BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Su, Xiaoyang

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

POSITION TITLE: Assistant Professor (Research), Co-Director of the Metabolomics Shared Resource

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
Tsinghua University, Beijing, China	B.S.	06/2004	Biochemistry
Tsinghua University, Beijing, China	M.S.	06/2007	Chemistry
Cornell University, Ithaca, NY	Ph.D.	05/2013	Biochemistry
Princeton University, Princeton, NJ	Postdoctoral	01/2017	Biochemistry

A. Personal Statement

My research focus is to use mass spectrometry to study metabolism in a quantitative manner. My lab has strong expertise in the design, data acquisition, result interpretation and data visualization of LC-MS metabolomics experiments, especially in the stable-isotope labeling studies. My lab also has background in computational biology, especially in metabolic flux analysis and untargeted metabolomic data annotation. As the Co-Director of the Metabolomics Shared Resource of Rutgers Cancer Institute of New Jersey, which is supported by NCI Cancer Center Support Grant, I am collaborating with more than 30 research groups in New Jersey on LC-MS metabolomics studies. This places me in an ideal position to leverage local expertise and resources in cancer metabolism and metabolomics for the proposed study. My facility has extensive experience in metabolic profiling and stable-isotope tracing experiments, as demonstrated by the following:

Citations:

1. Williams A, Chiles EN, Conetta D, Pathmanathan JS, Cleves PA, Putnam HM, Su X, Bhattacharya D. Metabolomic shifts associated with heat stress in coral holobionts. Sci Adv. 2021 Jan 1;7(1):eabd4210. doi: 10.1126/sciadv.abd4210. PMID: 33523848; PMCID: PMC7775768.
2. Zhang Z, Chen L, Liu L, Su X, Rabinowitz JD. Chemical Basis for Deuterium Labeling of Fat and NADPH. J Am Chem Soc. 2017 Oct 18;139(41):14368-14371. doi: 10.1021/jacs.7b08012. Epub 2017 Oct 4. PMID: 28911221; PMCID: PMC5748894.
3. Su X, Lu W, Rabinowitz JD. Metabolite Spectral Accuracy on Orbitraps. Anal Chem. 2017 Jun 6;89(11):5940-5948. doi: 10.1021/acs.analchem.7b00396. Epub 2017 May 18. PMID: 28471646; PMCID: PMC5748891.
4. Chen L, Vasoya RP, Toke NH, Parthasarathy A, Luo S, Chiles E, Flores J, Gao N, Bonder EM, Su X, Verzi MP. HNF4 Regulates Fatty Acid Oxidation and Is Required for Renewal of Intestinal Stem Cells in Mice. Gastroenterology. 2020 Mar;158(4):985-999.e9. doi: 10.1053/j.gastro.2019.11.031. Epub 2019 Nov 22. PMID: 31759926; PMCID: PMC7062567.

B. Positions, Scientific Appointments, and Honors

Positions and Employment

2021- Assistant Professor (Research), Department of Medicine, Rutgers University, New Brunswick, NJ
2017- Co-Director of the Metabolomics Shared Resources, Cancer Institute of New Jersey, Rutgers University, New Brunswick, NJ
2017-2021 Assistant Professor, Department of Medicine, Rutgers University, New Brunswick, NJ
2013-2016 Postdoctoral Associate, Lewis-Sigler Institute of Integrative Genomics, Princeton University, Princeton, NJ

Other Experience and Professional Memberships

2016- Member, American Society for Mass Spectrometry
2013- Member, American Society for Biochemistry and Molecular Biology
2012- Member, American Chemical Society

Honors

2012 Scholarship for Outstanding Self-Financed Students, Ministry of Education, China
2012 Tunis Wentink Prize, Cornell University, Ithaca, NJ
2009 Tsang Fellowship, Cornell University, Ithaca, NJ

