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高级研究员

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教育经历 :

1982-1986 大连理工大学, 化学工程学, 学士
1986-1989 北京基础医学研究所, 分子遗传学, 硕士
1989-1992 北京基础医学研究所, 分子生物学, 博士
1994-1999 耶鲁大学 (美国), 分子细胞生物学, 博士后
1999-2001 纽黑文大学 (美国), 计算机科学, 硕士

工作经历 :

2013-至今 高级研究员, 耶鲁大学医学院内科系肝脏中心
2013-至今 兼职教授, 中国医学科学院医学生物技术研究所
2015-至今 兼职教授, 第三军医大学西南医院消化科
2010-2013 研究员, 耶鲁大学医学院内科系肝脏中心
2004-2010 副研究员, 耶鲁大学医学院内科系肝脏中心
2002-2004 高级科学家, Xeotron 公司, 休斯顿, 德克萨斯州
1992 - 1994 研究助理, 北京基础医学研究所

荣誉及奖励 :

1992 1%提前晋升, 北京基础医学研究所
1993 国家科学与技术进步三等奖, 中国
2002 DARPA 杰出表现奖, Xeotron 公司, 休斯顿, 德克萨斯州

在研及即将到位的基金项目 :

NIDDK, 5R37 DK025636-38: "Mechanisms of Bile Secretion and Cholestasis"
July 2014-present. Role: co-Investigator

NIDDK, 5P30 DK34989-31: "Silvio O. Conte Digestive Diseases Research Core
Centers". September 2014-August 2019. Role: Assistant Director.

NIDDK, pending R01 "Role of Ca²⁺/NFAT signaling pathway in cholestatic liver
injury". April 2019 – March 2024. Role: PI.

曾经获得的基金项目:

The PSC Partners Seeking a Cure Foundation, Research grant: “Combination treatment with ursodeoxycholic acid and all-trans retinoic acid (atRA) for primary sclerosing cholangitis (PSC)”. Nov 2010 – Dec 2012. Role: PI.

American Liver Foundation, Special Research Initiative PBC Seed Grant: “Ursodeoxycholic Acid And Retinoic Acid Combinational Treatment For Primary Biliary Cirrhosis” Linda Shapiro (PD) July, 2007-Jan, 2010. Role: PI.

The Yale Liver Center, Pilot Project (NIDDK P30-34989): “Modulating FXR expression in Progressive Familial Intrahepatic Cholestasis type 1 (PFIC-1) disease”. July 2005-June 2006. Role: PI.

Mount Desert Inland Biological Lab, Center for Membrane Toxicity Studies, Pilot Project (NIEHS, P30 ES003828-20): “Bile Salts Modulate Lipid and Glucose Metabolisms in *Leucoraja erinacea*, The Little Skate” June 2006-August 2006. Role: PI.

Mount Desert Inland Biological Lab, Center for Membrane Toxicity Studies, Pilot Project (NIEHS, P30 ES003828-20): “Bile Salts Modulate Gene Regulation in *Leucoraja erinacea*, The Little Skate” June 2005-August 2005. Role: PI.

科学贡献 :

作为一名分子生物学家,我已经鉴定了许多基因在多种物种中的功能,包括人类、细菌和早期脊椎动物,我还揭示了许多基因的表达调控机制。此外,我积极探索了治疗啮齿动物模型中胆汁淤积性肝损伤的新方法,并参与了临床试验中新治疗方法的转化。这一系列已经发表的发现确实提高了我们在生物学和医学方面的知识。在这里,我总结了近年来在耶鲁大学肝脏中心工作时对肝脏生理和疾病的研究成果。

1.分子和细胞研究揭示在啮齿动物和患者中胆汁形成和对胆汁淤积的适应性反应里涉及到的基因调节机制。理解胆汁淤积性肝损伤的病理生理学有助于指导我们开发新的治疗胆汁淤积的方法。

2. 治疗啮齿动物和患者的胆汁淤积的新疗法。通过比较基因组的方法和胆汁形成的机制研究,我们开发了一种联合治疗胆汁淤积的方法,即 UDCA 和全反式维甲酸,因为全反式维甲酸可以有效抑制 CYP7A1(胆汁酸合成中的限速酶)在肝细胞的表达以及减少胆汁酸池大小。另外,我们正在进行的研究表明,胆汁酸引发的炎症反应在胆汁淤积性肝损伤中起重要作用,我们还探索了啮齿动物模型中胆汁淤积的另一种新型治疗方法,即 CVC (CCR2 和 CCR5 的趋化因子受体拮抗剂)与 维甲酸联合疗法。

