## Depletion of fat-resident Treg cells prevents age-associated insulin resistance.

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**Public Summary:**
Age-associated insulin resistance (IR) and obesity-associated IR are two physiologically distinct forms of adult-onset diabetes. While macrophage-driven inflammation is a core driver of obesity-associated IR, the underlying mechanisms of the obesity-independent yet highly prevalent age-associated IR are largely unexplored. Here we show, using comparative adipo-immune profiling in mice, that fat-resident regulatory T cells, termed fTreg cells, accumulate in adipose tissue as a function of age, but not obesity. Supporting the existence of two distinct mechanisms underlying IR, mice deficient in fTreg cells are protected against age-associated IR, yet remain susceptible to obesity-associated IR and metabolic disease. By contrast, selective depletion of fTreg cells via anti-ST2 antibody treatment increases adipose tissue insulin sensitivity. These findings establish that distinct immune cell populations within adipose tissue underlie ageing- and obesity-associated IR, and implicate fTreg cells as adipo-immune drivers and potential therapeutic targets in the treatment of age-associated IR.

**Scientific Abstract:**
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