Stearoyl-CoA desaturase (SCD) synthesizes oleate necessary for the biosynthesis of triglycerides and other lipids. Mice with a targeted disruption of the SCD1 gene are deficient in tissue oleate and have reduced expression of the sterol regulatory element-binding protein (SREBP) and its target genes. The SREBP-1c isoform is a known mediator of insulin action on hepatic gene expression, but its transcriptional effects due to glucose or fructose are still unclear. We found that fructose compared with glucose is a stronger inducer of SREBP-1c and lipogenic gene expression, causing a dramatic increase in hepatic triglyceride levels. However, when fed to the SCD1–/– mice, fructose failed to induce SREBP-1 or lipogenic genes and the triglyceride levels were not increased. Instead fructose feeding caused a decrease in hepatic triglycerogen and plasma glucose levels. The induction of SREBP-1 and lipogenic gene expression as well as the levels of liver triglycerides, glycogen, and plasma glucose was partially restored when the fructose diet was supplemented with very high levels of oleate (20% by weight) but not with palmitate, stearate, or linoleate. Fructose in a long term feeding induced the expression of SCD1 and that of other lipogenic genes in the liver of SREBP-1c–/– mice, and a further increase in expression of these genes occurred when the fructose diet was supplemented with oleate. Our observations demonstrated that oleate produced by SCD is necessary for fructose-mediated induction of lipogenic gene expression through SREBP-1c-dependent and -independent mechanisms and suggested that SCD1 gene expression is important in lipid and carbohydrate homeostasis.
SREBP-2 preferentially activates genes involved in cholesterol synthesis (37–39). The worldwide prevalence of obesity is increasing, and although it is probable that no single factor is responsible, environmental factors interacting with predisposing genetic factors are involved (40–42). One of these environmental elements is diet, and currently, changes in the diet are being studied as contributing factors to the development of obesity. Along with an increase in total energy consumption over the past decades, there has been a shift in the types of nutrients consumed worldwide (43). The consumption of fructose has increased, largely because of an increase in the consumption of soft drinks and many other beverages that contain high levels of fructose (43). The mechanisms by which fructose may contribute to the development of obesity and accompanying abnormalities of insulin resistance have not been well addressed.

We show in this study that when mice are fed either glucose or fructose individually, fructose is a stronger inducer of liver SREBP-1c and lipogenic gene expression than glucose. However, fructose failed to induce SREBP-1c and lipogenic gene expression in SCD1−/− mice. Fructose feeding was instead accompanied by a decrease in liver glycogen and plasma glucose levels. SREBP-1c and lipogenic gene expression, as well as triglyceride and glycogen levels, were partially restored in the SCD1−/− mice when the fructose diet was supplemented with high levels of dietary oleate and after feeding for 7 days. Separate or palmitate supplementation to the fructose diet did not induce SREBP-1c or lipogenic gene expression. Liver triglyceride, liver glycogen, and plasma glucose levels were not rescued. Long term feeding of fructose also induced the expression of SCD1 and other lipogenic genes in SCD1−/− mice. Supplemen
ting the fructose diet with oleate did change SCD1 mRNA levels but caused additional increase in the mRNA levels of FAS and ACC. Taken together, our observations demonstrated that fructose-mediated induction of SREBP-1c or lipogenic genes is highly dependent on SCD1 gene expression and suggested that regulation of SCD1 plays an important role in carbohydrate and lipid homeostasis.