3. 比较基因组方法揭示: 1) 胆盐转运蛋白和核受体的结构/功能关系; 2) 对胆汁淤积的适应性反应的新机制。这方面的研究成果已经引导我们设计出新的治疗胆汁淤积的方法。

专利:

China Patent (ZL 2015 1 0830392.9): Application of Arylsulfonylamino-benzanilides in protection of liver from injury and fibrosis. Granted on November 14, 2017. Role: Co-inventor.

China Patent (ZL 2015 1 0290719.8): Inhibitor of Na⁺-dependent taurocholate cotransporting polypeptide. Granted on May 17, 2017. Role: Co-inventor.

学术兼职 :

多种专业期刊杂志论文评审专家, 期刊包括 : Hepatology, Journal of Hepatology, American Journal of Physiology, J Pharmacol Exp Ther., World Journal of Gastroenterology, BBA - Molecular Basis of Disease.

《世界胃肠杂志》编委会成员 (2010-2013)

中国自然科学基金评审专家(2010, 2011)

美国肝脏疾病研究协会会员

在耶鲁大学和沙漠岛生物实验室指导博士后、研究生、本科生和高中生

发表论文 (同行评审) :

1. Pan Q, Zhang X, Zhang L, Cheng Y, Zhao N, Li F, Zhou X, Chen S, Li J, Xu S, Huang D, Chen Y, Li L, Wang H, Chen W, **Cai SY**, Boyer JL, Chai J. Solute Carrier Organic Anion Transporter Family Member 3A1 is a Bile Acid Efflux Transporter in Cholestasis. *Gastroenterology*. 2018 Jul 28. pii: S0016-5085(18)34819-4. [Epub ahead of print] PMID: 30063921.
2. Yu D, **Cai SY**, Mennone A, Vig P, Boyer JL. Cenicriviroc, a cytokine receptor antagonist, potentiates all-trans retinoic acid in reducing liver injury in cholestatic rodents. *Liver international*. 2018; 38(6):1128-1138. PMID: 29356312 PMCID: PMC6032984
3. Zhang N, Geng T, Wang Z, Zhang R, Cao T, Camporez JP, **Cai SY**, Liu Y, Dandolo L, Shulman GI, Carmichael GG, Taylor HS, Huang Y. Elevated hepatic expression of H19 long noncoding RNA contributes to diabetic hyperglycemia. *JCI insight*. 2018; 3(10). PMID: 29769440 PMCID: PMC6012507
4. Ouyang X, Han SN, Zhang JY, Dioletis E, Nemeth BT, Pacher P, Feng D, Bataller R, Cabezas J, Stärkel P, Caballeria J, LePine Pongratz R, **Cai SY**, Schnabl B, Hoque R, Chen Y, Yang WH, Garcia-Martinez I, Wang FS, Gao B, Torok NJ, Kibbey RG, Mehal WZ. Digoxin Suppresses Pyruvate Kinase M2-Promoted HIF-1 α Transactivation in Steatohepatitis. *Cell metabolism*. 2018; 27(5):1156. PMID: 29719229.

