

## Abstract of Presentation

**Note: This paper should be typed in “Times New Roman” of 12pt.**

Presentation Title(Should be no more than 20 words):

The role of mTOR signaling in the regulation of size in normal and diseased muscle

Abstract :

Mammalian target of rapamycin (mTOR) is a highly conserved protein kinase that assembles into two distinct multiprotein complexes, called mTOR complex 1 (mTORC1) and mTORC2. mTOR is expressed in many tissues and regulates cellular reactions to external stimuli. For example, mTOR has been shown to be involved in immune responses, tumor growth, obesity and longevity. Several lines of evidence show that mTORC1 is involved in the control of cell growth and is inhibited by the immunosuppressant rapamycin. In contrast, mTORC2 is thought to mainly regulate the cytoskeleton and not to be sensitive to rapamycin. To address the role of mTORC1 and mTORC2 in a tissue that strongly adapts its size to external stimuli, we generated mice that are deficient for mTORC1 or mTORC2 in skeletal muscle using tissue-specific deletion of obligatory components of each of the complex. We find that mTORC1-deficient muscles are slightly atrophic, less oxidative and become dystrophic. Moreover, the mice die when they are between 4 and 6 months old. In contrast, mTORC2 deficiency does not result in an overt phenotype. We are now studying the detailed molecular mechanisms underlying the phenotypes of these mice. Moreover, we use experimental paradigms that trigger atrophy or hypertrophy of muscle to study the role of mTORC1 and mTORC2. Our results show that mTORC1 function has a significant role in maintaining muscle mass in response to atrophying stimuli. Moreover, we find that mTORC1 deficiency in muscle makes mice unresponsive to a high fat diet, suggesting that muscle mTORC1 effects overall energy expenditure. In summary, our data suggest an unprecedented role of mTOR in the control of the metabolic and functional properties of skeletal muscle. As loss of muscle is a hallmark of several diseases including muscle dystrophies, AIDS, sepsis or cancer, our data may reveal new entry points for the treatment of such diseases.