BIOGRAPHICAL SKETCH

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NAME: Yao, Xiaolan

eRA COMMONS USER NAME (credential, e.g., agency login): Xiaolan

POSITION TITLE: Associate Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Zhengzhou University, Henan, China	A.B.	1994	Chemistry
Zhengzhou University, Henan, China	M.S.	1998	Chemistry
Iowa State University, Ames, IA	Ph.D.	2004	Biophysics
UT Southwestern Medical Center, Dallas, TX	Postdoctoral fellow	2010	Biophysics and biochemistry

A. Personal Statement

My research aims to understand the biochemical and biophysical basis of protein function, focusing on lipid transfer proteins. Lipid molecules are responsible for the fundamental bilayer structure of biological membranes. They are also increasingly being recognized as regulators of a plethora of cellular processes. In the past ten years or so, various lipid transfer proteins have been revealed as critical mediators in lipid metabolism, trafficking, and cellular signaling. My research at UMKC investigates the biochemical and biophysical mechanisms of these protein machineries. To this end, I integrate structure biology methods such as nuclear magnetic resonance (NMR) spectroscopy and x-ray crystallography with various biochemical techniques into my research tool kit. Our past investigations mainly focused on the ceramide transfer protein (CERT), which carries out the nonvesicular transfer of ceramide from ER to the *Trans*-Golgi for sphingomyelin synthesis. CERT function is required for embryo development and normal life span. Our investigations revealed the structural basis of CERT N-terminal pleckstrin-homolog (PH)-mediated *Trans*-Golgi membrane association and how the interaction between the PH domain and the C-terminal lipid transfer domain inhibits CERT binding to *Trans*-Golgi upon phosphorylation downregulation. We have also obtained multiple crystal structures of the lipid transfer domain of CERT complexed with various inhibitors, providing important insights into the structural basis of CERT inhibition (unpublished results). Current ongoing research in my lab investigates the role of a largely unstructured region of CERT (~200 residues), termed the middle region (MR). Multiple lines of data indicate MR is critical for CERT function and regulation. This notion is further supported by the identification of various *de novo* mutations in MR associated with developmental disorders. However, despite years of effort, the structural mechanism of how MR confers CERT regulation has been elusive. To overcome this challenge, I plan to acquire the skills for using another powerful tool, cryo-electron microscopy, to understand the structural basis of CERT regulation. Regions similar to MR in CERT are also found in many other lipid transfer proteins. Our findings in CERT will provide important insights into the regulation of lipid homeostasis and signaling in general. I plan to investigate other important lipid transfer proteins in the long run with the ultimate goal to understand how lipid transfer proteins mediate lipid metabolism, trafficking, and signaling.

Recent Support:

University of Missouri Kansas City Funding for Excellence 01/2022 -12/2022
Ceramide transfer protein regulation and its role in development
Role: PI

NIH R15 AREA, 1R15GM113200-01 Jan. 2015 – Dec. 2017
Structure and biochemical mechanisms of ceramide transfer protein functional regulation
Role: PI

Citations:

1. Prashek J, Bouyain S, Fu M, Li Y, Berkes D, and **Yao X**, CERT START domain interacts with PH domainand blocks PH binding to PtdIns(4)P. J Biol. Chem. 2017 Aug 27, 292, 14217-14288
2. Prashek J, Truong T, **Yao X**, Crystal structure of the pleckstrin homology domain from ceramide transferprotein: implications for conformational change upon ligand binding, PLoS One. 2013 Nov. 18;8(11):e79590. doi: 10.1371/journal.pone.0079590.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2018-current	Associate Professor, School of Biological Sciences, Division of Molecular Biology and Biochemistry, Universityof Missouri - Kansas City
2010-2018	Assistant Professor, School of Biological Sciences, Division of Molecular Biology and Biochemistry, University of Missouri - Kansas City
2004-2010	Postdoctoral fellow, University of Texas Southwestern Medical Center and Howard Hughes Medical Institute

Other Experience and Professional Memberships

2000 - 2006	Biophysical Society
2016 - 2017	Protein Society
2017- 2018	American Society for Biochemistry and Molecular Biology
2012, June 19-26	Argonne National Lab workshop on protein x-ray crystallography

2016 Reviewer for University of Missouri Research Board grant applications

Honors:

2018	UMKC Trustee Faculty Scholar Award

C. Contributions to Science

1. The main focus of my research lab has been the CERT protein. Its ceramide transfer function is among the earliest examples of nonvesicular lipid transfer or exchange inside the cell carried out by specific lipid

transfer proteins. We solved the crystal structure of the N-terminal PH domain of CERT and then used NMR to determine residues involved in PH interaction with Trans-Golgi-membrane mimic liposomes. The combined structure information from x-ray crystallography and NMR were used as input model and constrains for the generation of a structure model that shed light on the specificity of PH domain association with the Trans-Golgimembrane. Built on this study, we further investigated how CERT dissociates from the Golgi upon hyperphosphorylation. Our crystal structure of a complex between PH domain and the lipid transfer domain provided critical structural insight that the lipid transfer domain associates with PH domain in way that competes with PH binding to membrane. Currently we are carrying our experiments to understand how does hyperphosphorylation bring PH and the lipid transfer domain to proximity for the inhibition of PH.

- Prashek J, Bouyain S, Fu M, Li Y, Berkes D, and **Yao X**, *CERT START domain interacts with PHdomain and blocks PH binding to PtdIns(4)P. J Biol. Chem. 2017 Aug 27, 292, 14217-14288*
- Prashek J, Truong T, **Yao X**, Crystal structure of the pleckstrin homology domain from ceramide transfer protein: implications for conformational change upon ligand binding, PLoS One. 2013 Nov.18;8(11):e79590. doi: 10.1371/journal.pone.0079590.

2. In addition to the main focus of my own research program, I had collaborations with other research labs thathave complementary research expertise to understand the structural basis of ion channel modulation, bacterialprotein inhibition as well as the dynamic features of a novovirus protein.

- Jiang Q, Peterson AM, Chu Y, **Yao X**, Zha X-M, and Chu X-P, *Histidine Residues Are Responsible forBidirectional Effects of Zinc on Acid-Sensing Ion Channel 1a/3 Heteromeric Channels. Biomolecules 2020, 10, 1264.*
- Summers BJ, Garcia B L, Woehl JL, Ramyar KX, **Yao X**, Geisbrecht BV, *Identification of peptidic inhibitors of the alternative complement pathway based on Staphylococcus aureus SCIN proteins*, Mol.Immunol. 2015 Oct;67(2 Pt B):193-205
- Takahashi D, Hiromasa Y, Kim Y, Anbanandam A, **Yao X**, Chang K, Prakash O, *Structure anddynamics characterization of norovirus protease,* Protein Science, 22(3), 347-57, 2013.

Complete List of Published Work in MyBibliography:

https://www.ncbi.nlm.nih.gov/myncbi/1Jey8lsBRj3kM/bibliography/public/