# METABOLIC RESEARCH ALLIANCE: EMERGING PROJECT

## The Role of "Gatekeeper" MTCH2 in Controlling Obesity

THE METABOLIC RESEARCH ALLIANCE (MRA) is a consortium consisting of the University of Connecticut, Jackson Laboratory, Yale University, and The Weizmann Institute of Science. The primary goal of the Alliance is to take advantage of the inter-disciplinary strengths of the partner institutions for transformative research into metabolic diseases, especially pertaining to diabetes (T1D and T2D) and obesity. Our consortium is distinctly positioned to provide synergistic research expertise which could lead to prevention, treatment, and curative approaches to these devastating diseases. The UConn Foundation is leading efforts to raise $ 1 million in seed funding to launch this research.

### Emerging Research: MTCH2 and Obesity

One of the promising projects happening right now at the MRA is work being conducted by two nationally noted UConn School of Medicine researchers: Anthony Vella, Ph.D., of the Department of Immunology, and Atan Gross, Ph.D., of the Department of Biological Regulation, Weizmann Institute for Science, and Rehovot. Their work focuses on a mitochondrial membrane protein called mitochondrial carrier homolog 2 (MTCH2).

Cells require energy to execute biological function and hematopoietic cells are no exception. This is especially true for immune cells combating cancer, infection or other environmental stimuli. An excellent example are tumor-specific T cells which must be fortified with different capabilities of generating energy to tolerate the depleting pool of glucose and hypoxic environment generated by tumors. In particular, tumor cell consumption of glucose reduces availability to activated T cells, but mechanisms to overcome these deficits are beginning to be uncovered. In this proposal the collaborative teams of Vella and Gross will investigate the role of a key outer mitochondrial membrane protein called mitochondrial carrier homolog 2 (MTCH2). MTCH2 is regarded as a gatekeeper for oxidative phosphorylation (OXPHOS) since its absence profoundly enhances OXPHOS resulting in increased energy consumption. The team's overarching hypothesis is that MTCH2 controls the ability of anti-tumor specific T cells to attack tumors, but immune costimulation overcomes this process by uncoupling either expression of MTCH2 or its function. Although MTCH2 has been shown to control OXPHOS and its absence associated with increased metabolism or energy consumption, the interactome of MTCH2 remains unclear.

### A Second Hypothesis

The team's second hypothesis is that the absence of MTCH2 rearranges the mitochondrial proteome and will promote novel interactions that facilitate OXPHOS. This data will be clinically useful in the development of new ways to control obesity and hopefully unveil novel protein interactions that might be open to pharmaceutical targeting.

The MTCH2 research being done through the Metabolic Research Alliance could lead to new treatments for obesity.

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