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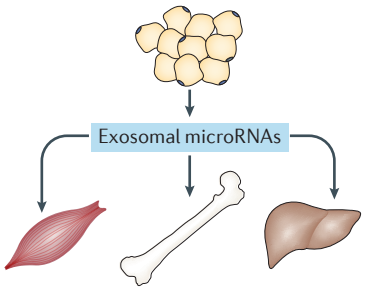
ADIPOSE TISSUE

Exosomal microRNAs — novel adipokines

New research has found that the exosomal microRNAs (miRNAs) produced by adipose tissue affect gene expression in distant organs, such as the liver. The researchers suggest that their findings indicate that exosomal miRNAs are a previously undescribed form of adipokine.

To investigate the role of miRNAs produced in adipose tissue, the researchers generated mice lacking Dicer (the enzyme that processes miRNAs) in adipose tissue using a Cre–*lox* gene recombination strategy. The resulting ADicerKO mice had an overall decrease in circulating levels of exosomal miRNAs compared with wild-type mice; levels of 419 miRNAs were significantly decreased, and those of three miRNAs were significantly increased. Similar results were found when the levels of miRNAs were analysed in serum from patients with congenital generalized lipodystrophy or HIV-associated lipodystrophy (who have low levels of Dicer in adipose tissue).



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Transplanting fat from normal mice into ADicerKO mice restored circulating levels of exosomal miRNAs to normal, an effect that was particularly marked when brown adipose tissue was transplanted. This finding confirms that adipose tissue is the source of these exosomal miRNAs.

Interestingly, ADicerKO mice had a threefold increase in circulating levels of fibroblast growth factor 21 (FGF21), compared with wild-type mice. Levels of *Fgf21* mRNA were also increased in liver, muscle, fat and pancreas. On transplantation of brown adipose tissue from control mice, levels of *Fgf21* mRNA in the livers of ADicerKO mice reduced by ~50%, which was accompanied by a reduction in circulating levels of FGF21. Thus, transplantation of brown adipose tissue seems to provide a factor that regulates FGF21 expression. Further analyses revealed that miR-99b, which is present in exosomes derived from brown adipose tissue, is the factor that is involved in regulating FGF21 expression in the liver.

"Our data show that adipose tissue is an important source of circulating exosomal miRNAs in both mice and humans," write the authors. They also conclude that these miRNAs could be involved in regulating whole-body metabolism and the translation of mRNAs in other tissues.

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ORIGINAL ARTICLE Thomou, T. *et al.* Adipose-derived circulating miRNAs regulate gene expression in other tissues. *Nature* http://dx.doi.org/10.1038/nature21365 (2017)

> "ADicerKO mice had a threefold increase in circulating levels of fibroblast growth factor 21"

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