CURRICULUM VITAE

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A. EDUCATION/POSITIONS:

2008-Present: Assistant Professor Research, Center for BioEnergetics, Biodesign Institute, ASU
2006-2008: Research Scientist, Department of Chemistry, University of Virginia
2004-2006: Postdoctoral Fellow, Department of Chemistry, University of Virginia
1998-2003: Ph.D., Institute of Medicinal Biotechnology, Chinese Academy of Medical Sciences & Peking Union Medical College.
1994-1998: B.Sc., Department of Pharmacy, Shandong Medical University.

B. RESEARCH INTERESTS:

Early diagnosis of HIV infection; Development of inhibitors against AIDS/HIV; Development of drugs and novel strategies to prevent cancer cell metastasis; Study of protein dynamics.

C. RESEARCH SUPPORT:

OPP1061337 S. Chen (PI) 5/1/2012 – 4/30/2014
Bill & Melinda Gates Foundation
Grand Challenges Explorations Grants
Fluorescent Protein Sensor to Diagnose HIV at Low Cost
The goal of this grant is to design and prepare a fluorescent sCD4 protein or peptide mimics that changes color when it binds to the HIV gp120 protein. By directly detecting a virus protein instead of antibodies or RNA, which take days to months to accumulate sufficiently to detect, HIV infection can be diagnosed immediately to help prevent the spread of the epidemic.

CA082013 S. Chen (PI) 8/1/2013 – 7/31/2015
Clinx American Inc.
Peptide-drug Conjugates to Target HER2-positive Cancers
The goal of this grant is to prepare a short peptide from *E. coli* and coupled it with small molecule drugs. These peptide-drug conjugates will specifically targeted to HER2-positive cancer cells and show a synergistic effect against cancer patients.

OPP1108171 S. Chen (PI) 5/1/2014 – 10/31/2015

Bill & Melinda Gates Foundation

Grand Challenges Explorations Grants

Novel Materials to Increase Pleasure and Enhance Erection

We propose to design and prepare a skin-like condom, which mimics the membrane of living cells to increase pleasure and enhance erection. Our final goal is to develop a low-cost novel condom that can prevent pregnancy and STIs; increase pleasure to both partners; and enhance a male erection and a female arousal.

D. RESEARCH EXPERIENCE:

2008-Present: Research Areas in Arizona State University:

1. A new strategy for monitoring small motions by FRET was conceived and implemented by using two small fluorescent amino acids that fit into the protein structure without distortion. Protein motion changes the dipole orientation between the probes, resulting in a significant change in FRET even in the absence of any large distance change.

2. A sCD4 protein was prepared in a cell-free translation system. It is going to be introduced a series of fluorescent amino acids at desired position. The fluorescent sCD4 protein mimics will change color while it binds to the HIV gp120 protein. Thus, it will be developed into a probe to diagnose HIV infection at an early stage to help prevent the spread of the epidemic.

3. Two pyrenylalanine analogs have been incorporated into dihydrofolate reductase (DHFR) at positions 16 and 49 to obtain an excimer formation, which is more sensitive to small changes in distance than FRET pairs (a constraint imposed by the dimensions of the enzyme). The excimer formation was used to study the dynamics of DHFR under both single and multiple turnover conditions. More fluorescent amino acids will be synthesized and incorporated into different positions of DHFR to study its function and dynamics in the near future.

4. Thiothreonine and its analogs were synthesized and incorporated into DHFR at predetermined position, and the elaborated proteins were modified site-specifically at the thiothreonine residue with a fluorophore. Aspartic acid derivatives also were synthesized and incorporated into DHFR at desired position to study the function of enzyme.

5. A *p*-thiophenylalanine was synthesized and incorporated into the active site (position 274) of vaccinia DNA topoisomerase IB by *in vitro* translation. The modification, which resulted in replacement of the nucleophilic tyrosine OH group with SH, retained DNA topoisomerase activity and did not alter the DNA

cleavage site. However, the modified topoisomerase effected relaxation of supercoiled plasmid DNA at a rate about 16-fold slower than the wild-type enzyme. The thiophenylalanine-induced DNA cleavage rate was 30 times lower than for the wild-type enzyme. The changed rates were due to alterations in the bond strengths of the obligatory intermediates.

2004-2008: Research areas in University of Virginia:

6. ^{13}C labeled dihydrofolate reductase (DHFR) was prepared and the catalyzed mechanism was analyzed using ^{13}C NMR. Also, a series of derivatives of aspartic acid were incorporated into the active site of dihydrofolate reductase and their activities were studied. Among them, the modified DHFRs, which containing a cysteic acid or cysteinesulfinic acid at 27 position (active site) had much higher activity than wild-type DHFR.

