Characterization of the Fasting-induced Adipose Factor FIAF, a Novel Peroxisome Proliferator-activated Receptor Target Gene*

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Fasting is associated with significant changes in nutrient metabolism, many of which are governed by transcription factors that regulate the expression of rate-limiting enzymes. One factor that plays an important role in the metabolic response to fasting is the peroxisome proliferator-activated receptor α (PPARα). To gain more insight into the role of PPARα during fasting, and into the regulation of metabolism during fasting in general, a search for unknown PPARα target genes was performed. Using subtractive hybridization (SABRE) comparing liver mRNA from wild-type and PPARα null mice, we isolated a novel PPARα target gene, encoding the secreted protein FIAF (for fasting induced adipose factor), that belongs to the family of fibrinogen/angiopoietin-like proteins. FIAF is predominantly expressed in adipose tissue and is strongly up-regulated by fasting in white adipose tissue and liver. Moreover, FIAF mRNA is decreased in white adipose tissue of PPARα−/− mice. FIAF protein can be detected in various tissues and in blood plasma, suggesting that FIAF has an endocrine function. Its plasma abundance is increased by fasting and decreased by chronic high fat feeding. The data suggest that FIAF represents a novel endocrine signal involved in the regulation of metabolism, especially under fasting conditions.

In many developed and developing countries, the prevalence of diabetes, particularly type II diabetes, is increasing at an alarming rate. Despite intensive research over the past decades, the knowledge about the metabolic derangements precipitating to and accompanying type II diabetes remains fragmentary. One factor that has limited progress of diabetes research has been a lack of clear understanding of the regulation of nutrient metabolism under normal, non-diabetic conditions. Indeed, much still needs to be learned about the genetics of metabolism during various physiological states, such as fasting.

Fasting can be described as a state when food intake has been arrested for a significant amount of time. The absence of energy entering the body evokes a complex physiological response aimed at maintaining whole body homeostasis. A critical event in the fasting response is the liberation of fatty acids from the adipose tissue and their preferential use as an energy substrate in tissues such as skeletal muscle and liver. The metabolic adaptations accompanying fasting are governed by numerous endocrine and cellular factors. Fasting results in pronounced changes in the plasma concentrations of important metabolic hormones such as insulin, glucocorticoids, leptin, and glucagon. In addition, fasting causes altered expression levels of important transcription factors, such as sterol response element-binding protein (1), c-Myc (2), and peroxisome proliferator-activated receptor α (PPARα) (3), directing specific changes in the expression of metabolic enzymes. We and others (3, 4) have recently shown the important role of PPARα in the fasting response. By stimulating the oxidation of fatty acids in liver, this transcription factor assures an efficient output of ketone bodies and glucose by the liver.

Besides PPARα, two other PPARs (β and γ) are currently known (5). All belong to the superfamily of nuclear hormone receptors, which encompasses a large collection of transcription factors that regulate transcription in response to small lipophilic compounds such as retinoic acid, vitamin D, thyroid hormone, and fatty acids (6). Like other nuclear hormone receptor, PPARs bind to the promoter of target genes and stimulate transcription after binding of a specific ligand. In the case of PPARα, a variety of fatty acids and fatty acid derivatives have been shown to bind and activate PPARα. This includes long-chain unsaturated fatty acids such as linoleic acid; branched, conjugated, and oxidized fatty acids such as phytanic acid and conjugated linoleic acid; and eicosanoids such as 8(S)-hydroxyeicosatetraenoic acid and leukotriene B4 (5).

Functionally, the PPARα and PPARγ isotypes have been relatively well characterized. For PPARα, it has been shown, both in vitro and in vivo, that this receptor plays an important role in the oxidation of fatty acids in the liver by activating the expression of many genes involved in this metabolic pathway (7, 8). PPARα also mediates the effect of peroxisome proliferators on hepatic cell proliferation, as demonstrated by the observation that mice that lack PPARα are refractory to the effects of peroxisome proliferators (9, 10). Whereas PPARα

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† The abbreviations used are: PPAR, peroxisome proliferator-activated receptor; FIAF, fasting-induced adipose factor; SABRE, selective amplification via biotin and restriction-mediated enrichment; GFF, green fluorescent protein; bp, base pairs; kb, kilobase(s); ORF, open reading frame; WAT, white adipose tissue; BAT, brown adipose tissue; HFARP, hepatic fibrinogen/angiopoietin-related protein; PAG, polyacrylamide gel electrophoresis.

