Fatty acids have been postulated to regulate adaptation of adipose tissue to nutritional changes by controlling expression of genes implicated in lipid metabolism via activation of nuclear receptors. Ectopic expression of the nuclear receptors PPARγ or PPARδ promotes adipogenesis in fibroblastic cells exposed to thiazolidinediones or long-chain fatty acids. To investigate the role of PPARδ in fatty acid regulation of gene expression and adipogenesis in a preadipose cellular context, we studied the effects of overexpressing the native receptor or the dominant-negative PPARδ mutant in Ob1771 and 3T3-F442A cells. Overexpression of PPARδ enhanced fatty acid induction of the adipose-related genes for fatty acid translocase, adipocyte lipid binding protein, and PPARγ and fatty acid effects on terminal differentiation. A transactivation-deficient form of PPARδ mutated in the AF2 domain severely reduced these effects. Findings are similar in Ob1771 or 3T3-F442A preadipose cells. These data demonstrate that PPARδ plays a central role in fatty acid-controlled differentiation of preadipose cells. Furthermore, they suggest that modulation of PPARδ expression or activity could affect adaptive responses of white adipose tissue to nutritional changes.

Dietary long-chain fatty acids (LCFA) control adipose tissue mass by regulating both the number and the size, i.e., the lipid accumulation, of adipocytes. This was illustrated in vivo by the findings that high fat diets promote hyperplastic and hypertrophic development of adipose tissue and massive obesity in adult rodents (1–3). Adipogenic effects of LCFA have also been documented in vitro by demonstrating that exposure of preadipose cells to native or non-metabolized fatty acids, such as 2-bromopalmitate (2BrP), increased the number of cells committed to differentiate as well as expression levels of adipose-related genes (4).

Cellular effects of fatty acids and some of their metabolites are related, at least in part, to activation of nuclear receptors called PPARs. Two different PPAR subtypes, δ and γ, are expressed in preadipose and adipose cells. PPARγ has been shown to play a central role in the control of gene expression and adipogenesis (5–8). Synthetic and naturally occurring PPARγ activators, such as thiazolidinediones or 15-deoxy-D12,14-prostaglandin J2, are potent stimulators of terminal differentiation of cultured preadipose cells (9, 10). We have recently proposed that PPARδ acts as an early player in LCFA induction of terminal differentiation by promoting PPARγ expression. Fibroblasts ectopically expressing PPARδ respond to LCFA by transcriptional activation of genes for fatty acid translocase (FAT/CBD36), adipocyte lipid binding protein (ALBP), and PPARγ. Although treatment with fatty acids alone was not sufficient to trigger adipogenesis, exposure to a combination of PPARδ and PPARγ activators, for example 2BrP and thiazolidinedione, or to a pan-PPAR activator, such as prostacyclin, promotes the expression of a typical adipose differentiation program and adipogenesis (11).

These experiments, which documented the role of PPARδ in the adiogenic action of LCFA, also illustrated a major difference between fibroblasts and preadipose cells. Fibroblasts expressing PPARδ strictly require exposure to strong PPARγ activators to trigger terminal differentiation, whereas preadipose cells do not. A similar situation had already been described for PPARγ-expressing fibroblasts (5). This discrepancy may reflect the ability of differentiating preadipose cells to synthesize and to accumulate enough endogenous PPARγ activator to undergo terminal differentiation. Because many other differences could exist between preadipose cells and PPAR-expressing fibroblasts, it is crucial to examine the role of these transcription factors in a preadipose cellular context to confirm their role in adipocyte differentiation. Therefore, we have investigated the effects of overexpression of PPARδ and dominant-negative PPARδ mutant on the control by LCFA of gene expression and terminal differentiation in Ob1771 preadipose cells. The dominant-negative PPARδ was generated by substitution of a glutamate residue by a proline in the loop preceding the AF2 domain. This domain is essential for coactivator binding and confers a dominant-negative phenotype (4).}

Published, JBC Papers in Press, September 15, 2000, DOI 10.1074/jbc.M006450200

Claire Bastie, Serge Luquet, Dorte Holst, Chantal Jehl-Pietri, and Paul A. Grimaldi‡

From the Institut de Recherche Signalisation, Biologie du Développement et Cancer, INSERM U470, Centre de Biochimie, Faculté des Sciences, Université de Nice-Sophia Antipolis, Parc Valrose, 06108 Nice Cedex 2, France

* The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked “advertisement” in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

‡ To whom correspondence should be addressed. Tel.: 33-492-07-64-02; E-mail: grimaldi@taloa.unice.fr.

