**microRNAs in obesity-associated inflammation of adipose tissue**

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**Introduction**

microRNAs (miRNAs) are a class of small (18-25 nucleotides), non-coding RNA molecules. They play an important role in the regulation of gene expression by either suppressing translation or inducing mRNA degradation. Adipocytes express at least 169 different miRNA species and 85 of them appear to be released from cells as they are detectable in cell culture supernatants (1). Their impact ranges from regulating adipogenesis and glucose metabolism to the modulation of inflammation (2).

Obesity leads to the infiltration of macrophages into white adipose tissue (WAT) local inflammation and decreased insulin sensitivity. In an Affymetrix miRNA array we found miR-146a expression strongly upregulated in adipocytes under inflammatory conditions.

miR-146a plays a central role in the regulation of the inflammatory response in cell types such as human keratinocytes (3), human monocytes (4) and human lung alveolar epithelial cells (5). Here the impact of miR-146a on adipocyte inflammation was investigated.

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**Summary**

This work identified miR-146a as a fine tuner of the inflammatory response in human adipocytes. In brief:

- Human adipocytes miR-146a is upregulated under inflammatory conditions.
- miR-146a targets IRAK1 and TRAF6.
- miR-146a counteracts the inflammation-induced activation of JNK and p38.
- miR-146a reduces the inflammation-induced expression and secretion of IL-8 and MCP-1.

Considering that the tissue macrophage of obese WAT is pro-inflammatory and that miR-146a is upregulated under these conditions, we hypothesize that it controls the inflammatory response in a negative feedback loop.

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**Results**

**miR-146a is upregulated in obesity and under inflammatory conditions**

![Figure 1](image1.png)

**Figure 1 | Obesity and inflammation stimulus lead to increased miR-146a expression**

(A) miR-146a expression in subcutaneous WAT from lean and obese females (+18 total) with n的例子 as reference gene. (B) miR-146a expression in subcutaneous WAT from female and male diet for 4 weeks with n的例子 as reference gene. (C) Effect of IRAK1 and TRAF6 on miR-146a expression in subcutaneous WAT from lean and obese males. Total RNA was normalized by 0, 6, 24, 48, 72 and 120 hours in reverse transcribed. The expression of miR-146a was assessed by qPCR. Data were analyzed using the ΔΔCT method with n的例子 as reference gene. The results are displayed as mean ± SEM of three independent experiments. Statistics: *p < 0.05, **p < 0.01, *** p < 0.001.

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**miR-146a damps the inflammatory response in human adipocytes**

![Figure 2](image2.png)

**Figure 2 | miR-146a mimic transfection reduces IL-8 and MCP-1 expression and secretion in 3T3-L1 adipocytes**

3T3-L1 adipocytes were transfected with miR-146a mimic (20 nM) or non-target control (20 nM). At 48 h, the cells were stimulated with Macrophage cell culture supernatant (MCT, 20 nM). At 48 h, the cells were stimulated with Macrophage cell culture supernatant (MCT, 20 nM). Total RNA was isolated after 48 h and protein after 48 h, 72 h, and 96 h. (A) IRAK1 and TRAF6 mRNA expression with SNCA as reference gene. (B) Representative Western blots for IRAK1 and TRAF6 and densitometric analysis with β-actin as loading control. Data are displayed as mean ± SEM of four to six independent experiments. Statistics: paired t-test, *p < 0.05, **p < 0.01, *** p < 0.001.

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**miR-146a reduces the activation of JNK and p38**

![Figure 3](image3.png)

**Figure 3 | miR-146a mimic transfection reduces IL-8 and MCP-1 expression and secretion in human adipocytes**

(A) miR-146a mimic was transfected into human adipocytes of these three cultures and stimulated as described in Figure 2. (B) The transfection of miR-146a mimic was assessed by qPCR with n的例子 as reference gene. (C) Secreted IL-8 and MCP-1 protein measured in media supernatants by ELISA. Data are displayed as mean ± SEM of four qPCR data or three ELISA independent experiments. Statistics: (A) paired t-test, (B-C) two-way ANOVA, *** p < 0.001, ** p < 0.01, * p < 0.05.

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**References**


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