重庆大学药学院

学 术 报 告 第 一百四十四 讲

报告题目：Selenium Nucleic Acids (SeNA) for Structure & Function Studies and Drug Innovation(硒核酸在结构功能研究以及药物创新中的应用)

报 告 人：黄震 教授

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时　　间：2018 年 8 月 2 日（周四）15:30

地　　点：重庆大学药学院学术报告厅

报告人简介：

2009- Professor, Georgia State University, Director of SeNA Research Institute

2004-2009 Associate Professor, Georgia State University

1998-2004 Assistant Professor, Brooklyn College, City University of New York

1994-1998 Postdoctoral Researcher, Harvard Medical School, Boston, USA

1994 Ph.D. Swiss Federal Institute of Technology (ETH), Zurich, Switzerland

1987 MS Peking University

1984 BS Sichuan University

Research Interests:

Nucleic Acid-Protein Structural Biology; Nucleic Acid Novel Drug & Target Discovery; Selenium Nucleic Acids (SeNA), Enzyme Structure and Function Studies; Direct RNA Detection & RNA Microchip;

黄震教授 (Zhen Huang)，1984 年于四川大学获得学士学位，1987 年获得北京大学硕士学位，1994 年在瑞士苏黎世联邦理工大学（ETH, Zurich) 获得 博士学位。同年，他加入了哈佛大学医学院遗传系为 博士后,师从于 2009 年诺贝尔医学奖得主 邵斯达克教授 (Professor Jack Szostak)。于 1998, 他应聘入纽约城市大学布鲁克伦学院为助理教授，2004 升为副教授, 并获得终身教授职称。于 2004 年,他被聘入乔治亚州立大学化学系,于 2009 年升为乔治亚州立大学正教授,获大学杰出教授奖,为乔治亚州杰出癌症研究专家。他的研究曾多次获奖, 他也热心为学术界做很多工作。他为中美化学及化学生物学教授协会(CAPA)第一任主席及三位 创办人之一. 美国联邦政府研究基金评审员. 也曾为几本书藉刊物 担任编辑或客座编辑. 他开创了硒核酸,碲核酸及蛋白晶体复合结构研究新领域. 目前他的 主要研究兴趣包括:硒以及碲核苷和核苷酸类似物的化学生物学合成,硒核酸的转化医学基础研究及应用, 核酸药物研究，核糖核酸衍生化和核酸 及蛋白晶体结构研究,核酸基因芯片检测和测序研究.他的若干研究项目已经得到了美国联邦政府多项研究基金,美国佐治亚州政府多项研究基金, 杰出癌症研究专家基金, 和企业多项研究基金。他的研究也已经获得美国及欧洲国家多项专利。

Biography:

Zhen Huang was born and raised in Sichuan, China. He received his B.S. degree from Sichuan University in 1984 (under the supervision of Professor Shulin Chen), M.S. from Peking University in 1987 (under the supervision of Professor Wen Zhong), and Ph.D. degree from Swiss Federal Institute of Technology (ETH, Zurich) in 1994 (under the supervision of Professor Steven Benner). In 1994, he joined the Department of Genetics at Harvard Medical School as a research fellow, in Laboratory of Professor Jack Szostak (Nobel Laureate in Medicine in 2009). He was hired in 1998 by Brooklyn College, City University of New York, as assistant professor and was later promoted to associate professor with tenure. Dr. Huang was recruited in 2004 to Chemistry Department, Georgia State University, currently is Professor of Chemistry and Chemical and Structural Biology, and is also University Distinguished Professor Awardee of Georgia State University. He has received several

awards, including Georgia Distinguished Cancer Scientists Award, from The State of Georgia (GCC), and University Distinguished Professor Award. He is also very active in community services: he has served as editors and guest editors for several journals and books, and is the first President of Chinese-American Chemistry & Chemical Biology Professors Association (CAPA; also one of the three Co-Founders). He has pioneered and developed selenium and tellurium derivatizations of nucleic acids for structure and function studies of nucleic acids, protein-nucleic acid complexes, and nucleic acid-small molecular ligands (such as anticancer drugs). His current research interests are in selenium and tellurium derivatizations of DNAs and RNAs for X-ray crystallographic studies of nucleic acids and protein complexes (especially for Cancer Research), synthesis of analogs of nucleosides and nucleotides for structure, function and anticancer studies, development of RNA microchip technology for direct detection and quantitation of gene expression profile for Cancer Early Detection, nanomaterial-assisted novel RNA microchip, modified nucleic acid-based nano-medicine (potential therapeutics), nucleic acid-based cancer diagnosis, in vitro selection, evolution and characterization of ligand-binding and catalytic RNAs and DNAs. His research has been funded by federal agencies, including NIH, NSF, DOD, and/or CDC, state funding agencies, the distinguished cancer scholar award, and private funds (such as industries). He has received several US and European patents, and many US and international patent applications are pending.

