Peptide YY Stimulates the Expression of Apolipoprotein *A-IV* Gene in Caco-2 Intestinal Cells (44490)

KEI SONOYAMA,[1] KEIKO SUZUKI, AND TAKANORI KASAI

Laboratory of Food Biochemistry, Department of Bioscience and Chemistry, Faculty of Agriculture, Hokkaido University, Sapporo 060–8589, Japan

Abstract. **The effect of peptide YY, a gastrointestinal hormone, on the expression of the apolipoprotein *A-IV* gene in the intestinal epithelial cell line Caco-2 was examined by semiquantitative RT-PCR followed by Southern hybridization with an inner oligonucleotide probe. Apolipoprotein A-IV mRNA levels were increased in response to peptide YY in a dose- and time-dependent fashion. Western blotting revealed that the exogenous peptide YY increased the intracellular concentration of apolipoprotein A-IV. In contrast, apolipoprotein A-I, B, and C-III mRNA did not respond to peptide YY. Differentiated Caco-2 cells expressed Y1- but not Y2- and Y5-receptor subtype mRNA. The present results suggest that peptide YY modulates apolipoprotein *A-IV* gene expression, likely *via* the Y1-receptor subtype in intestinal epithelial cells.**

[P.S.E.B.M. 2000, Vol 223]

Apolipoprotein (apo) A-IV is a component of triglyceride (TG)-rich lipoproteins mainly synthesized by enterocytes in the small intestine (1). Although the precise function of the *apo A-IV* gene is not known, it has been shown to modulate lipoprotein metabolism (2–6), food intake (7, 8), and gastric functions (9, 10). For this reason, information on the expression of *apo A-IV* in the small intestine should lead to a better understanding of the regulation of lipoprotein metabolism, feeding behavior, and gastric functions.

We previously reported that massive small bowel resection resulted in a rapid increase in apo A-IV mRNA levels in the remnant ileum of fasted rats (11–13). In addition, plasma apo A-IV concentrations following small bowel resection were transiently decreased initially before recovering to control levels (11). These observations suggest that enterocytes in the residual ileum respond to the loss of proximal intestine by a compensatory increase in *apo A-IV* gene expression. However, the mechanism for the up-regulation of the *apo A-IV* gene following small bowel resection remains unclear.

Peptide YY (PYY) is a gastrointestinal hormone synthesized in L-cells in the distal bowel (14, 15), and PYY mRNA expression in the residual ileum and plasma PYY concentrations have been reported to be elevated following massive small bowel resection in the rat (16–18). Therefore, we speculated that PYY may be associated with the upregulation of the *apo A-IV* gene following small bowel resection (11). To test this hypothesis, the present study investigated the effect of exogenous PYY on the expression of apo A-IV mRNA in the human colon adenocarcinoma cell line Caco-2. A number of studies have reported that Caco-2 cells differentiate after reaching confluence to form an epithelium that shares many characteristics with mature small intestinal mucosa *in vivo* and provides an excellent *in vitro* model for the investigation of intestinal apolipoprotein synthesis, lipoprotein secretion, and metabolism (19, 20).

Materials and Methods

Cell Culture. Caco-2 cells at passage 18 were obtained from the American Type Culture Collection. Cells were maintained in Falcon 75-cm^2 T-flasks (Nippon Becton Dickinson, Tokyo, Japan) in a standard culture medium at 37°C in a humidified atmosphere of 5% CO_2 and 95% air.

This work was partly supported by Grant-in-Aid for Encouragement of Young Scientists from The Ministry of Education, Science, Sports and Culture of Japan, by the Nutritional Science Institute of Meiji Milk Products Co., and by Yamanouchi Pharmaceutical Co.

[1]To whom requests for reprints should be addressed at Laboratory of Food Biochemistry, Faculty of Agriculture, Hokkaido University, Kita-9, Nishi-9, Sapporo 060–8589, Japan. E-mail: ksnym@chem.agr.hokudai.ac.jp

Received April 19, 1999. [P.S.E.B.M. 2000, Vol 223]
Accepted September 29, 1999.

