Max-Planck-**Innovation**

Technology Offer

A novel strategy for reducing inflammation by modulating immune cell metabolism

Remodeling the morphology of mitochondria to manipulate immune cell metabolism and hence reduce immune cell activation and effector functions

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Background

Inflammation is a protective immune response induced by the body during tissue injury or infection. Inflammation can, however, become harmful when not tightly regulated or if the immune system responds to inappropriate stimuli. If left uncontrolled, destruction of healthy tissue may occur and negatively impact patient quality of life, or lead to autoimmune disease. There is an urgent need for new and effective methods to regulate inflammatory immune cells and thereby alleviate many common disorders, like inflammatory bowel diseases, rheumatoid arthritis, atherosclerosis, obesity, or sepsis.

Previous research has shown that the metabolism of immune cells is directly tied to their ability to activate and cause inflammation. Specifically, immune cells such as dendritic cells, macrophages, and T cells modulate mitochondrial energy generation and engage aerobic glycolysis upon their activation into mature effector cells. The upregulation of aerobic glycolysis is also shared by cancer cells, classically termed the “Warburg effect”. Failure to utilize glycolysis impairs the activation and effector functions of these immune cells during inflammatory conditions, such as those observed during infection and autoimmunity. Thus, harnessing immune cell metabolism provides a powerful new approach to regulate immune cell function and inflammatory disease.

Technology

Researchers from the Max-Planck-Institute of Immunology and Epigenetics in Freiburg and Washington University in St. Louis, MO, discovered that mitochondrial dynamics, namely mitochondrial fission, fusion, and cristae remodelling, can signal and control the engagement of specific metabolic pathways, such as glycolysis (1). Their results demonstrate that exposure of T cells, macrophages, and dendritic cells to pharmacological inhibition of DRP1 (a GTPase involved in mitochondrial fission), blocks their ability to effectively engage aerobic glycolysis and as such, prevents their activation and ensuing inflammatory functions. On the other hand, blocking mitochondrial fission either directly or via genetic or drug induced enhancement of mitochondrial fusion, consequently enforces immune cells to adopt oxidative metabolism driven by fatty acid oxidation, characteristic of quiescent immune cell populations (Fig. 1).

From this evidence, targeting mitochondrial remodelling may serve to reduce immune cell activation and effector functions by manipulating their dynamic metabolic profile and thus, be used to treat a variety of immune related inflammatory conditions.

We are currently seeking a licensing partner for the further development of this exciting technology.

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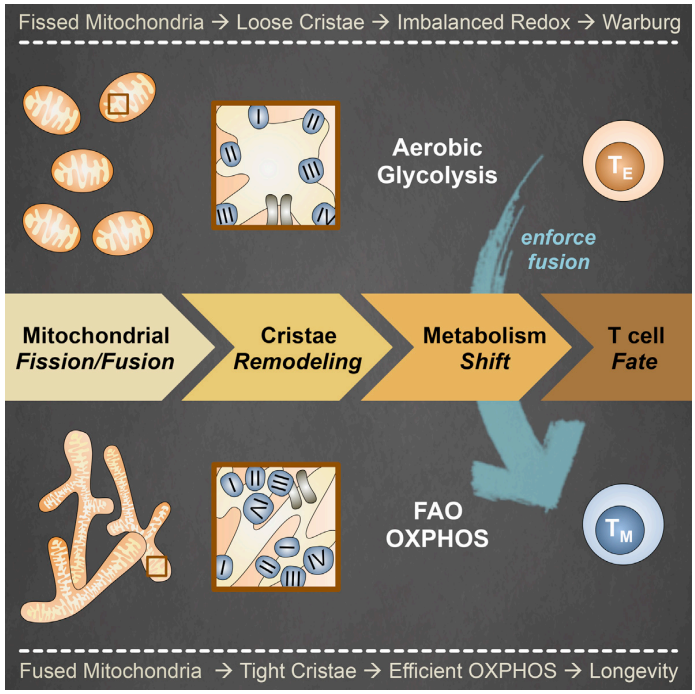

Figure 1: The fate of T-cells is the shape of their mitochondria. Remodelling mitochondrial cristae via fusion/fission instructs metabolic adaptations in T-cells and can be modulated to enhance antitumor immunity. Adapted from (1).

Patent Information:

A US priority application has been filed in June 2016.

Literature:

(1) Buck, M. et al., Cell 2016 Jun 30;166(1):63-76. doi: 10.1016/j.cell.2016.05.035