† The abbreviations used are: LCFA, long-chain fatty acid; ALBP, adipocyte lipid binding protein; 2BrP, 2-bromopalmitate; FAT, fatty acid transporter; GPDH, glycerophosphate dehydrogenase; PPAR, peroxisome proliferator-activated receptor; PPRE, PPAR responsive element; RXR, retinoid X receptor; kb, kilobase(s).
short term, i.e. activation of gene expression, and long term, i.e. adipogenesis, responses to LCFA.

EXPERIMENTAL PROCEDURES

Plasmids—The retroviral constructs containing PPARδ cDNA or PPARδE411P mutant cDNA were derived from pSG5-FAAR (20) and cloned into the BanHI site of pBizeoneo retroviral vector (Dr. K. Kristiansen, University of Odense, Denmark).

The PPARδE411F was obtained by the site-directed mutagenesis method of Viville (21) using the 5'-CATCATCTGGCCGCTGTGGGTTGACCGCGT-3' oligonucleotide, and the construct was verified by sequencing.

Cell Culture—Cells were grown in Dulbecco’s modified Eagle’s medium complemented with 8% fetal calf serum, 200 units/ml penicillin, 50 μg/ml streptomycin, 33 μM bovine, 17 μM calcium panthenolate (standard medium). For differentiation, cells were shifted after confluence to a standard medium supplemented with 17 μM insulin and 1 μM triiodothyronine (differentiation medium). Medium was changed every other day. Oil Red O staining was performed as described previously (22).

Stable Cell Lines—BOSC23 cells were transfected at 50–70% of confluence by lipofection (Fugene 6, Roche Molecular Biochemicals) by 8 μg of pBizeoneo or pBizeoneoPPARδ or pBizeoneoPPARδE411P expression vectors. After 8 h, cells were re-fed with fresh standard medium and viral supernatants were collected 48 h later. Ob1771 (23) or 3T3F442A (24) cells grown in standard medium were infected with equal titers of recombinant virus for 6 h and then maintained for 48 h in fresh standard medium and then replated with a 1:5 dilution in standard medium containing 0.4 μg/ml Geneticin. Stable populations were obtained after 7–10 days of selection.

Transient Transfection—HEK-293 cells were grown in standard medium and plated in 24-well plates. At 80% confluence, cells were transfected by Fugene 6 with 0.5 μg/well 3xACOPPRE-Tk luciferase reporter vector, 25 ng/well pCMV-RXRα expression vector, 15 ng/well pCMV-βGalactosidase vector, and various amounts of pBizeoneoPPARδ or pBizeoneoPPARδE411P expression vectors. After 6 h, cells were re-fed with fresh standard medium with or without 50 μM 2BrP. A 50 μM stock solution of 2BrP and dilutions were prepared in Me2SO. Luciferase and galactosidase activities were analyzed 48 h later using the luciferase assay system (Promega France), and the Galacto-Light assay system (Tropix, PerkinElmer, France), respectively. Each transfection was performed in triplicate, and the fluorescence of the samples was measured using a 1450 Micro Beta luminometer (Wallac, Finland).

RNA and Protein Analysis—Total RNA was prepared and analyzed by Northern blot as described previously (25). Probes were labeled with 32PdCTP using the random priming kit from Stratagene, and hybridizations were performed at 42 °C in a 50% formamide buffer. Blots were subjected to digital imaging (FujixBAS1000). GAPDH mRNAs were obtained for cells maintained in control medium and transfected with PPARδ (A) or PPARγ (B) vectors and are the mean ± S.D. of three separate experiments.

