# Shu Z. Wiley

Formerly Shu Zhou

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## Summary

I am a highly motivated biomedical researcher who has training in multi-disciplinary areas including Organic Chemistry, Biochemistry, and Molecular and Cell Biology. My expertise lies in drug target validation, G protein-coupled receptor (GPCR) signaling, ligand-receptor interaction, high throughput screening, assay development, assay quality control.

## Education

**Certificate, Clinical Research** **2013-2015**
University of California, San Diego, La Jolla, CA

**Ph.D., Biochemistry** **2006-2011**
Ohio University, Athens, OH
Dissertation Title: *Riboswitch Drug Discovery: Identification and characterization of T box antiterminator RNA ligands as potential antibacterial agents*

**B.S., Organic Chemistry** **2002-2006**
**Shanghai University**, Shanghai, China

## Research Experience

**Postdoctoral Fellow** **01/2013-present**
University of California, San Diego, La Jolla, CA
Department of Pharmacology
Dr. Paul Insel's lab (Collaborator: Andrew Lowy, MD)

- Conducted Taqman GPCR arrays and RNA-seq for gene expression profiling and identification of highly expressed GPCRs in primary human pancreatic cancer associated fibroblasts (CAFs)
- Validated GPCR biological functions in pancreatic CAFs and assessed their potential as novel therapeutic targets (cell viability, proliferation, alteration of gene expression, cytokine production, collagen synthesis)
- Developed a co-culture system to study tumor-stromal interactions in pancreatic cancer
- Identified GPCR signaling pathways in pancreatic CAFs (cAMP, PKA activation/inhibition, CREB phosphorylation, intracellular $Ca^{2+}$)
- Generated stable GPCR cell lines for high throughput screening

**Visiting Scientist** **06/2015-12/2015**
La Jolla Institute for Allergy and Immunology, La Jolla, CA
RNAi Center

- Developed a siRNA knockdown screening assay to identify GPCRs that regulate CAF fibrotic activities using in-cell western assays

**Postdoctoral Fellow** **01/2012-12/2012**
University of California, San Diego, La Jolla, CA
Department of Chemistry and Biochemistry
Dr. Thomas Hermann's lab

- Developed a FRET high throughput screening assay to identify inhibitors of HCV IRES RNA as potential antiviral agents
- Conducted HCV IRES-dependent *in vitro* translation assays
- Developed a UV-crosslinking method to study HCV IRES RNA-protein interaction

**Ph.D. Student** **09/2006-07/2011**
Ohio University, Athens, OH
Department of Chemistry and Biochemistry
Dr. Jennifer Hines' lab

- Developed a FRET high throughput screening assay to identify small molecules binding to T box antiterminator RNA targets
- Developed a fluorescence anisotropy high throughput screening assay to identify small molecules that can disrupt T box antiterminator RNA-tRNA interaction
- Developed a fluorescence-monitored thermal denaturation high throughput screening assay to identify small molecules that can affect T box antiterminator RNA stability
- Developed a multi-run *in vitro* transcription assay to monitor T box riboswitch regulated gene expression
- Measured T box antiterminator RNA stability using UV absorbance based thermal denaturation
- Determined T box antiterminator RNA secondary structure using both in-line and enzymatic probing methods
- Characterized the T box antiterminator RNA-ligand interaction (binding affinity and specificity, ligand-induced changes in RNA structure, computational docking)

**Visiting Scholar** **06/2009**
Leipzig University, Germany
Department of Pharmaceutical Analysis
Dr. Ralf Hoffmann's lab

- Determined T box antiterminator RNA-peptide interactions using fluorescence anisotropy screening assays

**Teaching Assistant** **09/2006-12/2007**
Ohio University, Athens, OH
Department of Chemistry and Biochemistry

- General chemistry
- Organic chemistry

## Research Skills

- Drug target validation, GPCR signaling, ligand-target interaction, high throughput screening, lead compound identification, assay development, and assay quality control
- Various ligand-binding techniques (FRET, FP, thermal denaturation shift, UV absorbance)
- Human primary cell culture
- Real-time PCR
- Molecular cloning
- Stable cell line generation
- Western blot
- Transfection/siRNA knockdown
- Immunofluorescence
- ELISA
- Cell proliferation and viability
- *In vitro* transcription and translation
- Protein expression and purification
- cAMP luminescence assay and cAMP radioimmunoassay
- FLIPR Intracellular $Ca^{2+}$ assay
- In-cell western fluorescence assay

