The pancreas secretes several different lipases. The most abundant is pancreatic triglyceride lipase (PTL). The pancreas also synthesizes two homologues of PTL, the pancreatic lipase-related proteins 1 and 2 (PLRP1 and PLRP2). Cytotoxic T-lymphocytes also express PLRP2 under certain conditions. We sought to determine the role of PLRP2 in fat absorption and in T-cell cytotoxicity by creating a PLRP2-deficient mouse. Adult PLRP2-deficient mice had normal fat absorption. In contrast, suckling PLRP2-deficient mice had fat malabsorption evidenced by increased fecal weight, increased fecal fats, and the presence of undigested and partially digested dietary triglycerides in the feces. As a result, the PLRP2-deficient pups had a decreased rate of weight gain. To assess T cell cytotoxicity, we immunized PLRP2-deficient mice with a mastocytoma cell line, P815, and determined the ability of splenocytes from the immunized mice to kill P815 cells in a 51Cr release assay. PLRP2-deficient cells had deficient killing activity in this assay, and PLRP2-deficient splenocytes released fewer fatty acid from the target cells than did control cells. Our results provide the first evidence of a physiological function for PLRP2. PLRP2 participates in T cell cytotoxicity, and PLRP2 performs a crucial role in the digestion of dietary fats in suckling animals.

During the last 10 years, data from cDNA and genomic cloning have provided evidence for a lipase gene family. The first speculation about a lipase gene family began after the cloning of cDNAs for hepatic lipase, lipoprotein lipase, and pancreatic triglyceride lipase (PTL) showed similarities among the predicted amino acid sequences of these lipases (1). Subsequently, the cloning of other cDNAs encoding lipases from various species and the realization that many lipases and other hydrolases share a common protein folding pattern expanded the family greatly (2). Two of the recently described lipases have higher sequence homology to PTL than any other members of the gene family. Because of their similarities to PTL, Giller et al. (3) named these two lipases pancreatic lipase-related proteins 1 and 2 (PLRP1 and PLRP2) (3).

One of these related proteins, PLRP2, was also independently cloned for reasons other than its similarity to PTL. Mouse PLRP2 was cloned as an interleukin-4-inducible gene in CD8+ T cells (4). Rat PLRP2 was cloned as GP3, a zymogen granule membrane-associate protein (5). These studies suggested potential physiological functions for PLRP2 in T cell-mediated cytotoxicity, in zymogen granule fusion with the acinar cell plasma membrane, and in the digestion of dietary fats. Additional investigations of PLRP2 have supported some of these functions. Each of these postulated functions requires that PLRP2 have lipase activity. Studies of recombinant PLRP2 have demonstrated a high level of triglyceride lipase activity similar to PTL (6). Unlike PTL, PLRP2 also hydrolyzes other lipid substrates and possesses phospholipase and galactolipase activities (6, 7). PLRP2 is also secreted by the pancreas and by isolated pancreatic acinar cells in culture (8, 9). This secretion places PLRP2 in the duodenum, where dietary fat digestion occurs. Secretion of PLRP2 by T cells has not been reported. Finally, the pancreas expresses mRNA encoding PLRP2 at birth but does not express mRNA encoding PTL until near the suckling-weanling transition (10). This temporal pattern of expression for mRNA encoding PLRP2 and PTL led to the speculation that PLRP2 mediates dietary fat digestion in suckling animals.

We sought to define the function of PLRP2 in dietary fat metabolism and in T cell cytotoxicity. To accomplish this aim, we created a line of PLRP2-deficient mice by homologous recombination. We characterized T cell function in adult animals and dietary fat absorption in animals at various ages.

MATERIALS AND METHODS

Targeting Construct and Generation of Mice with Null Allele for PLRP2—The targeting construct was made by cloning a Smal/ClaI fragment of the mouse PLRP2 gene into a vector containing a thymidine kinase cassette (Fig. 1) (11). The gene fragment contained exons 1–V from the 12 total PLRP2 exons (12). A LacZ/neomycin cassette was cloned into a unique BamHI site in exon IV (13). The LacZ fusion was created so that cells expressing the gene encoding PLRP2 could be detected in situ.