EXPERIMENTAL PROCEDURES

Animals and Diets—The generation of SCD1−/− mice has been described previously (44). Pre-bred homozygous (SCD1+/+) and wild-type (SCD1+/−) mice on a pure 129/Sv background were used. The SREBP-1c−/− mice were from the Jackson Laboratory and were bred into 129/SvEv background at least for five generations. 16–20-week-old mice were used in all of the experiments. Three mice were housed caged and fed a standard chow diet (number 7001, Harlan Teklad), a 60% fructose diet (catalog number TD02518, Harlan Teklad), or a 60% glucose diet (TD02519) for 2 or 7 days. Triolein, tripalmitin, and tristearin (99% purity, Sigma) were supplemented to the fructose diet at 20 g weight % of diet. Dietary fat absorption was assessed by delivering 2 nmol bovine serum albumin complex containing 1 μCi of [3H]palmitate and phosphatidylcholine-liposome containing 1 μCi of [3H]cholestanol (American Radiolabeled Chemicals) by oral gavage to the mouse after a 4-h fast. Animals were given ad libitum access to food and water after gavage. Total feces were collected for 3 days, and the ratio of 14C to 3H radioactivity in aliquots of fecal extracts was used to calculate the percent dietary fat absorption. The breeding and care of the animals are in accordance with the protocols approved by the Animal Care Research Committee (ACRC) of the University of Wisconsin-Madison.

Materials—Radioactive [32P]dCTP (3000 Ci/mmol) was obtained from PerkinElmer Life Sciences. Thin layer chromatography plates (TLC Silica Gel G60) were from Merck (Darmstadt, Germany). The cDNA probes for SCD1, FAS, and SREBP-1 have been described previously (25). All of the other chemicals were purchased from Sigma. SREBP-1 and SREBP-2 antibodies were from Dr. Jay Horton (University of Texas Southwestern Medical Center).

Isolation and Analysis of RNA—Total RNA was isolated from livers of SCD1−/− mice and SREBP-1c−/− mice as well as the appropriate wild-type controls using TRIzol reagent (Invitrogen). The isolated RNA from livers of 4–6 mice in each group were pooled, and 15 μg of total RNA were separated by 0.1% agarose/2.2% formaldehyde gel electrophoresis and transferred onto a nylon membrane. The membrane was hybridized with [32P]-labeled cDNA probes. The cDNA probes for long chain fatty acyl-CoA elongase (LFAE, GenBankTM accession number Y053453), acetyl-CoA carboxylase (ACC, GenBankTM accession numbers J03808, NM000664), fructokinase (FK, GenBankTM accession number Y09335), and aldolase B (GenBankTM accession number AH011101) were prepared by RT-PCR. The primers used for PCR were as follows. For ACC, the 5′ primer was 5′-GGGACCTTTGAAATTTGCG-TGATTCTCA-3′ and the 3′ primer was 5′-GTCATACCTCATCATT-TACCTCAATC-3′. For long chain fatty acyl-CoA elongase, the 5′ primer was 5′-CTCTGGTTTCTGCGTGTACGG-3′ and the 3′ primer was 5′-GAATGCATCCGCTATGTCAT-3′. For FK, the 5′ primer was 5′-GAAT-
Glucose and Glycogen Metabolism—Plasma glucose was measured according to the methods of Roehrig and Allred (49). One-way ANOVA or Student’s t test with statistical significance set at p < 0.05.

RESULTS

Fig. 1 shows a Northern blot of total RNA isolated from the liver of wild-type mice that were fed chow, high glucose, or fructose diets for 7 days measuring the mRNA levels of SREBP-1 and lipogenic genes. The 7-day feeding period was used to ensure maximum induction of mRNA levels. Dietary glucose increased the mRNA levels of SREBP-1, SCD1, LFAE, FAS, and ACC by 1.5-, 4.7-, 2.8-, 2.3-, and 1.9-fold, whereas fructose increased the levels of these mRNAs by 2.6-, 19.6-, 7.9-, 7.0-, and 9.1-fold, respectively, relative to chow diet. The effect of glucose or fructose on the expression of SREBP isoforms was analyzed by RT-PCR. Fig. 1B shows that glucose induced the mRNA level of SREBP-1c isoform by 1.5-fold, whereas fructose induced it by 2.9-fold relative to chow diet. Glucose or fructose did not induce SREBP-1a and SREBP-2 mRNA expression. Consistent with the Northern blot, fructose induced the mature form of SREBP-1 protein 3.8-fold, whereas glucose did not induce it (Fig. 1C). The levels of the mature form of SREBP-2 protein were not altered by either sugar. These experiments indicated that fructose is a stronger inducer of SREBP-1c and lipogenic gene expression than glucose.

