Title: Nucleic Acid-Protein Crystallography Facilitated by Selenium-Nucleic Acids (SeNA)

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Abstract

Selenium-atom-specifically-derivatized nucleic acids (SeNA) can offer nucleic acid-protein crystallography with many unique and novel strategies via the enhanced properties (such as facilitated crystallization, phase determination and high-resolution diffraction) without significant perturbation of nucleic acids and their protein complexes in 3D structures. In addition to the ability to store genetic information and participate in gene replication, transcription and translation, nucleic acids can fold to well-defined 3-demential structures and their structures can be readily adjusted to perform specific functions (such as signal transduction, catalysis, diagnosis and therapeutic applications). Although functions of numerous nucleic acids in catalysis, gene expression regulation, protein binding and therapeutics have been well demonstrated, structures of the nucleic acids and their protein complexes largely remain elusive, especially high-resolution structures. Recently, we have established a selenium strategy for nucleic acid derivatization. This novel Se-atom-specific derivatization and functionalization will provide important tools to study nucleic acids and their protein interactions, to investigate nucleic acid-protein structure/folding, recognition and catalysis, to study and improve biochemical and biophysical properties of nucleic acids, and to discover potential nucleic acid diagnostics and therapeutics. Herein, our presentation in X-ray crystallography and neutron crystallography will focus on the most recent progresses on our SeNA technologies and their applications in structure-function studies and molecular diagnosis-medicine discovery. Work is supported by NIH ES026935.

Selected Publications:

1. Yiqing Chen, Hehua Liu, Chun Yang, Yanqing Gao, Xiang Yu, Xi Chen, Ruixue Cui, Lina Zheng, Suhua Li, Xuhang Li, Jinbiao Ma, Zhen Huang*, Jixi Li* and Jianhua Gan*, "Structure of the error-prone DNA ligase of African swine fever virus identifies critical active site residues", *Nature Communications,* **2019**, *10*, 387.

2. Venu Gopal Vandavasi, Matthew P. Blakeley, David A. Keen, Lillian R. Hu, Zhen Huang* and Andrey Kovalevsky*, "Temperature-induced replacement of phosphate proton with metal ion captured in neutron structures of A-DNA", *Structure*, **2018**, *26*, 1-6.

3. **103.** Hehua Liu, Xiang Yu, Yiqing Chen, Jing Zhang, Baixing Wu, Lina Zheng, Phensinee Haruehanroengra, Rui Wang, Suhua Li, Jinzhong Lin, Jixi Li, Jia Sheng, Zhen Huang*, Jinbiao Ma*, and Jianhua Gan*, "Crystal structure of an RNA-cleaving DNAzyme", *Nature Communications,* **2017**, *8*, 2006.

4. Jing Zhang, Hehua Liu, Qingqing Yao, Xiang Yu, Yiqing Chen, R. Cui, B. Wu, L. Zheng, J. Zuo, Zhen Huang*, Jinbiao Ma* and Jianhua Gan*,"Structural basis for single-stranded RNA recognition and cleavage by C3PO", *Nucleic Acids Research*, **2016**, *44*, 9494–9504.

5. *Liqin Zhang, Zunyi Yang, Sefah, Bradley, Hoshika, M.-J. Kim, H.-J. Kim, Zhu, Sena Cansiz, I-Ting Teng, Carole Champanhac,* Christopher McLendon, Chen Liu, Wen Zhang, Dietlind L. Gerloff[3], Zhen Huang[*], Weihong Tan[*] and Steven A. Benner[*], "Crystal Structure, Evolution, and Function of Six-Nucleotide DNA. Exploring its Large Sequence Space"，Journal of American Chemical Society, **2015**, *137*, 6734−6737.

6. Rob Abdur, O. Gerlits, Jianhua Gan, J. Jiang, J. Salon, A. Kovalevsky, A. Chumanevich, I. Weber, Zhen Huang*, "Novel Complex MAD Phasing and RNase H Structural Insights by Selenium Oligonucleotides", **2014**, *Acta Crystallographica Section D*, **2014**, *D70*, 354-361.