Role of Sirtuin 3 in the differentiation of 3T3-L1 preadipocytes

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An adaptive capacity of white adipose tissues is essential to match energy intake and expenditure. Part of this adaptation is driven by the enrollment of new adipocytes, a phenomenon referred to "adipogenesis". Our current efforts are dedicated to the investigation of the putative role of the Sirtuin 3 (SIRT3), a NAD^+-dependent deacetylase and master regulator of several mitochondrial functions, in the differentiation of preadipocytes in white adipocytes. This is of particular relevance as mitochondrial biogenesis and activation of oxidative metabolism are promoted by SIRT3 and are known to be required for proper adipogenic differentiation. Moreover, SIRT3 was already reported to be required for proper differentiation of various other cell types such as skeletal myocytes [1] and brown adipocytes [2].
White 3T3-L1 adipoblasts were differentiated in adipocytes in the presence or in the absence of SIRT3 (invalidation using CIRSPR/Cas9-DN technology) and the expression of SIRT3 as well as markers of its activity were analysed during a differentiation programme of 12 days. In addition, ROS production as well as respiration (Oxygraph-2k, ORBOROS Instruments Corp) in cells in the presence or in the absence of SIRT3 were studied.
The results show that the expression of SIRT3 is induced during the differentiation programme. In addition, the absence of SIRT3 is reflected by a delay (but not the inhibition) of preadipocyte differentiation as demonstrated by a reduced content of triacylglycerols. We are currently investigating the underlying mechanisms that could postpone adipogenesis in the absence of the mitochondrial deacetylase such as modifications in reactive oxygen species production and putative alterations of OXPHOS that could connect SIRT3 to proper development of the adipose phenotype.
In conclusion, we showed that SIRT3 activity accompanies the adipogenic programme of 3T3-L1 preadipocytes and that the enzyme plays an important role in the kinetics of the differentiation programme. The identification of SIRT-3 dependent mechanisms playing a role in the differentiation of preadipocytes is ongoing.

[1] Khalek WA, Cortade F, Ollendorff V, Lapasset L, Tintignac L, Chabi B, Wrutniak-Cabello C (2014) SIRT3, a mitochondrial NAD+-dependent deacetylase, is involved in the regulation of myoblast differentiation. Plos One 9(12): e114388.

[2] Giralt A, Hondares E, Villena JA, Ribas F, Díaz-Delfín J, Giralt M, Iglesias R, Villarroya F (2011) Peroxisome proliferator-activated receptor-alpha Coactivator-1gamma controls transcription of the Sirt3 gene, an essential component of the thermogenic brown adipocyte phenotype. The journal of biological chemistry 286(19):16958–66.