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functions in lipid catabolism, the role of PPARγ seems to be geared toward anabolic pathways, particularly in adipose tissue. Activation of PPARγ in preadipocytes is sufficient to direct the cell toward the adipocyte differentiation program (11), leading to dramatic build-up of lipid inside the cell. Other tissues where PPARγ may play a role include the colon and monocytic/macrophages where PPARγ may play a role in cytokine production (12).

Studies with PPARα null mice have shown that PPARα becomes especially important during fasting (3, 4). When fasted, these mice suffer from a defect in fatty acid oxidation and ketogenesis, resulting in elevated plasma free fatty acid levels, hypoketonemia, hypothermia, and hypoglycemia. To gain more insight into the function of PPARα and to increase our understanding of the genetic regulation of metabolism during fasting, an unbiased subtractive hybridization assay was performed to search for unknown PPARα target genes. Here we describe the isolation and characterization of a novel PPARα target gene, FIAF, for fasting-induced adipose factor, implicated in the metabolic response to fasting.

EXPERIMENTAL PROCEDURES

Animals—Mice were housed in a temperature-controlled room (23 °C) on a 10-h dark, 14-h light cycle. Pure-bred wild-type or PPARα null mice on a C57BL/6J background were used (7). Animal experiments were approved by the animal authorization commission of the canton of Vaud (Switzerland). Fasted animals were deprived of food for 24 h, starting at the beginning of the light cycle. Fed animals were sacrificed at the end of the dark cycle. WY14643 was administered by dissolving it in the drinking water (0.1%) for 3 weeks. The high fat diet (3, 4) became especially important during fasting (3, 4). When fasted, tissues were homogenized with a Polytron homogenizer in lysis/denaturation solution (2.5 mg/ml) and further clarified by centrifugation via a Qiashredder (Qiagen). 20 μl of lysate was hybridized to 10 ng of specific FIAF probe (1 × 10^6 cpm/mg) and 10 ng of L27 probe (1 × 10^6 cpm/mg). RNase digestion (10 units/ml RNase A; 400 units/ml RNase T1) was carried out for all probes at 37 °C for 20 min. The products of ribonuclease protection assay were resolved in a 6% electrophoretic gradient denaturing polyacrylamide gel. Protein was precipitated by adding 8 volumes of cold acetone and leaving the medium at −20 °C for several hours. Protein was pelleted by centrifugation and, after washing, redissolved in SDS-PAGE loading buffer. SDS-PAGE was further performed according to standard procedures.