## Analytical Skills

- GraphPad Prism
- SigmaPlot
- IBM SPSS Statistics
- ChemDraw
- ImageJ
- Primer Premier 6
- MacroModel
- UNAFold
- RQ Manager

## Publications

**Wiley SZ**, Sriram K, Liang W, Chang SE, French R, McCann T, Sicklick JK, Nishihara H, Lowy AM and Insel PA. GPR68, a proton-sensing GPCR, mediates interaction of cancer associated fibroblasts and cancer cells. *FASEB J*. **2017** (Accepted pending with minor revision).

Liu J, Zeng C, Hogan V, **Zhou S**, Monwar MM, Hines JV. Identification of Spermidine Binding Site in T-box Riboswitch Antiterminator RNA. *Chem. Biol. Drug. Des.* **2016**, 87, 182-189.

Zeng C, **Zhou S**, Bergmeier SC, Hines JV. Factors that influence T box riboswitch efficacy and tRNA affinity. *Bioorg. Med. Chem.* **2015**, 23, 5702-5708.

Insel PA, Wilderman A, Zambon A, Snead A, Murray F, Aroonsakool N, McDonald D, **Zhou S**, McCann T, Zhang L, Sriram K, Chinn A, Michkov AV, Lynch R, Overland A, Corriden R. G Protein-Coupled Receptor (GPCR) Expression in Native Cells: "Novel" endoGPCRs as Physiologic Regulators and Therapeutic Targets. *Mol. Pharmacol.* **2015**, 88, 181-187.

Liu J, Zeng C, **Zhou S**, Means JA, Hines JV. Fluorescence assays for monitoring RNA-ligand interactions and riboswitch-targeted drug discovery screening. *Methods Enzymol*. **2015**, 550, 363-383.

**Zhou S**, Anupam R, Hines JV. Fluorescence anisotropy: analysis of tRNA binding to the T box riboswitch antiterminator RNA. *Methods Mol. Biol*. **2015**, 1240, 143-152.

Anupam R, **Zhou S**, Hines JV. Electrophoretic mobility shift assays: analysis of tRNA binding to the T box riboswitch antiterminator RNA. *Methods Mol. Biol.* **2015**, 1240, 135-142.

Dibrov SM, Parsons J, Carnevali M, **Zhou S**, Rynearson KD, Ding K, Garcia Sega E, Brunn ND, Boerneke MA, Castaldi MP, Hermann T. Hepatitis C virus translation inhibitors targeting the internal ribosomal entry site. *J. Med. Chem.* **2014**, 57, 1694-1707.

**Zhou S**, Rynearson KD, Ding K, Brunn ND, Hermann T. Screening for inhibitors of the hepatitis C virus internal ribosome entry site RNA. *Bioorg. Med. Chem.* **2013**, 21, 6139-6144.

**Zhou S**, Acquaah-Harrision G, Jack KD, Bergmeier SC, Hines JV. Ligand-induced changes in T box antiterminator RNA stability. *Chem. Biol. Drug Des.* **2012,** 79, 202-208.

**Zhou S**, Means JA, Acquaah-Harrison G, Bergmeier SC, Hines JV. Characterization of a 1,4-disubstituted 1,2,3-triazole binding to T box antiterminator RNA. *Bioorg. Med. Chem.* **2012,** 20, 1298-1302.

**Zhou S**, Acquaah-Harrison G, Bergmeier SC, Hines JV. Anisotropy studies of tRNA-T box antiterminator RNA complex in the presence of 1,4-disubstituted 1,2,3-triazoles. *Bioorg. Med. Chem. Lett.* **2011**, 21, 7059-7063.

Orac CM, **Zhou S**, Means JA, Boehm D, Bergmeier SC, Hines JV. Synthesis and stereospecificity of 4,5-disubstituted oxazolidinone ligands binding to T-box riboswitch RNA. *J. Med. Chem.* **2011**, 54, 6786-6795.

Maciagiewicz I, **Zhou S**, Bergmeier SC, Hines JV. Structure activity studies of RNA-binding oxazolidinone derivatives. *Bioorg. Med. Chem. Lett.* **2011**, 21, 4524-4527.

