

## AN

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## DN

PREV200600228562

## TI

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

## AU

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## CS

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## SO

Endocrinology, (FEB 2006) Vol. 147, No. 2, pp. 875-884.  
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## DT

Article

## LA

English

## ED

Entered STN: 12 Apr 2006  
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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  
Pathology - Therapy 12512  
Metabolism - Metabolic disorders 13020  
Nutrition - Malnutrition and obesity 13203  
Digestive system - Physiology and biochemistry 14004  
Endocrine - General 17002  
Endocrine - Pancreas 17008  
Muscle - Physiology and biochemistry 17504  
Pharmacology - Clinical pharmacology 22005  
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