RESULTS

We searched for unknown genes regulated by PPARα, we compared liver mRNA from wild-type and PPARα null mice by performing the subtractive hybridization assay SABRE described above (13). One of the cDNA fragments isolated corresponded to an unknown gene (further referred to as FIAF for reasons explained below), whose differential expression between wild-type and PPARα null mice was evident by Northern blot (Fig. 1A). To obtain the full-length mouse cDNA of FIAF, 5′- and 3′-RACE were carried out using internal primers of the 600-bp cDNA fragment (Fig. 1B). Primer extension revealed that the 5′-RACE fragment stopped about 25 bp short of the transcriptional start site. The genomic sequence could be directly extracted from the GenBank data base (accession number AF110520.1), because the mouse FIAF gene happens to be located in the mouse major histocompatibility complex II locus on chromosome 17, in a region that has been completely sequenced. With the genomic sequence information, the core promoter containing a putative TATA box could be located. The mouse FIAF gene contains seven exons and six introns, spanning about 7 kb (Fig. 1C). From the full-length cDNA an ORF of 1233 bp could be derived, giving rise to a protein of 410 amino acids and a predicted molecular mass of around 46 kDa (Fig. 1B). Further analysis of the primary sequence revealed similarity with a family of proteins that contain a so-called fibrinogen-like domain. In addition, a coiled-coil domain that typically precedes the fibrinogen-like domain was present. The highest similarity was found with a group of angiopoietins and with ficolin-A. Angiopoietins have been implicated in endothelial developmental processes, whereas ficolin seems to bind bacterial surfaces. However, we found that the primary amino acid level did not exceed 24%, suggesting that the function of FIAF is likely to be different from the angiopoietins and from ficolin. In analogy with other fibrinogen-like proteins, a putative signal sequence was found at the N terminus of FIAF, possibly directing secretion of the protein. To investigate whether the protein was indeed secreted, the ORF was sub-cloned into the green fluorescence protein (GFP) fusion vector pEGFP-N2 (Clontech), which contains a strong cylomegalovirus promoter, to create the mFIAF-GFP fusion construct (GFP is located toward the C terminus). To obtain mFIAF not fused to GFP, the termination codon of mFIAF was left intact. HEK293 cells were cultured in Dulbecco’s modified Eagle’s medium with 5% fetal calf serum. Cells were transfected with the vectors indicated above by calcium-phosphate precipitation immediately after transfection, medium was replaced by Dulbecco’s modified Eagle’s medium without calf serum. 24 h after transfection, the medium was harvested, centrifuged to remove remaining cells, and stored at −20 °C. Protein was precipitated by adding 8 volumes of cold acetone and leaving the medium at −20 °C for several hours. Protein was pelleted by centrifugation and, after washing, redissolved in SDS-PAGE loading buffer. SDS-PAGE was further performed according to standard procedures.
cloned behind a cytomegalovirus promoter and the vector was transfected into HEK293 cells. The ORF was also linked to green fluorescent protein to create a GFP fusion protein. A polyclonal antibody directed against a non-conserved peptide in the N-terminal region was synthesized. As shown in Fig. 2, FIAF could be detected in the culture medium by Western blot, both as the GFP fusion protein (lane 2), and as the native protein (lane 3), indicating that FIAF is indeed secreted.

Although FIAF was cloned from a liver cDNA library, it is probably expressed elsewhere as well. To examine the expression profile of FIAF, Northern blot was performed with liver RNA from wild-type and PPARα null mice killed in the middle of the light cycle. As shown in Fig. 2, FIAF could be detected in the culture medium by Western blot, both as the GFP fusion protein (lane 2), and as the native protein (lane 3), indicating that FIAF is indeed secreted.

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Because FIAF was less expressed in liver of PPARα null mice than in wild-type mice, it is possible that FIAF is a target gene of PPARα and of synthetic PPARα ligands such as fibrates. To study the effect of PPARα on FIAF expression, mice were treated with the potent PPARα ligand WY14643. In wild-type mice but not in PPARα null mice, WY14643 increased expression of FIAF, providing further evidence that FIAF is a PPARα target gene in liver (Fig. 4A). To study the factors influencing the expression of FIAF and thereby provide some clues about the possible function of this protein, the effect of fasting was examined. Fasting was chosen because it is accompanied by an increase in PPARα expression (3). Moreover, the effects of PPARα deletion become more manifest during fasting (3, 4).

Interestingly, fasting caused a dramatic increase in FIAF expression in liver, but the PPARα dependence was completely lost (Fig. 4B). A marked increase in FIAF expression was observed in white adipose tissue (WAT) as well. For this reason the protein was named FIAF, for fasting induced adipose factor. Remarkably, in WAT FIAF expression was higher in PPARα null mice than in wild-type mice.

WAT contains very little PPARα (15). In contrast, the PPARγ isotype is very abundant in WAT (15). To examine whether expression of FIAF in adipose tissue is under control of PPARγ,
FIAF mRNA was determined in WAT of heterozygous PPARγ mutant mice. Heterozygous PPARγ mutant mice were chosen, because homozygous null mice are embryonically lethal (16, 17). As shown in Fig. 5, mFIAF mRNA expression was down-regulated in PPARγ1/2 mice.