7. Aminoacyl t-RNAs were prepared for the introduction of noncoded amino acids into proteins by *in vitro* suppression. A series of derivatives of tyrosine were incorporated into 274 position of vaccinia topoisomerase I *in vitro* followed by purification using Ni-NTA. Among them, four mutant topoisomerases I showed different activity than wild-type topoisomerase I.

8. Myristinin, which has dual biochemical activity both as potent DNA damaging agents and as DNA polymerase inhibitors, was synthesized in 18 steps.

1998-2003: Ph.D. Research area in China:

9. New pyrrolidine derivatives, which bear an alkyloxime substituent in the 4-position and an amine substituent in the 3-position of the pyrrolidine ring, were synthesized and coupled with various quinolinecarboxylic acids to produce a series of new fluoroquinolone antibacterials. Their antibacterial activities were tested *in vitro*.

10. Design, synthesis, antibiotic activity studies of new erythromycins. A series of 3-keto-9-O-substituted oxime derivatives of 6-O-methyl erythromycin A were prepared using a novel synthetic route. The antibacterial activities of these compounds were tested in vitro against both erythromycin-susceptible and erythromycin-resistant organisms. Several of these derivatives showed improved antibacterial activity against some erythromycin-resistant organisms as compared to erythromycin A.

E. MAIN PUBLICATIONS:

1. Zhiqiang Yu, Bin Yu, Justin Boy Kaye, Chenhong Tang, Shengxi Chen, Chenbo Dong, and Bing Shen. Perspectives and Challenges of Cell-Penetrating Peptides in Effective siRNA Delivery. *Nano LIFE*, **4**,

1441016 (2014)

2. Xiaobo Yu, Poulami Talukder, Chandrabali Bhattacharya, Nour Eddine Fahmi, Jamie A. Lines, Larisa M. Dedkova, Joshua LaBaer, Sidney M. Hecht, Shengxi Chen*. Probing of CD4 binding pocket of HIV-1 gp120 glycoprotein using unnatural phenylalanine analogues. *Bioorg. Med. Chem. Lett.* **24**, 5699-5703 (2014).

3. Jamie A. Lines, Zhiqiang Yu, Larisa M. Dedkova and Shengxi Chen*. Design and expression of a short peptide as an HIV detection probe. *Biochemical and Biophysical Research Communications*, **443**, 308-312 (2014).

4. Poulami Talukder, Shengxi Chen, C. Tony Liu, Edwin A. Baldwin, Stephen J. Benkovic, and Sidney M. Hecht. Tryptophan Derivatives as Probes of Protein Conformational Changes. *Bioorganic & Medicinal Chemistry*, **22**, 5924-5934, (2014).

5. Poulami Talukder, Shengxi Chen, Pablo M. Arce and Sidney M. Hecht. Efficient asymmetric synthesis of trypophan analogues having useful photophysical properties. *Organic Letters*, **16**, 556-559 (2014).

6. Shengxi Chen, Nour Eddine Fahmi, Chandrabali Bhattacharya, Lin Wang, Yuguang Jin, Stephen J. Benkovic and Sidney M. Hecht. Fluorescent biphenyl derivatives of phenylalanine suitable for protein modification. *Biochemistry*, **52**, 8580-8589 (2013).

7. Shengxi Chen, Nour Eddine Fahmi, Lin Wang, Chandrabali Bhattacharya, Stephen J. Benkovic and Sidney M. Hecht. Detection of DHFR conformational change by FRET using two fluorescent amino acids. *Journal of the American Chemical Society*, **135**, 12924-12927 (2013).

8. Rumit Maini, Dan T. Nguyen, Shengxi Chen, Larisa M. Dedkova, Sandipan Roy Chowdhury, Rafael Alcala-Torano, Sidney M. Hecht. Incorporation of β-amino acids into dihydrofolate reductase by ribosomes having modifications in the peptidyltransferase center. *Bioorganic & Medicinal Chemistry*, **21**, 1088-1096 (2013).

9. Shengxi Chen, Lin Wang, Nour Eddine Fahmi, Stephen J. Benkovic and Sidney M. Hecht. Two pyrenylalanines in dihydrofolate reductase form an excimer enabling the study of protein dynamics. *Journal of the American Chemical Society*. **134**, 18883-18885 (2012).

10. Shengxi Chen, Nour Eddine Fahmi, Ryan C. Nangreave, Youcef Mehellou and Sidney M. Hecht. Synthesis of pdCpAs and transfer RNAs activated with thiothreonine and derivatives. *Organic & Biomolecular Chemistry*, **20**, 2679-2689 (2012).

