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Variability of the Intestinal Uptake of Lipids Is Genetically Determined in Mice

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Abstract

The response of the plasma cholesterol concentration to changes in dietary lipids varies widely in humans and animals. There are variations in the *in vivo* absorption of cholesterol between different strains of mice. This study was undertaken in three strains of inbred mice to test the hypotheses that: (i) there are strain differences in the *in vitro* uptake of fatty acids and cholesterol and (ii) the adaptability of the intestine to respond to variations in dietary lipids is genetically determined. An *in vitro* intestinal ring technique was used to assess the uptake of medium- and long-chain fatty acids and cholesterol into jejunum and ileum of adult DBA/2, C57BL/6, and C57L/J mice. The jejunal uptake of cholesterol was similar in C57L/J, DBA/2, or C57BL/6 fed *ad libitum* a low-fat (5.7% fat, no cholesterol) chow diet. This is in contrast to a previous demonstration that *in vivo* cholesterol absorption was lower in C57L/J than in the other murine strains. The jejunal uptake of several long-chain fatty acids was greater in DBA/2 fed for 4 wk the high-fat (15.8% fat and 1.25% cholesterol) as compared with the low-fat diet. Furthermore, on the high-fat diet, the uptake of many long-chain fatty acids was higher in DBA/2 than in C57BL/6 or C57L/J. The differences in cholesterol and fatty acid uptake were not explained by variations in food uptake, body weight gain, or the weight of the intestine. In summary: (i) there are strain differences in the *in vitro* intestinal uptake of fatty acids but not of cholesterol; (ii) a high-fat diet enhances the uptake of long-chain fatty acids in only one of the three strains examined in this study; and (iii) the pattern of strain- and diet-associated alterations in the *in vivo* absorption of cholesterol differs from the pattern of changes observed *in vitro*. We speculate that genetic differences in cholesterol and fatty acid uptake are explained by variations in the expression of protein-mediated components of lipid uptake.

The response of the plasma cholesterol concentration to changes in dietary lipids varies widely in humans and in animals (1-8). Alterations in the efficiency of cholesterol absorption can account for differences in serum cholesterol concentrations between hypo- and hyper-responding rabbits after feeding a cholesterol-rich diet (9). Using human intestinal biopsy samples, Safonova and co-workers (10) demonstrated that cholesterol uptake is clustered into low, medium, and high rates. The suggestion that cholesterol absorption might be regulated by specific gene(s) was strengthened by the recent study by Carter and co-workers using inbred strains of mice (11). They showed that cholesterol absorption measured with an *in vivo* fecal

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recovery technique varied between mouse strains under low dietary fat conditions. Furthermore, there were different changes between strains in cholesterol absorption observed in response to feeding a high-fat/cholesterol diet.

This study was undertaken to determine (i) if the initial uptake step in cholesterol absorption varied between three inbred mouse strains and in response to a high-fat diet and (ii) if the variability in cholesterol uptake also included the uptake of fatty acids. The results support the hypothesis that the specific gene(s) controlling cholesterol uptake are different from those which influence the uptake of long-chain fatty acids and that the adaptation of lipid uptake in response to alterations in dietary fats is also regulated by genetic factors. Furthermore, the reported genetically influenced differences in the *in vivo* absorption of cholesterol cannot be explained by variations in the uptake step demonstrated *in vitro*.

METHODS

Animals and diets

The C57BL6 and DBA/2 mice were purchased from Harlan Bioproducts (Indianapolis, IN), and C57L/J mice were obtained from The Jackson Laboratories (Bar Harbor, ME). Male chimeric mice derived from cholesterol esterase gene-targeted embryonic stem cells, with a 129/SvEv genetic background, were mated with female Black Swiss mice (12). Heterozygotes from different parents were mated with female Black Swiss mice. Black Swiss and 129/SvEv mice were obtained from Taconic Farms (Germantown, NY). Animals with the normal cholesterol esterase genotype were selected for the current study. The mice were housed in a temperature- and humidity-controlled room with a 12-h light/dark cycle for at least 7 d before experiments. Female mice between the ages of 10 and 12 wk were used for all experiments. The mice were fed either the basal nonpurified low-fat chow diet (Teklad LM485; Madison, WI) containing 5.7% fat and no cholesterol or a high-fat/high-cholesterol nonpurified diet (Purina Mouse Chow 5015 supplemented with 7.5% cocoa butter and 1.25% cholesterol to yield final concentrations of 15.8% fat and 1.25% cholesterol). Mice were fed *ad libitum* the high-fat/high-cholesterol diet for at least 4 wk, and up until the morning that the transport studies were performed. All experimental protocols described in the text were reviewed and approved by the Institutional Animal Care and Use Committee of the University of Cincinnati and the Health Sciences Animal Welfare Committee of the University of Alberta, in compliance with Guide for Care and Use of Laboratory Animals and the Canadian Committee on Animal Care, respectively.