Because FIAF is a secreted protein, it was of interest to investigate whether it may be circulating in the blood plasma. Interestingly, using the purified antibody against FIAF in Western blotting, a band could be detected in plasma at exactly the same molecular weight as FIAF protein produced in cell culture, suggesting that it corresponds to FIAF (Fig. 6A). This band was also observed in liver, kidney, WAT, and brown adipose tissue (BAT), tissues where FIAF is produced (Fig. 6, A and B). In kidney, BAT, and WAT, another band was observed with a slightly higher molecular weight than the original band. Most likely, this slower moving band represents FIAF immediately after synthesis, with the signal sequence still attached. It is also possible that the two bands represent different glycosylated forms of the protein, which have been previously shown to occur for the angiopoietins. To corroborate that the band observed in plasma truly represented FIAF protein, the effect of fasting was examined. Fasting caused an approximate 2-fold increase in the intensity of the putative FIAF band, in accordance with the mRNA expression data showing an increased FIAF expression during fasting (Fig. 6C). Interestingly, prolonged feeding of a high fat diet, which was accompanied by an average 2.2-fold increase in epididymal fat mass, decreased the intensity of the putative FIAF band by about 2-fold (Fig. 6D). Modulation of FIAF abundance in plasma was, however, not associated with altered expression of mRNA levels in liver (Fig. 7A) or WAT (Fig. 7B).

DISCUSSION

Besides being important for the storage and subsequent release of fatty acids, research over the past decade has shown that white adipose tissue also has an important endocrine function. Factors such as plasminogen activator inhibitor 1, tumor necrosis factor α, and leptin are produced by the adipose tissue to exert effects elsewhere in the body. Here we describe the cloning of a novel fibrinogen/angiopoietin-like factor, primarily secreted from the adipose tissue, whose production is elevated during fasting and whose mRNA expression is stimulated by PPARα in liver and by PPARγ in WAT.

In recent years, a wealth of data has accumulated about leptin, the product of the mouse ob gene. Initially viewed as a sensor of the fat stores that acts on the hypothalamus to inhibit food intake, leptin is now realized to have a much broader role in energy homeostasis (18). This is exemplified by the observation that the expression of leptin in WAT is acutely reduced by fasting (19, 20), suggesting that leptin is also involved in short term metabolic regulation. In contrast to leptin, expression of FIAF is up-regulated during fasting. Furthermore, the abundance of FIAF in plasma is decreased with high fat feeding and increased WAT mass, an effect directly opposite to that observed with leptin (18). Finally, leptin is a negative target of
PPARγ and is overexpressed in WAT of PPARγ+/− mice (16, 21, 22), whereas FIAF mRNA is down-regulated in these mice. Although it remains speculative to suggest that FIAF and leptin have antagonistic functions, the opposite regulation between leptin and FIAF expression/production during various nutritional states and by PPARγ is nevertheless very interesting.

Our data clearly show that the expression of FIAF is strongly increased during fasting in both liver and WAT. This, together with the observation that expression of FIAF is increased by PPARα, whose critical involvement in the adaptive response to fasting has been well established (3, 4), suggests that FIAF is mainly important under fasting conditions. Interestingly, PPARα deletion had no effect on FIAF expression in the liver of fasted mice, a phenomenon that was previously observed for other PPARα target genes such as short chain acyl-CoA dehydrogenase and carnitine palmitoyl acyl-transferase I, which are genes whose expression is strongly stimulated by fasting as well (3). Most likely, the loss of PPARα dependence can be ascribed to other signaling pathways activated during fasting, which override the effect of PPARα. FIAF expression was found to be somewhat higher in WAT of PPARα null mice than wild-type mice (mainly evident in the fed state). This could either reflect a negative regulation of FIAF expression by PPARα in WAT (either directly or via other transcription factors) or a consequence of the metabolic derangements present in PPARα null mice. Increased expression levels of genes implicated in metabolism in WAT of PPARα null mice have been observed previously. Future research will have to establish more precisely what role FIAF plays in the metabolic response to fasting.