0037-9727/00/2233-0270$15.00/0

The standard culture medium contained Dulbecco's modified Eagle's medium supplemented with 20% fetal bovine serum, 4 m*M* L-glutamine, 25 m*M* glucose, 1X nonessential amino acids (from 100X liquid, GIBCO-BRL, Tokyo, Japan), 100,000 U/l penicillin, 100 mg/l streptomycin, and 50 mg/l gentamycin. Media were replaced every 2 days or every day, depending on harvest times and degree of confluence. For experiments, subconfluent cells were plated onto Falcon 23.4-mm cell-culture inserts (pore size: 0.45 μm, Nippon Becton Dickinson) in six-well plastic plates at initial densities of 0.5×10^6 cells/well in standard medium. To test the effects of different concentrations of PYY on the expression of apolipoprotein genes in Caco-2 cells, the standard medium supplemented with 0, 1, 20, 50, 100, and 500 n*M* PYY (purified from human colon, purity > 96%, BACHEM AG, Budendorf, Switzerland) was supplied to the basolateral side of the monolayers at 10–14 days postconfluence. The cells were grown under the above conditions for an additional 12 hr and then harvested. To observe the time course of apolipoprotein and PYY receptor mRNA levels and apolipoprotein concentrations after addition of PYY in Caco-2 cells, the standard medium supplemented with 100 n*M* PYY was supplied to the basolateral side of the monolayers at 10–14 days postconfluence. The cells were cultured for 3, 6, 12, 24, and 72 hr and then harvested. Cells in the control wells were harvested prior to supplementation of PYY (0 time).

Extraction and Analysis of RNA. After washing with phosphate-buffered saline (PBS), the cell monolayers were added to a 1 ml/well Isogen (Nippon Gene, Tokyo, Japan), a reagent for RNA isolation, gently scraped with a plastic blade, and then transferred to a microcentrifuge tube. Thereafter, total RNA was isolated according to the manufacturer's protocol.

The steady-state levels of mRNA were semiquantitatively determined by reverse transcription polymerase chain reaction (RT-PCR) followed by Southern hybridization with an inner oligonucleotide probe. The total RNA samples were treated with DNase RQ1 (Promega, WI) to remove genomic DNA. Next, 5 μg of total RNA was annealed with 0.5 μg of oligo (dT) primer (GIBCO-BRL) at 70°C for 10 min, and first strand cDNA was then synthesized in a 20-μl solution containing 50 m*M* Tris-HCl pH 8.3, 75 m*M* KCl, 3 m*M* $MgCl_2$, 10 m*M* dithiothreitol (DTT), 0.5 m*M* dNTP, 25 U of RNase inhibitor, and 200 U of MMLV RTase (GIBCO-BRL) at 42°C for 50 min, followed by RNA digestion with RNase H (GIBCO-BRL). The first strand cDNA sample (0.5 μl) was added to 50 μl of a PCR reaction mixture containing 0.5 μ*M* gene-specific primers (Table I), 2 m*M* $MgCl_2$, 0.2 m*M* dNTP, and 1.25 U of EX-Taq polymerase (Takara, Otsu, Japan). Each cycle of PCR included 1 min of denaturation at 94°C, 1 min of primer annealing at different temperatures for each primer pair, and 2 min of extension at 72°C. The single band was detected by 2%

Table I. Oligonucleotide Primers Used for RT-PCR and Inner Oligonucleotide Probes Used for Southern Hybridization of RT-PCR Products

Target template		PCR primers	Product size (bp)
Apo A-I	Sense:	5′-CTGGCCCCCTACAGCGACGAG	253
	Antisense:	5′-GGGCGCCTCACTGGGTGTTGA	
Apo A-IV	Sense:	5′-TGAACACTTACGCAGGTGACC	866
	Antisense:	5′-GGTGCTGAAGAAGGAGTTGAC	
Apo B	Sense:	5′-CTGAATTCATTCAATTGGGAGAGACAAG	283
	Antisense:	5′-CACGGATATGATAGTGCTCAT	
Apo C-III	Sense:	5′-TCTGAGTTCTGGGATTTGGAC	189
	Antisense:	5′-AGGCATGAGGTGGGGTAGGAG	
Y1-receptor	Sense:	5′-AACAACCAAACCAATCAAAAT	362
	Antisense:	5′-ACTTACACATCGCCTCACCAA	
Y2-receptor	Sense:	5′-CATCATCTTGCTTGGGGTAAT	827
	Antisense:	5′-ATCCAGCCATAGAGAAGGGGA	
Y5-receptor	Sense:	5′-CAGAAAGCACAGAAGGAGGTA	285
	Antisense:	5′-GCGAACACGAGTATCAGTATG	
GAPDH	Sense;	5′-AAATCCCATCACCATCTTCCA	582
	Antisense:	5′-GCCTGCTTCACCACCTTCTTG	