Mice with a targeted disruption of the SCD1 isoform have
wild type mice was not different (data not shown). These ex-
some containing [3H]sitostanol in the feces of
SCD1
tose did not induce
respectively, in the wild-type mice relative to chow diet, fruc-
tose did not induce SREBP-1, FAS, and ACC mRNA expression in the SCD1+/− mice. Food intake of the fructose diet was not different between SCD1+/− and wild-type mice (3.1 ± 0.3 g/day SCD1+/− mice versus 2.9 ± 0.4 g/day wild-type mice). To check the nutritional status of the mice, we measured the mRNA expression of fructokinase and aldolase B genes. These genes encode for fructokinase and aldolase B enzymes, which are increased by fructose feeding (50). Fig. 2A shows that fructose induced fructokinase and aldolase B mRNA levels by >2-fold in both wild type and SCD1+/− mice, demonstrating that both groups of mice were correctly fed fructose. Consistent with the Northern blot (Fig. 2A), Fig. 2B shows that fructose increased the content of the precursor and mature forms of SREBP-1 protein by 1.8- and 4-fold, respectively, in the wild-type mice, but no such induction was observed in the SCD1+/− mice. The content of the precursor and mature forms of SREBP-2 proteins was not changed in the wild-type and SCD1+/− mice in response to fructose feeding.

Oleate is major product of SCD (48). To determine whether oleate is required for the induction of SREBP-1c and lipogenic gene expression, SCD1+/− mice were fed a fructose diet supplemented with 5% triolein (18:1) for 2 or 7 days and mRNA expression of SREBP-1, FAS, and ACC were measured. Because there was no increase in the levels of these mRNAs in the liver of SCD1+/− mice (data not shown), the amount of triolein supplemented to the fructose diet was increased to 20% by weight. A two-day feeding of fructose induced SREBP-1 and lipogenic genes in the wild-type mice but not in the SCD1+/− mice (data not shown). Fig. 2A shows that 20% triolein (18:1) supplementation to the fructose diet for 2 days still did not increase the mRNA for SREBP-1, FAS, and ACC in the SCD1+/− mice, but a 4.3-, 3.5-, and 7.0-fold induction, respectively, to the fructose-fed mice occurred after a 7-day feeding period. Triolein supplementation caused a further increase in the expression of SREBP-1, FAS, and ACC mRNA levels in the wild-type mice, but the mRNA level of SCD1 was not increased. Consistent with the Northern blot (Fig. 2), 20% triolein feeding increased the content of the mature SREBP-1 protein in the wild-type and SCD1+/− mice 6.7- and 5.3-fold, respectively, to a chow diet feeding (Fig. 2B). The content of precursor and mature forms of SREBP-2 proteins were not affected by triolein feeding. Fructose supplemented with triolein (18:0) did not induce SREBP-1, FAS, and ACC mRNA levels, and the content of the mature form of SREBP-1 protein was not increased in SCD1+/− mice (Fig. 2B). The content of the precursor and mature form of SREBP-2 protein was not changed. In another experiment, 20% tripalmitin (16:0) or trilinolein (18:2n-6) supplementation to the fructose diet did not induce the mRNA levels for SREBP-1, ACC, and FAS in the SCD1+/− mice (Fig. 2C) and the levels of the mature form of SREBP-1 protein were not increased (Fig. 2D).

