NUS National University of Singapore | Department of Biological Sciences, Faculty of Science

ON-SITE BIOLOGY COLLOQUIUM

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Hosted by Assoc. Prof Liou Yih-Cherng

Glucose availability controls health and lifespan

By **Sheng-Cai Lin**

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Glucose is the major energy source for most cells, from which ATP is generated via glycolysis and oxidative metabolism. It is known that AMPK and mTOR play central roles in the regulation of metabolic homeostasis. We have delineated the signaling pathways for the cellular sensing of low and high glucose, which link to the regulation of both AMPK and mTOR Complex1. These findings suggest that glucose, via its metabolite FBP, can act as a "messenger" for controlling both AMPK and mTOR. Based on this glucose sensing pathway, we identified an inhibitor termed as Aldometanib that prevents aldolase from binding to FBP, thus mimicking glucose starvation or calorie restriction to induce extension of health span as well as lifespan. Interestingly, we have shown that metformin signaling intersects, via the entry of the lysosomal proton pump v-ATPase, the glucose sensing pathway for activation of AMPK and inhibition of mTORC1, re-enforcing the important roles of this glucose sensing pathway in both health span and lifespan.

I will also present latest work on how glucose availability controls carbon source shift after glucose starvation via AMPK, and cell fate control via p53.

About the Speaker

Professor Sheng-Cai Lin received his Ph.D. in Biochemistry from the University of Texas Southwestern Medical Center at Dallas. He completed his postdoctoral training at the Howard Hughes Medical Institute, University of California at San Diego, where he cloned the receptor for growth hormone-releasing factor, a G-protein coupled receptor, and identified types of dwarfism associated with dysfunction of the receptor. In 1995, he established his laboratory in IMCB, Singapore, and in 2001, he joined Hong Kong University of Science and Technology as an Associate Professor. In 2006, he returned to Xiamen University as a Professor and later served as the Dean of School of Life Sciences, China.

During his career, Prof. Lin has made significant contributions to the field of regulators of G-protein signaling (RGS proteins) and the RGS-domain protein called AXIN, which regulates important biological processes such as the JNK/MAPK pathway and tumor suppressor p53 signaling. His most notable discovery is the identification of mechanisms for cellular AMPK activation, revealing that AXIN serves as a bridge for LKB1 to phosphorylate AMPK, and later that AMPK activation occurs on the surface of the lysosome. More recently, he has focused on understanding the maintenance of cell metabolism and the mechanisms of cellular perception of nutrients and energy and human diseases.

Prof. Lin has received numerous awards and honors, including the Changjiang Distinguished Professor awarded by the Ministry of Education, the Chief Scientist of the National Major Research Program, and the winner of the National Science Fund for Distinguished Young Scholars. In 2021, he was also elected as a Fellow of the Chinese Academy of Sciences.