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Preface

PI3K-AKT-FoxO axis in cancer and aging

AKT/Protein kinase B (PKB) had emerged during the past 20 years as a key signaling molecule that regulates diverse cellular functions related to metabolism, longevity and cellular senescence downstream of tyrosine kinase receptors and PI3K. Increased AKT activity, induced by deregulation of its upstream effectors, is observed in the majority of human cancers and is considered a main oncogenic event. Among the most evolutionarily conserved targets of AKT are the forkhead box O (FoxO) transcription factors. A vital breakthrough in understanding AKT function came from longevity studies in *C. elegans* establishing the DAF-16 transcription factor as a main mediator of AKT signaling. Follow-up studies in mammalian systems established a signaling cascade from AKT to the DAF-16 orthologues, the FoxO transcription factors. Research in the past 10 years uncovered a myriad of physiological roles of FoxO proteins including regulation of metabolism, cell cycle and response to stress factors orchestrated through complex FoxO regulation involving transcriptional and post-transcriptional mechanisms. The current special review issue provides an up-to-date review of the field, focusing on the regulation of FoxO transcription factors through a complex network of protein–protein interactions, phosphorylation, acetylation and ubiquitination and offers perspectives for future research directions.

Dr. Guri Tzivion is an Associate Professor at the Cancer Institute and Department of Biochemistry, University of Mississippi Medical Center. He obtained his PhD. degree in Immunology from the Hebrew University in Jerusalem, Israel and completed a postdoctoral training in 2000 in the laboratory of Dr. Joseph Avruch at the Department of Molecular Biology, Massachusetts General Hospital, Boston. He was a faculty member at Texas A&M University and Wayne State University, MI before obtaining his current position at the University of Mississippi in 2009. His research has been focused on understanding signaling processes and networking downstream of growth factor receptors at the molecular and mechanistic level and applying this knowledge to address cancer and lifespan related questions. Of specific interest are the Ras–Raf–MAPK and the PI3K–AKT–FoxO pathways. More recently, his work expanded also to studying the roles of nicotinamide modulation and the sirtuin deacetylase family in controlling metabolism and lifespan.

Nissim Hay received his PhD from the Weizmann Institute in 1984, working on attenuation of transcription using SV40 as a model system. He then moved to the University of California San Francisco for a postdoctoral work with Dr. J. Michael Bishop. In 1990 he joined the faculty of the University of Chicago, and in 1998 he moved to the University of Illinois, at Chicago, where he is a Professor in the Department of Biochemistry and Molecular Genetics. Since 1997, after work in his laboratory showed that the serine/threonine kinase Akt is the major downstream effector of growth factor mediated cell survival, and that Akt is sufficient and required for the activation of mTOR by growth factors, work in his laboratory has been focused on the PI3K/Akt/mTOR signaling pathway as well as on the Akt/FOXO axis. Studies in his laboratory explore the role of these pathways in apoptosis, cell proliferation, their relevance to the genesis of cancer and aging, and how these are coupled to energy metabolism, both at the cellular and organismal levels.

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