Acquaah-Harrison G, **Zhou S**, Hines JV, Bergmeier SC. Library of 1,4-disubstituted 1,2,3-triazole analogs of oxazolidinone RNA-binding agents. *J. Comb. Chem.* **2010**, 12, 491-496.

Means JA, Simson CM, **Zhou S**, Rachford AA, Rack JJ, Hines JV. Fluorescence probing of T box antiterminator RNA: insights into riboswitch discernment of the tRNA discriminator base. *Biochem. Biophys. Res. Commun*. **2009**, 389, 616-621.

**Conference Presentations**

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**Zhou S**, Chang S, McCann T, Nishihara H, French R, Lowy AM, Insel PA. *GPCRs expressed by cancer-associated fibroblasts are potential therapeutic targets in pancreatic cancer.* Poster presented at Experimental Biology Conference, San Diego, CA **(04/2016)**.

**Zhou S**, Chang S, McCann T, Nishihara H, French R, Lowy AM, Insel PA. *GPCRs as potential therapeutic targets in pancreatic cancer-associated fibroblasts.* Poster presented at AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics, Boston, MA **(11/2015)**.

**Zhou S**, McCann T, French R, Lowy AM, Insel PA. *GPCRs as potential therapeutic targets in pancreatic cancer-associated fibroblasts.* Poster presented at AACR special conference – Pancreatic Cancer: Innovations in Research and Treatment, New Orleans, LA **(05/2014)**.

**Zhou S**, McCann T, French R, Lowy AM, Insel PA. *GPCRs as potential therapeutic targets in pancreatic cancer-associated fibroblasts.* Poster presented at Experimental Biology Conference, San Diego, CA **(04/2014)**.

**Zhou S**, McCann T, French R, Lowy AM, Insel PA. *GPCRs as potential therapeutic targets in pancreatic cancer-associated fibroblasts.* Poster presented at AACR special conference - Cellular Heterogeneity in the Tumor Microenvironment, San Diego, CA **(02/2014)**.

**Zhou S**, Hines JV. *Riboswitch Drug Discovery: Development of high-throughput screening assays for identifying T box antiterminator RNA ligands*. Poster presented at Great Lakes Bioinformatics Conference, Athens, OH **(05/2011)**.

**Zhou S**, Acquaah-Harrison G, Maciagiewicz I, et al. *Fluorescence anisotropy screening for inhibitors of tRNA-T box antiterminator RNA.* Poster presented at 239th American Chemical Society National Meeting, San Francisco, CA **(03/2010)**.

**Zhou S**, Acquaah-Harrison G, Maciagiewicz I, et al. *Identification of small compounds as inhibitors for tRNA-T box antiterminator interaction*. Poster presented at 2009 Rustbelt RNA Meeting, Mt. Sterling, OH **(10/2009)**.

**Zhou S,** Acquaah-Harrison G, Maciagiewicz I, et al. *Fluorescence resonance energy transfer screening of small molecules as potential ligands for T box antiterminator model RNA*. Poster presented at 2008 Rustbelt RNA Meeting, Mt. Sterling, OH **(10/2008)**.

## Honors and Awards

- Young Scientist Travel Award, The American Society for Pharmacology and Experimental Therapeutics (ASPET), the ASPET/CNPHARS joint meeting **(2017)**
- First Place Postdoctoral Best Presentation Award, The Division for Cancer Pharmacology of The American Society for Pharmacology and Experimental Therapeutics (ASPET) **(2016)**
- Ruth L. Kirschstein National Research Service Award – Cancer Therapeutics Training Grant (**2013-2015**)
- Young Investigator Award, The Division for Drug Discovery and Development of The American Society for Pharmacology and Experimental Therapeutics (ASPET) (**2014**)
- Two-time second place award for outstanding presentation at Student Research and Creative Activity Fair, Ohio University (**2009 & 2010**)

- Outstanding graduate student award, Department of Chemistry and Biochemistry, Ohio University (**2007**)

- Three-time university scholarship recipient, Shanghai University (**2003-2005**)

**References**

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- Paul Insel, M.D.
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  Pharmacology Department, University of California, San Diego
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  Phone: 858-534-2295

- Thomas Hermann, Ph.D.
  Associated professor
  Chemistry and Biochemistry Department, University of California, San Diego
  Email: tch@ucsd.edu
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- Jennifer Hines, Ph.D.
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