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Dietary regulation of amino acid transport activity in the exocrine pancreatic epithelium

M. Muñoz *, P.W. Emery [b], S. Peran * and G.E. Mann [a]

Departments of [a] Physiology and [b] Nutrition, King's College London, London (U.K.)

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Dietary-induced alterations in exocrine pancreatic amino acid transport were investigated in rats adapted for 14 days to isocaloric diets of varying casein and carbohydrate content. The kinetics of unidirectional (15 s) L-phenylalanine and L-lysine transport were measured relative to D-mannitol (extracellular tracer) in the perfused pancreas isolated from dietary adapted animals. In rats adapted to a 20% casein diet a weighted non-linear regression analysis of phenylalanine transport (1–24 mM) indicated an apparent $K_t = 9.4 \pm 1.1$ mM and $V_{max} = 14.8 \pm 0.9$ μmol/min per g pancreas ($n = 6$). Saturation of lysine transport occurred at lower concentrations (0.05–10 mM) with an apparent $K_t = 2.40 \pm 0.09$ mM and $V_{max} = 2.44 \pm 0.18$ μmol/min per g ($n = 6$). The characteristics of phenylalanine transport were modified after adaptation to either high ($K_t = 3.6 \pm 1$ mM, $V_{max} = 8.2 \pm 0.9$ μmol/min per g, $n = 3$) or low ($K_t = 4.2 \pm 0.9$ mM, $V_{max} = 6.8 \pm 0.5$ μmol/min per g, $n = 3$) carbohydrate diets. Increasing the dietary protein content (0–45% casein) led to a linear increase in the K_t for phenylalanine transport whereas V_{max} values remained unchanged. Unlike phenylalanine, adaptation to a 0% casein diet significantly elevated the V_{max} for lysine transport (4.82 ± 0.21 μmol/min per g, $n = 4$) without altering the K_t (2.54 ± 0.23 mM). The present findings suggest that changes in dietary composition induce select adaptive responses in the transport activities of System L (phenylalanine) and System y^+ (lysine) in the basolateral membrane of the exocrine pancreatic epithelium.

Introduction

Enzyme synthesis in the mammalian exocrine pancreas appears to be directly influenced by dietary protein and carbohydrate intake [1–9], and adaptation of pancreatic lipase synthesis is dependent upon the amount and type of dietary fat [10–13]. Dietary control of pancreatic protein synthesis is known to be mediated by rapid, specific and reversible processes involving regulation of cytoplasmic mRNA levels [9,14]. It remains to be established whether changes in amino acid transport are associated with dietary-induced alterations in enzyme synthesis.

Previous studies in the perfused rat pancreas revealed that starvation, a condition known to reduce overall pancreatic protein synthesis (for review, see Ref. 15), elevated L-phenylalanine tranport [16] and increased pancreatic concentrations of large neutral amino acids [17]. The fasting-induced increase in phenylalanine transport may have been due to adaptive regulation (see

* Present address: Departamento de Bioquimica y Biologia Molecular, Facultad de Medicina, Universidad de Malaga, Spain.

Correspondence: G.E. Mann, Department of Physiology, King's College London, Campden Hill Road, London W8 7AH, U.K.

Refs. 18–21) and/or accelerated exchange diffusion [22] of phenylalanine for accumulated intracellular amino acid(s). Regulation of amino acid transport by substrate deprivation has mainly been ascribed to the Na^+-dependent System A (see Refs. 18–20), although other transporters including System Gly, N and L also undergo adaptive regulation (for review, see Ref. 19). In CHO-K1 cells Na^+-independent System L transport activity is modulated by leucine availability [21]. Control of System A appears to be transcriptional [18] whereas control of System L may be translational [21].

In the present study we have examined-dietary alterations in exocrine pancreatic amino acid transport. Transport kinetics were measured for the essential amino acids L-phenylalanine and/or L-lysine in the perfused rat pancreas isolated from animals adapted for 14 days to isocaloric diets of different protein, fat or carbohydrate content. Preliminary accounts of part of this work have been communicated [23,24].

Materials and Methods

Animals and diets

Male Sprague-Dawley rats weighing either between 85 and 125 g or 195 and 210 g (0% casein experiments) were housed individually in suspended wire-bottomed cages. Animals were offered water ad libitum and adapted for 14 days to isocaloric powered diets containing varying amounts of casein (0%–45%) and carbohydrate. Table I summarizes the composition of each diet.

Each animal's weight gain or loss and daily food intake were recorded throughout the dietary

TABLE I

COMPOSITION OF DIETS USED IN THE PRESENT STUDY

Animals were allowed food and water ad libitum and groups of animals were fed a given diet for 14 days prior to an experiment. Values are g of each component per 100 g food. Abbreviations HCHO and LCHO refer respectively to high and low carbohydrate diets.