Probe and marker compounds

[³H]-inulin was used as a nonabsorbable marker to correct for the adherent mucosal fluid volume. The [¹⁴C]-labeled probes included lauric acid (12:0), palmitic acid (16:0), stearic acid (18:0), oleic acid (18:1), linoleic acid (18:2n-6), linolenic acid (18:3n-3), and cholesterol. D- and L-glucose uptake was assessed as a control for the anticipated changes in lipid uptake. Unlabeled and [¹⁴C]-labeled probes were supplied by Sigma Co. (St. Louis, MO) and New England Nuclear (Boston, MA), respectively. Probes were shown by the manufacturer to be more than 99% pure by high-performance liquid chromatography.

Tissue preparation and determination of uptake rates

The *in vitro* uptake into everted intestinal rings was examined in mouse jejunum and ileum. Animals were weighed at the time of sacrifice. Animals were anesthetized by the intraperitoneal injection of Euthanyl® (pentobarbital, 35 mg/kg body weight; MTC Pharmaceuticals, Mississauga, Ontario, Canada). A midline incision was made into the peritoneal cavity. The ligament of Treitz, which marks the proximal end of the jejunum, was clamped and cut. The small intestine was pulled out until it reached the ileocecal junction, which marks the distal

end of the ileum. The whole length of small intestine was removed rapidly. In these studies, the jejunum was represented by the proximal third and the ileum by the distal third of the removed intestine; the middle third of the intestine was discarded.

The intestine was everted and cut into small rings of approximately 3 mm each, which were immersed immediately in pre-incubation beakers containing oxygenated Krebs-bicarbonate buffer (pH 7.2) at 37°C (13). The rings were allowed to equilibrate for approximately 5 min prior to commencement of the uptake studies. Nutrient uptake was initiated by the timed transfer of everted tissue rings into a shaking water bath (37°C) containing 5-mL plastic vials with oxygenated Krebs buffer plus [³H]-inulin and one of the following [¹⁴C]-labeled substrates: 0.1 mM fatty acids (12:0, 16:0, 18:0, 18:1, 18:2, 18:3), 0.05 mM cholesterol. The long-chain fatty acids and cholesterol were solubilized in 20 mM taurocholic acid. The uptake of glucose was also assessed to establish whether strain differences in lipid uptake also influenced the active carrier-mediated uptake of a water-soluble nutrient: the concentrations of D-glucose were 4, 8, 16, 32, and 64 mM, and L-glucose 16 mM. After incubation for 5 min, the uptake of nutrient was terminated by pouring the vial contents onto filters on an Amicon vacuum filtration manifold (Millipore Canada Ltd., Nepean, Ontario, Canada) maintained under suction, followed by washing the jejunal or ileal rings with ice-cold saline. The tissue was dried overnight at 55°C to a constant weight. The dry weight of tissues was determined, and the tissues were saponified with 0.75 N NaOH. Scintillation fluid was added, and radioactivity was determined by means of an external standardization technique to correct for variable quenching of the two isotopes.

Expression of the results

The rates of uptake were expressed as nanomoles of substrate taken up per milligram dry weight of tissue per minute (nmol·mg tissue⁻¹·min⁻¹). The values obtained from the dietary groups are reported as the means ± SEM for results obtained from five to six animals in each group.

Glucose uptake kinetics were determined by fitting the observed data points to the Michaelis-Menten equation and by nonlinear regression analysis using the Sigma Plot (Jandel Scientific, San Rafael, CA) program for best fit curves. As variance increased with the size of the y-axis variable (rate of uptake of glucose), data points were weighted in proportion to the reciprocal of the within-concentration estimates of variance (14).

Analysis of variance was used to test for a difference between the five dietary groups. Individual differences were determined using a Student Neuman-Keuls multiple range test. A value of $P < 0.05$ was accepted as statistically significant.