11. Larisa M. Dedkova, Nour Eddine Fahmi, Rakesh Paul, Melissa del Rosario, Liqiang Zhang, Shengxi Chen, Glen Feder and Sidney M. Hecht. β-Puromycin selection of modified ribosomes for in vitro incorporation of β-amino acids, *Biochemistry*, **51**, 401-415 (2012).

12. Shengxi Chen, Yi Zhang and Sidney M. Hecht. *p*-Thiophenylalanine-induced DNA cleavage and religation activity of a modified vaccinia topoisomerase IB, *Biochemistry*, **50**, 9340-9351 (2011).

13. Ryan C. Nangreave, Larisa M. Dedkova, Shengxi Chen and Sidney M. Hecht. A new strategy for the synthesis of bisaminoacylated tRNAs, *Organic Letters*, **13**, 4906–4909 (2011).

14. Shengxi Chen and Sidney M. Hecht. Synthesis of pdCpAs and transfer RNAs activated with derivatives of aspartic acid and cysteine, *Bioorganic & Medicinal Chemistry*, **16**, 9023-9031 (2008).

15. Maria Duca, Shengxi Chen and Sidney M. Hecht. Modeling the reactive properties of tandemly activated tRNAs. *Organic & Biomolecular Chemistry*, **6**, 3292-3299 (2008).

16. Maria Duca, Shengxi Chen and Sidney M. Hecht. Aminoacylation of transfer RNAs with one and two amino acids. *Methods*, **44**, 87-99 (2008).

17. Lyudmila Yakovleva, Shengxi Chen, Sidney M. Hecht, and Stewart Shuman. Chemical and traditional mutagenesis of vaccinia DNA topoisomerase provide insights to cleavage site recognition and transesterification chemistry. *Journal of Biological Chemistry*, **283**, 16093-16103 (2008).

18. David J. Maloney, Shengxi Chen and Sidney M. Hecht. Stereoselective synthesis of the atropisomers of myristinin B/C. *Organic Letters*, **8**, 1925-1927 (2006).

19. Shengxi Chen and Huiyuan Guo. Synthesis and antibacterial activity of 7-[(2S)-2-hydroxymethyl-4-amino-pyrrolindine-1-yl]-quinolone derivatives. *Chinese Journal of Pharmaceuticals*, **36**, 129-132 (2005).

20. Shengxi Chen and Huiyuan Guo. Synthesis and antibacterial activity of 7-[(2S)-2-aminomethyl -pyrrolindine-1-yl]-quinolone derivatives. *Chinese Journal of Antibiotics*, **29**, 397-400 (2004).

21. Shengxi Chen and Xiandong Xu. Synthesis of 9-oxime-6-O-methyl-3-oxo erythromycin. *Chinese Journal of Pharmaceuticals*, **34**, 58-59 (2003).

22. Shengxi Chen and Jie Dai. Research development of preventive and curative drugs against AIDS. *World Notes on Antibiotics*, **23**, 155-157 (2002).

23. Shengxi Chen and Huiyuan Guo. Novel fluoroquinoloe-gemifloxacin. *World Notes on Antibiotics*, **23**, 279-283 (2002).

24. Shengxi Chen, Xiandong Xu and Lanxiang Yu. Synthesis and antibacterial activity of 3-hydroxy-6-O-methylerythromycin-9-O-substituted oxime derivatives. *Acta Pharmaceutica Sinica*, **36**, 581-584 (2001).

25. Shengxi Chen and Huiyuan Guo. Pharmacokinetics and pharmacodynamics of fluoroquinoloe. *World Notes on Antibiotics*, **22**, 253-258 (2001).

26. Shengxi Chen, Xiandong Xu and Lanxiang Yu. 3-Keto-9-O-substituted oxime derivatives of 6-O-methyl erythromycin A, synthesis and in vitro activity. *J. Antibiotics*, **54**, 506-509 (2001).

F. PATENT:

1. Shengxi Chen. A fusion peptide for HIV gp120 antigen detection, USA patent (pending).

G. INVITED BOOK CHAPTER:

1. Shengxi Chen. HIV-1 integrase inhibitors to treat AIDS. In: Atta-ur-Rahman, Eds. Frontiers in Clinical Drug Research-HIV. Bentham Science Publishers (in press).

H. INVITED LECTURES:

1. Incorporation of Two Fluorescent Amino Acids into Dihydrofolate Reductase for its Conformational Monitoring. Hunan University, Changsha, China (March 19, 2014).