To determine whether oleate is required for fructose-mediated changes in triglyceride levels, we measured liver and plasma triglycerides in the SCD1+/+ and SCD1+/− mice after 7 days of feeding. Fig. 3A shows that fructose caused a 2.7-fold increase in liver triglyceride levels in the wild-type mice but that no increase in triglyceride content was observed in the SCD1+/− mice. Triolein (20%) supplementation caused a further 1.5-fold increase in liver triglyceride content relative to

Stearoyl-CoA Desaturase and Lipogenic Gene Expression

![Fig. 3. Liver triglycerides, plasma triglyceride, and liver fatty acid content of SCD1+/− and wild-type mice that were fed a diet of fructose or fructose supplemented with triolein, triglyceride, or tripalmitin. Mice (3–8 mice/group) were fed a chow diet (Chow), a high fructose fat-free diet (Fru), or a high fructose diet supplemented with 20% triolein (Fru+18:1), 20% triglyceride (Fru+18:0), or 20% tripalmitin (Fru+16:0) for 7 days. Plasma (A) and liver (B) triglyceride (TG) contents were measured as described under "Experimental Procedures." C, fatty acid contents in liver TG were analyzed by gas-liquid chromatography. #, p < 0.01 versus wild-type mice that were fed a chow diet; &, p < 0.05 versus wild-type mice that were fed the same diet; *, p < 0.05 versus SCD1+/− mice that were fed a fructose fat-free diet; $, p < 0.05 versus wild-type mice that were fed a fructose fat-free diet. MUFA, mono-unsaturated fatty acids. SFA, saturated fatty acids.](http://www.jbc.org/content/early/2017/10/20/JBC.M117.798220/F3.large.jpg)
fructose feeding in wild-type mice but caused a 4.8-fold increase in triglyceride content in the SCD1−/− mice. Tristearin or tripalmitin supplementation did not increase triglyceride levels in the SCD1−/− mice. Fig. 3B shows that fructose feeding did not cause a significant change in plasma triglyceride levels in the wild-type mice but caused a 54% decrease in plasma triglycerides in the SCD1−/− mice. The triglyceride levels were elevated to almost normal levels in the SCD1−/− mice when the fructose diet was supplemented with triolein. Tristearin or tripalmitin supplementation did not rescue plasma triglycerides in SCD1−/− mice. These observations indicated that oleate is required in the fructose-mediated elevation of liver triglyceride levels.

We then determined the total content of saturated and monounsaturated fatty acids in liver triglycerides of wild-type and SCD1−/− mice. Fig. 3C shows that fructose feeding increased the content of saturated and monounsaturated fatty acids 1.7- and 1.8-fold, respectively, in the wild-type mice relative to chow diet but that there was no increase in the content of these fatty acids in the SCD1−/− mice. Triolein (20%) supplementation increased the content of the saturated and monounsaturated fatty acids in the wild-type mice relative to the chow diet by a 2.8-fold and 3.6- and 3.1-fold increase in saturated and monounsaturated fatty acid content, respectively, in the liver of SCD1−/− mice. The increase in saturated fatty acid content of the triglyceride fraction suggested that triolein supplementation increased de novo fatty acid synthesis consistent with increased expression of SREBP-1, FAS, and ACC genes. Tristearin (20%) supplementation did not increase the content of saturated fatty acids but caused a 1.2-fold increase in the monounsaturated fatty acid content in the wild-type mice. Tristearin supplementation did not increase the content of saturated or monounsaturated fatty acids in the SCD1−/− mice.

