BIOGRAPHICAL SKETCH

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NAME: Li, Yuan

eRA COMMONS USER NAME (credential, e.g., agency login): YUANLI1

POSITION TITLE: Postdoctoral Scholar

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)*	Start Date MM/YYYY	Completion Date MM/YYYY	FIELD OF STUDY
Huazhong University of Science and Technology, China	BMed	09/2006	06/2011	Clinical Medicine
Central China Normal University, China	BA (minor)	03/2008	06/2011	English Language and Literature
University of Kansas Medical Center, U.S.	PhD	08/2012	10/2018	Toxicology
University of Kansas Medical Center, U.S.	PostDoc	12/2018	02/2019	Liver Diseases
Stanford University, U.S.	PostDoc	03/2019	present	Hepatology

A. Personal Statement

My overall research interests are liver biology, pathology, and therapeutics. The medical education in China has provided me a comprehensive perspective of human disease and treatment. At the later stage of my undergraduate study and one year after that, I was in Dr. De-An Tian's group in Tongji Hospital and worked on hepatocellular carcinoma (HCC). I helped to examine KLF17 expression in HCC patient liver tissues and human cancer cell lines and contributed to a publication. This research experience has sparked my interest in hepatology. As a graduate student in Dr. Wen-Xing Ding's lab in University of Kansas Medical Center (KUMC), I gained expertise in using transgenic mouse models to study liver lipid metabolism and xenobiotic-induced liver steatosis and injury. I also studied on the mechanism of chemoresistance in cancer cell lines. My graduate dissertation work got sponsored by the Biomedical Research Training Program in KUMC, and my several projects were presented in national or international meetings and published on peer-reviewed journals as first-author. In addition, in the doctoral program I had advanced education in molecular cell biology, pharmacology, and toxicology and obtained a solid understanding of liver metabolism. After a short transition period as a postdoc in Dr. Ding's lab, I recently started the postdoc training with Dr. Natalie J. Torok in Stanford University. As a physician-scientist in hepatology, Dr. Torok is internationally renowned for her specialty in liver fibrosis in non-alcoholic steatohepatitis (NASH) and is highly experienced in training postdocs and fellows. I plan to build up my expertise in liver research by studying NASH and liver cancers. In addition to the abundant resources in *in vivo* models and NASH study in Torok Lab, we will collaborate with external cancer experts to perfect this interdisciplinary project. At the same time, I am actively attending the postdoc workshops in Stanford including writing, speaking, and networking, which largely helps to train me to become an independent liver researcher.

B. Positions and Honors

Positions and Employment

2009 - 2011 Medical Intern, Tongji Hospital, China

2010 - 2012 Research Trainee, Institute of Liver Disease of Tongji Hospital, China
2012 - 2018 Graduate Research Assistant, University of Kansas Medical Center, U.S.
2018 - 2019 Postdoctoral Fellow, University of Kansas Medical Center, U.S.
2019 - present Postdoctoral Scholar, Stanford University, U.S.

Other Experience and Professional Memberships

2018 Selected Trainee for *Big Data Training for Translational Omics Research*, Purdue University, U.S.
2019 Trainee Member, American Association for the Study of Liver Disease

Honors and Awards

2014, 2015, 2017 Student Governing Council Travel Award, University of Kansas Medical Center, U.S.
2016, 2017 Graduate Student Professional Development Award, University of Kansas Medical Center, U.S.
2016 - 2018 Azarnoff Award, University of Kansas Medical Center, U.S.
2017 Biomedical Research Training Program ($12,000 stipend), University of Kansas Medical Center, U.S.

C. Contributions to Science

1. Role of adipocyte mTOR and autophagy in adipose atrophy and alcoholic liver disease. Alcoholic liver disease (ALD) is a worldwide health issue, and no ideal treatment, except for liver transplantation, is available for late-stage ALD such as liver cirrhosis and hepatocellular carcinoma. I believe that liver is not an isolated organ in ALD, and my doctoral dissertation studied the effect of alcohol on adipose tissue and its subsequent contribution to ALD pathogenesis. I found that chronic-plus-binge alcohol inhibited mTOR signaling, increased autophagic flux, and induced adipose tissue atrophy in mice. I further demonstrated that mice with chronic adipose tissue autophagy deficiency (adipose-Atg5 KO mice) were more resistant to alcohol-induced adipose atrophy. These data indicate that autophagy activation contributes to adipose dysfunction induced by alcohol. In addition, I demonstrated that adipose-Atg5 KO mice were more resistant to alcohol-induced liver injury, which was likely due to increased secretion of adiponectin and fibroblast growth factor 21 at basal levels. These data support an important role for the adipose-liver axis in the pathogenesis of ALD and suggest that targeting adipose tissue autophagy may be helpful for improving alcohol-induced liver injury. These studies led to two reviews, two AASLD meeting abstracts, and a manuscript in preparation. Based on this project, I received the Biomedical Research Training Program fellowship from KUMC in 2017.

