

New blood test might offer early warning of deep belly fat

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Measuring levels of a chemical found in blood offers the best indicator yet of the amount of fat surrounding abdominal organs, according to a new study of lean and obese individuals reported in the July issue of *Cell Metabolism*, a publication of Cell Press. The buildup of such “visceral fat” is of particular health concern as it has been linked to insulin resistance, type 2 diabetes, and heart disease risk.

The researchers, including Barbara Kahn and Timothy Graham of Harvard Medical School and Matthias Blüher of the University of Leipzig in Germany, showed that “retinol-binding protein 4” (RBP4) is produced in much greater amounts by visceral fat compared to the subcutaneous fat that lies just beneath the skin. Moreover, they report that blood serum levels of RBP4 jump in people who are obese, who have double or even triple the concentrations found in individuals of normal weight.

“We believe that in the near future, measurements of RBP4 serum concentrations might serve as a novel biomarker for visceral obesity and increased risk for type 2 diabetes and other adverse outcomes of visceral obesity,” said Blüher. “In addition, pharmacological interventions that reduce RBP4 levels might be a new approach in the treatment of metabolic syndrome and visceral obesity.”

Prior to 2005, when Kahn’s group showed that elevating RBP4 levels in mice causes insulin resistance and lowering them in obese mice can improve insulin sensitivity, the only known function of RBP4 was to

carry vitamin A (also known as retinol) in the blood, Kahn said.

The researchers went on to show that serum RBP4 concentrations are also elevated in insulin-resistant individuals with obesity, type 2 diabetes, or impaired glucose tolerance, and even in otherwise normal people with a strong family history of diabetes. Likewise, interventions designed to improve insulin sensitivity, such as exercise training, “lifestyle modification,” or gastric banding surgery also lead to a decline in RBP4 levels.

Serum RBP4 concentrations in humans also correlate highly with waist-to-hip circumference ratio (an estimate of intra-abdominal fat mass), waist circumference, and percent trunk fat. Those findings suggested that the amount of visceral fat might contribute directly to blood concentrations of RBP4, although the connection had not been clearly shown, the researchers said.

In a study of 196 people, the researchers now reveal that RBP4 is indeed preferentially produced in the deep fat that covers organs of the belly. RBP4 gene expression activity levels spiked about 60-fold in the visceral fat of viscerally obese relative to lean study participants, they found. By comparison, visceral fat RBP4 concentrations were increased just 12-fold in obese individuals with a preponderance of subcutaneous fat.

“We were surprised about the magnitude of RBP4 differences between obese and lean people,” Blüher said.

RBP4 in the blood rose along with its gene expression activity in fat and with intra-abdominal fat mass, independently of age, gender, and body mass index. Among several fat-secreted proteins considered to be important in regulating insulin/glucose balance, serum RBP4 concentrations appear to be the best indicator of insulin resistance and intra-abdominal fat mass, the researchers concluded.

“This suggests a potential role for RBP4 as a convenient marker not only for type 2 diabetes but also for cardiovascular risk,” they wrote. “In addition, RBP4 may provide a mechanistic link between visceral adipose tissue accumulation and the increased metabolic and cardiovascular risks associated with it.” Kahn said her group is “still investigating whether the effects of RBP4 depend on vitamin A or whether they are due to RBP4 protein itself.”

Source: Cell Press

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