C. Contributions to Science

1. **Study nutrient utilization and preference using stable-isotope tracing -** We used stable isotope tracing and mass spectrometry to study the substrate preference of metabolic pathways. My lab has strong expertise in the design and interpretation of stable-isotope labeling experiment and the metabolic flux analysis. We used deuterium tracer in the study of cellular NADPH production and found solvent hydrogen exchange results in the underestimation of contribution from oxidative pentose phosphate pathway. We used carbon and deuterium tracers in the study of whole-body NAD metabolism, and discovered liver is the major organ converting tryptophan to nicotinamide. We also used carbon tracers in the study of gluconeogenesis and found glycerol is an important substrate for glucose production.

    a. Chen, L., Vasoya, R.P., Toke, N.H., Parthasarathy, A., Luo, S., Chiles, E., Flores, J., Gao, N., Bonder, E.M., **Su, X.**, Verzi, M.P.* (2020), HNF4 Regulates Fatty Acid Oxidation and Is Required for Renewal of Intestinal Stem Cells in Mice. *Gastroenterology*.158(4), 985-999. DOI: 10.1053/j.gastro.2019.11.031. PMID: 31759926; PMCID: PMC7062567
    b. Zhang, Z., Chen, L., Liu, L., **Su, X.***, Rabinowitz, J.D.* (2017), Chemical Basis for Deuterium Labeling of Fat and NADPH, *J Am Chem Soc* 139(41),14368-14371. DOI: 10.1021/jacs.7b08012. PMID: 28911221; PMCID: PMC5748894
    c. Bhatt, V., Khayati, K., Hu, Z.S., Lee, A., Kamran, W., **Su, X.**, Guo, J.Y.* (2019), Autophagy modulates lipid metabolism to maintain metabolic flexibility for Lkb1-deficient kras-driven lung tumorigenesis, *Genes Dev*. 33, 150–165. DOI: 10.1101/gad.320481.118. PMID: 30692209; PMCID: PMC6362813
    d. Bott, A.J., Shen, J., Tonelli, C., Zhan L., Sivaram N., Jiang, Y., Yu, X., Bhatt, V., Chiles, E., Zhong, H., Maimouni, S., Dai, W., Velasquez, S., Pan, J., Muthalagu, N., Morton, J., Anthony, T.G., Feng, H., Lamers, W.H., Murphy, D.J., Guo, J.Y., Jin, J., Crawford, H.C., Zhang, L., White, E., Lin, R.Z., **Su, X.**, Tuveson, D.A., Zong, W. (2019). Glutamine Anabolism Plays a Critical Role in Pancreatic Cancer by Coupling Carbon and Nitrogen Metabolism, *Cell Rep*. 29(5), 1287-1298. DOI: 10.1016/j.celrep.2019.09.056. PMID: 31665640; PMCID: PMC6886125

2. **Develop tools for high-resolution mass spectrometry data analysis -** I have developed several software tools to process and analyze high-resolution mass spectrometry data. To facilitate the stable-isotope tracing experiments, I developed the isotope natural abundance correction tools that address the resolved

isotopologues in high-resolution mass spectrometry data. We have also developed tools to annotate the untargeted metabolomics dataset utilizing the metabolic incorporation of stable isotope traces.

a. **Su, X**.*, Chiles, E., Maimouni, S., Wondisford, FE., Zong, WX., Song, C.*, (2020). In-Source CID Ramping and Covariant Ion Analysis of Hydrophilic Interaction Chromatography Metabolomics, *Anal Chem*, 92(7), 4829–4837. DOI: 10.1021/acs.analchem.9b04181. PMID: 32125145; PMCID: PMC8141260
b. **Su, X.**, Lu, W., Rabinowitz, J.D. (2017). Metabolite Spectral Accuracy on Orbitraps, *Anal Chem*, 89(11), 5940-5948. DOI: 10.1021/acs.analchem.7b00396. PMID: 28471646; PMCID: PMC5748891
c. Du, D., Tan, L., Wang, Y., Peng, B., Weinstein, J.N., Wondisford, F.E., **Su, X.***, Lorenzi, P.L*. (2019). ElemCor: accurate data analysis and enrichment calculation for high-resolution LC-MS stable isotope labeling experiments; *BMC Informatics*, 20, 89. DOI: 10.1186/s12859-019-2669-9. PMID: 30782135; PMCID: PMC6381631
d. Lu, W., **Su, X.**, Klein, M.S., Lewis, I.A., Fiehn, O., Rabinowitz, J.D. (2017). Metabolite Measurement: Pitfalls to Avoid and Practices to Follow, *Annu Rev Biochem*, 86, 277-304. DOI: 10.1146/annurev-biochem-061516-044952. PMID: 28654323; PMCID: PMC5734093

