NUS National University of Singapore | Department of Pharmacy Faculty of Science

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Mechanisms linking glucose sensing to AMPK activation and implications

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Hosted by A/P Victor Yu

Glucose is not only the main source for energy, but also a precursor for the synthesis of many biomolecules. On entering glycolysis, glucose is converted in three steps to fructose-1,6-bisphosphate (FBP), which is then split into triose phosphates by FBP aldolases. Glucose deprivation activates AMP-activated protein kinase (AMPK), a sensor of cellular energy that monitors levels of AMP, ADP and ATP and plays a primary role in adaptive responses to energy stress, but it had been unclear how glucose deprivation is sensed and signals to activate AMPK. We have found that it is the aldolase that senses the availability of glucose and directly links to AMPK activating complex on the lysosome in a manner independent of energy status change. These findings have redefined AMPK, in that the ancestral role of AMPK is to sense a fall of glucose availability prior to decrease of energy levels. Glucose starvation-induced AMPK activation may also prime the response to subsequent energy shortage in an AMP-dependent manner. Biological/pharmaceutical implications of our new discoveries will be also discussed.

Dr. LIN Shengcai is currently a professor at the School of Life Sciences, Xiamen University. He graduated from Xiamen University in 1984, and received his Ph.D. from University of Texas Southwestern medical Center at Dallas in 1991, and finished his postdoc training at the Howard Hughes Medical Institute University of California at San Diego. He then moved to IMCB Singapore, in 1995, and stayed for 6 years before moving to Hong Kong University of Science and Technology. He became dean of the School of Life Sciences Xiamen University in 2003, until May of this year. His recent main achievement is the discovery and elucidation of the lysosomal pathway for AMPK activation and its role in glucose sensing. His AMPK work has led to a major paradigm shift on the mechanism of AMPK activation. His current research also aims to understand how fat synthesis is controlled.