma brucei*. *J. Am. Soc. Mass Spectrom.* **2014**, *25*, 1763–1770.
10. Fu LJ, Guerrero CR, Zhong N, Amato NJ, Liu YH, Liu S, Cai Q, **Ji DB**, Jin SG, Niedernhofer, LJ, Pfeifer, GP, Xu GL, Wang YS. Tet-Mediated Formation of 5-Hydroxymethylcytosine in RNA. *J. Am. Chem. Soc.* **2014**, *136*, 11582–11585.
11. Wang PC, Williams, RT, Guerrero CR, **Ji DB**, Wang YS. Fragmentation of Electrospray-Produced Deprotonated Ions of Oligodeoxyribonucleotides Containing an Alkylated or Oxidized Thymidine. *J. Am. Soc. Mass Spectrom.* **2014**, *25*, 1167–1176.
12. Wang L, Zhou YJ, **Ji DB**, Lin XP, Liu YX, Zhang YX, Liu WJ, Zhao, ZB. Identification of UshA as a Major Enzyme for NAD Degradation in *Escherichia coli*. *Enzyme. Microb. Tech.* **2014**, *59*, 75–79.
13. Wang L, Zhou YJ, **Ji DB**, Zhao, ZB. An Accurate Method for Estimation of the Intracellular Aqueous Volume of *Escherichia coli* Cells. *J. Microb. Meth.* **2013**, *93*, 73–76.
14. Hou SH, Liu WJ, **Ji DB**, Wang Q, Zhao ZB. Synthesis of 1,2,3-Triazole Moiety Containing NAD Analogs and Their Potential as Redox Cofactors. *Tetrahedron Lett.* **2011**, *52*, 5855–5857.
15. Hou SH, Liu WJ, **Ji DB**, Zhao ZB. Efficient Synthesis of Triazole Moiety-containing Nucleotide Analogs and Their Inhibitory Effects on a Malic enzyme. *Bioorg. Med. Chem. Lett.* **2011**, *21*, 1667–1669.
16. Liu SX, **Ji DB**, Yang YH, Zhen XL, Tian X, Han JR. A Practical Procedure for Efficient Synthesis of alpha-Amino Acids. *Lett. Org. Chem.* **2009**, *6*, 156–158.

## CONFERENCE POSTERS AND PRESENTATIONS

1. **Ji DB**, Wang L, Hou SH, Liu WJ, Wang JX, Wang Q, Zhao ZB. Assembling of Bioorthogonal Redox Systems Depending on NAD Analogs. Gordon Research Conference in Bioorganic Chemistry June 12–17, 2011. Poster 115.
2. **Ji DB**, Wang L, Liu WJ, Zhao ZB. Assembling of Bioorthogonal Redox Systems. Cold Spring Harbor Asia Conferences: Design & Synthesis of Biological Systems November 7–11, 2011.

## PRESENT RESEARCH FOCUS

My current research is to find a simple and rapid ways to detect the cellular genetic mutations that cause cancer and drug resistance and develop new nucleoside analogs as next generation DNA sequencing tools and imaging agents.

## RESEARCH FOCUS AT UC RIVERSIDE

My postdoctoral research has focused on DNA damage. In this research area, I have been using a multi-pronged approach, encompassing synthetic organic chemistry, biochemistry and molecular biology tools, mass spectrometry-based analytical chemistry, to understand, at the molecular level, how various DNA damage products are repaired, and how they perturb the efficiency and fidelity of flow of genetic information during DNA replication and transcription.

### 1. Chemical synthesis of oligodeoxynucleotides harboring structurally defined DNA lesions.

I employed traditional phosphoramidite chemistry and automated solid-phase DNA synthesis to prepare oligodeoxynucleotide (ODN) substrates containing site-specifically incorporated and structurally defined DNA modifications. These substrates were then used for assessing the repair and biological consequences of these DNA modifications.

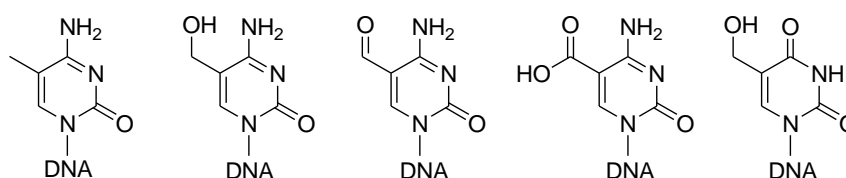


Fig. 1 ODN containing 5-methylcytosine and its oxidized products

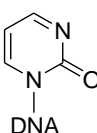


Fig. 2 ODN containing zebularine for determine the crystal structure of DNMT 3a

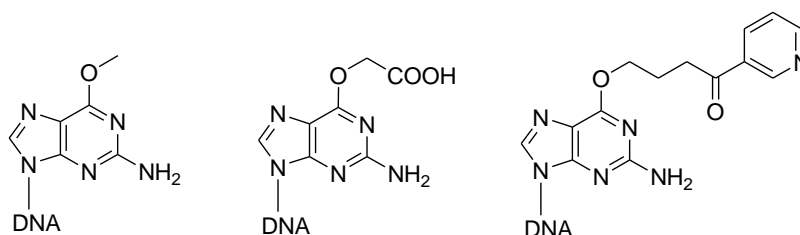


Fig. 3 Syntheses of ODN containing O<sup>6</sup>-MG O<sup>6</sup>-CMG and O<sup>6</sup>-pobG