	Inner oligonucleotide probes
Apo A-I	5′-CTCTCCAGCACGGGCAGCAGGCCTTGGCGGAGGTCCTCGAGCGCGGGCTTGGCC
Apo A-IV	5′-CTCCTCCAGCTCCTTCCCAATCTCCTCCTTCAGTTTCTCCGAGTCCTTGGCCAG
Apo B	5′-AATCATGTAAATCATAACTATCTTTAATATACTGA
Apo C-III	5′-GCAGGATGGATAGGCAGGTGGACTTGGGGTATTGAGGTCTCAGGCAGCCACGGC
Y1-receptor	5′-TGATCAAGGCCAGGTTTCCAGAGACACCAAGAATGATCACAGCTCCATAAGCAA
Y2-receptor	5′-TGGGCATAGGGCACCAGGTGGCACAGGACAGGACCCATTTTCCACTCCCCCATT
Y5-receptor	5′-TGGGACCCCTGGAATGACCTTACTGGATGGCGACAGCTGGCTACGGACGGAGGC
GAPDH	5′-TCCATGGTGGTGAAGACGCCAGTGGACTCCACGACGTACTCAGCGCCAGCATCG

Note. Primer and probe sequences correspond to the sequences for human and rat (for Y5-receptor) cDNAs deposited to GenBank.

agarose gel electrophoresis of PCR products, and the size of each product was consistent with the predicted size (data not shown). For each combination of primers the kinetics of amplification was studied in preliminary experiments, and PCR was performed within an exponential range. The PCR products separated on 2% agarose gel electrophoresis were transferred to a nylon membrane (Biodyne Plus, Pall, NY), and the blots were hybridized with each inner oligonucleotide probe (Table I) labeled with digoxigenin using a DIG oligonucleotide tailing kit (Boehringer Mannheim, Mannheim, Germany). Prehybridization, hybridization, and detection were carried out with a DIG luminescence detection kit (Boehringer Mannheim). The hybridization was performed at 42°C overnight, and posthybridization washing was performed with 0.1 X standard saline citrate (SSC), 0.1% sodium dodecyl sulfate (SDS) at 60°C three times for 15 min each wash. The bands developed on x-ray film were quantitated using NIH Image. The signal intensity of each apolipoprotein relative to that of glyceraldehyde-3-phosphate dehydrogenase (GAPDH), which was used as an internal control of PCR, was expressed as relative intensity. The results shown in Figures 1, 2, and 3 are from a representative experiment. The experiment was repeated three times, and similar results were obtained.

Western Blot Analysis. After washing with PBS, the cell monolayers were added to 1 ml/well of cell lysis buffer composed of 10 m*M* Tris-HCl pH 7.4, 150 m*M* NaCl, 1 m*M* EDTA, 10 μg/ml aprotinin, and 0.5% NP40, and incubated for 30 min on ice. The cell lysate was centrifuged (12,000*g*) for 20 min at 4°C, and a part of the supernatant (20 μg total protein) was subjected to 7.5% SDS-PAGE under reducing conditions. Electrophoresed proteins were electrophoretically transferred to a nitrocellulose membrane (Hybond C extra, Amersham International plc., Buckinghamshire, U.K.) and immunostained with the antihuman apo A-IV monoclonal antibody (Boehringer Mannheim) or the Sheep antihuman apo A-I serum (The Binding Site Ltd., Birmingham, UK) as previously described (11). The relative quantities of apo A-IV and apo A-I were estimated by using NIH Image.

Results

Figure 1 shows the results of Southern hybridization analysis of semiquantitative RT-PCR products for apolipoproteins in Caco-2 cells cultured for 12 hr with or without exogenous PYY. Apo A-IV mRNA levels progressively increased in response to the graded concentrations of PYY. In contrast, no changes in apo A-I, B, C-III, or GAPDH mRNA levels were observed. The time-course experiment demonstrated that apo A-IV mRNA began to increase at 3 hr following the addition of 100 n*M* of PYY, reaching a maximum value by 6 hr (Fig. 2). Although apo A-IV mRNA levels decreased somewhat 24 hr following the addition of PYY, they recovered to maximum levels at 72 hr. In contrast, mRNA encoding of other apolipoproteins or of GAPDH showed no change during the culture period following supplementation of PYY. Similarly, cellular concentrations of apo A-IV protein began to increase at 6 hr, whereas apo A-I protein concentrations were relatively constant throughout the culture period (Fig. 3).