D3 embryonic stem cells were transfected with the targeting construct. We screened for targeted stem cells by Southern blot of genomic DNA isolated from neomycin-resistant clones and digested with EcoRI. The blot was hybridized to a 5'-probe, which detected a 5-kilobase pair wild-type band and a 7-kilobase pair fragment from the targeted allele. The targeting efficiency was 5.6% (7/129). Embryonic stem cells from a targeted clone were injected into BALB/c mouse blastocysts to generate chimeric animals whose offspring from BALB/c matings were subsequently screened for the targeted allele by a polymerase chain reaction with three primers (lipase upstream, 5'-GTAACGTATTTGCGTTGA-
matings of mice heterozygous for the PLRP2 allele. The quenched with 0.3% hydrogen peroxide in H2O. After washing three in PBS-T (137 mM NaCl, 2.7 mM KCl, 4.3 mM Na2HPO4, 0.2% Tween 20) containing 2 mM MgCl2. The slides were then processed as for adult animals. The mice were adapted to the diet for at least 2 weeks before samples were collected. Nursing mothers were fed standard 5053 chow.

Fecal Fat Analysis—Adult mice were placed in a cage with a metabolic screen. They were given water but no food during the 4-h collection period. The stool was dried to a constant weight, and fats were extracted as described (16). To obtain stool from suckling animals, 10-day-old animals were sacrificed, and the entire colon was removed. The feces were removed by extrusion and processed as for adult animals. The percentage of recovery was 90 ± 2.0% as determined by the recovery of radiolabeled triolein.

Analysis of Lipid Classes—Extracted fecal fats from 100 mg of dried feces were dissolved in 1 ml of chloroform, and 10 μl of each sample was

![Diagram](Image)

**Fig. 1.** Targeting construct for creating PLRP2-deficient mice and polymerase chain reaction (PCR) screening of tail DNA from matings of mice heterozygous for the PLRP2 allele. The top half of the figure shows a schematic map of the PLRP2 wild-type allele (top), targeting construct (middle), and the targeted allele (bottom). Exons are numbered with roman numerals. The positions of the polymerase chain reaction primers and fragments used for Southern analysis are indicated. th, thymidine kinase. The bottom half of the figure shows a representative polymerase chain reaction screening of tail DNA. Samples were separated by agarose gel electrophoresis and stained with ethidium bromide. Markers are in the first lane. The next nine lanes show the results from screening. The upper, 190-base pair band is the targeted allele, and the lower, 113-base pair band is the wild-type allele.

3' lipase downstream, 5'-ACCGACAACATGACACAA-3' and LacZ, 5'-ATTCAAGGCCTGGCGAAGTGT-3' (Fig. 1). These primers amplified a 113-base pair wild-type fragment and a 190-base pair fragment from the targeted allele (Fig. 1). Mice with the targeted allele were backcrossed six generations to BALB/c mice before intercrossing.

RNA Analysis—We isolated total RNA from the pancreas of animals at birth, 10 days, 21 days, and 4 months of age as described previously (10). The integrity of the RNA was assessed by denaturing agarose gel electrophoresis (14). The mRNA encoding PTL, PLRP1, and PLRP2 was quantitated by an RNase protection assay utilizing 300-base pair probes complementary to each mRNA species. The PTL and PLRP1 probes went from the middle of exon 3 to the middle of exon 5, and the PLRP2 probe extended from the middle of exon 2 to the middle of exon 4 and was 5' of the LacZ-neomycin cassette. Standard curves were prepared by hybridizing the probe to known amounts of in vitro transcribed mRNA encoding each individual lipase. Values were normalized to levels of cyclophilin. The cyclophilin standard cDNA was obtained from Ambion, Inc. mRNA transcription was done with reagents from Ambion, Inc. (Austin TX) according to the manufacturer’s directions. The Ambion RPA II kit was used for the RNase protection assay. The products were separated by acrylamide gel electrophoresis according to the instructions with the kit and were transferred to Ambion’s BrightStar Plus membrane in a semidry electroblot apparatus (Bio-Rad). Bands were detected with the BrightStar BioDetect (Ambion) kit according to the instructions. The signal from the standard curves and the unknowns was quantitated using SigmaGel software (SSPS, Inc., Chicago, IL), and the amount of mRNA was determined from the standard curve.