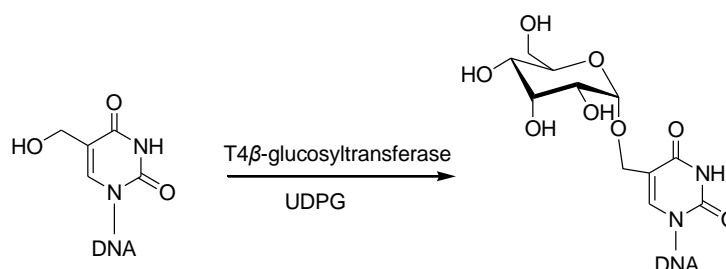


Fig. 4 Syntheses of base J containing ODN using an enzyme catalyzed method



### 3. Using a LC-MS method to determine the effects of Tet-induced oxidation products of 5-methylcytosine on Dnmt1- and DNMT3a-mediated cytosine methylation

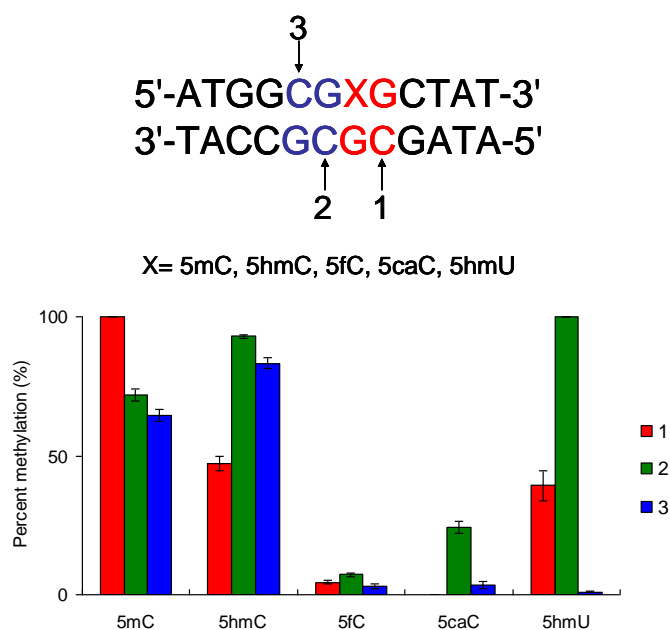


Fig. 7 Levels of cytosine methylation in different substrates methylated by Dnmt1 at three different CpG sites.

### 4. Synthesis of GTP analog probe for quantitative affinity profiling of their binding proteins

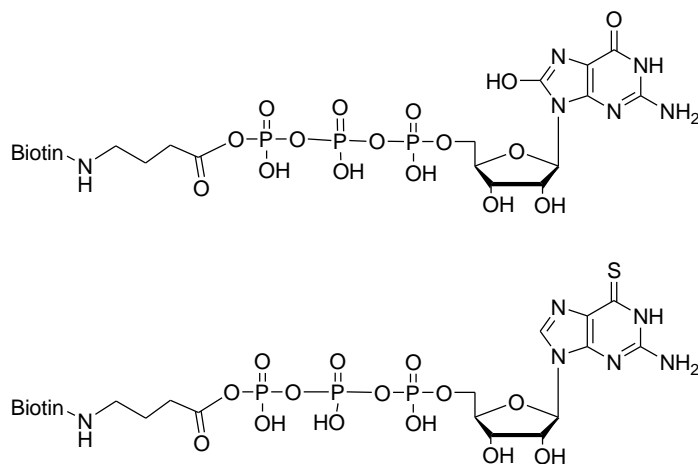


Fig.8 Structure of 6SGTP and 8-Oxo-GTP affinity probes

## PH.D. RESEARCH FOCUS

I created a bioorthogonal system that catalyzes the oxidative decarboxylation of L-malate with a dedicated abiotic cofactor. Firstly, I realized the preparation of various  $\text{NAD}^+$  analogs. Secondly, taking NAD-dependent malic enzyme (ME) as the model, I constructed multi-site saturated mutagenesis library of ME. After screening the  $\text{NAD}^+$  analog library against the mutant enzyme libraries, I identified a couple of bioorthogonal redox pairs, in which the mutant enzyme ME L310R/Q401C specifically recognizes nicotinamide flucytosine dinucleotide ( $\text{NFCD}^+$ ) but not  $\text{NAD}^+$ . The catalytic efficiency of ME-L310R/Q401C with  $\text{NFCD}^+$  was comparable to that of ME with  $\text{NAD}^+$ .

