Dr. Herbert and Nicole Wertheim Leadership in Healthcare and Medicine Lectureship

Novel Insights on Mitochondrial Regulation of Cancer Immunity

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Biography

Prof. Basel al-Ramadi is Professor of Immunology in the Department of Medical Microbiology and Immunology, College of Medicine & Health Sciences, United Arab Emirates University. He received his B.Sc. in 1984 from the University of Edinburgh (Scotland) and Ph.D. in Microbiology and Immunology in 1990 from Temple University School of Medicine, Philadelphia (USA). In 1993, he joined Yale University faculty as Associate Research Scientist, a position he held until 1997. Subsequently, he joined the College of Medicine and Health Sciences, United Arab Emirates University and served as the Chair of the Department of Medical Microbiology and Immunology from 2010 to 2016. Prof. al-Ramadi's research interests are focused on immunoregulatory aspects of the immune system in cancer and, in particular, on modalities of boosting anti-tumor immunity. He has published more than 75 papers in peer reviewed international journals with a cumulative impact factor of >500, receiving >2800 citations, and a Hirsch index of 27. He has made more than 130 contributions to medical scientific conferences in the form of invited seminars and poster presentations.

Abstract

Aerobic glycolysis (or the Warburg effect) by tumor cells is considered a hallmark of all cancers. The utilization of aerobic glycolysis within the tumor microenvironment, a process that is bioenergetically less efficient than mitochondrial oxidative phosphorylation, the alternative ATP-generating process, has been associated with tumor progression. Accumulating evidence indicates that the use of aerobic glycolysis by tumors represents a form of metabolic reprogramming aimed at suppressing anti-tumor T cell responses. The activity of tumor-infiltrating leukocytes (TILs) is regulated by a variety of immune as well as metabolic checkpoints. Competition for nutrients, in particular glucose, between tumor cells and TILs underlies this form of metabolic checkpoint inhibition, thereby enhancing tumor progression and metastasis.

We recently demonstrated that Methylation Controlled J (MCJ) protein, which is localized to the mitochondrial inner membrane and is an endogenous inhibitor of Complex I of the electron transport chain, plays a critical role in resistance to chemotherapy treatment in breast cancer patients. Interestingly, MCJ is also highly expressed in CD8+ T lymphocytes, one of the critical cell populations with anti-tumor function. In our effort to further dissect the role of metabolic programming on anti-tumor immunity, we have utilized MCJ-deficient mice to investigate the interplay between TILs and tumor cells in syngeneic models of implantable tumors. Data will be presented that highlights the profound alterations in tumor growth in these mice compared to normal controls. Our findings indicate that a better understanding of the metabolic challenges within the tumor microenvironment and their impact on immune cell function could contribute to more efficient approaches to rewire metabolic fitness of TILs and boost existing immunotherapies.