a. **Li Y**, Chao X, Wang S, Ni HM, Ding WX. Acute-On-Chronic Alcohol Induces Adipose Tissue Atrophy, Hepatic Steatosis and Liver Injury via Inhibition of mTORC1 in Adipose Tissue in Mice [abstract]. In: The 68th Annual Meeting of the American Association for the Study of Liver Diseases: The Liver Meeting 2017; 2017 Oct 20–24; Washington, D.C: ***Hepatology***; 2017 Oct. Abstract nr 1295.
b. **Li Y**, Ni HM, Chao X, Ding WX. Impaired Adipocyte Autophagy Promotes White Adipocyte Browning and Protects against Alcohol-Induced Liver Injury [abstract]. In: The 67th Annual Meeting of the American Association for the Study of Liver Diseases: The Liver Meeting 2016; 2016 Nov 11–15; Boston, MA: ***Hepatology***; 2016 Oct. Abstract nr 1223.
c. **Li Y**, Ding WX. Adipose Tissue Autophagy and Homeostasis in Alcohol-Induced Liver Injury. ***Liver Res*****.** 2017 Jun;1(1):54-62. doi: 10.1016/j.livres.2017.03.004. Epub 2017 Apr 26. PMID: 29109891
d. **Li Y**, Wang S, Ni HM, Huang H, Ding WX. Autophagy in Alcohol-Induced Multiorgan Injury: Mechanisms and Potential Therapeutic Targets. ***Biomed Res Int*****.** 2014;2014:498491. PMID: 25140315

2. Autophagy in liver lipid droplet homeostasis. Autophagy is important in maintaining the homeostasis of intracellular lipid droplets (LDs) in cultured cells and in mice. However, it is still controversial and unclear how impaired autophagy in hepatocytes affects LD biogenesis. I compared the phenotype and lipid metabolism among WT mice and liver-specific Atg5 and/or Nrf2 KO mice in response to starvation. I demonstrated that hepatic autophagy-deficient (L-Atg5 KO) mice had impaired adaptation to fasting-induced hepatic biogenesis of LDs, which was corrected in L-Atg5/Nrf2 double KO mice. I originally found the contribution of persistent Nrf2 activation to impaired LD biogenesis, and this finding helps to explain the altered lipid metabolism in mice with deficient liver autophagy. Besides a publication on this project, we were invited for two comments in the field.

a. **Li Y**, Chao X, Yang L, Lu Q, Li T, Ding WX, Ni HM. Impaired Fasting-Induced Adaptive Lipid Droplet Biogenesis in Liver-Specific Atg5-Deficient Mouse Liver Is Mediated by Persistent Nuclear Factor-Like 2

Activation. ***Am J Pathol.*** 2018 Aug;188(8):1833-1846. doi: 10.1016/j.ajpath.2018.04.015. Epub 2018 May 25. PMID:29803835

b. **Li Y**, Zong WX, Ding WX. Recycling the Danger via Lipid Droplet Biogenesis after Autophagy. ***Autophagy.*** 2017 Sep 5:1-3. doi: 10.1080/15548627.2017.1371394. PMID: 28873005

c. **Li Y**, Ding WX. Impaired Rab7 and Dynamin2 Block Fat Turnover by Autophagy in Alcoholic Fatty Livers. ***Hepatol Commun*****.** 2017 Aug;1(6):473-476. doi: 10.1002/hep4.1067. PMID: 29124250