3. **Elucidation of diphthamide biosynthesis pathway -** Diphthamide is a post-translational modification found on the translation elongation factor-2 of all eukaryotic species. This modification is thought to regulate the fidelity of protein translation. I discovered two genes YBR246W and YLR143W in yeast that are required for diphthamide biosynthesis. Our biochemical characterization revealed that human gene WDR85 and ATPDB4, with previously unknown functions, are diphthamide biosynthetic genes, catalyzing the demethylation and amidation steps respectively. The entire diphthamide biosynthetic pathway can now be reconstituted in vitro using purified enzymes, demonstrating our full knowledge of this biochemical process.

a. **Su, X.**, Chen, W., Lee, W., Jiang, H., Zhang, S., Lin, H. (2012). YBR246W Is Required for the Third Step of Diphthamide Biosynthesis, *J Am Chem Soc*, 134 (2), 773–776. DOI: 10.1021/ja208870a. PMID: 22188241; PMCID: PMC3264676
b. **Su, X.**, Lin, Z., Chen, W., Jiang, H., Zhang, S., Lin, H. (2012). A chemogenomic approach identified yeast YLR143W as diphthamide synthetase, *Proc Natl Acad Sci USA*, 109 (49), 19983-19987. DOI: 10.1073/pnas.1214346109. PMID: 23169644; PMCID: PMC3523822
c. **Su, X.**, Lin, Z., Lin, H. (2013). The biosynthesis and biological function of diphthamide, *Crit Rev Biochem Mol Bio*, 48(6), 515-521. DOI: 10.3109/10409238.2013.831023. PMID: 23971743; PMCID: PMC4280834
d. Lin, Z., **Su, X.**, Chen, W., Ci, B., Zhang S., Lin, H., (2014). Dph7 catalyzes a previously unknown demethylation step in diphthamide biosynthesis, *J Am Chem Soc* 136 (17), 6179-6182. DOI: 10.1021/ja5009272. PMID: 24739148; PMCID: PMC4015618

4. **Discovery of lysine succinylation modification and identified Sirtuin 5 as desuccinylase -** Sirtuins are a family of NAD-dependent deacetylases. However, some family members do not have robust activity in removing lysine acetylation. We found that Sirt5 is effectively a mitochondrial de-succinylase. Lysine succinylation, which was not previously identified, was found at many lysine acetylation sites on mitochondrial proteins. Moreover, the activities of mitochondrial enzymes, such as carbamoyl phosphate synthase 1, are regulated through de-succinylation by Sirt5. Since this ground-breaking work, many new lysine acylation has been discovered.

a. Du, J., Zhou, Y., **Su, X. (co-first author)**, Yu, J.J., Khan, S., Jiang, H., Kim, J., Woo, J., Kim, J.H., Choi, B.H., He, B., Chen, W., Zhang, S., Cerione, R.A., Auwerx, J., Hao, Q., Lin, H. (2011). Sirt5 is a NAD-dependent protein lysine demalonylase and desuccinylase, *Science* 334 (6057), 806-809. DOI: 10.1126/science.1207861. PMID: 22076378; PMCID: PMC3217313
b. Lin, H., **Su, X.**, He, B. (2012). Protein lysine acylation and cysteine succination by intermediates of energy metabolism. *ACS Chem Bio*, 7(6), 947-60. DOI: 10.1021/cb3001793. PMID: 22571489; PMCID: PMC3376250

Complete List of Published Work in myBibliography (62 Publications):
https://www.ncbi.nlm.nih.gov/myncbi/1R7T8dKyqrpswh/bibliography/public/