RESULTS

There were no differences between the three strains of mice in the rates of jejunal or ileal uptake of cholesterol when the animals were fed either chow or the high-fat diet (Table 1). When fed chow, the jejunal uptake of 12:0 was highest and 18:3 was lowest in the C57L/J mice as compared with the other animals, whereas the ileal uptake of 18:0 was highest. When the animals were fed the high-fat diet, the jejunal uptake of 16:0, 18:2, and 18:3 was highest in DBA/2, and the ileal uptakes of 16:0 and 18:1 were also highest in this strain. In C57L/J fed chow or the high-fat diet, the jejunal uptake of 12:0 was greater than in DBA/2 or C57BL6.

The chow and high-fat/cholesterol diets were not isocaloric, but the animals were fed *ad libitum* and there were no differences in food intake (Table 2). The rate of body weight gain was lower in C57L/J fed either chow or the high-fat diet, as compared with DBA/2 or C57BL6. The variations in fatty acid uptake were not due to any differences in the animals' food intake, the weight of the intestine, or the weight of the mucosa (Table 2).

A curvilinear relationship was noted between glucose concentration and uptake (data not shown). In the jejunum the rate of uptake of L-glucose was unchanged by diet or by the strain of mouse. In the ileum, uptake of L-glucose was lower in C57L/J mice fed the basal diet. When the high-fat diet was fed, the uptake of L-glucose was higher in C57L/J than in the other two strains. After correcting for the minor differences in passive uptake, there were no differences in the maximal transport rate ($V_{\max}$) or the apparent Michaelis affinity constant (K_m) for jejunal or ileal glucose uptake between DBA/2, C57BL6, or C57L/J (Table 3).

DISCUSSION

The topic of the intestinal absorption of lipids has been reviewed (15,16). Once cholesterol or long-chain fatty acids have been solubilized in bile salt micelles in the intestinal lumen, they diffuse across the intestinal unstirred water layer (UWL). The lipids then partition from the micelle, either directly into the lipophilic enterocyte brush border membrane (BBM) or into an aqueous phase, and then diffuse across the BBM. There also may be a carrier-mediated component to the uptake of fatty acids and cholesterol (7,8,10,17-20).

There was no difference in the initial step of cholesterol uptake observed between the three murine strains (Table 1). The greater *in vitro* uptake of 12:0 into the jejunum of C57L/J fed chow or the high-fat diet suggests but does not prove that the UWL resistance is lower in these animals than in the DBA/2 or C57BL6 mice (21). The measurement of the uptake of fatty acid 12:0 is not the ideal measure of UWL resistance, and the value of the diffusion coefficient for cholesterol under these conditions is unknown. Thus, the BBM permeability of cholesterol in C57L/J is either similar to or higher than in the two other strains of mice. This is in contrast to the lower *in vivo* absorption of cholesterol in the C57L/J mice when fed either the low-fat chow or the high-fat diet (11). Thus, the strain differences in the intestinal absorption of cholesterol observed *in vivo* (11) cannot be explained simply on the basis of variations in the uptake step when studied *in vitro*. Although these strain differences in the *in vivo* as compared with *in vitro* absorption of cholesterol may result from the presence of bile, an intact blood circulation, diet, or desquamated cells, the possibility exists that there may be genetic variations related to the process of digestion of the luminal lipids prior to absorption by the enterocytes, intracellular metabolism, or transport out of the enterocyte.

Genetic differences in the lipid uptake of long-chain fatty acids have not been reported. In this study the mice fed chow did not display major differences in jejunal or ileal uptake of long-chain fatty acids, but, when fed the high-fat diet, the uptake of most fatty acids was greater in DBA/2 than in C57BL6 or C57L/J mice (Table 1). DBA/2 mice also had a greater uptake of lipids when fed the high- as compared with the low-fat diet. This suggests that uptake of long-chain fatty acids is also genetically influenced and that the pattern is different from changes observed in the *in vivo* absorption of cholesterol (11). Of note, the uptake of only some fatty acids was affected by strain differences. This argues for the change in the uptake process not being the result of a general alteration in the lipophilic properties of the BBM, which would have been expected to have altered the uptake of all lipids. Instead, the finding of the change in the uptake of only some fatty acids argues in favor of there being BBM or cytosolic proteins mediating the uptake of only some lipids, or having a greater affinity for the transport of some lipids. Furthermore, the variability in lipid uptake between the three strains when fed chow was different when they were fed the high-fat diet. This suggests that there may be involvement of a protein-mediated component in lipid absorption, as has been proposed by others (7,19, 21-23).

