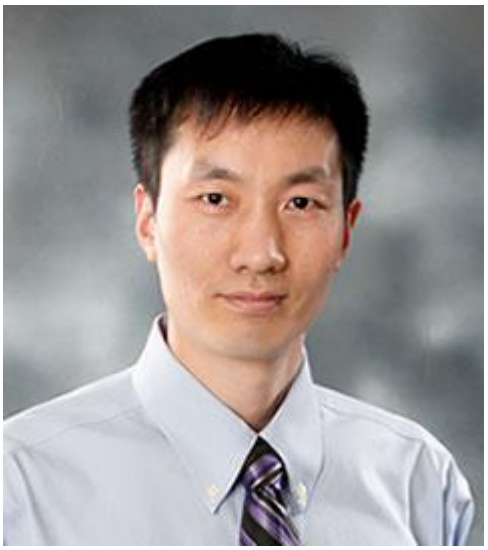
宋保亮



职称职务：教授、院长
Appointment: Professor, Dean
学科专业：生物化学
Department: Biochemistry
研究方向：胆固醇代谢与代谢性疾病
Research: Cholesterol metabolism and met

教育经历/Education

1993－1997　南京大学生物科学与技术系，学士
B.S. Biology, Nanjing University, Nanjing, China

1997－2002　中科院上海生命科学研究院生物化学与细胞生物学研究所，博士
Ph.D. Institute of Biochemistry and Cell Biology, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences.

工作经历与任职/Professional Experience

2002－2005　美国德克萨斯大学西南医学中心，博士后
Post-doctoral research fellow, UT Southwestern Medical Center, Mentors: Drs. Mike Brown, Joe Goldstein, Russell DeBose-Boyd

2005－2014　中科院上海生命科学研究院生物化学与细胞生物学研究所，研究组长，研究员，博士生导师，“百人计划”择优支持，“百人计划”终期评估优秀。分子生物学国家重点实验室副主任（2012-2014），生化细胞所所长助理（2013-2014）。
Principle Investigator, Institute of Biochemistry and Cell Biology, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences.

2014－至今　武汉大学生命科学学院，教授，院长

Professor and Dean, College of Life Sciences, Wuhan University, Wuhan, China

学术兼职：

2009－至今　中国生物物理学会理事会理事

2010－至今　J. of Molecular Cell Biology, Associate Editor

2012－至今　J. Biol. Chem., Editorial Board Member

2014－2016　International Conference on the Bioscience of Lipids (ICBL) 筹划委员

2014－至今　中国生物化学与分子生物学理事会，常务理事

获奖及荣誉：

国家杰出青年科学基金（2009）

国家重大科学研究计划首席科学家（2009）

中科院优秀研究生指导教师（2010）

陈嘉庚青年科学奖（首届，2012）

万人计划科技创新领军人才入选者（2012）

中科院优秀研究生指导教师（2013）

亚太 Arthur Kornberg Memorial Award（2013）

新世纪百千万人才工程国家级人选（2013）

中国青年科技奖（2013）

谈家桢生命科学创新奖（2014）

长江学者特聘教授（2015）

中国细胞生物学学会-普洛麦格创新奖（2015）

研究概述/Research Description

我们主要从事与心脑血管疾病发生密切相关的胆固醇代谢平衡调控的研究。首次提出并证明了小肠细胞对饮食胆固醇吸收的分子模型，发现了该途径中的多个蛋白因子；深入探索了内源胆固醇合成的负反馈调控机制—HMGCR 蛋白的受控降解，揭示了肝脏脂质合成与棕色脂肪能量代谢的联系；构建了基于胆固醇合成负反馈调控途径的筛选体系，并获得了能同时降低胆固醇和甘油三酯的活性化合物白桦酯醇。这些原创性成果不仅丰富了胆固醇代谢平衡调控的基础理论，并且对研发新型的降脂药物具有重要意义。

主要研究方向包括：1）小肠胆固醇吸收的分子途径；2）细胞内胆固醇动态运输的分子机制；3）胆固醇代谢调控的信号转导途径和机理；4）胆固醇代谢的药靶系统及新药研发。

实验室的长期目标是揭示胆固醇代谢的分子机制，发展治疗胆固醇相关疾病的新策略。

Dr. Song’s lab works on cholesterol homeostasis that is closely related to cardiovascular disease. His group has dissected the molecular pathway of intestinal cholesterol absorption and identified most of the protein in this process. He has uncovered the mechanism of sterol-regulated degradation of HMG-CoA reductase, which is a major feed-back regulation of de novo cholesterol biosynthesis. His group also

identified betulin, a small molecule, which can decrease both cholesterol and fatty acid levels by inhibiting SREBP pathway.

