Expression of AdipoR1 In Vivo in Skeletal Muscle Is Independently Associated With Measures of Truncal Obesity in Middle-Aged Caucasian Men

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The study protocol was undertaken with local research ethics committee approval, and informed consent was obtained from all subjects. Fifteen middle-aged (42–64, mean age 53.2 ± 5.8 years), healthy Caucasian men with a wide range of BMIs (21–39 kg/m², 30.63 ± 5.48) were recruited. Waist circumference was measured over bare skin midway between the costal margin and the iliac crest. Percentage of body fat was measured using bioelectrical impedance (Bodystat 1500, Bodystat, Isle of Man, U.K.). DEXA scanning was undertaken on a Delphi W instrument (Hologic, Bedford, MA) using a standard visual method to divide images into trunk, limb, and head. Detailed information about visceral fat was obtained from MRI images from five noncontinuous slices extending from 5 cm below to 15 cm above L4-L5 (9). A 3-h hyperinsulinemic-euglycemic clamp was performed with insulin infused at 1.5 mU·kg⁻¹·min⁻¹ and whole blood glucose clamped at 5 mmol/l. The glucose infusion rate in the final steady state was used as a measure of skeletal muscle insulin sensitivity (M value). Fat insulin sensitivity was assessed by percentage free fatty acid (FFA) suppression [FFA (time) – FFA (fast)]/FFA (time) on a 75-g oral glucose tolerance test (3,10–13).

RESULTS — Plasma adiponectin concentrations were negatively correlated with BMI (r = −0.79, P < 0.001), waist circumference (r = −0.80, P < 0.001), and positively correlated with skeletal muscle insulin sensitivity (M values, r = 0.71, P = 0.001), which were consistent with previous findings (2,3,19,20).

mRNA levels of AdipoR1 and -R2 in skeletal muscle were approximately fourfold greater than those of AdipoR2 (P < 0.0001) and were strongly correlated with each other (r = 0.63, P = 0.006). These in vivo data were consistent with data obtained from human myotubes (21).

There was a trend toward significant correlation between mRNA levels of AdipoR1 and muscle insulin sensitivity...
(M values, \( r = 0.41; P = 0.063 \)), which were consistent with data obtained from Mexican Americans (8) and animal studies (22). In contrast, mRNA levels of AdipoR1 and -R2 did not correlate with insulin sensitivity in fat assessed by percentage of FFAsuppression.

mRNA levels of AdipoR1 were correlated with different measures of body and truncal fat, including waist circumference and truncal fat by DEXA (Table 1). There was a similar trend toward significant correlation between mRNA levels of AdipoR1 and total fat by DEXA or bioimpedance and plasma leptin level (\( P = 0.086 \), Table 1), a marker of fat mass (23,24). Plasma leptin levels were strongly correlated with total fat (\( r = 0.85, P < 0.001 \)) and trunk fat (\( r = 0.85, P < 0.001 \)) measured on DEXA. In contrast, there was no significant association between mRNA levels of AdipoR1 and lean mass measured by DEXA (\( r = -0.058, P = 0.42 \)) and MRI visceral fat (\( P = 0.29, Table 1 \)). No significant correlations between mRNA levels of AdipoR2 and measures of body fat (Table 1) and plasma leptin level were observed (Table 1).

mRNA levels of AdipoR2 were correlated with fasting plasma FFA concentrations (\( r = -0.48, P = 0.036 \)). In contrast, there was no significant correlation between AdipoR1 and age (\( r = 0.092, P = 0.37 \)), fasting plasma triglycerides (\( r = -0.043, P = 0.44 \)), cholesterol (\( r = 0.022, P = 0.47 \)), HDL cholesterol (\( r = 0.11, P = 0.35 \)), FFA (\( r = -0.11, P = 0.35 \)), and adiponectin concentrations (\( r = 0.19, P = 0.25 \)). Similarly, no significant correlations were found between AdipoR2 mRNA levels and age (\( r = -0.001, P = 0.50 \)), fasting plasma triglycerides (\( r = -0.075, P = 0.40 \)), cholesterol (\( r = -0.18, P = 0.27 \)), HDL cholesterol (\( r = -0.07, P = 0.40 \)), and adiponectin concentrations (\( r = 0.064, P = 0.41 \)).

Multivariate stepwise linear regression modeling showed that percentage truncal fat by DEXA independently predicted AdipoR1 mRNA levels in a model including M values. Approximately 27.5% (\( r^2 = 0.275, P < 0.05 \)) of the variation in skeletal muscle AdipoR1 could be explained by percentage truncal fat.

**CONCLUSIONS** — Skeletal muscle AdipoR1 expression is independently and inversely correlated with measures of central obesity including waist circumference and truncal fat by DEXA, suggesting a novel mechanism linking skeletal muscle adiponectin signaling, central obesity, and insulin resistance. Further studies are required to determine whether muscle AdipoR1 expression is regulated by insulin or molecules released from adipocytes such as FFA (because fasting FFA concentration is associated with AdipoR2) and adipokines (such as leptin).

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**References**


In vivo expression of AdipoR1 in muscle in men

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