Mammalian TOR signaling in lymphocyte growth and development

Abstract
Mammalian target of rapamycin complex 2 (mTORC2) is a key downstream mediator of phosphoinositide-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