The closest family members of FIAF, the angiopoietins, are secreted proteins that act as ligands for receptor-like tyrosine kinases such as TIE2 (23, 24). Similar to the angiopoietins, it is likely that FIAF exerts its effect distant from its site of production, probably by binding to some kind of receptor. The detection of FIAF in plasma suggests that FIAF’s mode of action is endocrine, rather than autocrine or paracrine, although this remains to be proven. At the present time, no information is available regarding the molecular target of FIAF or about its target tissue(s).

It was observed that the abundance of FIAF in plasma is decreased on a chronic high fat diet. Remarkably, this was not accompanied by changes in mRNA expression in two major FIAF-producing tissues, liver and WAT. Besides being possibly caused by post-transcriptional effects, it is also conceivable that a high fat diet lowers plasma FIAF abundance by increasing its rate of breakdown. In the absence of any information on the identity and location of the putative FIAF receptor, this hypothesis would be very difficult to test.

It is remarkable that, despite much higher mRNA expression levels in WAT, FIAF protein seems to be more highly present in liver and kidney. One possibility that could explain this apparent discrepancy is that FIAF protein is stored in the latter tissues, whereas it is immediately secreted after synthesis in WAT. Alternatively, it is conceivable that the concentrated production of FIAF protein in liver and kidney reflects uptake rather than production. Again, to test this hypothesis, more information about the target tissues of FIAF is needed.

While this manuscript was in preparation, Kim et al. (25) reported on a hepatic fibrinogen/angiopoietin-related protein (HFARP) that is identical to our FIAF. As was found for FIAF, HFARP was secreted by COS-7 cells and was detected in circulating blood. The highest expression of HFARP was found in

2 S. Kersten and W. Wahl, unpublished data.
the liver, but WAT and BAT, where we found much higher expression levels, were omitted. According to these authors, HFARP acts as an apoptosis survival factor for vascular endothelial cells. It is not easy to reconcile this function with the predominant expression of FIAF/HFARP in adipose tissue and its marked up-regulation by fasting. Given the large divergence in sequence between FIAF and angiopoietins, these proteins are likely to have quite different functions.

In conclusion, we have isolated a novel gene that is a PPARα target gene in liver, and probably a PPARγ target gene in WAT, that encodes the secreted protein FIAF. Its high expression in adipose tissue and its up-regulation by fasting suggest an involvement of FIAF in the metabolic response to fasting. Moreover, its plasma levels are reduced by chronic high fat feeding. Future studies are needed to establish more precisely the role of FIAF in energy homeostasis.