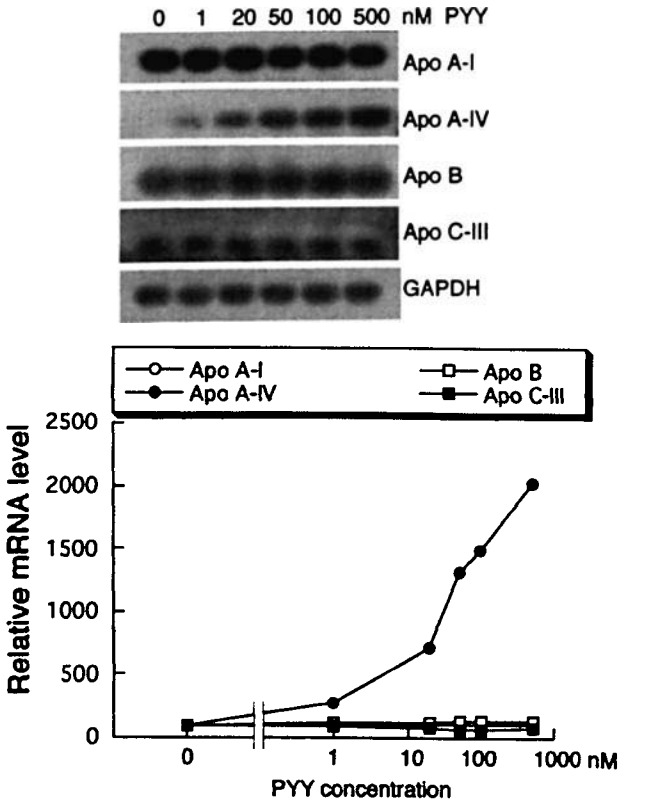

Figure 1. Effect of graded concentrations of PYY on mRNA expression of apolipoproteins in Caco-2 cells. Total RNA was isolated from Caco-2 cells cultured with or without PYY for 12 hr and subjected to semiquantitative RT-PCR followed by Southern hybridization with each inner oligonucleotide probe. The inset illustrates the representative Southern blots of RT-PCR products. GAPDH was used as the internal control for PCR. The signal intensity of each apolipoprotein relative to that of GAPDH is expressed as relative intensity, and the values on each point are expressed relative to values without PYY that are taken as 100. The results shown are from a representative experiment. The experiment was repeated three times, and similar results were obtained.

The major apolipoproteins reported to have been expressed in the enterocytes of the small intestine include apo A-I, A-IV, and B48 (21–24). In the present study, semiquantitative RT-PCR followed by Southern hybridization demonstrated that Caco-2 cells expressed mRNA that encoded the above apolipoproteins, suggesting that the cells showed an enterocyte-like phenotype when under experimental conditions like those used in the present study. In addition, apo A-I, C-III, and A-IV are reportedly encoded in a gene cluster localized in human chromosome 11 (11q23-qter) (25), and the present study detected apo C-III mRNA in Caco-2 cells. Among the apolipoproteins mentioned previously, apo A-IV was clearly shown to be the only one whose mRNA levels increased as a result of exogenous PYY in a dose- and time-dependent fashion, suggesting the specific upregulation of the *apo A-IV* gene by the gastrointestinal hormone PYY. Additionally, the increase in cellular

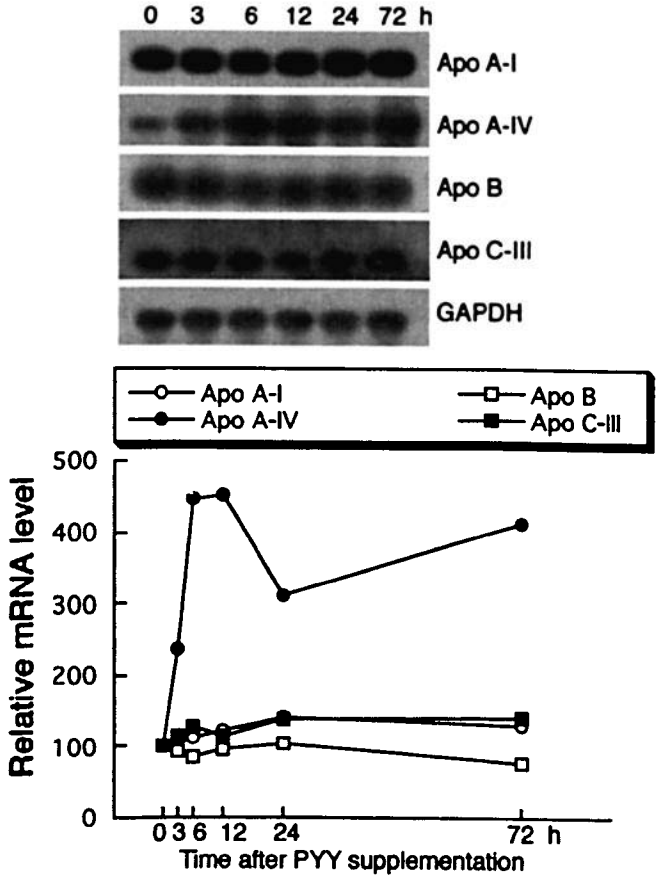

Figure 2. Time course of changes in mRNA levels of apolipoproteins in Caco-2 cells after supplementation of PYY. Total RNA was isolated from Caco-2 cells cultured with 100 n*M* of PYY for 0, 3, 6, 12, 24, and 72 hr and analyzed as described in Figure 1. The inset illustrates the representative Southern blots of RT-PCR products. The signal intensity of each apolipoprotein relative to that of GAPDH is expressed as relative intensity, and the values on each time point are expressed relative to values of 0 time, which are taken as 100. The results shown are from a representative experiment. The experiment was repeated three times, and similar results were obtained.

