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DN

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TI

peroxisome proliferator-activated receptor-gamma transcriptionally up-regulates hormone-sensitive lipase via the involvement of specificity protein-1.

AU

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SO

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DT

Article

LA

English

ED

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AB

Both peroxisome proliferator-activated receptor (PPAR)-gamma and hormone-sensitive lipase (HSL) play important roles in lipid metabolism and insulin sensitivity. We demonstrate that expression of the HSL gene is up-regulated by PPAR gamma and PPAR gamma agonists (rosiglitazone and pioglitazone) in the cultured hepatic cells and differentiating preadipocytes. Rosiglitazone treatment also results in up-regulation of the HSL gene in liver and skeleton muscle from an experimental obese rat model, accompanied by the decreased triglyceride content in these tissues. The proximal promoter (-87 bp of the human HSL gene) was found to be essential for PPAR gamma-mediated transactivating activity. This important promoter region contains two GC-boxes and binds the transcription factor specificity protein-1 (Sp1) but not PPAR gamma. The Sp1-promoter binding activity can be endogenously enhanced by PPAR gamma and rosiglitazone, as demonstrated by analysis of EMSA and chromatin immunoprecipitation assay. Mutations in the GC-box sequences reduce the promoter binding activity of Sp1 and the transactivating activity of PPAR gamma. In addition, mithramycin A, the specific inhibitor for Sp1-DNA binding activity, abolishes the PPAR gamma-mediated up-regulation of HSL. These results indicate that PPAR gamma positively regulates the HSL gene expression, and up-regulation of HSL by PPAR gamma requires the involvement of Sp1. Taken together, this study suggests that HSL may be a newly identified PPAR gamma target gene, and up-regulation of HSL may be an important mechanism involved in action of PPAR gamma agonists in type 2 diabetes.

CC

Cytology - Animal 02506
Cytology - Human 02508
Genetics - General 03502
Genetics - Animal 03506
Genetics - Human 03508
Biochemistry studies - Lipids 10066
Enzymes - General and comparative studies: coenzymes 10802
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Endocrine - Pancreas 17008
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Pharmacology - Blood and hematopoietic agents 22008
Pharmacology - Cardiovascular system 22010
Pharmacology - Endocrine system 22016
Pediatrics 25000

IT

Major Concepts
Molecular Genetics (Biochemistry and Molecular Biophysics); Enzymology (Biochemistry and Molecular Biophysics); Endocrine System (Chemical Coordination and Homeostasis)

IT

Parts, Structures, & Systems of Organisms
liver: digestive system; skeletal muscle: muscular system;
preadipocyte; hepatic cell: digestive system

IT

Diseases
type 2 diabetes: endocrine disease/pancreas, metabolic disease
Diabetes Mellitus, Non-Insulin-Dependent (MeSH)

IT

Diseases
obesity: nutritional disease
Obesity (MeSH)

IT

Chemicals & Biochemicals
triglyceride; peroxisome proliferator-activated receptor-alpha;
hormone-sensitive lipase; pioglitazone: antidiabetic-drug;
specificity protein 1; mithramycin A: enzyme inhibitor-drug;
rosiglitazone: antidiabetic-drug, thrombolytic-drug, hematologic-drug,
cardiovascular-drug, vasodilator-drug

IT

Methods & Equipment
immunoprecipitation: laboratory techniques, immunologic techniques;
electrophoresis mobility shift assay [EMSA]: electrophoretic
techniques, genetic techniques, laboratory techniques

IT

Miscellaneous Descriptors
lipid metabolism; insulin sensitivity

ORGN

Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
SMMC-7721 cell line (cell_line): human hepatoma cells
CCC-L cell line (cell_line): human fetal liver cells
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

ORGN

Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
Wistar rat (common): newborn
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals,
Rodents, Vertebrates

RN

9001-62-1 (hormone-sensitive lipase)
111025-46-8 (pioglitazone)
97666-60-9 (mithramycin A)
122320-73-4 (rosiglitazone)

GEN

rat HSL gene [rat hormone-sensitive lipase gene] (Muridae): up-regulation