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Cell fate decisions and anti-tumor effects of the mRNA translation initiation factor eIF2

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The lecture will address the function of the translation initiation factor eIF2 in stressed-induced tumorigenesis as well as in anti-tumor treatments with chemotherapeutic drugs. eIF2 is a master regulator of stress through its ability to control protein synthesis in response to various forms of stress including DNA damage, oxidative stress, oncogenic stress as well as stress in the tumor microenvironment. Cells respond to stress by inducing the phosphorylation of the alpha (α) subunit of eIF2 at serine 51 (S51) (herein referred to as eIF2 α P), a modification that leads to the inhibition of global protein synthesis. eIF2 α P is mediated by four kinases, namely HRI, PKR, PERK/PEK and GCN2 each of which becomes activated to distinct form of stress. Despite the general inhibition of protein synthesis, specific mRNAs can bypass the blockade, and in fact, be efficiently translated under stress. Such mRNAs encode for proteins that facilitate cell adaptation to stress as shown for transcription factors ATF4 and ATF5 in mammalian cells or GCN4 in yeast. Our work focuses on eIF2 α P function as a cell fate decision maker through its ability to induce either cell survival or death in stressed tumor cells. We investigate how the dual but opposing function of eIF2 α P relates to the activation of the MAPK and Akt/PKB-mTORC1 pathways in stressed cells. Our work suggests that inhibition of eIF2 α P is a powerful approach to disarm cell survival and induce death in tumor cells treated with pro-oxidant drugs or drugs targeting the PI3K-Akt/PKB-mTORC1 pathway.

Biography

Antonis E Koromilas holds a BSc in Chemistry and a PhD in Biochemistry from the Aristotelian University of Thessaloniki, Greece. He pursued his Post-graduate studies in Immunology (Stockholm University, Sweden), Molecular Immunology (Kyoto University, Japan) and Biochemistry (McGill University, Canada). He is Professor in the Department of Oncology, Faculty of Medicine, McGill University and Senior Scientists and Group Leader at Lady Davis Institute-Sir Mortimer B. Davis Jewish General Hospital, Montreal. He has won many Canadian and international research grants and personal awards, and he has served as an Editorial Board Member in international journals.

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