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Hypoxia modulates monocarboxylate transporter (MCT) expression in human adipocytes

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Hypoxia has been proposed to occur in hypertrophied adipose tissue[1,2] and may underlie the inflammatory response in the tissue and the subsequent development of obesity-associated disorders. Adipocytes switch to a glycolytic metabolism in response to hypoxia, involving an up-regulation of glucose transporter expression (particularly GLUT-1) and increased glucose uptake[3]. Consequently, lactate rises and needs to be removed from the cell. The transport of lactate, and similar metabolites, is mediated through the proton-linked MCT family. Currently, there are fourteen known MCT, four of which (MCT-1–4) transport lactate[4]. One transporter, MCT-4, has been reported to be up regulated by hypoxia in certain cell types[5]. The objective of the present study was to determine whether the MCT-1–4 are expressed in human adipocytes and whether hypoxia modulates their expression.

Human SGBS adipocytes were used to screen for the expression of the MCT-1–4 genes by RT–PCR. Adipocytes at day 14 post induction of differentiation were cultured under normoxia (21 % (v/v) O_2) or hypoxia (1 % (v/v) O_2) for different periods and MCT mRNA levels quantified by quantitative PCR. Another group of cells was treated with the hypoxia mimetic, $CoCl_2$, to assess whether the key hypoxia-responsive transcription factor hypoxia-inducible factor 1 (HIF-1)[6] was involved in any changes.

The ubiquitous MCT-1 was found to be expressed in both preadipocytes (0 d) and fully-differentiated adipocytes, as was MCT-2 and MCT-4 (Figure). Expression of MCT-3 was less clear. Hypoxia significantly increased lactate levels in the culture medium, and had a significant effect on MCT gene expression, up regulating MCT-1 and MCT-4 mRNA levels (8.5-fold and 14-fold respectively at 48 h; $P<0.001$), while down regulating MCT-2 (4-fold at 48 h; $P<0.05$). These changes on MCT gene expression were reversed on return to normoxia, and mirrored by $CoCl_2$ treatment.

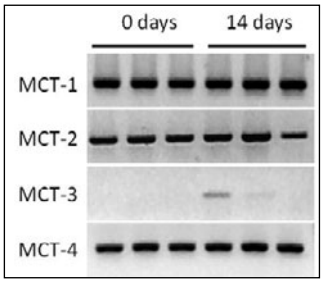

Figure. MCT1-4 mRNA in human adipocytes (SGBS cells) by RT-PCR.

The present study demonstrates for the first time that MCT-1, MCT-2 and MCT-4 are each expressed in human adipocytes. Furthermore, this expression is significantly modified by hypoxia in a type-specific manner, via the transcription factor HIF-1. MCT-1 and MCT-4 are likely to be important in exporting increased lactate produced by adipocytes under the hypoxic conditions that appear to characterize adipose tissue in obesity; besides, lactate may impact on the development of local inflammatory processes[7]. Therefore, the observed hypoxia-related increase in lactate transport from adipocytes could constitute a further link between obesity, inflammation and the metabolic syndrome.

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