RESULTS

Characterization of a Dominant-Negative PPARδ Mutant—The PPARδE411F mutant was obtained by replacing Glu-411 by a proline residue. This mutated PPARδ was assayed for activation of a PPAR-responsive reporter gene and for dominant-negative activity against either native PPARδ or PPARγ. HEK-293 cells were transfected with a PPAR-responsive luciferase reporter (27) and an expression vector for the obligate partner RXRα. As shown in Fig. 1, treatment of these cells with 2BrP, a non-metabolized long-chain fatty acid (28) and potent activator of PPARδ (20) resulted in a very moderate induction of luciferase. Cells transfected with the PPARδ expression vector showed a 12-fold 2BrP-dependent activation. In contrast, no activation was observed in cells transfected with the mutated PPARδ, indicating that this mutant is inactive.

The dominant-negative activity of PPARδE411F was then
investigated by transfection of HEK-293 cells with a constant amount of PPARδ (Fig. 1A) or PPARγ (Fig. 1B) expression vector and increasing amounts of PPARδE411P expression vector. These experiments revealed that PPARδE411P inhibits, in a dose-dependent manner, the PPARδ-mediated transactivation. Luciferase induction was decreased by 50% and 85% when the mutated PPARδ was used in a 4- and 20-fold excess, respectively (Fig. 1A). In contrast, PPARδE411P did not inhibit rosiglitazone-induced and PPAR-Y-mediated transactivation of the reporter gene (Fig. 1B). Taken together, these observations indicated that the PPARδE411P exerts a dominant-negative activity specifically on the PPARδ-mediated transactivation.

Isolation of Stable Ob1771 Cell Population Expressing Either Native or Dominant-Negative Mutant PPARδ—Expression of either PPARδ or dominant-negative mutant PPARδE411P was accomplished in Ob1771 by retroviral infection (11). As shown in Fig. 2A, Ob1771Biz cells expressed at day 1 post-confluence the endogenous PPARδ mRNA at the expected size of 3.5 kb. A stronger signal was found at about 5 kb corresponding to the viral transcript in both Ob1771PPARδ and Ob1771PPARδE411P. Further experiments revealed that the level of endogenous PPARδ mRNA increased by 4-fold during the first week after confluence in all cell populations, whereas expression of BizeoneoPPARδ and BizeoneoPPARδE411P mRNA remained unchanged (not shown). Western blot analysis, performed with an antiserum directed against the PPAR δA/B domain and thus cross-reacting with both native and mutated proteins, revealed that at day 1 post-confluence Ob1771PPARδ and Ob1771PPARδE411P cells contained, respectively, 8- and 6-fold more PPARδ protein than did control Ob1771Biz cells (Fig. 2B).

Effects of PPARδ and PPARδE411P Expression on Fatty Acid Responsiveness—To investigate the effects of PPARδ and the dominant-negative PPARδ mutant on responsiveness to LCFA-induced transcription, Ob1771Biz, Ob1771PPARδ, and Ob1771PPARδE411P cell populations were grown to confluence and then exposed for 2 days to increasing concentrations of 2BrP. As described previously for parental Ob1771 cells (29), control Ob1771Biz cells showed a fatty acid dose-dependent induction of the fatty acid transporter FAT and ALBP mRNA (Fig. 3). Induction of these genes was markedly enhanced in Ob1771 overexpressing PPARδ. These cells were also more sensitive to 2BrP than control cells (EC₅₀ of about 10 μM in Ob1771PPARδ versus greater than 30 μM in Ob1771Biz).

In contrast, Ob1771 expressing the dominant-negative PPARδ displayed a reduced induction of FAT and ALBP mRNA even at higher fatty acid concentrations. Interestingly, the mutated protein did not completely abolish the transcriptional response to 2BrP.
Adipogenic Potential of Fatty Acid-activated PPAR®

Effects of PPAR® and dominant-negative PPAR® on GPDH expression in Ob1771 cells. Ob1771Biz (■), Ob1771PPAR® (●), and Ob1771PPAR®E411P (▲) cells were maintained as in Fig. 4 and GPDH specific activity was determined as described under “Experimental Procedures” at days 9 and 14 post-confluence. Results are the mean ± S.D. from three separate experiments.

Effects of PPAR® and PPAR®E411P on Expression of PPAR®—Because PPAR® plays a crucial role in terminal differentiation, we investigated its expression pattern in the three cell populations treated with 25 μM 2BrP during the first 5 days with increasing concentrations of 2BrP. Adipogenesis was estimated by Oil Red O staining (Fig. 4) and by determination of cellular triglyceride amounts (Fig. 5) at day 14 post-confluence and measurements of GPDH activity at days 9 and 14 (Fig. 6).