5. Li M, **Cai SY**, Boyer JL. Mechanisms of bile acid mediated inflammation in the liver. *Molecular aspects of medicine*. 2017; 56:45-53. PMID: 28606651
PMCID: PMC5662014
6. **Cai SY**, Boyer JL. Studies on the mechanisms of bile acid initiated hepatic inflammation in cholestatic liver injury. *Inflammation and cell signaling*. 2017; 4(2). PMID: 28804737
PMCID: PMC5553904.
7. Yu D, Zhang H, Lionarons DA, Boyer JL, **Cai SY**. Na⁺-taurocholate cotransporting polypeptide (NTCP/SLC10A1) ortholog in the marine skate *Leucoraja erinacea* is not a physiological bile salt transporter. *American journal of physiology. Regulatory, integrative and comparative physiology*. 2017; 312(4):R477-R484. PMID: 28077388
PMCID: PMC5407083.
8. **Cai SY**, Ouyang X, Chen Y, Soroka CJ, Wang J, Mennone A, Wang Y, Mehal WZ, Jain D, Boyer JL. Bile acids initiate cholestatic liver injury by triggering a hepatocyte-specific inflammatory response. *JCI insight*. 2017; 2(5):e90780. PMID: 28289714
PMCID: PMC5333973.
9. **Cai SY**, Boyer JL. The Role of Inflammation in the Mechanisms of Bile Acid-Induced Liver Damage. *Digestive diseases* (Basel, Switzerland). 2017; 35(3):232-234. PMID: 28249287
PMCID: PMC6051694.
10. Assis DN, Abdelghany O, **Cai SY**, Gossard AA, Eaton JE, Keach JC, Deng Y, Setchell KD, Ciarleglio M, Lindor KD, Boyer JL. Combination Therapy of All-Trans Retinoic Acid With Ursodeoxycholic Acid in Patients With Primary Sclerosing Cholangitis: A Human Pilot Study. *Journal of clinical gastroenterology*. 2017; 51(2):e11-e16. PMID: 27428727
PMCID: PMC5218875
11. Chai J, **Cai SY**, Liu X, Lian W, Chen S, Zhang L, Feng X, Cheng Y, He X, He Y, Chen L, Wang R, Wang H, Boyer JL, Chen W. Canalicular membrane MRP2/ABCC2 internalization is determined by Ezrin Thr567 phosphorylation in human obstructive cholestasis. *Journal of hepatology*. 2015; 63(6):1440-8. PMID: 26212029
PMCID: PMC4686151.
12. Yu DK, Zhang CX, Zhao SS, Zhang SH, Zhang H, **Cai SY**, Shao RG, He HW. The anti-fibrotic effects of epigallocatechin-3-gallate in bile duct-ligated cholestatic rats and human hepatic stellate LX-2 cells are mediated by the PI3K/Akt/Smad pathway. *Acta pharmacologica Sinica*. 2015; 36(4):473-82. PMID: 25832428
PMCID: PMC4387300.
13. **Cai SY**, Mennone A, Soroka CJ, Boyer JL. Altered expression and function of canalicular transporters during early development of cholestatic liver injury in

- Abcb4-deficient mice. *American journal of physiology. Gastrointestinal and liver physiology*. 2014; 306(8):G670-6. PMID: 24481602 PMCID: PMC3989703.
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 18. Chai J, He Y, **Cai SY**, Jiang Z, Wang H, Li Q, Chen L, Peng Z, He X, Wu X, Xiao T, Wang R, Boyer JL, Chen W. Elevated hepatic multidrug resistance-associated protein 3/ATP-binding cassette subfamily C 3 expression in human obstructive cholestasis is mediated through tumor necrosis factor alpha and c-Jun NH2-terminal kinase/stress-activated protein kinase-signaling pathway. *Hepatology* (Baltimore, Md.). 2012; 55(5):1485-94. PMID: 22105759 PMCID: PMC3297707.
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- expression. *American journal of physiology. Gastrointestinal and liver physiology*. 2010; 299(1):G126-35. PMID: 20395535 PMCID: PMC2904108.
22. Thomas DJ, Nava GM, **Cai SY**, Boyer JL, Hernández-Zavala A, Gaskins HR. Arsenic (+ 3 oxidation state) methyltransferase and the methylation of arsenicals in the invertebrate chordate *Ciona intestinalis*. *Toxicological sciences*. 2010; 113(1):70-6. PMID: 19833739 PMCID: PMC2902911.
 23. Nava GM, Lee DY, Ospina JH, **Cai SY**, Gaskins HR. Genomic analyses reveal a conserved glutathione homeostasis pathway in the invertebrate chordate *Ciona intestinalis*. *Physiological genomics*. 2009; 39(3):183-94. PMID: 19470804 PMCID: PMC2789670.
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- and physiology. Part B, Biochemistry & molecular biology.* 2006; 144(2):167-79. PMID: 16567119.
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 33. Denk GU, **Cai SY**, Chen WS, Lin A, Soroka CJ, Boyer JL. A comparison of gene expression in mouse liver and kidney in obstructive cholestasis utilizing high-density oligonucleotide microarray technology. *World journal of gastroenterology.* 2006; 12(16):2536-48. PMID: 16688799 PMCID: PMC4087986.
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