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Uncover the molecular mechanism that regulates the RAF/MEK/ERK kinase cascade by characterizing the oncogenic RAF/MEK mutants

Although extensively studied for three decades, the molecular mechanism that regulates the RAF/MEK/ERK cascade remains ambiguous. Recent studies identified the dimerization of RAF as a key event in the activation of this cascade. Here, we show that in-frame deletions in the β3-αC loop activate ARAF, BRAF and MEK1 as well as other kinases in cancer genomes by enforcing homodimerization. These RAF and MEK1 mutants exhibit a strong oncogenic potential and differential inhibitor resistance. Using these unique mutants, we further demonstrate that RAF activates MEK in a dimer-to-dimer manner and that MEK is able to activate itself by homodimerization-driven transphosphorylation. This study defines a special catalogue of oncogenic kinase mutations and illustrates key steps in the activation of the RAF/MEK/ERK cascade.

Biography

Jiancheng Hu has completed his PhD training in 2007 from University of Colorado Health Sciences Centre and Postdoctoral studies in 2014 from Howard Hughes Medical Institute and Washington University in St. Louis. He is the Principal Investigator of Cellular and Molecular Research Division, National Cancer Centre Singapore. He has published more than 15 papers in reputed journals.

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