Immunohistochemistry and β-Galactosidase Staining—For Immunoperoxidase staining, tissues were fixed in 10% formalin and embedded in paraffin, and thin sections were made. Paraffin was removed with xylene and isopropyl alcohol washes followed by three 5-min rinses in PBS-T (137 mM NaCl, 2.7 mM KCl, 4.3 mM Na2HPO4-H2O, 1.4 mM KH2PO4, 0.2% Tween 20). Endogenous peroxidase activity was quenched with 0.3% hydrogen peroxide in H2O. After washing three times for 5 min in PBS-T, the slides were incubated in blocking serum, 1.5% preimmune goat serum in PBS-T for 30 min. They were then incubated with the primary antibody diluted 1:2000 in PBS-T overnight at 4 °C. The primary antibody was a rabbit polyclonal antibody prepared against a unique peptide from mouse PLRP2 (422TVQRGK-DGKEFNFCA T) coupled to keyhole lympet hemocyanin. The slides were washed with PBS-T three times for 5 min each wash and processed following the directions in the Vectastain Elite ABC Kit (Vector Laboratories, Burlingame CA). The slides were viewed under a standard light microscope.

β-Galactosidase staining was done on fresh frozen sections embedded in O.C.T. (Sakura Finetek, Inc., Torrance CA). The sections were air-dried and postfixed in 0.5% glutaraldehyde in PBS (PBS-T without the Tween 20) containing 2 mM MgCl2. The slides were then processed as described (15).

**Animal Diets**—Diets were from PicoLab™. The standard chow was 5053 and contained 11.9% of energy as fat, 23.6% as protein, and 64.5% as carbohydrate. The medium fat diet was 5058, and the high fat diet was 5059, and contained 21.6% of energy as fat, 21.9% as protein, and 56.5% as carbohydrate. The latter had 59.7% of energy as fat, 15% as protein, and 25.3% as carbohydrate. The fat was derived from lard and corn oil in the same proportions for all diets. Ad libitum access to food and water was allowed. The mice were adapted to the diet for at least 2 weeks before samples were collected. Nursing mothers were fed standard 5053 chow.

**Fecal Fat Analysis**—Adult mice were placed in a cage with a metabolic screen. They were given water but no food during the 4-h collection period. The stool was dried to a constant weight, and fats were extracted as described (16). To obtain stool from suckling animals, 10-day-old animals were sacrificed, and the entire colon was removed. The feces were removed by extrusion and processed as for adult animals. The percentage of recovery was 90 ± 2.0% as determined by the recovery of radiolabeled triolein.

**Analysis of Lipid Classes**—Extracted fecal fats from 100 mg of dried feces were dissolved in 1 ml of chloroform, and 10 μl of each sample was
PLRP2 Function in Fat Digestion and T Cell Cytotoxicity

RESULTS

PLRP2-deficient Mice—To investigate the role of PLRP2 in dietary fat digestion and T cell-mediated cytotoxicity, we generated PLRP2-deficient mice by targeted homologous recombination. Adult and suckling PLRP2-deficient mice were grossly indistinguishable from wild-type and heterozygote littersmates. Adult mice had normal numbers and populations of cells in peripheral lymphoid organs. The frequency of PLRP2-deficient mice in heterozygote by heterozygote matings was diminished. The ratio of wild-type:heterozygous:homozygous deficient pups was 1.3:1.9:0.8 in over 300 live births.

Analysis of PLRP2 Expression—Expression of PLRP2 was determined by immunohistochemistry and by β-galactosidase histochemistry. A polyclonal rabbit antibody against a carboxyl-terminal peptide unique to PLRP2 was generated. This antibody recognized purified rat PLRP2 but not purified rat PTL or PLRP1 on a protein immunoblot. Sections of pancreas from wild-type and PLRP2-deficient mice were immunoperoxidase-stained using the anti-PLRP2 antibody as the primary reagent. No staining was detected in the acinar cells of the PLRP2-deficient pancreas (Fig. 2A), whereas acinar cells in the wild-type pancreas stained with the antibody (Fig. 2B). The staining pattern was heterogeneous with some acinar cells staining darkly and others not staining at all. The absence of PLRP2 immunoreactivity confirms that the mice containing the targeted allele did not synthesize PLRP2 protein.

β-Galactosidase activity could also be detected in the acinar cells of the PLRP2-deficient animals (Fig. 2C). Staining was not present in the islets. The acinar cell-specific expression of β-galactosidase was consistent with proper targeting of the PLRP2 gene. Like the staining pattern of the antibody, β-galactosidase activity varies over regions of the pancreas. Not all acinar cells stain to the same extent, demonstrating that individual acinar cells express PLRP2 at different levels.

