Regulation of Dicer Expression and Its Role During Adipocyte Differentiation

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Introduction and objectives

Dicer is a type III endoribonuclease that converts pre-miRNAs into mature miRNAs. Dicer is upregulated during adipocyte differentiation and is required for the formation/maturation of brown/beige adipocytes. Here we tested whether Dicer overexpression is sufficient to determine brown/beige adipocyte differentiation. Moreover, we studied how Dicer expression is controlled during adipocyte differentiation.

Materials and methods

We used a clonal cell lineage of murine 3T3-F442A preadipocytes transduced with lentiviruses expressing either human Dicer (H8) or Empty vector as the control. Cells were differentiated into adipocytes under high (850 nM) or low (20 nM) insulin concentrations. Adipocyte markers and Dicer expression was assessed. Results were analyzed using ANOVA when more than two groups where present or student's t test otherwise.

Results and Discussion

H8 cells differentiated spontaneously and were more prone to adipogenesis under low insulin concentration, as determined by higher expression of pan-adipocyte markers [*aP2* (130%) and *Pparg* (92%)] and increased triglyceride accumulation (274%) at the end of the differentiation protocol. These differences were not observed under high insulin concentration. H8 cells displayed insulin resistance induced by chronic insulin exposure, as observed by lower phosphorylation of Akt (70%), Erk1 (76%) and Erk2 (57%) after 8 hours of stimulation with 20 nM insulin. We also observed higher expression of brown/beige adipocyte markers [*Elovl3* (276%), *Eva1* (74%) and *Ppargc1a* (92%)] in the H8 versus the controls after differentiation. Dicer protein expression was higher in adipocytes than in preadipocytes, with no changes at the mRNA level. Moreover, the half-life of Dicer protein was extremely rapid in adipocytes (~1 hour).

Conclusions

Dicer overexpression in preadipocytes favors adipogenesis, lipid accumulation, brown/beige adipocyte marker expression, and insulin resistance under chronic insulin exposure. Furthermore, Dicer expression is stabilized during adipocyte differentiation due to translational or post-translational regulation, most likely controlled by degradation.

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