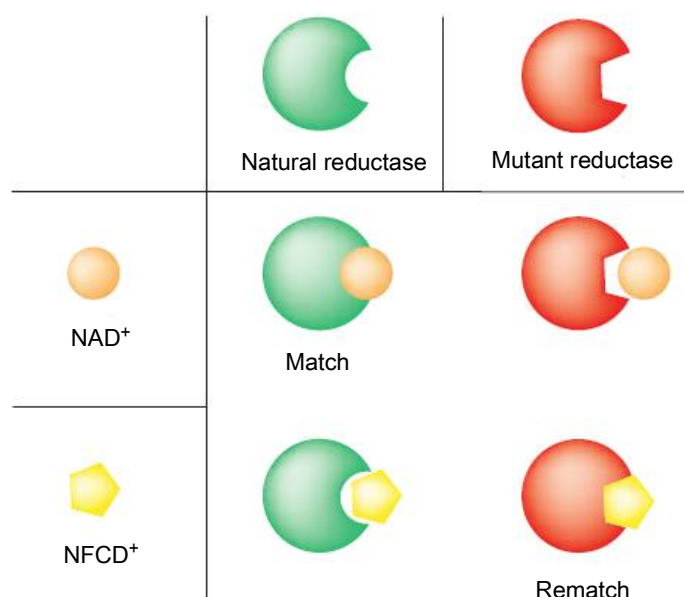


Fig.9 Scheme illustrating bioorthogonal redox system

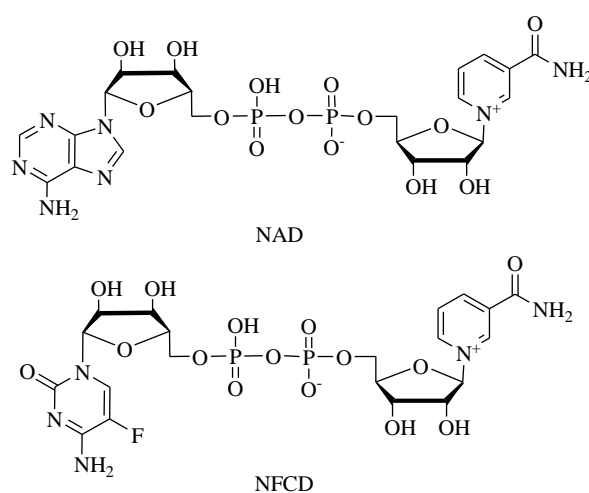


Fig.10 Chemical structure of NAD<sup>+</sup> and NFC D<sup>+</sup>.

It should be pointed out that the L310 residue is located immediately at the N-terminus of the conserved GXGXXG sequence in Rossmann fold motif of ME. Changing the particular residue to R in other NAD-dependent oxidoreductases could also yield active mutants that take NFC D<sup>+</sup> as the cofactor. And this speculation was supported by the one point mutant V152R of D-lactate dehydrogenase and L6R of malate dehydrogenase. With ME-L310R/Q401C and DLDH-V152R in hand, we were able to demonstrate the regeneration of NFC D<sup>+</sup> *in vitro*. These data suggested that NFC D<sup>+</sup> could be potentially applied *in vivo* to drive or control a naturally NAD<sup>+</sup> dependent reaction independent of the cellular NAD<sup>+</sup> level.

The present study provided a conceptually novel approach for the selective manipulation of a targeted NAD-dependent process. The accessibility of such systems should provide unique tools for synthetic biology to assemble pathway-specific redox chemistry and for systems biology to elucidate the contributions of individual redox steps in the metabolic network.

I synthesized a series of 3-arylalanine in a new way and get the enantiomers by biocatalysts resolution using *Aspergillus oryzae*.

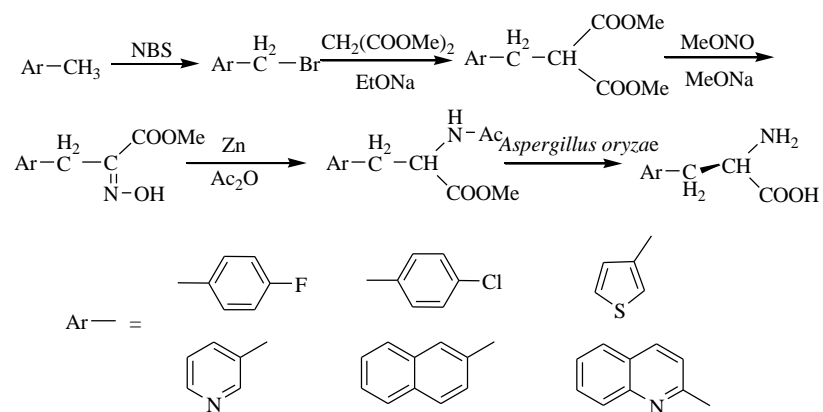


Fig.11 Synthesis of 3-arylalanine