mTOR in Aging and Age-Related Diseases

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Abstract

Caloric Restriction (CR), a dietary regimen that delays aging and the onset of age-associated diseases, induces a reprogramming of energy metabolism that may be important in its mechanisms of action. In mice, the effect of CR on adipose tissue is particularly striking and presents a possible means to integrate the CR response among tissues through changes in adipose tissue-derived systemic signaling. Leptin, a hormone secreted by adipose tissue, is a key factor in regulating energy homeostasis and is important in the regulation of appetite, metabolism, and adiposity. CR decreases leptin levels in mice, and leptin is involved in the regulation of energy metabolism. CR decreases the expression of leptin in adipose tissue, and leptin levels are increased in adipose tissue from mice fed a high-fat diet. The leptin levels in adipose tissue are increased in mice fed a high-fat diet, and leptin levels are decreased in adipose tissue from mice fed a high-fat diet. The leptin levels in adipose tissue are increased in mice fed a high-fat diet, and leptin levels are decreased in adipose tissue from mice fed a high-fat diet.

Results

Rapamycin alters mitochondrial metabolism in adipose tissue

Rapamycin impacts PGC-1α stability in adipose tissue

Conclusions

Rapamycin increases inhibitory phosphorylation of GSK3β and enhances activity of PGC-1α-dependent processes.

Rapamycin disrupts GSK3β-mediated regulation of PGC-1α within adipocytes during differentiation.

Inappropriate levels of PGC-1α impair lipids accumulation.

Protein levels of PGC-1α and its regulator, GSK3β, are altered in adipose tissue from rapamycin-fed mice.

We hypothesize that the interaction between mTOR signaling and PGC-1α through GSK3β is a conserved feature of aging and age-associated disease risk.

References


Schinke T, Phillips D, et al. The eukaryotic target of rapamycin (mTOR) pathway regulates mitochondrial dysfunction mediated by decreased oxygen consumption and oxidative capacity.

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