Feeding a sunflower oil-enriched diet upregulated fatty acid transporter (FAT) mRNA 2.6-fold over feeding a medium-chain triglyceride-enriched diet (21). The increases in linoleic acid and linolenic acid uptake in DBA/2 mice after fat and cholesterol feeding reported in the present

study may be associated with the upregulation of FAT. The binding of several long-chain fatty acids (stearic acid, oleic acid, arachidonic acid) to FAT was not significantly different from each other (22), but studies were not done on linoleic acid, linolenic acid, docosahexaenoic acid, or short-chain fatty acids. Furthermore, the differences in lipid uptake between strains fed the low-fat vs. the high-fat diet raise the possibility that there may be several genes modifying cholesterol and long-chain fatty acid uptake.

The uptake of glucose is mediated by a sodium-dependent transporter in the BBM, SGLT1 (24). The activity of SGLT1 may be influenced by the lipophilic properties of the BBM (25). For this reason, we speculated that if the strain-associated alterations in cholesterol and long-chain fatty acid absorption were on the basis of changes in the lipophilic properties of the BBM, then glucose uptake also might have been influenced. However, there was no effect of strain differences on the values of the $V_{\max}$ or K_m for glucose uptake (Table 3). Therefore, this also suggests that the mechanism(s) responsible for the strain-associated change in the uptake of cholesterol and long-chain fatty acids is not a process caused by generalized alterations in the lipophilic properties of the BBM.

The lower rate of body weight gain in C57L/J as compared with DBA/2 or C57BL6 fed either chow or the high-fat diet occurred despite similar amounts of food being ingested (Table 2). The lower rate of uptake of some long-chain fatty acids in C57L/J fed the high-fat diet may have contributed in part to their lower body weight gain as compared with DBA/2, in which fatty acid uptake and weight gain were both higher. However, this would not explain the greater weight gain in C57BL6 than C57L/J, since there were similar rates of fatty acid uptake (Table 1). Presumably, the lower rate of weight gain in C57L/J was due to lower total lipid absorption, and not just to lower rates of lipid uptake. This speculation of the difference between murine strains and the *in vitro* fatty acid uptake vs. *in vivo* absorption is supported by the variations between the *in vivo* absorption and the *in vitro* uptake of cholesterol, in which absorption was lowest in C57L/J (11) but *in vitro* uptake was similar in the three strains (Table 1).

In this study we did not determine which protein-mediated component might be responsible for the strain-associated variations in fatty acid uptake observed when the mice were fed the low- or the high-fat diets. The failure of some strains to modify their lipid uptake when switched from a high- to a low-fat diet leads us to speculate that dietary lipid modification is likely to be a successful therapeutic strategy to modify the exogenous contribution of lipids to hyperlipidemia only in those strains which are genetically capable of modifying their lipid absorption in response to dietary lipid changes. We speculate that these genetically determined differences in cholesterol and fatty acid uptake and absorption also may exist in humans and may be responsible for known variations in cholesterol absorption between individuals (i.e., hypo- and hyper-responsiveness), as well as their variable responses to a high-cholesterol/lipid diet (1-6,9,10,18). If a marker could be discovered in humans for high rates of lipid uptake and absorption, this would potentially lead the way to screening young persons before the development of hyperlipidemia. Such a marker also would be useful to determine which persons with hyperlipidemia would be most likely to respond to dietary treatment with a low-fat/cholesterol diet. Finally, finding the gene products responsible for the variations in cholesterol and fatty acid uptake and absorption would open the way to the development of targeted therapeutic agents which could reduce the absorption of lipids for the treatment of hyperlipidemia or obesity.

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Abbreviations

BBM, brush border membrane; FAT, fatty acid transporter; UWL, unstirred water layer.

