

Date / Time:
Tuesday 14 February 2012
12pm – 1pm

Venue:
CeLS Auditorium
Centre for Life Sciences,
Level 1,
28 Medical Drive
Singapore 117456

Convener:
Dr Zhang Yongliang

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Mammalian TOR signaling in lymphocyte growth and development

Abstract

Mammalian target of rapamycin complex 2 (mTORC2) is a key downstream mediator of *phosphoinositol*-3-kinase (PI3K) dependent growth factor signaling. In lymphocytes, mTORC2 has emerged as an important regulator of cell development, homeostasis and immune responses. However, our current understanding of mTORC2 functions and the molecular mechanisms regulating mTORC2 signaling in B and T cells are still largely incomplete. Recent studies have begun to shed light on this important pathway. We demonstrate that mTORC2 mediates the growth factor dependent phosphorylation of Akt and facilitates the Akt dependent phosphorylation and inactivation of the transcription factors FoxO1 and FoxO3a. We have revealed the functions of mTORC2 in B cells in regulating survival and immunoglobulin (Ig) gene recombination of bone marrow B cells through an Akt2-FoxO1 dependent mechanism. Our results raise the possibility that genetic or pharmacologic inhibition of mTORC2 may promote B cell tumor development as a result of inefficient suppression of Ig recombination in dividing B cells.

Selected Publications

You-Tong Wu, Weiming Ouyang, Adam S Lazorchak, Dou Liu, Han-Ming Shen*, and **Su B***. mTOR Complex 2 Targets Akt for Proteasomal Degradation via Phosphorylation at the Hydrophobic Motif. **J Biol Chem.** 2011. 286: 14190-14198.

Xing Chang, Fang Liu, Xiaofang Wang, and **Su B.** MEKK2 and MEKK3 regulate TGF- β -mediated helper T cell differentiation. **Immunity.** 2011. **34**: 201-212.

Adam S Lazorchak, Dou Liu, Valeria Facchinetti, Annarita Di Lorenzo, William C Sessa, David G Schatz & **Su B.** Sin1 suppresses *rag1/2* and *il7r* gene expression through Akt2 in B cells. **Mol. Cell.** 2010. 39: 433-443.

Valeria Facchinetti*, Weiming Ouyang, Hua Wei, Nelyn Soto, Adam Lazorchak, Christine Gould, Carolyn Lowry, Alexandra C. Newton, Yuxin Mao, Robert Q. Miao, William C. Sessa, Jun Qin, Pumin Zhang, **Su B***, and Estela Jacinto*. The mammalian target of rapamycin complex 2 controls folding and stability of Akt and protein kinase C. **EMBO J.** 2008. 27(14):1932-43. (*Corresponding authors)

Jacinto E, Facchinetti V, Liu D, Soto N, Wei S, Jung SY, Huang Q, Qin J*, **Su B.*** SIN1/MIP1 maintains rictor-mTOR complex integrity and regulates Akt phosphorylation and substrate specificity. **Cell.** 2006. 127(1):125-37. (*corresponding authors).