As described previously for the original Ob1771 cell line (4), 2BrP treatment during the preadipose state enhanced terminal differentiation in Ob1771Biz cells in a dose-dependent manner, as shown by the tremendous increase of triglyceride accumulation (Figs. 4 and 5). The adipogenic effect of the fatty acid was also illustrated by the induction of GPDH activity during the course of differentiation (day 9) or at the end of the process (day 14).

Compared with control cells, Ob1771PPAR® cells displayed an increased ability to differentiate and enhanced fatty acid sensitivity. This is illustrated by greater increases of both triglyceride accumulation (Figs. 4 and 5) and GPDH activity (Fig. 6) occurring at lower 2BrP concentrations. Interestingly, as shown by the Oil Red O staining, adipose differentiation was nearly complete when the cells were treated by 25 μM fatty acid, which suggests that PPAR® overexpression dramatically promoted the commitment of preadipose cells to terminal differentiation.

The decrease of PPAR® activity in Ob1771, expressing the dominant-negative form of this nuclear receptor, resulted in a significant reduction of adipose differentiation. Indeed, Ob1771PPAR®E411P cells did not accumulate lipids when maintained in low 2BrP concentrations. At high concentrations of 2BrP, these cells displayed moderate adipogenesis (Fig. 4) and contained less triglyceride than control cells (Fig. 5). This is confirmed by the significantly lower GPDH activities measured in Ob1771PPAR®E411P than in control cells under all conditions assayed (Fig. 6).

Effects of PPAR® and PPAR®E411P on Expression of PPAR®—Because PPAR® plays a crucial role in terminal differentiation, we investigated its expression pattern in the three cell populations treated with 25 μM 2BrP during the first 5 days after confluence. As described for the original Ob1771 line (20), in Ob1771Biz cells, PPAR® mRNA emerged after confluence and gradually increased until terminal differentiation (Fig. 7). In Ob1771PPAR®, PPAR® mRNA was already detected at confluence and accumulated thereafter to reach a maximal value at day 6. Noteworthy, at the end of adipose differentiation, i.e. day 14, PPAR® mRNA amounts were nearly similar in the two cell populations. In contrast, expression of the dominant-negative PPAR® resulted in a marked down-regulation of PPAR® mRNA. Expression levels remained relatively low and were, at day 14 post-confluence, 6-fold lower than those measured in control cells.

Expression of the Dominant-Negative PPAR® Severely Decreased 3T3-F442A Cell Differentiation—The effects of dominant-negative PPAR® were also investigated in the 3T3-F442A preadipose cell line, which was established from mouse embryo (24). Cell populations were obtained after infection with retroviral pBizeoneo vector with or without the dominant-negative PPAR® coding sequence. Fig. 8A shows that 442Abiz cells expressed a significant level of PPAR® at confluence, whereas PPAR® protein was 8-fold more abundant in confluent 442APPAR®E411P cells. Exposure for 4 days after confluence to 10 μM 2BrP was associated with low adipogenesis in 442APPAR®E411P cells, indicating that the dominant-negative PPAR® mutant strongly repressed the process. This is evidenced by the marked reduction of Oil Red O staining in 442APPAR®E411P population. Although treatment of these cells with 2BrP significantly increased lipid accumulation, levels still remained lower than those observed in 442Abiz cells maintained in control medium without 2BrP (Fig. 8B). The time course of PPAR® gene expression was investigated in 442Abiz and 442APPAR®E411P cells exposed to 2BrP. In 442Abiz, PPAR® mRNA emerged at day 2 post-confluence and then accumulated rapidly to reach a maximal level at day 5. On the other hand, the induction of PPAR® mRNA was seriously delayed and reduced in 442APPAR®E411P cells, i.e. emerging only at day 5 and remaining lower than in control cells at all times of determination (Fig. 8C). Consistent with the Oil Red O staining, 442APPAR®E411P cells expressed lower amounts of...
ALBP, FAT, and GPDH mRNAs as control cells when maintained in the absence or presence of 2BrP treatment (Fig. 5D). These findings demonstrate that PPARδ is important for LCFA regulation of 3T3-F442A differentiation.