REFERENCES

1. Aubert R, Perdereau D, Roubiscoul M, Herzog J, Lemonnier D. Genetic Variations in Serum Lipid Levels of Inbred Mice and Response to Hypercholesterolemic Diet. *Lipids* 1988;23:48–54. [PubMed: 3352472]
2. Bhattacharyya AK, Baker HN, Eggen DA, Malcolm GT, Roheim PS, Strong JP. Effect of Cholesterol Feeding on Lipolytic Activities in High- and Low-Responding Rhesus Monkeys. *Arteriosclerosis* 1989;9:380–389. [PubMed: 2497721]
3. Bhattacharyya AK, Eggen DA. Studies on the Mechanisms of High Intestinal Absorption of Cholesterol and Campesterol in High-Responding Rhesus Monkeys. *Atherosclerosis* 1988;72:109–114. [PubMed: 3214463]
4. Kirk EA, Moe GL, Caldwell MT, Lernmark JA, Wilson DL, LeBoeuf RC. Hyper- and Hypo-Responsiveness to Dietary Fat and Cholesterol Among Inbred Mice: Searching for Level and Variability Genes. *J. Lipid Res* 1995;36:1522–1532. [PubMed: 7595076]
5. McNamara DJ, Kolb R, Parker TS, Batwin H, Simon P, Brown CD, Ahrens EH. Heterogeneity of Cholesterol Responsiveness in Man. *J. Clin. Invest* 1987;79:1729–1739. [PubMed: 3584466]
6. Mahley RW, Weisgraber KH, Innerarity TL. Canine Lipoproteins and Atherosclerosis II. Characterization of the Plasma Lipoproteins Associated with Atherogenic and Nonatherogenic Hyperlipidemia. *Circ. Res* 1974;35:722–733. [PubMed: 4138629]
7. Thurnhofer HJ, Schnabel J, Betz M, Lipka G, Pidgeon C, Hauser H. Cholesterol-Transfer Protein Located in the Intestinal Brush-Border Membrane. Partial Purification and Characterization. *Biochim. Biophys. Acta* 1991;1064:275–286. [PubMed: 2036443]
8. Lipka G, Schulthess G, Thurnhofer H, Wacker H, Wehrli E, Zeman K, Weber FE, Hauser H. Characterization of Lipid Exchange Proteins Isolated from Small Intestinal Brush Border Membrane. *J. Biol. Chem* 1995;270:5917–5925. [PubMed: 7890723]
9. Overturf ML, Smith SA, Gotto AM. Dietary Cholesterol Absorption and Sterol and Bile Acid Excretion in Hypercholesterolemia-Resistant White Rabbits. *J. Lipid Res* 1990;31:2019–2027. [PubMed: 2086701]
10. Safonova IG, Sviridov DD, Roytman A, Rytikov FM, Dolgov VV, Nano JL, Rampal P, Repin VS. Cholesterol Uptake in the Human Intestine. *Biochim. Biophys. Acta* 1993;1166:313–316. [PubMed: 8443250]
11. Carter CP, Howles PN, Hui DY. Genetic Variation in Cholesterol Absorption Efficiency Among Inbred Strains of Mice. *J. Nutr* 1997;127:1344–1348. [PubMed: 9202089]
12. Howles PN, Carter CP, Hui DY. Dietary Free and Esterified Cholesterol Absorption in Cholesterol Esterase (bile salt-stimulated lipase) Gene-Targeted Mice. *J. Biol. Chem* 1996;271:7196–7202. [PubMed: 8636157]
13. Perin N, Keelan M, Clandinin MT, Thomson ABR. Ontogeny of Intestinal Absorption Adaptation in Rats in Response to Isocaloric Changes in Dietary Lipids. *Am. J. Physiol* 1997;273:G713–G720. [PubMed: 9316476]
14. Fingerote RJ, Doring KA, Thomson ABR. Gradient for Glucose and Linoleic Acid Uptake Along the Crypt-Villus Axis of Rabbit Jejunal Brush Border Membrane Vesicles. *Lipids* 1994;29:117–127. [PubMed: 8152345]
15. Tso, P. Physiology of the Gastrointestinal Tract. Raven Press; New York: 1994. Intestinal Lipid Absorption; p. 1867–1907.
16. Thomson ABR, Schoeller C, Keelan M, Smith L, Clandinin MT. Lipid Absorption: Passing Through the Unstirred Layers, Brush Border Membrane and Beyond. *Can. J. Physiol. Pharm* 1993;71:531–555.

