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Hypoxia mimetic blocks adipocyte differentiation but induces lipid accumulation

Obesity is one of the most immediate health threats in industrialized countries, increasing morbidity and mortality. It is characterized by an excessive increase of white adipose tissue. Adipose tissue is a tissue with high plasticity, having the ability to expand throughout the entire lifespan. In obesity, adipocytes become very large and the vasculature of adipose tissue is unable to grow along to provide oxygen to adipocytes, leading to local adipose tissue hypoxia. Hypoxia was reported to occur in adipose tissue in obese mice and humans. Hypoxia has a high impact in adipose tissue homeostasis, contributing to adipose tissue dysfunction in obesity. However, the impact of hypoxia on adipocyte physiology is not fully understood.

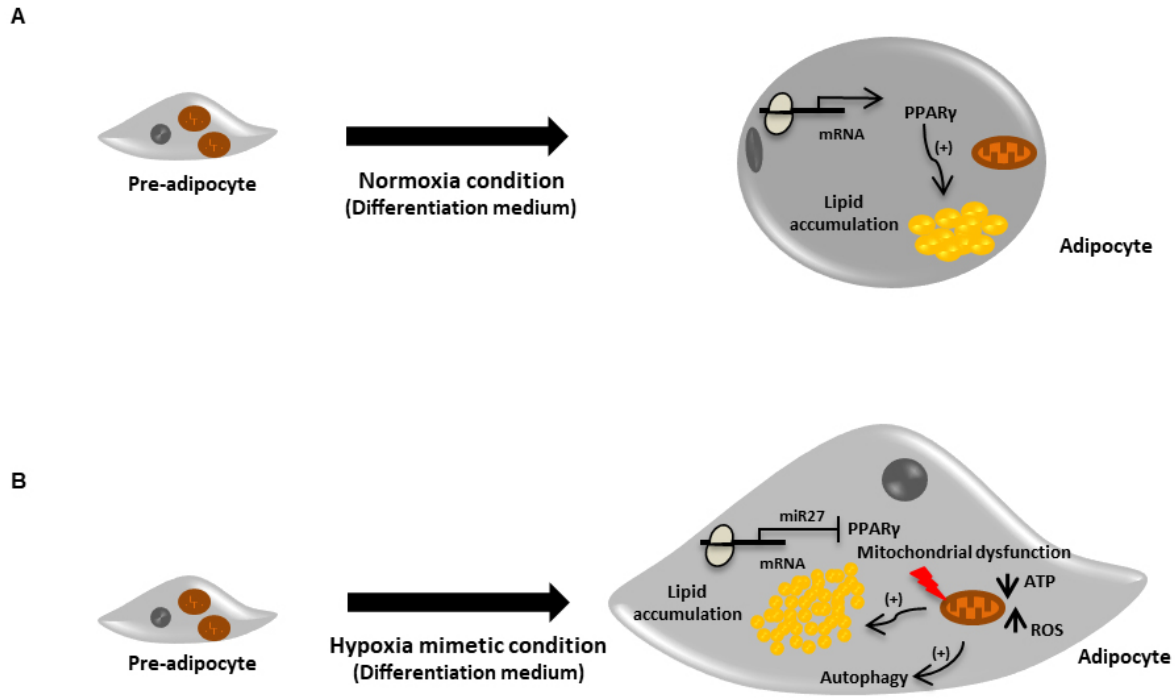

Fig. 1. Effects of normoxia (A) and hypoxia mimetic (B) in the physiology of adipocyte. (A) In normoxia conditions, adipocytes differentiate with an increase of PPARγ2 expression and increase of lipid accumulation (B) In hypoxic conditions (mimetic), adipocytes do not express PPARγ2 but with increased lipid accumulation. Hypoxia mimetic also increases miR27a and miR27b expression. Cobalt chloride also induces the production of reactive oxygen species and autophagy and decreases ATP production.

In the paper that we published we evaluated the impact of the oxygen decrease (hypoxia) in adipose tissue by treating adipocytes with hypoxia mimetics, cobalt chloride and deferoxamine. We observed that hypoxia mimetic has several deleterious effects in normal adipocyte function. Hypoxia blocks the differentiation of adipocytes but increases the accumulation of lipids by these cells.

Furthermore, hypoxia mimetic induces mitochondrial dysfunction, lactate and reactive oxygen species production and decreases ATP, decreasing the energy needed for the normal function of the cell. These results together suggest that hypoxia effects on adipocyte function occur through mitochondrial dysfunction and reactive oxygen species production. Hypoxia was also observed to induce autophagy, which is a physiological protective mechanism that is also described to be mediated by reactive oxygen species.

Although further studies are needed for a better understanding of the effect of hypoxia in adipocyte physiology, these results highlight the importance of hypoxia in adipocyte function and provides a possible explanation for hypoxic lipogenesis.

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Publication

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