BIOGRAPHICAL SKETCH

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NAME: Liquan Cai

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

POSITION TITLE: Assistant Investigator

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
Xinyang Normal University--Henan, China	B. S.	07/1994	Biology Science
Beijing Normal University--Beijing, China	M. S.	07/1997	Animal Physiology
Chinese Academy of Sciences--Beijing, China	Ph.D.	06/2000	Animal Physiology
Carnegie Institution at Baltimore, MD, USA	Postdoc.	07/2007	Dev. Biology

A. Personal Statement

After completing a bachelor's degree in Biological Science, I underwent a Master program at Beijing Normal University (1994-1997), where I studied the regulation of body metabolism and thermogenesis by thyroid hormones in mammals. Next, I completed a PhD program at the Institute of Zoology of the Chinese Academy of Sciences (1997-2000), where I studied embryo implantation in the mouse. Since then, my research focus has been on gene regulatory pathways in animal development and human diseases. Through over twenty years of research experience, I have accumulated knowledge and technical expertise in stem cell biology, cell/developmental biology, and human genetics. As concrete examples, I have conducted and supervised studies using gene manipulation in the cultured cells and animals as a tool to dissect out the molecular basis underlying the developmental control of tissue morphogenesis (2000-2007 at Carnegie Institution for Science at Baltimore and 2008-2014 at University of Pittsburgh). I have also conducted and supervised research studies using CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) technology and generated single-cell mutants of smooth muscle progenitor cells at the Centre for Research in Vascular Biology, University College Cork in Ireland. Finally, I have extensive experience in gene silencing and gene targeting in mammalian cells and animal models including mouse, *Xenopus laevis*, and *C. elegans*. Since joining Marshall, I have been studying the Na^+/K^+-ATPase (NKA) signaling function in human diseases using CRISPR genome editing and iPSC (induced pluripotent stem cells) as the major tools.

B. Positions, Scientific Appointments, and Honors

Positions and Employment

2000-07 Postdoctoral Fellow, Department of Embryology, Department of Embryology, Carnegie Institution for Science, 3520 San Martin Drive, Baltimore, MD, USA.
2007-08 Research Instructor, Department of Pharmacology, University of Illinois at Chicago, IL, USA.
2008-14 Research Assistant Professor, Department of Urology, University of Pittsburgh, PA, USA.
2014-15 Senior Scientist, University College Cork, Ireland
2015-25 Assistant Investigator at MIIR, Marshall University, WV, USA.
2025- Assistant Professor, Department of Biomedical Sciences, Joan C Edwards School of Medicine Marshall University, WV, USA.

Honors

2010 Society of Urology Basic Research meeting Poster Travel Award

2000 President Award for excellent PhD students in Chinese Academy of Science.
1995-97 Excellent Undergraduate Student Awards in Xinyang Normal University

C. Contributions to Science

1. CRISPR and stem cell biology. My current studies focus on genome editing in human iPSC. CRISPR technology is used to dissect out the specific role of Na^+/K^+-ATPase in myocyte (skeletal and cardiac muscles) or adipocyte differentiation and physiological function. In a longer term, patient-derived iPSC will be established as a "disease-in-a-dish" modeling system where candidate molecules will be tested *in vitro,* or new drugs will be identified through high-throughput screening from compound libraries. The CRISPR technology was implemented in my previous studies to create smooth muscle progenitor cell lines with the deletion mutation of a crucial transcription factor, Klf4. The mutant progenitor cells had altered cell fate determination. This body of work resulted in the following publications.

1) Huang M, Wang X, Chen Y, Pessoa M, Terrell K, Zhang J, Tian J, Xie Z, Pierre SV, **Cai L** (2024) Role of Na/K-ATPase α1 caveolin-binding motif in adipogenesis. *Am J Physiol Cell Physiol.* 27(1):C48-C64. (corresponding author)
https://pubmed.ncbi.nlm.nih.gov/38708522/
2) Huang M, Wang X, Banerjee M, Mukherji ST, Kutz LC, Zhao A, Sepanski M, Fan C, Zhu G, Tian J, Wang D, Zhu H, Xie Z, Pierre SV, **Cai L** (2022) Regulation of Myogenesis by a Na/K-ATPase a1 Caveolin Binding Motif. *Stem Cells* (Corresponding author)
https://pubmed.ncbi.nlm.nih.gov/35257186/
3) Wang X, **Cai L**, Xie J, Cui X, Zhang J, Wang J, Chen Y, Larre I, Shapiro J, Pierre S, Wu D, Zhu G and Xie Z (2020) A Caveolin Binding Motif in Na/K-ATPase is Required for Stem Cell Differentiation and Organogenesis in Mammals and *C. elegans*. *Science Advances*. 6(2) (Co-first author)
https://advances.sciencemag.org/content/6/22/eaaw5851
4) Turner EC, Huang CL, N. Sawhney N, K. Govindarajan K, Clover AJP, Martin K, Browne TC, Whelan D, Kumar AHS, Mackrill JJ, Wang S, Schmeckpeper J, Stocca A, Pierce WG, Leblond AL, **Cai L**, O'Sullivan DM, Buneker CK, Choi J, MacSharry J, Ikeda Y, Russell SJ, Caplice NM (2016) A novel selectable ISL-1 positive progenitor cell reprogrammed to expandable and functional smooth muscle cells. *Stem Cells*. 34(5):1354-68.
https://stemcellsjournals.onlinelibrary.wiley.com/doi/full/10.1002/stem.2319