The temporal pattern of expression for mRNA encoding PTL, PLRP1, and PLRP2 was quantitated by an RNase protection assay. Total RNA was prepared from wild-type and PLRP2-deficient pancreas taken from mice at different ages. Fig. 3 shows the temporal pattern of expression for the mRNAs encoding the three lipase species. The expression pattern of mRNA encoding PLRP1 and PLRP2 in wild-type mice mirrored the pattern previously reported in the rat (Fig. 3, A and B). Both were present at birth, and expression persisted throughout adulthood. mRNA encoding PTL was not detected at birth or 10 days of age but was present in both wild-type and PLRP2-deficient mice at 21 days of age and 4 months of age (adults). A faint signal with the PLRP2 probe was found in the PLRP2-deficient animals. The signal was about 5% of the signal in wild-type mice and, presumably, represented a chimeric mRNA between the 5'-end of the PLRP2 mRNA and the β-galactosidase mRNA because the targeted deletion was downstream from the region complementary to the probe. Representative gels are shown in Fig. 3C. No expression of PTL was detected in newborn and 10-day-old mice even with overexposure of the gel (Fig. 3C, far right part). Importantly, these results demonstrate that the temporal pattern of expression for the genes encoding PTL, PLRP1, and PLRP2 are the same in the mouse as in the rat and that expression of PTL and PLRP1 was not altered in the PLRP2-deficient animals.
Absorption of Dietary Fats—We next addressed the role of PLRP2 in dietary fat digestion. The secretion of PLRP2, a lipase with high triglyceride lipase activity, by the pancreas suggests that it may play a role in dietary fat digestion. Because earlier studies showed that newborn and suckling animals express PLRP2 but not PTL, we examined both suckling and adult animals. We determined if PLRP2 contributes significantly to fat digestion by measuring fecal fat. The feces from the PLRP2-deficient suckling mice were loose, yellow, and of larger volume than the formed brown feces of wild-type and heterozygous pups. This observation was supported by the increased dry weight of the colonic contents from the PLRP2-deficient pups (Table I). These findings suggested that the PLRP2 pups had steatorrhea.

We confirmed that the pups had fatty stools by measuring the fecal fat content in the stools (Fig. 4). Fats comprised 55% of the fecal dry weight in the PLRP2-deficient pups compared with 10.6% in heterozygous and 7.5% in wild-type pups. There were no differences in fecal fat between wild-type and PLRP2-deficient mice by 23 days of age. Challenging the adult mice with higher fat diets did not cause the PLRP2-deficient mice to malabsorb fat (Fig. 4). These findings demonstrated that PLRP2 makes a major contribution to the digestion of dietary fats in suckling animals but not in adult animals. The observation that the defect disappears as the pups age can be explained by the induction of pancreatic triglyceride lipase, which compensates for the lack of PLRP2 activity in the older pups.

The malabsorbed lipid classes were identified by thin layer chromatography. The extracted lipids were separated in a two-solvent, one-dimensional system and quantitatively stained with cupric acetate/phosphoric acid. Fatty acids were the predominant species in the feces from wild-type and heterozygous suckling mice (Fig. 5, lanes 1 and 2) and in adult wild-type and PLRP2-deficient mice (Fig. 5, lanes 5 and 6). In contrast, diglycerides and triglycerides comprised a much greater proportion of the lipids in the feces of PLRP2-deficient animals (Fig. 5, lanes 3 and 4). These results confirm that suckling animals require PLRP2 for efficient dietary fat digestion and show that diglycerides and triglycerides are physiological substrates for PLRP2.

Growth of PLRP2-deficient Mice—If the PLRP2-deficient mice malabsorb fat, their rate of weight gain might be affected. To test this possibility, we weighed all of the pups in multiple litters of heterozygous intercrosses from day 4 to weaning at day 23 (Fig. 6). The curves for the wild-type and heterozygote pups overlap and were not significantly different by two-way

<table>
<thead>
<tr>
<th>Genotype</th>
<th>No. of mice</th>
<th>Stool mg/mouse</th>
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<tbody>
<tr>
<td>+/+</td>
<td>44</td>
<td>5.5 ± 0.2</td>
</tr>
<tr>
<td>+/−</td>
<td>49</td>
<td>5.5 ± 0.3</td>
</tr>
<tr>
<td>−/−</td>
<td>25</td>
<td>13.8 ± 0.8*</td>
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* p < 0.05 compared with +/+ and +/− by Student’s t test.
The error bars are one S.D. Heterozygote adults were not studied. The fecal fat is significantly different for the 10-day animals compared with the corresponding genotype in the other groups (p < 0.05). In the 10-day group, the value for the PLRP2-deficient mice is significantly different from the wild-type and heterozygote animals; p < 0.0001 for both.

