

# METABOLIC RESEARCH ALLIANCE: EMERGING PROJECT

## Autoimmunity, cancer, and the microbiome

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: Autoimmunity, cancer, and the microbiome

Kevan Herold, M.D., Professor of Immunobiology and Internal Medicine, Yale School of Medicine, is involved in cutting-edge research in the growing field of autoimmunity and cancer. His work will dig deeper into the role of the microbiome in modifying autoimmunity and the effects of immune agents on autoimmune therapies such as anti-CD3 antibody and others. In preliminary studies the team has found that change in the microbiome, induced by antibiotics, can alter the effects of immune agents in humanized mice. In this model system, treatment of mice with human immune systems can block the effects of anti-CD3 antibody on preventing transplant rejection. Other studies, of agents such as anti-PD-L1 and anti-CTLA-4 antibodies have also shown that the effects of the drugs on cancer are modified by the microbiome of the host.

Yale researchers propose to evaluate the effects of the microflora on human immune responses following treatment with biologic agents in humanized mice. Specifically, researchers propose to identify which organisms are important, how they modify immune cells, and determine whether the composition of the microbiome can determine responses to biologics among patients with autoimmunity and cancer.

Important research  
will be energized by  
the collaboration  
among UConn,  
Jackson Labs, the  
Weizmann Institute  
of Science, and Yale  
through MRA.

Yale's team plans a collaboration with colleagues at the Weizmann Institute, Jackson Labs, and UConn who have expertise in the biology of the human microbiome and the effects of the microbiome on immune responses.

The collaboration will involve using model systems, bioinformatics, and analytics that have been developed at the three institutions. In some cases, investigators will travel to the other site to help establish models that may be used by collaborating research groups. Data can be shared electronically and web conferences can be used to enable teams to collaborate. Clinical material, from patients with autoimmunity and cancer can be obtained at Yale.

Dr. Herold notes and he anticipates that this collaboration will synergize efforts of research teams that are already working in this rapidly expanding area of investigation.