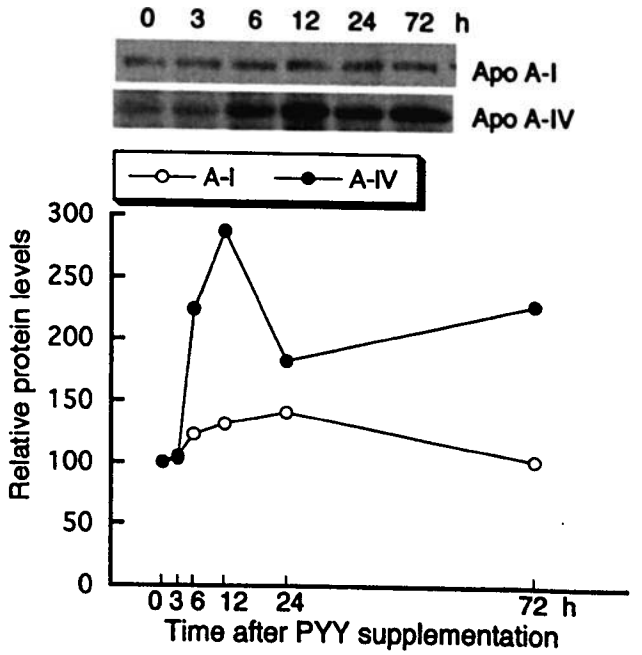

Figure 3. Time course of changes in relative concentrations of apolipoproteins in Caco-2 cells after supplementation of PYY. Cells were lyzed at 0, 3, 6, 12, 24, and 72 hr after adding 100 n*M* of PYY, and the cell lysates were subjected to Western blot analysis. The inset illustrates the representative Western blots. The values on each time point are expressed relative to values of 0 time, which are taken as 100. The results shown are from a representative experiment. The experiment was repeated three times, and similar results were obtained.

concentrations of apo A-IV protein after adding the PYY suggests that exogenous PYY stimulates apo A-IV synthesis at pretranslational levels in Caco-2 cells. As the PYY release from enteroendocrine cells in the distal bowel has been shown to be stimulated by dietary fat (26–28), the PYY modulation of *apo A-IV* gene expression may, at least in part, explain the stimulation of intestinal *apo A-IV* gene expression by dietary fat (29).

Discussion

We previously demonstrated that massive small bowel resection led to a rapid increase in apo A-IV mRNA levels in the remnant ileum of the rat (11–13). Given that PYY mRNA levels in the residual ileum and the plasma PYY concentrations were reported to be elevated following massive small bowel resection (16–18), we suspected the involvement of PYY in the postresectional increase in *apo A-IV* gene expression in the residual ileum. The present results suggest that increased concentrations of plasma PYY following small bowel resection may, at least in part, contribute to the upregulation of the *apo A-IV* gene in the residual ileum.

Halldén and Aponte (30) demonstrated that the expression of the intestinal fatty acid binding protein (*I-FABP*) gene was stimulated by 100 n*M* of PYY in the small intestinal somatic cell hybrids (hBRIE 380i cells). Additionally, *I-FABP* was shown to be a cytosolic protein abundantly expressed in enterocytes (31), which are involved in the intracellular trafficking and/or metabolism of free fatty acids (FFAs) in the enterocytes (32). The synthesis of *I-FABP* in enterocytes has been shown to be stimulated by a high-fat diet (33). Furthermore, Rubin *et al.* (34) reported that, as with apo A-IV mRNA, I-FABP mRNA was increased in the residual ileum following massive small bowel resection in the rat. Given the above findings, it was believed that under conditions of increased availability of intestinal fatty acids derived from diet and bile (e.g., a high-fat diet and small bowel resection), the increased concentrations of PYY would induce both I-FABP and apo A-IV, and thus facilitate intracellular trafficking and/or metabolism of FFAs followed by assembly and/or secretion of TG-rich lipoproteins in the enterocytes.

