REGULATION OF DICER EXPRESSION IN ADIPOSE TISSUE IS SENSITIVE TO SULFUR AMINO ACID LEVELS AND CONTRIBUTES TO METHIONINE RESTRICTION-INDUCED BROWNING IN MICE


1 Federal University of São Paulo.
2 Orentreich Foundation for the Advancement of Science, USA.
3 University of Campinas.

Introduction: Dietary restriction (DR) promotes beneficial health effects and prolongs lifespan in several species. Recently, it has been reported that DR prevents the adipose tissue specific decline in the expression of microRNAs and their processing enzymes, particularly Dicer, that occurs with aging. Objectives: To identify how nutritional interventions affect the processing of miRNAs in fat. Methods: We performed a series of experiments where we modified the period and the composition of the diet and analyzed the effects on subcutaneous fat. Results: Here we determined that the maximum effects of DR on adipose tissue Dicer expression can be achieved after only one week of a 10% dietary restriction. To test whether specific nutrient restriction was responsible for Dicer upregulation upon DR, we performed a nutrient screen in preadipocytes and identified that methionine or cysteine restriction was sufficient to increase Dicer mRNA expression in these cells. Consistently, mice subjected to DR supplemented with methionine, cysteine or casein (as a protein source) had adipose tissue Dicer expression levels similar to ad libitum (AL) fed mice and lower than DR mice. This was not the case when carbohydrates or lipids were supplemented to DR. Moreover, methionine restriction (MR) in rodents resulted in weight loss, improved glucose tolerance and increased expression of Dicer in adipose tissue. Interestingly, we found that the serum levels of adiponectin correlated with Dicer expression across different nutritional conditions. Serum adiponectin was also reduced in fat-specific Dicer knockout mice (AdicerKO) both under AL and MR conditions. Most importantly, MR-induced recruitment of beige adipocytes to subcutaneous adipose tissue was abrogated in AdicerKO mice. Conclusion: This study proposes new mechanisms of regulation of Dicer expression and reveals that Dicer upregulation in adipose tissue upon dietary interventions that reduce the levels of sulfur amino acids contributes to metabolic adaptations promoted by these diets.

Key Words: Adipose Tissue, Dicer and Methionine Restriction.

Nota: O Sistema não aceitou a inserção da autora Carmen Perrone porque ela não possui identidade nacional e nem cpf, se trata de uma autora estrangeira.