**DISCUSSION**

This study is a first examination of the role of PPARδ in mediating LCFA regulation of gene expression and adipogenesis in preadipose cells. Two complementary approaches have been used in the study, i.e. overexpression of the native nuclear receptor and expression of a dominant-negative PPARδ mutant.

As would be predicted based on studies with other nuclear receptors (17), the substitution of a glutamate residue by a proline at position 411 in PPARδ generates a protein without transcriptional activity and which exerts an inhibitory effect on the endogenous PPARδ. With other nuclear receptors, such mutations yield proteins that bind the ligand and the DNA-responsive element but that constitutively remain in a repressed form (19). Consequently, the inhibitory action of the constitutively repressed PPARδE411P mutant may reflect its competition with endogenous native PPARδ for binding to the PPRE. However, regardless of the underlying mechanism behind the dominant-negative activity of PPARδE411P, it is worth noting that the mutant did not exert a complete inhibition on the native receptor even when used in high excess (Fig. 1A) and did not affect the transcriptional activity of PPARγ (Fig. 1B). The lack of effect on PPARγ probably relates to the higher affinity of the γ isoform for the PPRE as compared with that of PPARδ. Such a difference in binding affinities between the two isoforms for several natural PPRE has been previously documented by electrophoretic mobility shift assay experiments (30).

This work clearly demonstrates that a change in PPARδ level or activity strongly alters the response of Ob1771 cells to LCFA and that this nuclear receptor acts early in the adipose differentiation time course. Preadipose Ob1771PPARδ cells, in which the PPARδ level was increased by retroviral infection, display a magnified response to fatty acids as shown by higher induction of FAT and ALBP gene expression at low fatty acid concentrations (Fig. 3).

The adipogenic action of fatty acids in promoting terminal differentiation also occurs at lower concentration in Ob1771PPARδ as shown by Oil Red O staining (Fig. 4), by GPDH activity (Fig. 5), and by triglyceride accumulation (Fig. 6). Furthermore, the almost complete terminal differentiation, shown by the homogenous Oil Red O staining observed in Ob1771PPARδ exposed for only the first 5 days to 2BrP (Fig. 4), strongly supports a crucial role of LCFA activated-PPARδ during early confluent phase in promoting the commitment of preadipocytes to adipogenesis. In addition to enhancing the effects of added fatty acids, the increase in PPARδ expression also exerts a potent action on terminal adipose differentiation of cells maintained in control medium. Ob1771PPARδ cells accumulate significantly more lipids (Fig. 5) and express more GPDH activity (Fig. 6) than do control cells. The considerable increase of terminal differentiation observed in the absence of added 2BrP could be explained by increased sensitivity to the effects of LCFA from the serum or from endogenous origin or to other naturally occurring activators such as prostacyclin, a potent PPARδ activator (7) synthesized by early confluent Ob1771 cells (31).

The role of PPARδ as a nuclear mediator of LCFA effects on gene transcription and adipose differentiation is confirmed by the demonstration that expressing the dominant-negative mutant in Ob1771 cells considerably attenuates 2BrP-induced transcriptions of FAT and ALBP genes in preadipose cells (Fig. 3) and 2BrP enhancement of adipogenesis (Fig. 4). However, the cells remain able to respond to the fatty acid derivative, as shown by exposure to high concentrations of 2BrP. Morphological (Fig. 4) and biochemical investigations (Figs. 5 and 6) indicate that expression of the dominant-negative mutant, by partially inhibiting action of the endogenous PPARδ, dramatically impairs terminal differentiation of Ob1771 cells. Ob1771PPARδE411P cells do not undergo terminal differentiation when maintained in medium containing low concentrations of activator but display adipogenesis when high concentrations of 2BrP are used. Residual responses during short term or long term exposure to high concentrations of LCFA are not surprising, because transactivation experiments revealed that the dominant-negative PPARδ mutant, even when used at a high excess, does not completely suppress fatty acid activation of the native nuclear receptor (Fig. 1). The amount of the mutated protein expressed in Ob1771PPARδE411P at day 1 after confluence was estimated to be approximately 6-fold
higher than the endogenous PPAR (Fig. 2B). Thus, in Ob1771PPARδE411P cells exposed to high concentrations of 2BrP, the amount of activated native PPARδ may be high enough to effectively compete with the mutated repressed receptor for binding to the PPRE and to allow transcription of LCFA-responsive genes. It is possible that, at high concentrations of LCFA, there is accumulation of ligand-activated native PPARδ, which favors the binding of the active transcription factor to the PPRE of LCFA-responsive gene promoters.