3. A cell-based high throughput screening of autophagy modulators. Autophagy is a promising target of cancer clinical trials. Meanwhile more accurate tools for autophagy measurement are needed. We collaborated with Dr. Menghang Xia's group from NIH, who employed a high throughput image-based screening for autophagy modulators in mouse embryonic fibroblasts stably expressing the autophagy marker GFP-LC3 using a library of pharmacologically active compounds. I examined the screening data and summarized potential autophagy inducers and inhibitors. In addition, I selected a few novel autophagy inducers which were known as dopamine inhibitors/antagonists, validated their autophagy induction in various cell lines, and explored their mechanisms of autophagy induction. This screening provides useful resources to discover new pharmacological agents for autophagy modulation. Since my lab previously found that autophagy protects against acetaminophen (APAP)-induced liver injury, I also tested the effect of the autophagy inducer chlorpromazine, a famous anti-psychotic medication, on APAP-induced injury in mice. I originally discovered that chlorpromazine treatment effectively protected against APAP via autophagy-dependent and JNK-dependent pathways. This study further supports the screening and brings new understanding to the mechanism and usage of old drugs.

a. **Li Y**, Ni HM, Jaeschke H, Ding WX. Chlorpromazine Protects Against Acetaminophen-Induced Liver Injury in Mice by Modulating Autophagy and c-Jun N-terminal Kinase Activation. ***Liver Res***. 2019 Feb https://doi.org/10.1016/j.livres.2019.01.004

b. **Li Y**, McGreal S, Zhao J, Huang R, Zhou Y, Zhong H, Xia M, Ding WX. A Cell-Based Quantitative High-Throughput Image Screening Identified Novel Autophagy Modulators. ***Pharmacol Res*****.** 2016 Aug;110:35-49. doi: 10.1016/j.phrs.2016.05.004. PMID:27168224

4. Autophagy and Nrf2 signaling in differential chemoresistance of cancers. Cancers are highly diverse in terms of chemoresistance. For example, the diabetic drug metformin is beneficial against various tumors in some epidemiological studies but not in other studies. We found that metformin can inhibit hepatic tumor cell growth *in vitro* likely through the inhibition of mTOR. However, different levels of basal autophagy and feedback activation of Akt by mTORC2 in different hepatic tumor cells may determine the sensitivity of these cells in response to metformin-induced growth inhibition. For another example, non-small cell lung cancer (NSCLC) responds differently or gradually develops chemoresistance to epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors. We found that the drug resistance of NSCLC involves multiple signaling pathways including EGFR, Nrf2 and autophagy. These studies help to explain the heterogeneity of cancers and suggest that autophagy and/or Nrf2 signaling are potential adjuvant targets. In these two projects, I contributed by characterizing the autophagy status and cell survival in response to drugs in several cancer cell lines.

a. Zhou Y, **Li Y**, Ni HM, Ding WX, Zhong H. Nrf2 but Not Autophagy Inhibition is Associated with the Survival of Wild-Type Epidermal Growth Factor Receptor Non-Small Cell Lung Cancer Cells. ***Toxicol Appl Pharmacol.*** 2016 Nov 1;310:140-149. doi: 10.1016/j.taap.2016.09.010. PMID:27639429

b. Yang H, Peng YF, Ni HM, **Li Y**, Shi YH, Ding WX, Fan J. Basal Autophagy and Feedback Activation of Akt Are Associated with Resistance to Metformin-Induced Inhibition of Hepatic Tumor Cell Growth. ***PLoS One*****.** 2015 Jun 25;10(6):e0130953. PMID: 26111001

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/myncbi/browse/collection/42909238/

D. Additional Information: Research Support and/or Scholastic Performance

Scholastic Performance

YEAR	COURSE TITLE	GRADE
	University of Kansas Medical Center	
2012	Introduction to Biomedical Research I	S

YEAR	COURSE TITLE	GRADE
2012	Introduction to Faculty Research	S
2012	Introduction to Research Ethics	S
2012	Biographics	S
2012	Scientific Communication	P
2012	Molecular Genetics	B
2012	Proteins and Metabolism	C
2012, 2013	Research Rotations	S
2013	Introduction to Biomedical Research II	S
2013	Comprehensive Human Physiology	B
2013	Research	P
2013	Cellular Structure	B
2013	Cell Communication	B
2013	Advanced Topics	A
2014	Essential Pharmacology	B
2014	Graduate Histology	B
2014	Principles of Toxicology	A
2014, 2015	Research in Toxicology	P
2014-2017	Seminar in Pharmacology	A
2015	Toxicology	B
2015	Techniques in Industry Toxicology	A
2016	Toxicologic Pathology	B
2016	Disposition of Xenobiotics	B
2016	Research Dissertation in Toxicology	P
2017, 2018	Dissertation in Toxicology	P

In University of Kansas Medical Center, courses are grades as S(satisfactory)/U(unsatisfactory), P(passed)/F(failed), or A(>90)/B(90-80)/C(80-70)/D(70-60)/F(failed).