To determine whether SCD1 deficiency might affect fructose metabolism downstream of the fructokinase and aldolase B steps in the liver, the amount of liver glycogen and plasma glucose levels were measured. Fig. 4A shows that the amount of glycogen in the liver of wild-type mice was increased 1.4-fold after fructose feeding, but glycogen levels were decreased by 69% in the liver of the SCD1−/− mice. Fructose feeding decreased plasma glucose levels in the SCD1−/− by 36% (Fig. 4B). Triolein (20%) supplementation restored liver glycogen and plasma glucose levels in the SCD1−/− mice close to the levels found in the wild-type mice (Fig. 4, A and B). Tristearin
or triplamitin feeding did not restore liver glycogen or plasma glucose levels in the SCD1−/− mice. To determine whether fructose induction of lipogenic genes in liver is SREBP-1c-dependent, we fed the fructose diet to wild-type and SREBP-1c-deficient male mice for 7 days and then used Northern blot analysis to measure the expression of lipogenic genes. Fig. 5A shows that fructose increased SCD1 expression by 20.6-fold and that of ACC and FAS by 6.8- and 4.8-fold, respectively, in the SREBP-1c−/− mice. The fold changes of ACC and FAS mRNAs in the SREBP-1c−/− mice are comparable to 5.4- and 5.2-fold, respectively, increased by fructose in the wild-type mice. Triolein supplementation caused a further increase in ACC and FAS mRNA levels in both wild-type and SREBP-1c−/− mice. The levels of SCD1 mRNA were not increased in the wild-type and SREBP-1c−/− mice upon triolein supplementation. Fructokinase and aldolase-B mRNA levels were not increased in response to triolein supplementation. Short term feeding (2 days) of fructose did not induce lipogenic gene expression (data not shown). Fructose feeding increased oleate content by 2.6-fold in the SREBP-1c−/− mice, and triolein (18:1) supplementation increased it to 5.6-fold relative to chow diet-fed mice. These data indicated that oleate plays a role in fructose-mediated induction of lipogenic gene expression through a mechanism that is independent of SREBP-1c expression.

**DISCUSSION**

Stearoyl-CoA desaturase is a regulatory enzyme in lipogenesis, catalyzing the rate-limiting step in the overall de novo synthesis of unsaturated fatty acids from acyl-CoA substrates (1–5, 50). SCD1 gene expression in liver tissue is regulated by numerous stimuli including diet and hormones (3, 4, 51). We are interested in why SCD is such a highly regulated enzyme, even though oleate, the major product of this enzyme, is one of the most abundant fatty acids in the diet and therefore is readily available. For instance, dietary oleate is well known for its hypotriglyceridemic effects and, as a major component of olive oil present in the Mediterranean diet, is expected to have beneficial effects. However, high SCD activity has been implicated in diabetes, obesity, and atherosclerosis in several animal models (2–5), and therefore, the role that oleate plays in these states has to be carefully evaluated. By using the SCD1−/− mice, which are deficient in tissue oleate, we begin to learn more about the physiological role of SCD gene expression and oleate in normal and disease states. We found previously that SCD1−/− mice have a deficiency in triglyceride and cholesterol ester in liver, and we suggested that endogenously synthesized monounsaturated fatty acids by SCD most probably serve as the main substrates for the synthesis of these lipids (3, 4).

Feeding high carbohydrate diets containing glucose or fructose induces fatty acid and triglyceride synthesis in both humans and rodents (28–29, 43). Fructose apparently is more lipogenic than glucose, and ingestion of this monosaccharide in high concentrations has been correlated with hypertriglyceridemia, insulin resistance, and obesity (43). The induction of hepatic fatty acid and triglyceride synthesis is mediated by SREBP-1c, which binds to the sterol regulatory elements present in lipogenic genes and activates their transcription (35). We show in this study that, when fed to SCD1−/− mice, fructose does not induce SREBP-1c or lipogenic genes and liver triglyceride levels are not increased. Fructose feeding instead caused a decrease in hepatic glycogen and plasma glucose levels in the SCD1−/− mice. The failure to induce lipogenic gene expression could not be rescued by supplementing the fructose diet with 5% (by weight) of oleate, which is normally present in the diet and was previously used (25). However, very high levels of oleate (20% by weight) followed by long term feeding increased the mRNA levels for SREBP-1c and lipogenic genes but not to levels found in the wild-type mice that were fed the fructose diet. These results suggested that the endogenously synthe-
sized oleate is a readily more accessible regulator of lipogenic gene expression than dietary oleate. The mechanism by which oleate mediates or induces SREBP-1c and lipogenic gene expression remains to be explored. Several in vitro studies have shown that oleate suppresses the proteolytic processing of SREBP-1 protein and reduces SREBP-1 and lipogenic gene expression (52–54). The inhibitory effect has been proposed to be attributed to the increase in the release of ceramide from sphingomyelin (55). The opposite effect between in vitro and in vivo results is a common feature in the studies of nutrient-gene interaction. Our results strongly suggest that oleate modulates a signaling pathway that is unique to the in vivo situation.