ANOVA analysis. The rate of weight gain for the PLRP2-deficient pups differed from the rates for the wild-type and heterozygote pups (0.33 g/day versus 0.43 and 0.44 g/day). Two-way ANOVA revealed a significant difference between the PLRP2-deficient pups and the wild-type pups (F(1, 19) = 78.9, p < 0.0001) and the heterozygote pups (F(1, 19) = 87.9, p < 0.0001). The decreased weight gain in PLRP2-deficient pups confirmed the importance of PLRP2 in dietary fat digestion by suckling animals.

Cytotoxic Activity in PLRP2-deficient Mice—Since murine PLRP2 was originally identified as an interleukin-4-inducible gene in CD8+ T cells, we also examined the PLRP2-deficient mice for alterations in cytotoxic activity (4). To determine whether PLRP2 plays an important role in T cell-mediated cytotoxicity, we immunized wild-type and PLRP2-deficient mice with the P815 mastocytoma cell line. P815 was derived from DBA/2 mice and is syngeneic at the major histocompatibility complex locus (H-2d) but has other histocompatibility differences from the BALB/c background of the mice. Ten days following injection of tumor cells, mice were sacrificed and spleen cells were tested as effectors in a 51Cr release assay. Control splenocytes displayed a dose-dependent cytotoxicity against 51Cr-labeled P815 targets (Fig. 7A). However, PLRP2-deficient splenocytes killed targets at a significantly lower level.

In parallel, splenocytes were expanded in vitro by stimulation with mitomycin C-treated P815 cells. After 6 days in culture, cells were used as effectors in a cytotoxic assay with 51Cr-labeled P815 targets. Cytotoxicity as measured by 51Cr release was similar to the results of the primary assay. CTL from wild-type mice killed targets in a dose-dependent manner, but killing was less efficient by PLRP2-deficient cells (Fig. 7B). This deficiency in killing activity was not due to differences in the percentages of CD8+ cells in the cultures (data not shown). Furthermore, levels of granzyme A production by wild-type and PLRP2-deficient mice were indistinguishable. A similar defect in killing was seen in assays using RENCA cells, another syngeneic tumor target (data not shown).

CTL-mediated lysis has been shown to result in the liberation of free fatty acids from target cells through an undefined mechanism (19). To determine whether free fatty acid release was affected by PLRP2 deficiency, we used [3H]oleic acid-labeled P815 cells as targets in the CTL assay described above. Fig. 7C demonstrates that free fatty acid release from syngeneic targets is decreased when PLRP2-deficient CTLs are used as effectors compared with wild-type cells. This correlates with the decreased cytotoxicity seen in the 51Cr release assays.

**DISCUSSION**

Lipases are ubiquitous enzymes present in many tissues and organisms. One recently described lipase, PLRP2, is expressed in pancreas and cytotoxic T cells (4, 5, 10). Although the func-
immunized as in the case of several independent experiments. B, C, A, and P815 cells for 6 days. Cultures were then used as effector cells as in the assay as described in [3H]oleic acid. Supernatants were collected after 3 h for scintillation counting.

Supernatants were collected and counted in a counter. Symbols represent the mean \( \pm S.E. \) of triplicate determinations and are representative of several independent experiments. B, splenocytes from mince immunized as in A were stimulated in vitro with mitomycin C-treated P815 cells for 6 days. Cultures were then used as effector cells as in A. C, in vitro cultured splenocytes were used as effectors in a cytotoxic assay as described in A with P815 cells that had been labeled with [3H]oleic acid. Supernatants were collected after 3 h for scintillation counting.

**Fig. 7. Cytotoxicity in PLRP2-deficient mice.** A, wild-type (circles) and PLRP2-deficient (diamonds) mice were immunized with P815 tumors. Ten days after immunization, splenocytes were removed and incubated at indicated dilutions with [3H]Cr-labeled target cells for 4 h. Supernatants were collected and counted in a counter. Symbols represent the mean \( \pm S.E. \) of triplicate determinations and are representative of several independent experiments. B, splenocytes from mince immunized as in A were stimulated in vitro with mitomycin C-treated P815 cells for 6 days. Cultures were then used as effector cells as in A. C, in vitro cultured splenocytes were used as effectors in a cytotoxic assay as described in A with P815 cells that had been labeled with [3H]oleic acid. Supernatants were collected after 3 h for scintillation counting.