2. *In vitro* Expression of Fluorescent Amino Acids into Dihydrofolate Reductase to screen its inhibitors. Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China (March 25, 2014).

I. PRESENTATIONS:

<u>Conference presentations</u>

1. Development of erythromycin, Chinese Pharmaceutical Association 2000 National Conference (2000, Ningbo, China). Oral presentation.

2. *p*-Thiolphenylalanine induced DNA cleavage and religation activity of vaccinia topoisomerase I, American

Chemical Society Fall 2010 National Meeting & Exposition (August, 2010 Boston). Poster presentation.

3. Incorporation of two fluorescent amino acids into dihydrofolate reductase for its conformational monitoring, Arizona Biophest 2013 Meeting (April, 2013 Tempe). Oral presentation.

Literature club oral presentations (selected from 35 presentations)

4. Oxidation state of the active-site cysteine in protein tyrosine phosphatase 1B (September, 2005, UVA).

5. Synthesis of mono-, bis-aminoacyl-pdCpA: The new source for aminoacyl t-RNA (October, 2005, UVA).

6. Synthesis of vaccinia topoisomerase I and its analogues (June, 2006, UVA).

7. The crystal of Cys-tRNACys-EF-Tu-GDPNP reveals general and specific features in the ternary complex and in tRNA (October, 2006, UVA).

8. MicroRNA, (December, 2007, UVA).

9. A small molecule enhances RNA interference and promotes microRNA processing (October, 2008, ASU).

10. Novel enzyme model for screening HIV-RT RNase H inhibitors (March, 2009, ASU).

11. A chemical genetic method for generating bivalent inhibitors of protein kinase (September, 2009, ASU).

12. A new potent secondary amphipathic cell–penetrating peptide for siRNA delivery into mammalian cells (October, 2009, ASU).

13. Dynamic copper (I) imaging in mammalian cells with a genetically encoded fluorescent copper (I) sensor (February, 2010, ASU).

14. Novel dual inhibitory function aptamer–siRNA delivery system for HIV-1 therapy (August, 2010, ASU).

15. A convenient catalyst for aqueous and protein Suzuki−Miyaura cross-coupling (August, 2010, ASU).

16. Incorporate fluorophores into DHFR to study protein dynamics (November, 2010, ASU).

17. Mammalian cell penetration, siRNA transfection, and DNA transfection by supercharged proteins (February, 2011, ASU).

18. Small-molecule activators of a proenzyme (July, 2011, ASU).

19. Bioluminescence is produced from a trapped firefly luciferase conformation predicted by the domain alternation mechanism (August, 2011, ASU).

20. Peroxide-dependent sulfenylation of the EGFR catalytic site enhances kinase activity (June, 2012, ASU).

21. Tetrazine-based cycloadditions: application to pretargeted live cell imaging (July, 2012, ASU).

(UVA: University of Virginia; ASU: Arizona State University)

J. AWARDS & SCHOLARSHIPS:

1. Outstanding university students in Beijing, 2001.

2. Excellent student scholarship for 3 years in Chinese Academy of Medical Sciences, 1999-2002.

3. First-rank student scholarship for 3 years in Shandong Medical University, 1994-1997.

K. ADVISING AND MENTORING EXPERIENCE:

1. Khalid Salim, undergraduate student who I mentored in protein synthesis (2010; he was enrolled by the University of Arizona, College of Medicine for a M.D.).

2. Jamie Lines, undergraduate student who I mentored in developing a fluorescent probe to diagnose HIV infection (she graduated in 2014).

3. Xiyi Liu, undergraduate student who I mentored in developing a novel strategy to prevent breast cancer metastasis (2012-2013, she graduated in 2014).

4. Chandrabali Bhattacharya, graduate student who I mentored in synthesis of fluorescent amino acids for developing a fluorescent probe. (2012-2013, she will graduate in 2015).

5. Ryan C. Nangreave, graduate student who I supervised for his research project of preparation of bis-aminoacylated tRNAs (2010-2012, he has recently accepted a postdoctoral position at the Arizona State University).

6. Basab Roy, graduate student who I supervised for his research project of preparation of mutant luciferase

(2010-2011, he will graduate in 2014).

7. Edwin A. Baldwin, undergraduate student who I mentored in synthesis of fluorescent DHFR to study the enzyme conformation (2014-, he will graduate in 2015).

L. SERVICE ACTIVITIES:

Manuscript Reviewer: *Retrovirology*; *Acta Biochimica et Biophysica Sinica (ABBS); International Journal of Nanomedicine.*

M. REFERENCES:

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