Retinol-binding protein-4 (RBP4), a 21-kDa protein synthesized in the liver and adipose tissue, has recently been described as a murine adipokine involved in the development of insulin resistance. The expression of the gene encoding RBP4 was increased in the adipose tissue, but not in the liver, of insulin-resistant adipose GLUT4(-/-) mice and five other mouse models of obesity and insulin resistance. In addition, intraperitoneal injection or transgenic overexpression of RBP4 in mice induced insulin resistance. While experimental clinical approaches (mostly applying clamp techniques) in humans confirmed correlations of RBP4 with insulin resistance, studies in larger groups out of clinical routine failed to demonstrate a connection with alternative measures of insulin sensitivity. Yet, significant associations of RBP4 with atherogenic lipids were found and a focus of future studies should be the influence on atherosclerosis and related complications. Based on current data, the function of RBP4 as an adipokine exerting metabolic effects in glucose metabolism in humans remains uncertain and might be restricted to rodent models.