



BIOMARKERS

Mannose levels predict insulin resistance

Plasma levels of mannose are positively associated with insulin resistance independent of BMI, according to new research published in *Cell Metabolism*. The findings could facilitate stratification and early treatment of individuals with obesity who are at risk of developing comorbidities associated with insulin resistance, such as type 2 diabetes mellitus (T2DM).

Explaining the rationale for their study, lead investigator Adil Mardinoglu says “we used a systems biology approach to identify novel small molecules that can predict future risk of obesity-associated complications such as T2DM, cardiovascular disease and nonalcoholic fatty liver disease.” The investigators performed transcriptomic analysis on liver and adipose tissue depots (subcutaneous, mesenteric and omental) isolated from 12 individuals with morbid obesity (BMI >40 kg/m²) who were undergoing bariatric

surgery. These data were then incorporated into cell-specific (hepatocyte, myocyte and adipocyte) integrated networks, which were created by combining different -omics information (including DNase-sequencing data, protein–protein interaction networks and genome-scale network models).

Comparing obesity-specific integrated networks with those generated from healthy, lean individuals, the team found that mannose metabolism was dysregulated in states of obesity. Specifically, mannose metabolism and the expression of genes associated with mannose utilization were decreased in the livers of individuals with obesity. As these effects should increase plasma levels of mannose, the investigators measured levels of the metabolite by liquid chromatography–mass spectrometry in three independent mixed-sex patient cohorts (399 individuals who were lean, overweight or had obesity; 79 individuals with

obesity who were either insulin sensitive or insulin resistant; and 80 individuals with impaired fasting glucose levels and/or impaired glucose tolerance). In all three cohorts, plasma levels of mannose were positively associated with insulin resistance and negatively associated with insulin sensitivity, independent of BMI.

The findings suggest that mannose is one of the best plasma metabolites to explain the variance in obesity-independent insulin resistance. Plasma levels of mannose could, thus, be used to identify and initiate early treatment in individuals with obesity who are at high risk of developing comorbidities associated with insulin resistance and/or impaired insulin secretion.

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