The fructose diet supplemented with 20% tripalmitin (16:0), tristearin (18:0), or trilinolein (18:2 n-6) did not increase mRNA levels for SREBP-1 and lipogenic genes. The inability of triolein to increase SREBP-1 gene expression was not unexpected, because polyunsaturated fatty acids in general repress SREBP-1 gene expression and protein maturation in vivo and in vitro (52, 56). The observed effects of the saturated fatty acids on SREBP-1 expression and maturation in SCD1−/− mice may suggest that in oleate deficiency saturated fatty acids (i.e. palmitate) can directly repress SREBP-1 gene expression and protein maturation. There is precedence for this speculation, because palmitate has been shown to regulate the maturation of SREBP in Drosophila through increased synthesis of phosphatidylethanolamine (57, 58). Phosphatidylethanolamine levels are increased in the livers of SCD1−/− mice. Further studies will be required to determine whether saturated fatty acids inhibit SREBP maturation in mammals.

On a chow diet, SCD1−/− mice have lower liver triglyceride levels than wild-type mice. Upon fructose feeding, SCD1−/− mice did not increase liver triglycerides but reduced their plasma triglycerides by 54%. This observation is consistent with reduced triglyceride synthesis in liver of SCD1−/− mice and suggests that newly synthesized triglycerides are preferred for secretion into plasma. The liver glycogen content and plasma glucose levels were also decreased in SCD1−/− mice despite the increased expression of fructose-metabolizing enzymes, fructokinase and aldolase B, suggesting that SCD1 deficiency affects a step downstream of these enzymes in the synthesis of glucose from fructose. Upon triolein supplementation, the liver triglyceride and glycogen as well as plasma triglyceride and glucose levels were restored. Supplementation of the diet with tristearin or tripalmitin did not increase triglyceride levels, and the liver glycogen and plasma glucose levels were not restored. Surprisingly, the content of the 16:0 or 18:0 fatty acids did not increase in the SCD1−/− mice upon tripalmitin or tristearin supplementation, respectively, although the food intake was similar between the wild type and SCD1−/− mice. The fate of these saturated fatty acids is not clear at the moment, but we speculate that in oleate deficiency, the saturated fat is oxidized so that a constant ratio of monounsaturated to saturated fatty acids is maintained. We already have evidence that SCD1−/− mice have increased fatty acid oxidation in the liver as well as other tissues (22, 26). Taken together, the data suggest that oleate levels play a major role in the regulation of carbohydrate and lipid homeostasis in liver.