17. Schroeder F, Jefferson JR, Powell D, Incerpi S, Woodford JK, Colles SM, Myers-Payne S, Emge T, Hebbell T, Moncecchi D. Expression of Rat L-FABP in Mouse Fibroblasts: Role in Fat Absorption. *Mol. Cell. Biochem* 1993;123:73–83. [PubMed: 8232270]
18. Paigen B. Genetics of Responsiveness to High-Fat and High-Cholesterol Diets in the Mouse. *Am. J. Clin. Nutr* 1995;62:458S–462S. [PubMed: 7625360]
19. Schoeller C, Keelan M, Mulvey G, Stremmel W, Thomson ABR. Oleic Acid Uptake into Rat and Rabbit Jejunal Brush Border Membrane. *Biochim. Biophys. Acta* 1995;1236:51–64. [PubMed: 7794955]
20. Stremmel W. Uptake of Fatty Acids by Jejunal Mucosal Cells Is Mediated by a Fatty Acid-Binding Membrane Protein. *J. Clin. Invest* 1988;82:2001–2010. [PubMed: 3198762]
21. Poirier H, Degrace P, Niot I, Bernard A, Besnard P. Localization and Regulation of the Putative Membrane Fatty-Acid Transporter (FAT) in the Small Intestine. Comparison with Fatty Acid-Binding Proteins (FABP). *Eur. J. Biochem* 1996;238:368–373. [PubMed: 8681947]
22. Baille AGS, Coburn CT, Abumrad NA. Reversible Binding of Long-Chain Fatty Acids to Purified FAT, the Adipose CD36 Homolog. *J. Membr. Biol* 1996;153:75–81. [PubMed: 8694909]
23. Ibrahimi A, Sfeir Z, Magharaie H, Amri E, Grimaldi P, Abumrad NA. Expression of the CD36 Homolog (FAT) in Fibroblast Cells: Effect on Fatty Acid Transport. *Proc. Natl. Acad. Sci. USA* 1996;93:2646–2651. [PubMed: 8610095]
24. Hediger MA, Rhoads DB. Molecular Physiology of Sodium-Glucose Cotransporters. *Physiol. Rev* 1994;74:993–1026. [PubMed: 7938229]
25. Meddings JB, Theisen S. Development of Rat Jejunum: Lipid Permeability, Physical Properties, and Chemical Composition. *Am. J. Physiol* 1989;256:G931–G940. [PubMed: 2719114]

TABLE 1
Effect of Dietary Lipids on the *in vitro* Uptake of Lipids in Different Strains of Mice^a

Lipid	DBA/2 ^b	C57BL6 ^b	Chow diet C57L/J ^c	DBA/2	C57BL6	High-fat/cholesterol diet C57L/J
Jejunum						
Fatty acids						
12:0	11.1 ± 2.1	16.1 ± 1.0 ^d	18.3 ± 1.2 ^d	11.3 ± 1.5	13.8 ± 1.1	17.5 ± 2.2 ^d
16:0	2.3 ± 0.4	2.5 ± 0.3	2.0 ± 0.3	4.1 ± 0.6 ^d	2.3 ± 0.3 ^a	2.8 ± 0.4 ^d
18:0	2.0 ± 0.4	1.9 ± 0.3	1.6 ± 0.2	2.7 ± 0.3	2.1 ± 0.2	2.2 ± 0.5
18:1	2.2 ± 0.4	2.0 ± 0.4	2.3 ± 0.2	3.2 ± 0.4	2.1 ± 0.2	2.3 ± 0.4
18:2	1.7 ± 0.4	2.0 ± 0.3	1.5 ± 0.2	3.4 ± 0.5 ^c	1.8 ± 0.3 ^a	1.2 ± 0.3 ^d
Cholesterol	2.0 ± 0.2	1.7 ± 0.2	1.0 ± 0.2 ^{a,b}	3.2 ± 0.5 ^c	1.8 ± 0.3 ^a	2.0 ± 0.5 ^d
Ileum	0.6 ± 0.2	0.4 ± 0.1	0.7 ± 0.2	0.8 ± 0.4	0.7 ± 0.4	0.5 ± 0.1
Fatty acids						
12:0	17.2 ± 2.9	13.0 ± 1.9	9.1 ± 1.5	21.8 ± 2.8	12.8 ± 1.3 ^d	15.8 ± 1.9
16:0	1.8 ± 0.6	1.7 ± 0.3	1.2 ± 0.3	3.8 ± 0.8 ^c	0.9 ± 0.2 ^a	1.8 ± 0.5 ^d
18:0	1.1 ± 0.2	1.7 ± 0.2	2.4 ± 0.5 ^d	2.2 ± 0.4	1.4 ± 0.4	1.6 ± 0.3
18:1	1.5 ± 0.6	0.9 ± 0.1	2.1 ± 0.6	3.0 ± 0.6	1.2 ± 0.3 ^a	1.6 ± 0.3 ^d
18:2	1.0 ± 0.2	0.8 ± 0.2	1.5 ± 0.5	2.3 ± 0.8	0.9 ± 0.5	1.6 ± 0.4
18:3	1.2 ± 0.2	1.6 ± 0.2	1.4 ± 0.5	2.9 ± 0.6	2.7 ± 0.8	1.6 ± 0.3
Cholesterol	0.8 ± 0.4	0.4 ± 0.1	0.3 ± 0.2	0.6 ± 0.3	0.6 ± 0.1	0.2 ± 0.1