The respective positive or negative actions of either native or dominant-negative PPARδ on terminal differentiation are a likely consequence of the alterations of PPARγ expression. Although overexpression of the native nuclear receptor did not significantly change the maximal expression of PPARγ, it resulted in the earlier induction of its expression when compared with control cells. Expression of the dominant-negative mutant led to an impairment of PPARγ expression during the differentiation phase (Fig. 7). Thus, the pattern of PPARγ expression in the three different Ob1771-derived cell lines used in this study supports the interpretation that LCFA-activated PPARδ controls PPARγ gene expression and that PPARγ is crucial for the induction of genes related to terminal differentiation.

These findings were applicable to both Ob1771 and 3T3F442A cells and indicated that they are not dependent on nor specific to a particular cell line. For example, despite the fact that terminal differentiation of 3T3-F442A cells is less dependent on fatty acid supply as shown for 442Abiz cells (Fig. 8, A and C), expression of the dominant-negative PPARγ in 3T3-F442A cells severely reduces adipogenesis in a way similar to Ob1771 cells.

In summary, the observations reported in this study, clearly establish the role for PPARδ as nuclear mediator of LCFA-mediated transcriptional and adipogenic actions in a preadipose cell context. The findings suggest that changes in the amount or activity of this nuclear receptor in preadipose cells may have important functional consequences with respect to the response of adipose mass to nutritional changes. Possibly, up-regulation of the receptor would result in hypersensitivity to LCFA effects in increasing adipose tissue mass, whereas down-regulation may confer resistance to LCFA. PPARδ is also expressed in various tissues, including heart, skeletal muscle, and intestine, and it would be of interest to characterize what tissue-specific effects up- or down-regulation of this nuclear receptor would have in the whole animal. The dominant-negative PPARδ mutant described in this study can be used to selectively inhibit LCFA-induced transcriptional activation in particular tissues. The construction of transgenic animals expressing the PPARδE411P mutant in a tissue-specific manner would provide valuable information on the role of PPARδ in various tissues.

Acknowledgments—We thank Nada A. Abumrad (Stony Brook, NY) and Ellen Van Obberghen-Schilling (Nice, France) for critical comments and review of the manuscript and Delphine Brignon for expert technical assistance.