2. Skeletal muscle development and muscle-nerve junction formation. Myogenesis in vertebrate animals shares the conserved regulatory genetics. Xenopus limb formation entails muscle and nerve development and interaction which is controlled by thyroid hormone. We dissected the molecular mechanisms through transgenesis, consisting of the tetracycline inducible system and the tissue/cell type specific promoters (muscle, neural, intestine, fibroblast) controlling the transgene expression in a time and cell-type specific manner. Inhibition of thyroid hormone action through this transgene in the muscle or nerve led to the same defect, the paralyzed limb and eventually tadpole death at around climax of metamorphosis. But the mechanisms are different. We observed the arrested muscle development including disrupted gene expression of myogenesis markers and histology. However, the myoblast or satellite cells were abundantly present, mimicking the muscle atrophy diseases in humans. Moreover, the defective phenotype is restricted by the promoters used, leaving the unaffected development in other tissues/cell types. The results are published in the following papers.

1) Kutz LC, Cui X, Xie JX, Mukherji ST, Terrell KC, Huang M, Wang X, Wang J, Martin AJ, Pessoa MT, **Cai L**, Zhu H, Heiny JA, Shapiro JI, Blanco G, Xie Z, Pierre SV. (2021) The Na/K-ATPase α1/Src interaction regulates metabolic reserve and Western diet intolerance. *Acta Physiol (Oxf)*.
https://pubmed.ncbi.nlm.nih.gov/33752256/
2) **Cai L**, Das B and Brown DD (2007) Changing a limb muscle growth program into a resorption program. *Developmental Biology*. 304:260-271.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1868508/
3) Marsh-Armstrong N, **Cai L**, Brown DD. (2004) Thyroid hormone controls the development of connections between the spinal cord and limbs during *Xenopus laevis* metamorphosis. *Proc Natl Acad Sci U S A*. 101(1):165-70.
https://www.pnas.org/content/101/1/165

4) Brown DD, **Cai L**, Das B, Marsh-Armstrong N, Schreiber AM, Juste R. (2005) Thyroid hormone controls multiple independent programs required for limb development in *Xenopus laevis* metamorphosis. *Proc Natl Acad Sci U S A*. 102(35):12455-8. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1194953/

3. Cell, developmental biology and molecular genetics. Most of the genetic pathways are conserved among all species and can be transformed into the study of human diseases. Human diseases are associated with the dysregulation of specific biological events which are, in normal conditions, elaborately controlled in the body. My earlier studies have been focused on the basic biological questions involved in thermogenesis, reproduction, and embryo development in vertebrate animals. This background gives me a broad perspective and insights into the study of human diseases, such as cancers, obesity, diabetes as well as disorders in skeletal and cardiac muscle cells. The following collection reflects my background on this topic.

1. Huang M, Wang X, Banerjee M, Mukherji ST, Kutz LC, Zhao A, Sepanski M, Fan C, Zhu G, Tian J, Wang D, Zhu H, Xie Z, Pierre SV, **Cai L** (2022) Regulation of Myogenesis by a Na/K-ATPase a1 Caveolin Binding Motif. *Stem Cells* (Corresponding author) https://pubmed.ncbi.nlm.nih.gov/35257186/
2) Wang X, **Cai L**, Xie J, Cui X, Zhang J, Wang J, Chen Y, Larre I, Shapiro J, Pierre S, Wu D, Zhu G and Xie Z (2020) A Caveolin Binding Motif in Na/K-ATPase is Required for Stem Cell Differentiation and Organogenesis in Mammals and *C. elegans*. *Science Advances*. 6(2) (Co-first author) https://advances.sciencemag.org/content/6/22/eaaw5851
3) **Cai L**, Das B and Brown DD (2007) Changing a limb muscle growth program into a resorption program. *Developmental Biology*. 304:260-271. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1868508/
4) Schreiber MA, **Cai L** and Brown DD (2005) Remodeling of the intestine during metamorphosis of Xenopus laevis. *Proc Natl Acad Sci U S A*. 2005 102(10):3720-5. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC553331/