A few potential limitations of the present study should be noted at this point. First, although Savage *et al.* (16) previously reported that the plasma concentrations of PYY were 28 and 85 p*M* in sham-operated and small bowel–resected rats, respectively, the increase in apo A-IV mRNA

in Caco-2 cells was observed when PYY was added at concentrations of over 1 n*M*. Thus, Caco-2 cells likely require supraphysiological concentrations of PYY for the upregulation of the *apo A-IV* gene. One possible explanation for this problem is that there may be certain defects in the signal transduction pathway of PYY in Caco-2 cells. The present study investigated the gene expression of recently cloned Y1, Y2 and Y5 receptor subtypes that have similar affinity for PYY and neuropeptide Y (35). Southern hybridization of RT-PCR products indicated that mRNA for the Y1 receptor was detected in Caco-2 cells and transiently increased by 100 n*M* PYY (Fig. 4). However, in the case of Y2 and Y5 receptor mRNA, no signal was detected even when the number of PCR cycles was increased to 40 (data not shown). These findings suggest that modulation of *apo A-IV* gene expression by PYY is likely through the Y1-receptor subtype in Caco-2 cells and that the Y1-receptor gene is upregulated by its putative ligand, PYY. However, it remains unclear whether the abundance, structure, and function of the receptor in Caco-2 cells are similar to those in the enterocyte *in vivo*. In addition, there is no information on the integrity of intracellular machinery for signal transduction of PYY in Caco-2 cells. Nevertheless, given the dose- and time-dependent increase in apo A-IV mRNA levels in the present study, it is likely that the upregulation of the *apo A-IV* gene in Caco-2 cells is a physiological response to PYY. Thus, further studies are necessary to clarify not only the molecular mechanisms underlying the regulation of the *apo A-IV* gene by PYY but also the integrity of signal transduction of PYY in Caco-2 cells.

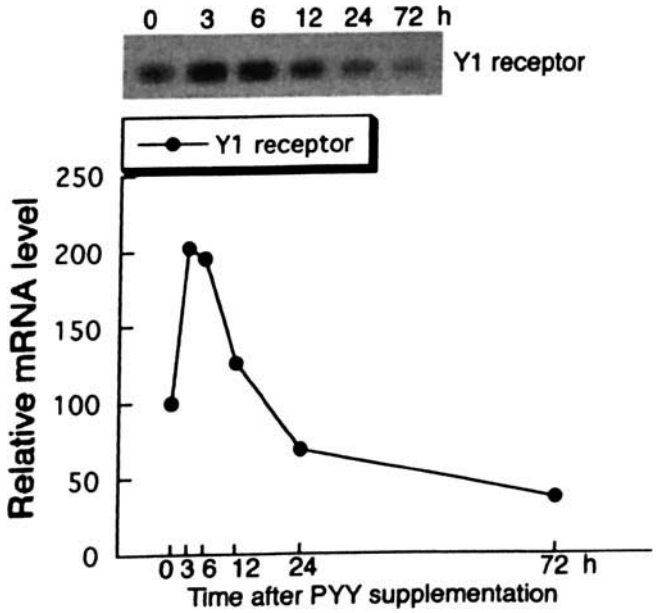

Figure 4. Time-course of changes in mRNA levels of the PYY/Y1 receptor in Caco-2 cells after supplementation of 100 n*M* PYY. The same samples used in Figure 2 were analyzed for Y1 receptor mRNA. The inset illustrates the representative Southern blots of RT-PCR products. The signal intensity of each apolipoprotein relative to that of GAPDH is expressed as relative intensity, and the values on each time point are expressed relative to values of 0 time, which are taken as 100. The results shown are from a representative experiment. The experiment was repeated three times, and similar results were obtained.

Secondly, although we demonstrated that exogenous PYY increased both mRNA and protein levels of apo A-IV in Caco-2 cells in the present study, Kalogeris *et al.* (36) recently reported that intravenous infusion of physiological doses of PYY resulted in a significant increase in the synthesis and lymphatic output of apo A-IV protein, with no corresponding changes in mRNA levels in the jejunum of rats. Similarly, we confirmed that intravenous infusion of PYY (1–100 pmole/kg hr for 8 hr) did not stimulate the *apo A-IV* gene in either the jejunum or ileum of rats (unpublished data). Although one may consider that lower concentrations of PYY can stimulate apo A-IV synthesis without increasing mRNA levels, our preliminary experiment showed that physiological concentrations of PYY (1–100 p*M*) could stimulate neither protein contents (analyzed by Western blotting) nor mRNA levels of apo A-IV in Caco-2 cells (unpublished data). Despite the lack of any experimental evidence to date to explain the above inconsistent observations, it is possible that there may be species-dependent differences in the PYY modulation of intestinal *apo A-IV* expression. Another possibility is that PYY stimulation of *apo A-IV* synthesis *in vivo* would be mediated by indirect mechanisms that may not be accompanied by the induction of mRNA expression. Thus, since inhibition of proximal gut function as part of the "ileal brake" by systemic PYY has been shown to be mediated by the vagus nerve (37), and since *apo A-IV* has been reported to share the "ileal brake" with PYY (9, 10), it is theoretically possible that PYY may stimulate *apo A-IV* synthesis *via* the vagus nerve. Therefore, it is of interest to investigate whether PYY stimulation of *apo A-IV* synthesis is diminished by blockade of the vagus nerve.