Selected Publications (out of more than 100):

1. 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, 2018, in press.

2. Yiqing Chen, Jing Zhang, Hehua Liu, Yanqing Gao, Xuhang Li, Lina Zheng, Ruixue Cui, Qingqing Yao, Liang Rong, Jixi Li, Zhen Huang*, Jinbiao Ma* and Jianhua Gan*, “Unique 50-P recognition and basis for dG:dGTP misincorporation of

ASFV DNA polymerase X", PLoS Biology, 2017, 15, e1002599.

3. Jing Zhang, Hehua Liu, Qingqing Yao, Xiang Yu, et al, 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.

4. Liqin Zhang, Zunyi Yang, Kwame Sefah, et al, 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.

5. Rob Abdur, Oksana O. Gerlits, et al, Zhen Huang*, "Novel Complex MAD Phasing and RNase H Structural Insights by Selenium Oligonucleotides", 2014, Acta Crystallographica Section D, 2014, D70, 354-361.

6. Jia Sheng, Jianhua Gan, Alexie Soars, Jozef Salon and Zhen Huang*, "Structural Insights of Non-canonical U•U Pair and Hoogsteen Interaction Probed with Se Atom", 2013, Nucleic Acids Research, 41, 10476-10487.

7. Huiyan Sun, Sibo Jiang, et al and Zhen Huang*, "2-Selenouridine Triphosphate Synthesis and Se-RNA Transcription", RNA, 2013, 19, 1309-1314.

8. Jozef Salon, Jianhua Gan, Rob Abdur, Hehua Liu and Zhen Huang*, "Synthesis of 6-Se-Guanosine RNAs for Structural Study", Organic Letter, 2013, 15, 3934-3937.

9. 2. Huiyan Sun, Jia Sheng, et al and Zhen Huang*, "Novel RNA Base Pair with Higher Specificity using Single Selenium Atom", Nucleic Acids Res., 2012, 40, 5171-5179.

10. Jia Sheng, Wen Zhang, Abdalla E. A. Hassan, Jianhua Gan, Alexei Soares, Song Geng, Yi Ren, Zhen Huang*, "Hydrogen Bond Formation between the Naturally Modified Nucleobase and Phosphate Backbone", Nucleic Acids Research, 2012, 40, 8111-8118.

报告简介

Title: Selenium Nucleic Acids (SeNA) for Structure & Function Studies and

Drug Innovation (硒核酸在结构功能研究以及药物创新中的应用)

Abstract

Nucleic acid is composed of five essential elements (H, C, N, O and P). Atom-specifically functionalized nucleic acids by introducing an additional element (such as Se) can offer nucleic acids with many unique and novel properties (such as facilitated crystallization and phase determination) without significant perturbation of 3D structures of nucleic acids and their protein complexes. Atom-specific replacement of nucleic acid oxygen with selenium means the substitution of O with Se atom. Nucleic acids possess not only the ability to store genetic information and participate in replication, transcription and translation, but also the capacity to adopt well-defined 3D structures, which can be readily adjusted to meet various functional needs (such as catalysis and therapeutics). Although the importance of numerous nucleic acids in catalysis, gene expression, protein binding and therapeutics has been acknowledged by the entire scientific society, current understanding of nucleic acid-protein interactions, functions and structures is still limited, especially due to lack of high-resolution structures. Thus, this novel selenium atom-specific mutagenesis provides important tools to explore potential nucleic acid therapeutics and diagnostics via novel target identification, to investigate nucleic acid structure/folding, recognition and catalysis, to study nucleic acids and their protein interactions, to improve biochemical and biophysical properties of nucleic acids, and to facilitate gene silencing and RNA & DNA nanotechnology. Our presentation will focus on the most recent selenium-atom functionalization of nucleic acids and their potential applications in 3D structure-and-function studies and anticancer therapeutics in molecular medicine. The research work is supported by NIH (R01GM095881, GM095086, ES026935), NSF (MCB-0824837 & CHE-0750235), and CNSF-21572146.