Education

B.S. Fundamental Sciences, Tsinghua University, China
Ph.D. Biophysics, The Ohio State University

Professional Activities

Postdoctoral Researcher: Davis Heart and Lung Research Institute, Department of Physiology and Cell Biology, The Ohio State University
Research Scientist: Davis Heart and Lung Research Institute, Department of Physiology and Cell Biology, The Ohio State University

Statement of Research Interests

Calcium (Ca) is required for cardiac contraction. It controls not only the strength of cardiac contraction, but also heart rhythm. Within a cardiac muscle cell, Ca cycles on a beat-to-beat basis, in a way that is consistent with the rhythmic cardiac activity. Ca is released from the intracellular Ca store sarcoplasmic reticulum (SR) through the channel protein ryanodine receptor (RyR2) to induce contraction; the released Ca must be brought back to the Ca store to allow relaxation to occur.

This Ca cycling process is sometimes adversely altered. For instance, instead of the regulated Ca release with every heartbeat, Ca can leak from the RyR2 channel spontaneously, which contributes to cardiac pathologies such as ventricular arrhythmias and even heart failure. Catecholaminergic polymorphic ventricular tachycardia (CPVT) is a life-threatening Ca-dependent arrhythmia caused by genetic mutations identified in the RyR2 channel complex. The mechanism of CPVT involves aberrant spontaneous Ca release through dysregulated or “leaky” RyR2 channels, which activates Ca-dependent depolarizing currents, thereby causing triggered arrhythmia.

My research interest focuses on understanding the molecular mechanism underlying Ca-dependent cardiac dysfunctions and developing novel mechanism-based therapeutics. One of the current projects is to develop a therapeutic calmodulin molecule to treat CPVT caused by genetic mutations identified in the other proteins of the cardiac SR Ca-releasing channel RyR2 complex. Primary experimental approaches include intracellular Ca imaging using fluorescent confocal microscopy and *in vivo* cardiac functional studies, such as electrocardiogram (ECG) recordings in genetic mouse models of cardiac diseases.

Selected Publications

Györke S, Belevych AE, **Liu B**, Kubasov IV, Carnes CA, Radwański PB. The role of luminal Ca regulation in Ca signaling refractoriness and cardiac arrhythmogenesis. *J Gen Physiol*. 2017 Sep 4;149(9):877-888.

Ho HT, Belevych AE, **Liu B**, Bonilla IM, Radwański PB, Kubasov IV, Valdivia HH, Schober K, Carnes CA, Györke S. Muscarinic Stimulation Facilitates Sarcoplasmic Reticulum Ca Release by Modulating Ryanodine Receptor 2 Phosphorylation Through Protein Kinase G and Ca/Calmodulin-Dependent Protein Kinase II. *Hypertension*. 2016 Nov;68(5):1171-1178.

Davis JP, Shettigar V, Tikunova SB, Little SC, **Liu B**, Siddiqui JK, Janssen PM, Ziolo MT,Walton SD. Designing proteins to combat disease: Cardiac troponin C as an example. *Arch Biochem Biophys*. 2016 Jul 1;601:4-10. doi: 10.1016/j.abb.2016.02.007.

Liu B, Ho HT, Brunello L, Unudurthi SD, Lou Q, Belevych AE, Qian L, Kim do H, Cho C, Janssen PM, Hund TJ, Knollmann BC, Kranias EG, Györke S. Ablation of HRC alleviates cardiac arrhythmia and improves abnormal Ca handling in CASQ2 knockout mice prone to CPVT. *Cardiovasc Res*. 2015 Nov 1;108(2):299-311. doi: 10.1093/cvr/cvv222. Epub 2015 Sep 25.

Lou Q, Belevych AE, Radwański PB, **Liu B**, Kalyanasundaram A, Knollmann BC, Fedorov VV, Györke S. Alternating membrane potential/calcium interplay underlies repetitive focal activity in a genetic model of calcium-dependent atrial arrhythmias. *J Physiol*. 2015 Mar 15;593(6):1443-58. doi: 10.1113/jphysiol.2014.280784. Epub 2014 Dec 2.

Curran J, Makara MA, Little SC, Musa H, **Liu B**, Wu X, Polina I, Alecusan JS, Wright P, Li J, Billman GE, Boyden PA, Gyorke S, Band H, Hund TJ, Mohler PJ. EHD3-Dependent Endosome Pathway Regulates Cardiac Membrane Excitability and Physiology. *Circ Res*. 2014 Jun 20;115(1):68-78.doi:10.1161/CIRCRESAHA.115.304149.

Liu B, Ho HT, Velez-Cortes F, Lou Q, Valdivia C, Knollmann B, Valdivia H, Gyorke S. Genetic ablation of ryanodine receptor 2 phosphorylation at Ser-2808 aggravates Ca2+-dependent cardiomyopathy by exacerbating diastolic Ca2+ release. *J Physiol*. 2014 May 1;592(Pt 9):1957-73. doi: 10.1113/jphysiol.2013.264689.

Liu B, Lopez JJ, Biesiadecki BJ, Davis JP. Protein kinase C phosphomimetics alter thin filament Ca^{2+} binding properties. *PLoS One*. 2014 Jan 22;9(1):e86279.

Ho HT, **Liu B**, Snyder JS, Lou Q, Brundage EA, Velez-Cortes F, Wang H, Ziolo MT, Anderson ME, Sen CK, Wehrens XH, Fedorov VV, Biesiadecki BJ, Hund TJ, Györke S. Ryanodine receptor phosphorylation by oxidized CaMKII contributes to the cardiotoxic effects of cardiac glycosides. *Cardiovasc Res*. 2014 Jan 1;101(1):165-74.

Liu B, Tikunova SB, Kline KP, Siddiqui JK, Davis JP. Disease-Related Cardiac Troponins Alter Thin Filament Ca^{2+} Association and Dissociation Rates. *PLoS One*. 2012;7(6):e38259.

Liu B, Lee RS, Biesiadecki BJ, Tikunova SB, Davis JP. Engineered Troponin C Constructs Correct Disease-related Cardiac Myofilament Calcium Sensitivity. *J Biol. Chem*. 2012 Jun 8;287(24):20027-36.

Tikunova SB[#], **Liu B**[#], Swindle N, Little SC, Gomes AV, Swartz DR, Davis JP. Effect of Calcium-sensitizing Mutations on Calcium Binding and Exchange with Troponin C in Increasingly Complex Biochemical Systems. *Biochemistry*. 2010 Mar 9;49(9):1975-84.

[#]**These two authors contributed equally to the manuscript.**