A boost in microRNA may protect against obesity and diabetes

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Obesity, which is associated with low-grade inflammation, is an important contributor in the development of diabetes and cardiovascular disease. While the role of several organs including adipose tissue have been implicated in this process, the cell types and factors driving this process have not been clear. Using a pre-clinical model of obesity, researchers at Brigham and Women's Hospital (BWH) have discovered that a small, non-coding RNA molecule called miR-181b is an important determinant of obesity-induced changes in adipose tissue by controlling the function of the vessels in adipose tissue. The findings could point toward new targets for the development of treatment or obesity and diabetes. The study is published in the March 4 edition of *Circulation Research*.

The researchers identified that the expression of miR-181b was lower in adipose tissue endothelial cells, but not adipocytes, after just one week of high-fat feeding in mice. The team hypothesized that reconstituting this microRNA in obese mice might improve the development of insulin resistance/diabetes. Indeed, they found that injections of a miR-181b mimic into obese mice markedly improved insulin sensitivity, glucose levels and reduced inflammation in adipose tissue.

The team found that the protein phosphatase PHLPP2 is a direct target of miR-181b, and that suppression of the protein also improved insulin sensitivity, glucose levels and inflammation in mice, providing an additional new target for therapy.

Finally, the team noted that levels of PHLPP2 were higher in endothelial cells from diabetic patients than healthy patients, suggesting the new findings in mice are relevant to human disease.

"We have discovered a microRNA that functions to dampen the inflammatory response in the vasculature of adipose tissue by targeting endothelial cells that surround adipocytes and a pathway that leads to increased nitric oxide production," said senior author Mark W. Feinberg, an associate physician at BWH. "The beneficial role of this microRNA in obesity is likely the tip of the iceberg since excessive inflammation is a pervasive finding in a wide-range of chronic inflammatory diseases."

An accompanying editorial in the journal notes that "using microRNAs to modulate adipocyte-endothelial cell axis in adipose tissue may offer new tools to combat the growing epidemic of obesity and its associate comorbidities."

More information: Xinghui Sun et al. MicroRNA-181b Improves Glucose Homeostasis and Insulin Sensitivity by Regulating Endothelial Function in White Adipose TissueNovelty and Significance, *Circulation Research* (2016). DOI: 10.1161/CIRCRESAHA.115.308166

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