Expression in Pancreas—Our evaluation of PLRP2 expression by immunohistochemistry and \( \beta \)-galactosidase histochemistry revealed patchy expression of PLRP2 by acinar cells, suggesting that acinar cells contain varying amounts of PLRP2. The notion of heterogeneous stores of pancreatic exocrine enzymes is not new (23, 24). Earlier studies demonstrated that enzyme contents differ among individual zymogen granules and that enzyme secretion is nonparallel. The heterogeneity of exocrine proteins in acinar cells provides a potential explanation for the nonparallel, adaptive changes in relative amounts of digestive enzymes in response to diet.

**PLRP2 in Dietary Fat Digestion**—Although the role of pancreatic lipases in dietary fat absorption is widely accepted, the participation of PLRP2 in fat digestion has not been established. The PLRP2-deficient mice provided the opportunity to directly test the function of PLRP2 in dietary fat digestion. Our results demonstrate that adult mice do not require PLRP2 for efficient dietary fat digestion. Although PLRP2 did not make a significant contribution to overall fat absorption in the adult, we did not eliminate the possibility that PLRP2 hydrolyzes a minor species of dietary fat. Also, the potential participation of PLRP2 in zymogen granule release was not tested in these studies. If PLRP2 has an important function in the adult animals, additional investigations are required to define that role.

In contrast, PLRP2 was essential for efficient fat digestion in suckling mice. We found that the PLRP2-deficient suckling mice had 10–15 times more fat in their feces than wild-type or heterozygote animals, suggesting a marked decrease in fat absorption. The fecal fat from PLRP2-deficient mice contained undigested and partially digested acylglycerides, confirming the importance of PLRP2 in dietary triglyceride digestion. Additionally, the weight gain of the suckling animals was decreased compared with wild type and heterozygotes, which is consistent with significant loss of calories through fat malabsorption. Clearly, PLRP2 contributes significantly to dietary fat digestion in suckling animals.

Our findings provide an explanation for the efficient fat digestion in suckling animals. Newborns have a relative PTL deficiency (25). Yet, newborn infants do not have significant steatorrhea despite consuming 3–5-fold more fat per kg, body weight, than adults. Previous models of fat absorption in newborns centered on the ready absorption of undigested monoacylglycerols, which made the complete digestion of dietary fats unnecessary for efficient absorption, or on the presence of bile salt-stimulated lipase in breast milk, which could compensate for the lack of PTL (26–28).

Against these models are in vitro experiments demonstrating that a combination of gastric lipase, bile salt-stimulated lipase, and PTL are required for efficient digestion of breast milk triglycerides (28–30). Digestion was incomplete unless all three lipases were present. In addition, there is ample evidence that the low intraluminal concentrations of bile salts found in premature and full-term infants not only decrease bile salt-stimulated lipase activity but favor the absorption of fatty acids over monoacylglycerols, making the complete digestion of triglycerides beneficial for the newborn (31–33). Given these data, the low levels of PTL in newborns should hamper the digestion of PLRP2 in these tissues is not known, one hypothesis is that pancreatic PLRP2 participates in dietary fat digestion and that cytosolic T cell PLRP2 mediates cell lysis by hydrolyzing membrane lipids. To address the physiological function of PLRP2, we created and characterized mice deficient in PLRP2. Our results show that PLRP2 contributes to cytosolic T cell cytotoxicity and to fat digestion in the suckling animal.

**PLRP2 in Cytotoxic T Cells**—PLRP2-deficient mice had a clear decrease in cytotoxicity as measured by both [51]Cr and [3H]-fatty acid release when compared with normal cytotoxic T cells. The decrease was greater than the decrease in cytotoxicity observed in granzyme B-deficient mice, but the defect was not as great as when pathways dependent on perforin or Fas were compromised (20–22). Each of these pathways has been implicated in cytosolic T cell killing activity. These findings suggested that PLRP2 may play an auxiliary role in some types of cytosolic T cell-mediated lysis. The molecular details of PLRP2-mediated cytotoxicity remain unclear, and further studies are necessary to elucidate these mechanisms.

**PLRP2 Function in Fat Digestion and T Cell Cytotoxicity**

[Image 68x260 to 278x729]
of dietary fats, but most newborns efficiently absorb their large dietary fat intakes, suggesting that other lipases may be active. PLRP2 is clearly one of those lipases.

REFERENCES


Decreased Neonatal Dietary Fat Absorption and T Cell Cytotoxicity in Pancreatic Lipase-related Protein 2-Deficient Mice

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