Ongoing projects in this laboratory include:

1) Dissecting the molecular pathway of dietary cholesterol absorption.

2) Studying mechanism and function of intracellular cholesterol trafficking.

3) Uncovering the regulatory mechanisms of cholesterol metabolism.

4) Screening for small chemical compounds controlling cholesterol metabolism.

The long-term goals of these studies are to reveal the molecular mechanism of cholesterol metabolism and develop novel strategies to treat cholesterol-related diseases.

发表文章/Publications

Representative Publications:

1) Chu BB, Liao YC, Qi W, Xie C, Du X, Wang J, Yang H, Miao HH, Li BL and **Song BL***. Cholesterol Transport through Lysosome-Peroxisome Membrane Contacts. *Cell*, 161(2):291-306, 2015

2) Li PS, Fu ZY, Zhang YY, Xu CQ, Ma YT, Li BL and **Song BL***. The clathrin adaptor Numb regulates intestinal cholesterol absorption through dynamic interaction with NPC1L1. *Nature Medicine*, 20(1): 80-86, 2014

3) Liu TF, Tang JJ, Li PS, Shen Y, Li JG, Miao HH, Li BL* and **Song BL***. Ablation of gp78 in liver improves hyperlipidemia and insulin resistance by inhibiting SREBP to decrease lipid biosynthesis. *Cell Metabolism*, 16: 213-225, 2012

4) Tang JJ, Li JG, Qi W, Qiu WW, Li PS, Li BL and **Song BL***. Inhibition of SREBP by a small molecule, betulin, improves hyperlipidemia and insulin resistance and reduces atherosclerotic plaques. *Cell Metabolism*, 13: 44-56, 2011

5) Ge L, Wang J, Qi W, Miao HH, Cao J, Qu YX, Li BL and **Song BL***. The cholesterol absorption inhibitor ezetimibe acts by blocking the sterol-induced internalization of NPC1L1. *Cell Metabolism*,7: 508-519, 2008

6) Cao J, Wang J, Qi W, Miao HH, DeBose-Boyd RA, Wang J, Li BL* and **Song BL***. Ufd1 is a cofactor of gp78 and plays a key role in cholesterol metabolism. *Cell Metabolism*, 6:115-128, 2007

7) Ge L, Qi W, Wang LJ, Miao HH, Qu YX, Li BL and **Song BL***. Flotillins play an essential role in Niemann-Pick C1 Like 1-mediated cholesterol uptake. *PNAS*, 108(2): 551-6, 2011

8) **Song BL**, Sever N, and DeBose-Boyd RA. Gp78, a membrane anchored ubiquitin ligase, associates with Insig-1 and couples sterol-regulated ubiquitination to degradation of HMG CoA reductase. *Molecular Cell*. 19(6):829-840, 2005

9) **Song BL**, Javitt NB, and DeBose-Boyd RA. Insig-mediated degradation of HMG CoA reductase stimulated by lanosterol, an intermediate in the synthesis of cholesterol. *Cell Metabolism*, 1: 179-189, 2005

10) Sever N#, **Song BL#**, Yabe D#, Goldstein JL, Brown MS, and DeBose-Boyd RA. Insig-dependent ubiquitination and degradation of mammalian 3-Hydroxy-3-methylglutaryl-CoA reductase stimulated by sterols and geranylgeraniol. *J Biol Chem*, 278: 52479-52490, 2003

Other Publications:

11) Wei J, Fu ZY, Li PS, Miao HH, Li BL, Ma YT, **Song BL*.** The Clathrin Adaptor Proteins ARH, Dab2, and Numb Play Distinct Roles in Niemann-Pick C1-Like 1 Versus Low Density Lipoprotein Receptor-mediated Cholesterol Uptake. *J Biol Chem*, 289(48):33689-700, 2014