4. RNA-seq and gene expression profiling. I have been working on gene expression, microarray analysis, and RNA-seq for many years. These technologies are instrumental to current biomedical research. When I worked at Carnegie Institution at Baltimore, I conducted cDNA microarray analysis to pursue the molecular mechanisms of the thyroid hormone-regulated developmental program called metamorphosis. This is a unique growth period in amphibians, when the larval tadpole turns into an adult frog. This transition of the body growth involves fundamental questions in cell biology: cell death, cell proliferation, and cell differentiation. All the diverse programs are controlled by a single molecule, thyroid hormone. Through gene array studies, we identified the diverse sets of genes controlled by this hormone in different tissues and organs. This revealed how the genetic toolbox is utilized and controlled by a single molecule to trigger cell death, proliferation or remodeling in response to the needs in different cell types. Similarly, I performed a cDNA microarray study when I used *C. elegans* as a model system to dissect the genetic signaling pathway for the tumor suppressor, also an androgen-regulated gene, *eaf2*.The following publications represent the above research involved in this technology.

1. Huang M, Wang X, Banerjee M, Mukherji ST, Kutz LC, Zhao A, Sepanski M, Fan C, Zhu G, Tian J, Wang D, Zhu H, Xie Z, Pierre SV, **Cai L** (2022) Regulation of Myogenesis by a Na/K-ATPase a1 Caveolin Binding Motif. *Stem Cells* (Corresponding author) https://pubmed.ncbi.nlm.nih.gov/35257186/
2) Wang X, **Cai L**, Xie J, Cui X, Zhang J, Wang J, Chen Y, Larre I, Shapiro J, Pierre S, Wu D, Zhu G and Xie Z (2020) A Caveolin Binding Motif in Na/K-ATPase is Required for Stem Cell Differentiation and Organogenesis in Mammals and *C. elegans*. *Science Advances*. 6(2) (Co-first author) https://advances.sciencemag.org/content/6/22/eaaw5851
3) **Cai L**, Phong B, Fisher A, Wang Z (2011) Regulation of fertility, survival, and cuticle collagen function by *C. elegans eaf-1* and *ell-1*. *J Biol Chem.* 286(41):35915-21. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3195645/
4) **Cai L** and Brown DD (2004) Expression of type II iodothyronine deiodinase marks the time that a tissue responds to thyroid hormone-induced metamorphosis in *Xenopus laevis*. *Developmental Biology*. 266(1):87-95.

https://www.sciencedirect.com/science/article/pii/S0012160603006183?via%3Dihub

5. Gene function study using transgene overexpression, RNAi knockdown, and knockout. RNAi or gene silencing technology has been frequently used in my studies to address specific gene functions. To dissect the genetic signaling pathways of the tumor suppressor *Eaf2* gene, I implemented the *C. elegans* model system due to its powerful genetics. I discovered collagen as the downstream target of this transcription factor in *C. elegans*. This regulation plays essential roles in *C. elegans* cuticle morphogenesis and body movement. Moreover, due to the ease of use of RNAi in *C. elegans*, I have performed the RNAi library screen including the gene selection for the *C. elegans* transcription factors, chromatin factors, kinases, and phosphatases. This study leads to the identification of the genetic interactions between the tumor suppressor *Eaf2* and *FoxA1* and the retinoblastoma signaling. Through protein co-immunoprecipitation and other cell or molecular methods, I also tested this genetic interaction, as well as the role in androgen signaling in prostate cancer cells. The above findings are published in the following references.

1. Huang M, Wang X, Banerjee M, Mukherji ST, Kutz LC, Zhao A, Sepanski M, Fan C, Zhu G, Tian J, Wang D, Zhu H, Xie Z, Pierre SV, **Cai L** (2022) Regulation of Myogenesis by a Na/K-ATPase a1 Caveolin Binding Motif. *Stem Cells* (Corresponding author) https://pubmed.ncbi.nlm.nih.gov/35257186/
2) Wang X, **Cai L**, Xie J, Cui X, Zhang J, Wang J, Chen Y, Larre I, Shapiro J, Pierre S, Wu D, Zhu G and Xie Z (2020) A Caveolin Binding Motif in Na/K-ATPase is Required for Stem Cell Differentiation and Organogenesis in Mammals and *C. elegans*. *Science Advances*. 6(2) (Co-first author) https://advances.sciencemag.org/content/6/22/eaaw5851
3) **Cai L**, Phong B, Fisher A, Wang Z (2011) Regulation of fertility, survival, and cuticle collagen function by *C. elegans eaf-1* and *ell-1*. *J Biol Chem*. 286(41):35915-21. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3195645/

D. Additional Information

Complete List of Published Work in MyBibliography

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