学位論文抄録
Abstract of Thesis

SIRT7 regulates lipogenesis in adipocytes through deacetylation of PPARγ2

（SIRT7 は PPARγ2 の脱アセチル化を介して脂質合成を制御する）

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Aims/Introduction

Peroxisome proliferator-activated receptor (PPAR)-γ2 is a transcription factor crucial for regulating adipogenesis and glucose/lipid metabolism, and synthetic PPARγ ligands, such as thiazolidinediones, are effective oral medication for type 2 diabetes. Sirtuin 7 (SIRT7), a nicotinamide adenine dinucleotide-dependent deacetylase, also controls metabolism. However, it is not known whether SIRT7 regulates the function of PPARγ2 by its deacetylation.

Materials and Methods

Physical interaction between SIRT7 and PPARγ2, the effect of SIRT7 on PPARγ2 acetylation, and the deacetylation residue targeted by SIRT7 were investigated. The effects of PPARγ2 K382 acetylation on lipid accumulation, gene expression in C3H10T1/2 cell-derived adipocytes, and ligand-dependent transactivation activity were also evaluated.

Results

We demonstrated that SIRT7 binds to PPARγ2 and deacetylates PPARγ2 at K382. C3H10T1/2-derived adipocytes expressing PPARγ2^{K382Q} (a mimic of acetylated K) accumulated much less fat than adipocytes expressing wild-type PPARγ2 or PPARγ2^{K382R} (a mimic of nonacetylated K). Global gene expression analysis of adipocytes expressing PPARγ2^{K382Q} revealed that K382Q caused the dysregulation of a set of genes involved in lipogenesis, including *Srebp1c*, *Acaca*, *Fasn*, and *Scd1*. The rosiglitazone-dependent transcriptional activity of PPARγ2^{K382Q} was reduced compared with that of PPARγ2^{K382R}.

Conclusion

Our findings indicate that SIRT7-dependent PPARγ2 deacetylation at K382 controls lipogenesis in adipocytes.