12) Jiang W, Tang JJ, Miao HH, Qu YX, Qin J, Xu J, Yang J, Li BL, **Song BL*.** Forward Genetic Screening for Regulators Involved in Cholesterol Synthesis Using Validation-Based Insertional Mutagenesis. *PLoS One*, 9(11):e112632, 2014

13) Jiang W, **Song BL*.** Ubiquitin ligases in cholesterol metabolism. *Diabetes Metab J.* 38(3):171-80, 2014

14) Rogers MA, Liu J, **Song BL**, Li BL, Chang CC, Chang TY. Acyl-CoA: cholesterol acyltransferases (ACATs/SOATs): Enzymes with multiple sterols as substrates and as activators. *J Steroid Biochem Mol Biol*. S0960-0760(14): 00207-6, 2014

15) Xiao X*, **Song BL**. SREBP: a novel therapeutic target.*Acta Biochim Biophys Sin (Shanghai).*45(1):2-10, 2013

16) **Song BL*.** A special issue on 'Metabolism'. *Acta Biochim Biophys Sin (Shanghai).*45(1):1, 2013

17) Xu J, Hu G, Lu M, Xiong Y, Li Q, Chang CC, **Song BL**, Chang TY, Li BL. MiR-9 reduces human acyl-coenzyme A:cholesterol acyltransferase-1 to decrease THP-1 macrophage-derived foam cell formation.*Acta Biochim Biophys Sin (Shanghai).*45(11):953-62, 2013

18) Lu M, Hu XH, Li Q, Xiong Y, Hu GJ, Xu JJ, Zhao XN, Wei XX, Chang CC, Liu YK, Nan FJ, Li J, Chang TY, **Song BL***, Li BL*.A specific cholesterol metabolic pathway is established in a subset of HCCs for tumor growth.*J Mol Cell Biol.* 5:404-15,2013

19) Hu GJ, Chen J, Zhao XN, Xu JJ, Guo DQ, Lu M, Zhu M, Xiong Y, Li Q, Chang CC, **Song BL**, Chang TY, Li BL. Production of ACAT1 56-kDa isoform in human cells via trans-splicing involving the ampicillin resistance gene.*Cell Res.* 23(8):1007-24, 2013

20) Liu Y, Xu XH, Chen Q, Wang T, Deng CY, **Song BL**, Du JL, Luo ZG. Myosin Vb controls biogenesis of post-Golgi Rab10 carriers during axon development.*Nat Commun.* 4:2005.2013

21) Xie C, Zhou ZS, Li N, Bian Y, Wang YJ, Wang LJ, Li BL* and **Song BL***. Ezetimibe blocks the internalization of NPC1L1 and cholesterol in mouse small intestine. *J Lipid Res*, 53: 2092-2101, 2012

22) Wang LJ and **Song BL***. Niemann-Pick C1-Like 1 and cholesterol uptake. *Biochim Biophys Acta*, 1821(7):964-72, 2012

23) Xie C, Li N, Chen ZJ, Li BL, **Song BL***. The small GTPase Cdc42 interacts with Niemann-Pick C1 Like 1 (NPC1L1) and controls its movement from endocytic recycling compartment to plasma membrane in a cholesterol dependent manner.*J Biol Chem*, 286(41):35933-42, 2011

24) Zhang JH, Ge L, Qi W, Zhang L, Miao HH, Li BL, Yang M and **Song BL***. The N-terminal domain of NPC1L1 protein binds cholesterol and plays essential roles in cholesterol uptake. *J Biol Chem*, 286(28): 25088-97, 2011

25) Wang LJ, Wang J, Li N, Ge L, Li BL and **Song BL***. Molecular characterization of the NPC1L1 variants identified from cholesterol low absorbers. *J Biol Chem,* 286(9): 7397-7408, 2011

26) Miao HH, Jiang W, Ge L, Li BL, **Song BL***. Tetra-glutamic acid residues adjacent to Lys248 in HMG-CoA reductase are critical for the ubiquitination mediated by gp78 and UBE2G2. *Acta Biochim Biophys Sin*, 42(5): 303-310, 2010

27) Chu BB, Ge L, Xie C, Zhao Y, Miao HH, Wang J, Li BL and **Song BL***. Requirement of Myosin Vb/Rab11a/Rab11-FIP2 complex in cholesterol-regulatedtranslocation of Niemann-Pick C1 Like 1 protein to the cell surface. *J Biol Chem*, 284: 22481-90, 2009.