The present study findings taken as a whole demonstrated that the gastrointestinal hormone PYY specifically stimulated the expression of the *apo A-IV* gene in the human intestinal cell line Caco-2. The results suggest that PYY may play an important role in the regulation of *apo A-IV* gene expression, likely *via* the PYY/Y1 receptor in the enterocytes. This may, at least in part, explain the upregulation of *apo A-IV* expression in the residual ileum following massive small bowel resection.

We are grateful to Dr. Gregory W. Aponte for helpful suggestions.

1. Elshourbagy NA, Boguski MS, Liao WSL, Jefferson LS, Gordon JI, Taylor JM. Expression of rat apolipoprotein *A-IV* and *A-I* genes: mRNA induction during development and in response to glucocorticoids and insulin. Proc Natl Acad Sci U S A **82**:8242–8246, 1985.
2. Chen CH, Albers JJ. Activation of lecithin: Cholesterol acyltransferase by apolipoproteins E-2, E-3, and A-IV isolated from human plasma. Biochim Biophys Acta **836**:279–285, 1985.
3. Dvorin E, Gorder NL, Benson DM, Gotto AM Jr. Apolipoprotein A-IV: A determinant for binding and uptake of high density lipoproteins by rat hepatocytes. J Biol Chem **261**:15714–15728, 1986.

