The mammalian target of rapamycin (mTOR) is a key cell growth regulator that forms two complexes, mTORC1 and mTORC2. mTORC1 is regulated by a wide range of cellular signals, including growth factors, energy, and nutrients. High mTORC1 promotes cell growth while inhibition of mTORC1, such as under nutrient starvation, induces autophagy, which is a self-degradative process of cellular components in order to maintain essential cellular activity and viability. Extensive genetic and biochemical evidence has shown that the yeast Atg1 kinase plays an essential role in autophagy induction. Mammals contain two Atg1 homologs known as ULK1 and ULK2, which have been implicated in autophagy regulation. However, the mechanism of ULK1/2 regulation is unclear. We investigated the role of AMPK (AMP activated protein kinase, a cellular energy sensor) and mTORC1 in ULK1 regulation. We observed that ULK1 activity and function is directly regulated by AMPK and mTORC1. Our study not only established a molecular basis of AMPK and mTORC1 in autophagy regulation but also revealed a biochemical mechanism for ULK1 activation in response to nutrient starvation.