



Specific and Novel Mode of Treatment for Age-Related Insulin Resistance

INVENTION: Our investigators explored the key immune cell types that drive age-associated insulin resistance using comparative adipo-immune profiling. They found that fat-resident regulatory T cells (fTregs) accumulate in adipose tissue as a function of age, and their accumulation in adipose is a driver of age-associated insulin resistance. They then looked at the IL-33 receptor ST2 in the fTreg cell cluster as it has been recently implicated in effector Treg and fTreg cell development, and discovered that ST2 is expressed on the cell surface of most fTreg cells but not on splenic Tregs. Consistent with that finding, the scientists showed that treatment of mice with anti-ST2 depleting antibodies depletes fTregs while preserving splenic Treg numbers. Additionally, adipose from aged mice treated with anti-ST2 antibody has increased insulin sensitivity compared to controls. Therefore, specific depletion of fTregs can decrease age-related fTreg accumulation and restore insulin sensitivity, thereby treating age-related insulin resistance, Type 2 diabetes and related disorders.

APPLICATIONS:

Specific and novel mode of treatment of age-associated insulin resistance, Type 2 diabetes and other related disorders

ADVANTAGES:

Elucidation of a mechanism for age-associated insulin resistance distinct from obesity-associated insulin resistance provides for a way to develop specific treatments.

STAGE OF DEVELOPMENT:

BACKGROUND: Aging and obesity are the two primary causes of insulin resistance and diabetes, which are now the defining epidemics of the modern world. It is known that there is a complex interplay between the immune system and inflammation of the adipose tissue that drives obesity-associated insulin resistance. What is not known are the mechanisms underlying aging-associated insulin resistance, which is an urgent concern due to its prevalence. In the U.S. alone, incidence of diabetes among adults ages 65-79 years old has more than doubled in the past 30 years. Over 25% of all Americans over 60 years old have Type 2 diabetes and more than 50% of that population are insulin-resistant. Our investigators' research explored the key immune cell types that drive age- versus obesity-associated insulin resistance, including regulatory T-cells (Tregs), whose mainly known function is to suppress the immune system in order to prevent an unwanted autoimmune reaction. Our scientists found that a specific population of Tregs, termed fat-resident regulatory T-cells (fTregs), accumulate in adipose tissue as a function of age, but not obesity, and are thus potential therapeutic targets in the treatment of age-associated insulin resistance.

INVENTORS: Dr. Ye Zheng, Dr. Ronald Evans, Dr. Michael Downes

PATENT STATUS: Patent application pending

PUBLICATIONS: Bapat, et al. 2015. Depletion of fat-resident Treg cells prevents age-associated insulin resistance. Nature, 528:137-141

CONTACT: Melissa Rodgers; mroddgers@salk.edu; (858) 453-4100 x1481

TECHNOLOGY ID: S2015-005