28) Wang J, Chu BB, Ge L, Li BL, Yan Y* and **Song BL***. Membrane topology of human NPC1L1, a key protein in enterohepatic cholesterol absorption. ***J Lipid Res***, 50: 1653-62, 2009

29) Lei L, Xiong Y, Chen J, Yang JB, Wang Y, Yang XY, Chang CCY, **Song BL**, Chang TY and Li BL*. TNF-alpha stimulates the ACAT1 expressionin differentiating monocytes to promote the CE-laden cell formation. ***J Lipid Res***, 50: 1057-67, 2009

30) Zhao XN, Chen J, Lei L, Hu GJ, Xiong Y, Xu JJ, Li Q, Yang XY, Chang C, **Song BL**, Chang TY and Li BL. The optional long 5'-untranslated region of human ACAT1 mRNAs impairs the production of ACAT1 protein by promoting its mRNA decay. ***Acta Biochim Biophys Sin***, 41: 30-41, 2009

31) Chen J, Zhao XN, Yang L, Hu GJ, Lu M, Xiong Y, Yang XY, Chang CC, **Song BL**, Chang TY, Li BL. RNA secondary structures located in the interchromosomal region of human ACAT1 chimeric mRNA are required to produce the 56-kDa isoform. ***Cell Res***, 18: 921-936, 2008

32) Qi W and **Song BL***. Dissecting the NPC1L1-mediated cholesterol absorption. ***Future Lipidology***, 3: 481-484, 2008

33) Cao J, Qi W and **Song BL***. Tocotrienols and the regulation of cholesterol biosynthesis. Chapter 18 (p237-256) In:***Tocotrienols: Beyond Vitamin E,*** *CRC press*, 2008

34) Lee JN, **Song BL**, DeBose-Boyd RA, Ye J. Sterol-regulated degradation of Insig-1 mediated by the membrane-bound ubiquitin ligase gp78. ***J Biol Chem***, 281:39308-39315, 2006

35) **Song BL*** and Debose-Boyd RA*. Insig-dependent ubiquitination and degradation of 3-Hydroxy-3-methylglutaryl-Coenzyme A stimulated by {delta}- and {gamma}-Tocotrienols. ***J Biol Chem***, 281: 25054-25061, 2006

36) **Song BL**, Wang CH, Yao XM, Yang L, Zhang WJ, Wang ZZ, Zhao XN, Yang JB, Qi W, Yang XY, Inoue K, Lin ZX, Zhang HZ, Kodama T, Chang CC, Liu YK, Chang TY and Li BL. Human acyl-CoA:cholesterolacyltransferase 2 gene expression in intestinal Caco-2 cells and in hepatocellular carcinoma. ***Bio chem J***, 394: 617-626, 2006

37) Yao XM, Wang CH, **Song BL**, Yang XY, Wang ZZ, Qi W, Lin ZX, Chang CC, Chang TY andLi BL. Two human ACAT2 mRNA variants produced by alternative splicing and coding for novel isoenzymes. ***Acta Biochim Biophys Sin***, 37: 797-806, 2005

38) Sever N, Lee PCW, **Song BL**, Rawson RB, and DeBose-Boyd RA. Isolation of mutant cells

lacking Insig-1 through selection with SR-12813, an agent that stimulates degradation of 3-Hydroxy-3-methylglutaryl-Coenzyme A reductase. *J Biol Chem*, 279: 43136-43147, 2004

39) Song BL and Debose-Boyd RA. Ubiquitination of 3-Hydroxy-3-methylglutaryl-CoA reductase in permeabilized cells mediated by cytosolic E1 and a putative membrane-bound ubiquitin ligase. *J Biol Chem*, 279: 28798-28806, 2004