Mammalian Target Of Rapamycin (mTOR) plays an evolutionary conserved role in the control of organismal growth depending on nutrient availability. In the last few years our laboratory has investigated the functions of the mTOR substrates, Akt and S6 kinases. I will present evidence that Akt2 and S6K1 have complementary roles in the control of nutrient homeostasis.

S6K1 is a nutrient-sensitive kinase controlling cell size. One of the most common hypotheses is that S6K1 may act on cell growth by up-regulating protein synthesis. However by a number of techniques including microarray analysis on polysomal fractions, we fail to uncover a translational control by S6 kinases. Importantly S6 kinases regulate the expression of nucleolar proteins involved in rRNA processing and ribosome assembly. Since genetic screening for cell size regulators in yeast and Drosophila are enriched in nucleolar factors, our data reveal an evolutionary conserved signal transduction pathway that functionally links ribosome biogenesis and cell size.

Akt2 is involved in the metabolic action of insulin, as underlined by the insulin resistance of the Akt2 knockout mice for their glycemic control. By using liver specific deletion of the tumour suppressor PTEN, we identify Akt2 are an essential factor promoting steatosis-associated tumorigenesis through the transcription factor PPARγ and metabolic gene program.