In previous studies, we showed that dietary fructose induces the transcription of SCD1 in the liver of streptozotocin-induced diabetic mice, suggesting that fructose-mediated induction of SCD1 transcription is independent of insulin signaling (59). However, the exact mechanism by which dietary fructose regulates the transcription of the SCD1 gene remained unclear. A series of studies (35, 37, 38, 60–64) demonstrate that SREBP-1c controls the expression of numerous genes related to fatty acid and triglyceride synthesis including SCD1, FAS, ACC, and GPAT through the insulin signaling pathway. Therefore, we postulated that in vivo fructose induces SCD1 as well as other lipogenic genes through an SREBP-1c-dependent mechanism. We show in this report that dietary fructose induced SREBP-1c mRNA expression and that both the precursor and mature forms of SREBP-1 protein were increased in the wild-type mice (Fig. 1). The expression of the lipogenic genes including SCD1 was also induced (Figs. 4 and 5). These data suggested that the induction of SCD1 and other lipogenic genes is dependent on SREBP-1c expression and would be consistent with published reports (32–34). However, using SREBP-1c−/− mice, we found that, unlike in short term feeding (data not shown), the long term feeding of fructose induced SCD1, ACC, and FAS mRNAs to levels comparable to the levels induced by fructose in the wild-type mice (Fig. 5), suggesting that fructose-mediated induction of lipogenic genes is independent of SREBP-1c expression. Triolein supplementation further increased the levels of ACC and FAS mRNAs in both wild type and SREBP-1c−/− mice. Triolein supplementation did not increase SCD1 mRNA levels, suggesting that oleate is not required in fructose-mediated induction of SCD1 gene expression in vivo. Overall, the studies indicated that the maximum induction of lipogenic genes by fructose requires endogenous oleate produced by up-regulation of SCD1 gene expression and occurs through an SREBP-1c-independent pathway.

In conclusion, our findings indicate that oleate is necessary for fructose-mediated induction of lipogenic genes through SREBP-1c-dependent and -independent mechanisms. As indicated in Fig. 6, we propose that fructose induces SCD1 gene expression via a mechanism that is unknown at present leading to the de novo synthesis of oleate. In a minor pathway, oleate mediates the induction of SREBP-1c expression and maturation, which in turn induces the expression of lipogenic genes consistent with published reports (34–39, 57, 60, 61). SREBP-1c in a feedback loop can induce SREBP gene expression by its capacity to bind to the sterol regulatory enzymes, fructokinase and aldolase B, suggesting that SCD1 deficiency affects a step downstream of these enzymes in the synthesis of glucose from fructose. Upon triolein supplementation, the liver triglyceride and glycogen as well as plasma triglyceride and glucose levels were restored. Supplementation of the diet with tristearin or tripalmitin did not increase triglyceride levels, and the liver glycogen and plasma glucose levels were not restored. Surprisingly, the content of the 16:0 or 18:0 fatty acids did not increase in the SCD1−/− mice upon tripalmitin or tristearin supplementation, respectively, although the food intake was similar between the wild type and SCD1−/− mice. The fate of these saturated fatty acids is not clear at the moment, but we speculate that in oleate deficiency, the saturated fat is oxidized so that a constant ratio of monounsaturated to saturated fatty acids is maintained. We already have evidence that SCD1−/− mice have increased fatty acid oxidation in the liver as well as other tissues (22, 26). Taken together, the data suggest that oleate levels play a major role in the regulation of carbohydrate and lipid homeostasis in liver.

In previous studies, we showed that dietary fructose induces the transcription of SCD1 in the liver of streptozotocin-induced diabetic mice, suggesting that fructose-mediated induction of SCD1 transcription is independent of insulin signaling (59). However, the exact mechanism by which dietary fructose regulates the transcription of the SCD1 gene remained unclear. A series of studies (35, 37, 38, 60–64) demonstrate that

---

A. Dobryn and J. M. Ntambi, unpublished data.

Acknowledgment—We thank Jay Horton for the SREBP-1 and -2 antibodies.

REFERENCES

Stearoyl-CoA Desaturase 1 Gene Expression Is Necessary for Fructose-mediated Induction of Lipogenic Gene Expression by Sterol Regulatory Element-binding Protein-1c-dependent and -independent Mechanisms
Makoto Miyazaki, Agnieszka Dobrzyn, Weng Chi Man, Kiki Chu, Harini Sampath, Hyoun-Ju Kim and James M. Ntambi

doi: 10.1074/jbc.M402781200 originally published online April 5, 2004

Access the most updated version of this article at doi: 10.1074/jbc.M402781200

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 61 references, 37 of which can be accessed free at http://www.jbc.org/content/279/24/25164.full.html#ref-list-1