REFERENCES

1. Faust, I. M., Johnson, P. R., Stern, J. S., and Hirsch, J. (1978) Am. J. Physiol. 235, E279–E286
2. Klyde, J. B., and Hirsch, J. (1979) J. Lipid Res. 20, 705–715
3. Shillabeer, G., and Lau, D. C. (1994) J. Lipid Res. 35, 592–600
4. Amri, E. Z., Ailhaud, G., and Grimaldi, P. A. (1994) J. Lipid Res. 35, 930–937
5. Tontonoz, P., Hu, E., and Spiegelman, B. M. (1994) Cell 79, 1147–1156
6. Spiegelman, B. M., and Flier, J. S. (1996) Cell 87, 377–389
7. Brun, R. P., Tontonoz, P., Forman, B. M., Ellis, R., Chen, J., Evans, R. M., and Spiegelman, B. M. (1996) Genes Dev. 10, 974–984
8. Gurnell, M., Wentworth, J. M., Agostine, M., Adams, M., Collingwood, T. N., Provenzano, C., Browne, P. O., Rajanayagam, O., Burris, T. F., Schwabe, J. W., Lazar, M. A., and Chatterjee, V. K. (2000) J. Biol. Chem. 275, 5734–5739
9. Lehman, J. M., Moore, L. B., Smith-Oliver, T. A., Wilkinson, W. O., Wilson, T. M., and Kliewer, S. A. (1995) J. Biol. Chem. 270, 12953–12956
10. Forman, B. M., Tontonoz, P., Chen, J., Burris, R. P., Spiegelman, B. M., and Evans, R. M. (1995) Cell 83, 803–812
11. Bastie, C., Holat, D., Gaillard, D., Jehl-Pietri, C., and Grimaldi, P. A. (1999) J. Biol. Chem. 274, 21920–21925
12. Schulman, I. G., Juguillon, H., and Evans, R. M. (1996) Mol. Cell. Biol. 16, 3907–3913
13. Fritsch, M. C., Leary, C. M., Furlow, J. D., Ahrens, H., Schuh, T. J., Mueller, G. C., and Gorski, J. (1992) Biochemistry 31, 5303–5311
14. Voegel, J. J., Heine, M. J., Zechel, C., Chambon, P., and Gronemeyer, H. (1996) EMBO J. 15, 3667–3675
15. Tate, B. F., and Grippo, J. F. (1995) J. Biol. Chem. 270, 20258–20263
16. Banaihmad, A., Leng, X., Burris, T. P., Tsai, S. Y., Tsai, M. J., and O'Malley, B. W. (1995) Mol. Cell. Biol. 15, 76–86
17. Durand, B., Saunders, M., Gaudon, C., Roy, B., Losson, R., and Chambon, P. (1994) EMBO J. 13, 5370–5382
18. Xu, H. E., Lamber, M. H., Montana, V. G., Parks, D. J., Blanchard, S. G., Brown, P. J., Sternbach, D. B., Lehmann, J. M., Wisely, G. B., Wilson, T. M., Kliexer, S. A., and Milburn, M. V. (1999) Mol. Cell 3, 397–403
19. Glass, C. K., Rose, D. W., and Rosenfeld, M. G. (1997) Proc. Natl. Acad. Sci. U. S. A. 94, 5370–5382
20. Amri, E. Z., Bonino, F., Ailhaud, G., Abumrad, N. A., and Grimaldi, P. A. (1995) J. Biol. Chem. 270, 2367–2371
21. Viville, S. (1995) Methods Mol. Biol. 31, 57–65
22. Green, H., and Kehinde, O. (1994) Cell 7, 113–116
23. Amri, E. Z., Dani, C., Doglio, A., Etienne, J., Grimaldi, P., and Ailhaud, G. (1986) Biochem. J. 238, 115–122
24. Green, H., and Kehinde, O. (1994) Cell 7, 105–113
25. Negrel, R., Grimaldi, P., and Ailhaud, G. (1978) Proc. Natl. Acad. Sci. U. S. A. 75, 6054–6058
26. Lowry, O. H., Rosebrough, N. J., Farr, A. L., and Randall, R. J. (1951) J. Biol. Chem. 193, 173–181
27. Kliexer, S. A., Umesono, K., Nooan, D. J., Heyman, R., and Evans, R. M. (1992) Nature 358, 771–774
28. Grimaldi, P. A., Kozubel, S. M., Whitesell, R. R., and Abumrad, N. A. (1992) Proc. Natl. Acad. Sci. U. S. A. 89, 10930–10934
29. Amri, E. Z., Bertrand, B., Ailhaud, G., and Grimaldi, P. (1991) J. Lipid Res. 32, 1449–1456
30. Juge-Aubry, C., Pernin, A., Favez, T., Burger, A. G., Wahli, W., Meier, C. A., and Desvergne, B. (1997) J. Biol. Chem. 272, 25252–25259
31. Negrel, R., and Ailhaud, G. (1981) Biochem. Cell Biol. Commun. 59, 768–777
Alterations of Peroxisome Proliferator-activated Receptor δ Activity Affect Fatty Acid-controlled Adipose Differentiation
Claire Bastie, Serge Luquet, Dorte Holst, Chantal Jehl-Pietri and Paul A. Grimaldi

J. Biol. Chem. 2000, 275:38768-38773.
doi: 10.1074/jbc.M006450200 originally published online September 15, 2000

Access the most updated version of this article at doi: 10.1074/jbc.M006450200

Alerts:
• When this article is cited
• When a correction for this article is posted

Click here to choose from all of JBC's e-mail alerts

This article cites 31 references, 16 of which can be accessed free at
http://www.jbc.org/content/275/49/38768.full.html#ref-list-1