Metabolic Regulation for proliferation and function of Natural Killer T cells

In conventional T cells, signaling pathways that control cellular metabolism have a crucial role in dictating the outcome of T cell activation and their effector function. However, little is known about metabolic regulation and its role for cellular functions of Natural Killer T (NKT) cells. NKT cells are a heterogeneous population that shows a high degree of phenotypic and functional specialization. When activated, unlike conventional T cells, NKT cells exhibit a fast and robust effector function such as cytokine release or cytotoxicity. Thus, the metabolic regulation in NKT cells likely plays an important role in immune diseases. To understand how NKT cells regulate their metabolism to mediate an appropriate immune response under a different environment, we measured parameters that associate with the metabolic capacity and compared them with that of CD4 T cells. Our study revealed that NKT cells are very different from CD4 T cells in many ways. Unlike CD4 T cells that switch metabolism to aerobic glycolysis upon activation, NKT cells rely more on oxidative phosphorylation for their survival. Furthermore, NKT cell survival is compromised if the glycolytic potential is elevated. Promyelocytic leukemia zinc finger (PLZF) plays an essential role for regulating NKT cells' glucose metabolism. Ectopic expression of PLZF in CD4 T cells shifted glucose metabolism to oxidative phosphorylation and, conversely, NKT cells with haplodeficient PLZF became more glycolytic. Overall, our study reveals for the first time that NKT cells use distinct arms of glucose metabolism for their survival and function.