4. Stein O, Stein Y, Lefevre M, Roheim PS. The role of apolipoprotein A-IV in reverse cholesterol transport studied with cultured cells and liposomes derived from an ether analog of phosphatidylcholine. Biochim Biophys Acta **878**:7–13, 1986.
5. Steinmetz A, Utermann G. Activation of lecithin: Cholesterol acyltransferase by human apolipoprotein A-IV. J Biol Chem **260**:2258–2264, 1985.
6. Steinmetz A, Barbaras R, Ghalim N, Clavey V, Fruchart JC, Ailhaud G. Human apolipoprotein A-IV binds to apolipoprotein A-I/A-II receptor sites and promotes cholesterol efflux from adipose cells. J Biol Chem **265**:7859–7863, 1990.
7. Fujimoto K, Cardelli JA, Tso P. Increased apolipoprotein A-IV in rat mesenteric lymph after lipid meal acts as a physiological signal for satiation. Am J Physiol **262**:G1002–G1006, 1992.
8. Fujimoto K, Fukagawa K, Sakata T, Tso P. Suppression of food intake by apolipoprotein A-IV is mediated through the central nervous system in rats. J Clin Invest **91**:1830–1833, 1993.
9. Okumura T, Fukagawa K, Tso P, Taylor IL, Pappas TN. Intracisternal injection of apolipoprotein A-IV inhibits gastric secretion in pylorus-ligated conscious rats. Gastroenterology **107**:1861–1864, 1994.
10. Okumura T, Fukagawa K, Tso P, Taylor IL, Pappas TN, Uehara A, Kohgo Y. Delayed gastric emptying by central apolipoprotein A-IV in rats. Gastroenterology **108**:A996, 1995.
11. Sonoyama K, Kiriyama S, Niki R. Adaptive response of apolipoprotein A-I and A-IV mRNA in residual ileum after massive small bowel resection in rats. J Nutr Sci Vitaminol **41**:253–264, 1995.
12. Sonoyama K, Nakamura Y, Kiriyama S, Niki R. Upregulation of apolipoprotein *A-IV* gene expression in residual ileum after massive small bowel resection requires the biliary secretion in rats. Proc Soc Exp Biol Med **211**:273–280, 1996.
13. Sonoyama K, Aoyama Y. Different responses of apolipoprotein *A-I, A-IV,* and *B* gene expression during intestinal adaptation to a massive small bowel resection in rats. Biosci Biotechnol Biochem **61**:1810–1813, 1997.
14. Ali-Rachedi A, Varndell IM, Adrian TE, Gapp DA, Van Noorden S, Bloom SR, Polak JM. Peptide YY (PYY) immunoreactivity is co-stored with glucagon-related immunoreactants in endocrine cells of the gut and pancreas. Histochemistry **80**:487–491, 1984.
15. Bottcher G, Sjolund K, Ekblad E, Hakanson R, Schwartz TW, Sundler F. Coexistence of peptide YY and glicentin immunoreactivity in endocrine cells of the gut. Regul Pept **8**:261–266, 1984.
16. Savage AP, Gornacz GE, Adrian TE, Ghatei MA, Goodlad RA, Wright NA, Bloom SR. Is raised plasma peptide YY after intestinal resection in the rat responsible for the trophic response? Gut **26**:1353–1358, 1985.
17. Taylor RG, Beveridge DJ, Fuller PJ. Expression of ileal glucagon and peptide tyrosine-tyrosine genes: Response to inhibition of polyamine synthesis in the presence of massive small-bowel resection. Biochem J **286**:737–741, 1992.
18. Fuller PJ, Beveridge DJ, Taylor RG. Ileal proglucagon gene expression in the rat: Characterization in intestinal adaptation using *in situ* hybridization. Gastroenterology **104**:459–466, 1993.
19. Gordon JI. Intestinal epithelial differentiation: New insights from chimeric and transgenic mice. J Cell Biol **108**:1187–1194, 1989.
20. Levy E, Mehran M, Seidman E. Caco-2 cells as a model for intestinal lipoprotein synthesis and secretion. FASEB J **9**:626–635, 1995.
21. Davidson NO, Magun AM, Brasitus TA, Glickman RM. Intestinal apolipoprotein A-I and B-48 metabolism: Effects of sustained alterations in dietary triglyceride and mucosal cholesterol flux. J Lipid Res **28**:388–402, 1987.
22. Fidge NH. The redistribution and metabolism of iodinated apolipoprotein A-IV in rats. Biochim Biophys Acta **619**:129–141, 1980.
23. Hayashi H, Fujimoto K, Cardelli JA, Nutting DF, Bergstedt S, Tso P. Fat feeding increases size, but not number, of chylomicrons produced by small intestine. Am J Physiol **259**:G709–G719, 1990.
24. Weinberg RB, Dantzker C, Patton CS. Sensitivity of serum apolipoprotein A-IV levels to changes in dietary fat content. Gastroenterology **98**:17–24, 1990.
25. Karathanasis SK. Apolipoprotein multigene family: Tandem organization of human apolipoprotein *AI, CIII,* and *AIV* genes. Proc Natl Acad Sci U S A **82**:6374–6378, 1985.
26. Pappas TN, Debas HT, Goto Y, Taylor IL. Peptide YY inhibits meal-stimulated pancreatic and gastric secretion. Am J Physiol **248**: G118–G123, 1985.
27. Aponte GW, Fink AS, Meyer JH, Tatemoto K, Taylor IL. Regional distribution and release of peptide YY with fatty acids of different chain length. Am J Physiol **249**:G745–G750, 1985.
28. Aponte GW, Park K, Hess R, Garcia R, Taylor IL. Meal-induced peptide tyrosine tyrosine inhibition of pancreatic secretion in the rat. FASEB J **3**:1949–1955, 1989.
29. Gordon JI, Smith DP, Alpers DH, Strauss AW. Cloning of a complementary deoxyribonucleic acid encoding a portion of rat intestinal preapolipoprotein AIV messenger ribonucleic acid. Biochemistry **21**:5424–5431, 1982.
30. Halldén G, Aponte GW. Evidence for a role of the gut hormone PYY in the regulation of intestinal fatty acid-binding protein transcripts in differentiated subpopulations of intestinal epithelial cell hybrids. J Biol Chem **272**:12591– 12600, 1997.
31. Gordon JI, Elshourbagy N, Lowe JB, Liao WS, Alpers DH, Taylor JM. Tissue-specific expression and developmental regulation of two genes coding for rat fatty acid binding proteins. J Biol Chem **260**:1995–1998, 1985.
32. Hsu KT, Storch J. Fatty acid transfer from liver and intestinal fatty acid binding proteins to membranes occurs by different mechanisms. J Biol Chem **271**:13317– 13323, 1996.
33. Bass NM. The cellular fatty acid binding proteins: Aspects of structure, regulation, and function. Int Rev Cytol **111**:143–184, 1988.
34. Rubin DC, Swietlicki EA, Wang JL, Dodson BD, Levin MS. Enterocytic gene expression in intestinal adaptation: Evidence for a specific cellular response. Am J Physiol **270**:G143–G152, 1996.
35. Blomqvist AG, Herzog H. Y-receptor subtypes: How many more? Trends Neurosci **20**:294–298, 1997.
36. Kalogeris TJ, Qin X, Chey WY, Tso P. PYY stimulates synthesis and secretion of intestinal apolipoprotein A-IV without affecting mRNA expression. Am J Physiol **275**:G668–G674, 1998.
37. Chen CH, Rogers RC. Central inhibitory action of peptide YY on gastric motility in rats. Am J Physiol **269**:R787–R792, 1995.