# Summary

Sirtuin 1 may regulate glucose and lipid metabolism. We aimed to assess adipose tissue and skeletal muscle sirtuin 1 expression in relation to insulin sensitivity, the expression of proinflammatory and metabolic genes, and to study the regulation of sirtuin 1 expression by hyperinsulinemia and circulating free fatty acids elevation.

We examined 60 normal-weight, 42 overweight and 15 obese young subjects. The hyperinsulinemic-euglycemic clamp technique was applied to measure insulin sensitivity. In 20 subjects, two 6h clamps were performed, one of them with the concurrent Intralipid/heparin infusion. Biopsies of subcutaneous adipose tissue and skeletal muscle were collected for the measurement of gene and protein expression.

Obese subjects had lower adipose sirtuin 1 in comparison with normal-weight and overweight participants. Muscle sirtuin 1 did not differ between the groups. Adipose tissue sirtuin 1 was related to insulin sensitivity, adipose tissue *SLC2A4*. The relationship between adipose tissue sirtuin 1 and insulin sensitivity was still present after controlling for BMI, however, it disappeared after controlling for adipose tissue *SLC2A4*. Muscle sirtuin 1 was not related to insulin sensitivity. Hyperisulinemia decreased adipose tissue and increased muscle sirtuin 1 expression. Intralipid/heparin infusion negated these effects.

Adipose tissue, but not muscle, sirtuin 1 is associated with insulin sensitivity in humans, possibly because of its correlation with adipose tissue *SLC2A4* expression. Insulin differentially regulates adipose tissue and skeletal muscle sirtuin 1 expression in short-term and circulating free fatty acids elevation negates these effects, which may be associated with lipid-induced insulin resistance.