REFERENCES

1. Horton, J. D., Bashmakov, Y., Shimomura, I., and Shimano, H. (1998) Proc. Natl. Acad. Sci. U. S. A. 95, 5987–5992
2. Corcos, D., Vaulont, S., Denis, N., Simon, M. P., Kitzis, A., Kahn, A., and Kruh, J. (1997) Oncogene Res. 2, 193–199
3. Kersten, S., Seydoux, J., Peters, J. M., Gonzalez, F. J., Desvergne, B., and Wahli, W. (1999) J. Clin. Invest. 103, 1489–1498
4. Leone, T. C., Weinheimer, C. J., and Kelly, D. P. (1999) Proc. Natl. Acad. Sci. U. S. A. 96, 7473–7478
5. Desvergne, B., and Wahli, W. (1999) Endocr. Rev. 20, 649–688
6. Gronemeyer, H., and Laudet, V. (1995) Protein Profile 2, 1173–1308
7. Lee, S. S., Pineau, T., Drago, J., Lee, E. J., Owens, J. W., Kroetz, D. L., Fernandez-Salguero, P. M., Westphal, H., and Gonzalez, F. J. (1995) Mol. Cell. Biol. 15, 3012–3022
8. Peters, J. M., Aoyama, T., Cattley, R. C., Nobumitsu, U., Hashimoto, T., and Gonzalez, F. J. (1998) Carcinogenesis 19, 1889–1994
9. Peters, J. M., Hennuyer, N., Staels, B., Fruchart, J.-C., Fievet, C., Gonzalez, F. J., and Auwerx, J. (1997) J. Biol. Chem. 272, 27307–27312
10. Aoyama, T., Peters, J. M., Iritani, N., Nakajima, T., Furihata, K., Hashimoto, T., and Gonzalez, F. J. (1998) J. Biol. Chem. 273, 5678–5684
11. Wu, Z., Puigserver, P., and Spiegelman, B. M. (1999) Curr. Opin. Cell Biol. 11, 689–694
12. Ricoe, M., Huang, J. T., Welch, J. S., and Glass, C. K. (1999) J. Leukocyte. Biol. 66, 733–739
13. Lavery, D. J., Lopez-Molina, L., Fleury-Olela, F., and Schibler, U. (1997) Proc. Natl. Acad. Sci. U. S. A. 94, 6831–6836
14. Haines, D. S., and Gillespie, D. H. (1992) BioTechniques 12, 736–741
15. Braissant, O., Poufelle, F., Scitto, C., Ducia, M., and Wahli, W. (1996) Endocrinology 137, 354–366
16. Kubota, N., Terauchi, Y., Miki, H., Tatemoto, H., Yamauchi, T., Kameda, K., Satoh, S., Nakano, R., Ishii, C., Sugiyama, T., Eto, K., Tsuhimoto, Y., Okuno, A., Murakami, K., Sekihara, H., Hasegawa, G., Naito, M., Taya, Y., Tanaka, S., Shiota, K., Kitamura, T., Fujita, T., Ezaki, O., Aizawa, S., Nagai, R., Tobe, K., Kimura, S., and Kadowaki, T., et al. (1999) Mol. Cell. 4, 587–609
17. Barak, Y., Nelson, M. C., Ong, E. S., Jones, Y. Z., Ruiz-Llorente, P., Chien, K. R., Koder, A., and Evans, R. M. (1999) Mol. Cell. 4, 597–609
18. Friedman, J. M., and Halaas, J. L. (1998) Nature 395, 763–770
19. Trayhurn, P., Thomas, M. E., Duncan, J. S., and Rayner, D. V. (1995) FEBS Lett. 368, 488–490
20. Vidal-Puig, A., Jimenez-Linan, M., Lovell, B. B., Hamann, A., Hu, E., Spiegelman, B., Flier, J. S., and Moller, D. E. (1996) J. Clin. Invest. 97, 2553–2561
21. Hellenberg, A. N., Susulic, V. S., Madura, J. P., Zhang, B., Moller, D. E., Tontonoz, P., Sarraf, P., Spiegelman, B. M., and Lovell, B. B. (1997) J. Biol. Chem. 272, 5283–5290
22. De Vos, P., Lefebvre, A. M., Miller, S. G., Guerre-Millo, M., Wong, K., Saladin, R., Hamann, L. G., Staels, B., Briggs, M. R., and Auwerx, J. (1996) J. Clin. Invest. 98, 1004–1009
23. Suri, C., Jones, P. F., Patan, S., Bartunkova, S., Maisonneuve, P. C., Davis, S., Sato, T. N., and Yancopoulos, G. D. (1996) Cell 87, 1171–1180
24. Davis, S., Aldrich, T. H., Jones, P. F., Acheson, A., Compton, D. L., Jain, V., Ryan, T. E., Bruno, J., Radziejewski, C., Maisonneuve, P. C., and Yancopoulos, G. D. (1996) Cell 87, 1171–1180
25. Kim, I., Kim, H.-G., Kim, H., Kim, H.-H., Park, S. K., Uhm, C.-S., Lee, Z. L., and Koh, G. Y. (2000) Biochem. J. 346, 603–610
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