

EP B002

SIRT1-SRSF10 PATHWAY PROMOTES BROWN-LIKE FEATURES OF WHITE ADIPOCYTES

https://doi.org/10.15605/jafes.039.S1.204

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INTRODUCTION/BACKGROUND

Energy expenditure predominantly occurs in brown adipose tissue (BAT), therefore promoting BAT-like features or inducing the browning of white adipose tissue (WAT) can be an attractive approach to reduce obesity. Studies have found the interplay between splicing factor SRSF10 and Sirt1-mediated pathway during adipocyte differentiation and lipid metabolism in obese liver. Therefore, we aimed to investigate whether activation of Sirt1-SRSF10 can lessen lipid accumulation in white adipocytes and induce the expression of typical genes of BAT *in vitro*.

CASE

3T3-L1 cells were differentiated into mature adipocytes for 10 days. The cells were also treated with Sirt1 activator, Sirt1 Inhibitor or Rosiglitazone throughout the adipogenic differentiation period and gene expression was analysed by real-time polymerase chain reaction.

Upregulation of Sirt1 was directly proportional to the level of SRSF10 in differentiated adipocytes resulting in lesser intracellular lipid accumulation. Expectedly, attenuation of Sirt1 activity enhanced lipid production in the cells. Lipin1, one of SRSF10-affected splicing events implicated in adipogenesis was further investigated and its variant *Lipin1a* was found significantly increased as compared to *Lipin1b*. Finally, the expression of 'browning' genes such as *PGC1a* and *Cidea* were upregulated in Sirt1-activated adipocytes.

CONCLUSION

Overall, Sirt1 affects important splicing events via SRSF10 during adipocyte differentiation hence preventing excessive lipid accumulation in vitro. It also promotes the browning of white adipose tissue, indicating that the Sirt1-SRSF10 pathway can be a potential drug target to reduce obesity.