

## *RBP4: a new player in the insulin, obesity and diabetes story*

### *Lowering RBP4 could be a new strategy for treating type 2 diabetes*

One of the unexpected players in the nutrition and metabolism story is a small protein called RBP4. Until recently known only as a retinol (vitamin A) binding protein, its appearance in blood was surprisingly discovered to be a correlate of insulin resistance. Beyond a simple association a number of very elegant experiments have supported the idea that RBP4 has a causal role in insulin metabolism, obesity and diabetes.

One of the characteristics of obesity and type 2 diabetes is reduced expression of the glucose transporter (GLUT4) in fat cells (adipocytes). GLUT4 allows cells to take up glucose in response to insulin and when cells become insulin resistant, or under conditions of obesity or type 2 diabetes, there are fewer of these carriers. Barbara Kahn and coworkers explored this process by preparing a genetically-modified mouse lacking GLUT4 receptors on adipocytes, that is, an adipose-specific GLUT4 knockout (adipose-Glut4  $-/-$ ). In addition to fat cells not responding to insulin, these mice show insulin resistance secondarily in muscle and liver, suggesting that fat cells might secrete something that affected insulin resistance in other tissues. RBP4 turned out to be the agent.

Kahn's group found that drugs that improve insulin-resistance return RBP4 levels to normal and conversely, mice that overexpression of RBP4 or injection of RBP4 in normal mice caused insulin resistance. Genetic deletion of RBP4 enhances insulin sensitivity. So, it seems to be that RBP4 is a kind of signal that fat cells generate that may contribute to the development of diabetes and lowering RBP4 could be a new strategy for treating type 2 diabetes.