^aMeans ± SEM, nmol·100 mg⁻¹·min⁻¹·0.1 mM⁻¹, *P* < 0.05, vs. DBA/2, *P* < 0.05, vs. C57BL6, *P* < 0.05, high-cholesterol diet vs. standard chow diet.

^a*P* < 0.05, vs. DBA/2.

^b*P* < 0.05, vs. C57BL6.

^c*P* < 0.05, high-cholesterol diet vs. standard chow diet.

^bHarlan Bioproducts (Indianapolis, IN).

^cThe Jackson Laboratories (Bar Harbor, ME).

TABLE 2

Effect of Dietary Lipids on Animal Characteristics^a

	DBA/2	Chow diet C57BL/6	C57L/J	DBA/2	High-fat/cholesterol diet C57BL/6	C57L/J
Food intake (g/mouse/d)	3.5 ± 0.2	5.4 ± 1.3	3.5 ± 0.6	2.5 ± 0.5	7.4 ± 1.2	2.9 ± 0.5
Body weight gain (g/mouse/d)	0.39 ± 0.10	0.22 ± 0.04	0.00 ± 0.02 ^{a,b}	0.24 ± 0.09	0.34 ± 0.07	0.07 ± 0.04 ^b
Jejunum						
Mucosa (mg/cm)	2.5 ± 0.5	4.1 ± 1.1	4.4 ± 0.5	4.6 ± 0.9	3.5 ± 0.6	4.1 ± 0.7
Remainder of intestine (mg/cm)	3.3 ± 0.3	2.4 ± 0.2	4.5 ± 0.6	4.2 ± 0.9	2.9 ± 0.3	3.2 ± 0.4
Ileum						
Mucosa (mg/cm)	1.7 ± 0.4	2.4 ± 0.4	1.7 ± 0.3	3.0 ± 0.6	2.8 ± 0.6	2.7 ± 0.5
Remainder of intestine (mg/cm)	1.9 ± 0.3	3.5 ± 0.8	1.7 ± 0.3	1.8 ± 0.2	2.5 ± 0.6	2.0 ± 0.2

^aSignificance: $P < 0.05$, vs. DBA/2. $P < 0.05$, vs. C57BL/6. See Table 1 for company sources.^a $P < 0.05$, vs. DBA/2.^b $P < 0.05$, vs. C57BL/6. See Table 1 for company sources.

TABLE 3
Effect of Dietary Lipids on *in vitro* Uptake of Glucose in Different Strains of Mice^a

	DBA/2	Standard chow diet C57BL/6	C57L/J	DBA/2	High-cholesterol diet C57BL/6	C57L/J
Jejunum						
V_{max}	441 ± 143	653 ± 136	1121 ± 357	685 ± 119	652 ± 214	815 ± 107
K_m	11.9 ± 4.2	7.9 ± 3.7	12.2 ± 3.2	3.3 ± 1.2	10.6 ± 3.0	7.9 ± 2.7
Ileum						
V_{max}	450 ± 119	851 ± 194	559 ± 198	777 ± 210	445 ± 129	232 ± 70
K_m	8.0 ± 0.6	4.9 ± 2.8	9.0 ± 3.0	8.6 ± 2.5	7.8 ± 5.6	4.0 ± 0.6

^a V_{max} maximal transport rate (nmol·mg tissue⁻¹·min⁻¹); K_m apparent Michaelis constant (mM). These values are not statistically different from each other ($P > 0.05$) and represent the means ± SEM of estimates calculated from individual animals. See Table 1 for company sources.