Journal of Molecular Imaging & Dynamics
ISSN: 2155-9937
Short Communication

Improving the outcome of T-cell immunotherapy of cancers by pre-conditioning T cell metabolism towards fatty acid catabolism

Hildegund C.J. Ertl
The Wistar Institute, USA

Abstract

Recent years have shown tremendous progress in active immunotherapy of cancers through tumor antigen (TA)-specific vaccines, adoptive T cell transfer or check point inhibitors. Nevertheless complete cures remain rare. TA-specific CD8+ T cells rapidly become exhausted once they enter solid tumors. This exhaustion, causing loss of tumor infiltrating CD8+ T cells during tumor progression, is in part cause by metabolic constrains, such as hypoxia and hypoglycemia, within the tumor microenvironment (TME). Lack of glucose forces T cells to switch from glycolysis for energy and biomass production to fatty acid catabolism. Most T cells are apparently unable to adjust their metabolism within the TME and as a consequence loose functions and eventually die. Pre-conditioning T cells during their initial activation in lymphatic tissues or their expansion in vitro towards fatty acid beta oxidation (FAO) preserves their functions and allows them to more effectively reduce tumor burden. CD8+ T cell metabolism can be modified by different types of manipulations such as knockdown of HIF-1a or other key factors of the glycolysis pathway to reduce the cells' reliance on glucose. FAO can be enhanced directly by strengthening signaling through PPAR-a, the master regulator of lipid metabolism.

Biography

Hildegund C.J. Ertl, Professor in Wistar Institute, Philadelphia, PA and Associate Professor of Pathology and Laboratory Medicine, Associate Faculty of the School of Medicine, University of Pennsylvania, Philadelphia, PA Program Director, Immunology Program, The Wistar Institute, Philadelphia, PA, Adjunct Professor of Pediatrics of the Children's Hospital of Philadelphia, Director, Wistar Vaccine Center and World Health Organization (WHO) Reference Center for Reference and Research on Rabies journals.

Citation: Hildegund C.J. Ertl | Improving the outcome of T-cell immunotherapy of cancers by pre-conditioning T cell metabolism towards fatty acid catabolism | Journal of Molecular imaging and Dynamics(JMID)