Component	Casein				HCHO	LCHO
	0%	10%	20%	45%		
Casein [a]	0	10	20	45	15	15
Sugar	18	18	18	18	18	18
Corn starch	60	50	40	15	56	0
Corn oil	10	10	10	10	5	30
Cellulose	6	6	6	6	0	31
Vitamin mix [b]	2	2	2	2	2	2
Mineral mix [c]	4	4	4	4	4	4

[a] Amino acid content (%): lysine (0.85), methionine (0.54), tryptophan (0.21), threonine (0.59), arginine (1), methionine + cystine (0.81).

[b] Vitamins/100 g diet: Rovimix A325 (2.5 mg, Roche), Rovimix A325/D_3 (1.5 mg), thiamine (1 mg), riboflavin (1 mg), B_6 (1 mg), B_{12} (0.1 mg), Rovimix E25 (30 mg), K_3 (0.1 mg), folic acid (0.1 mg), nicotinic acid (6 mg), pantothenic acid (4 mg), ascorbic acid (7.5 mg), choline bitartrate (0.18 g).

[c] Minerals/100 g diet: iron (0.17 mg), copper (1.5 mg), manganese (18 mg), zinc (3 mg), iodine (0.1 mg), magnesium (0.3 g), sodium (1.4 g), chloride (0.8 g), potassium (0.8 g), phosphate (0.74 g), calcium (2.1 g).

TABLE II

EFFECTS OF ALTERED DIETARY CASEIN AND CARBOHYDRATE COMPOSITION ON WEIGHT GAIN OR LOSS AND FOOD CONSUMPTION IN RATS FED THE RESPECTIVE DIETS FOR 14 DAYS

The dietary compositions and abbreviations are defined in Table I. Food consumption was measured daily and is expressed as grammes consumed per 100 g body weight per 24 h. Values denote mean ± S.E. of measurements in (n) animals.

	Casein				HCHO	LCHO
	0%	10%	20%	45%		
Initial weight (g)	196 ± 5 (8)	93 ± 2 (12)	87 ± 2 (8)	106 ± 3 (12)	126 ± 3 (7)	135 ± 4 (7)
Final weight (g)	159 ± 5	117 ± 7	166 ± 5	185 ± 5	199 ± 4	232 ± 9
Weight gain (g)	−37 ± 3	24 ± 5	79 ± 5	78 ± 3	73 ± 3	98 ± 6
% Change	−19	+26	+90	+75	+52	+72
Food consumed (g/100 g per day)	8 ± 0.3	14 ± 0.6	11 ± 0.3	11 ± 0.3	11 ± 0.4	12 ± 0.4

adaptation period (see Table II). The initial weights varied marginally to ensure successful isolation and perfusion of the pancreas, and our previous findings indicate that transport does not vary over this weight range. As rats adapted to a 0% casein diet lost weight, it was necessary to study animals with an initial weight between 195 and 210 g. Fed animals were anesthetized between 9 a.m. and 1 p.m. with sodium pentobarbitone (60 mg/kg 'Sagatal' i.p.), and supplementary anesthetic was administered intravenously.

Isolation and perfusion of the pancreas

As previously described [16,23–27], the pancreas was perfused at constant flow (approx. 1.8 ml/min) with a heated (38°C), oxygenated Krebs-Henseleit bicarbonate solution containing 2.5 mM D-glucose, bovine serum albumin (0.25% w/v, Cohn Fraction V, Sigma Chemical Co., Dorset, U.K.) and Dextran T70 (5% w/v, Meito Sangyo Co., Japan). The pH, p_{O_2}, and p_{CO_2} of arterial perfusates and the pancreatic venous effluent were monitored during experiments using an ABL2 Acid-Base Laboratory (Radiometer, Copenhagen, Denmark). Venous effluent samples were collected at 10 min intervals in glass capillary tubes and processed immediately. Pancreatic oxygen consumption was estimated from: $(p_{aO_2} - p_{vO_2}/p_{atmosphere}) \cdot S \cdot F$, where S is the solubility of O_2 in water at 37°C and 760 mmHg and F is the perfusion rate in ml/min per gram pancreas wet weight. Basal O_2 consumption (9–10 µl/min per g) remained constant over a 1 h perfusion interval (Fig. 1) and was not altered after adaptation to the different diets (data not shown).

Measurement of amino acid transport

Kinetics of pancreatic amino acid transport were quantitated using a rapid dual tracer dilution technique [28] previously applied in the perfused pancreas [16,23–26]. Unidirectional uptake was measured by comparing portal vein dilution curves for a tritiated L-amino acid and D-[^{14}C]mannitol (extracellular tracer) following an intra-arterial injection (100 µl/2 s) of perfusate containing both tracer molecules:

$$\text{uptake} = 1 - (\text{L-[}^3\text{H]amino acid}/\text{D-[}^{14}\text{C]mannitol})$$

Influx (v) was calculated from the maximal fractional L-[^{3}H]amino acid uptake (U_{max}), flow (F, ml/min per g) and the perfusate concentration (C_a) of unlabelled substrate (see Refs. 16 and 25):

$$v = -F \cdot \ln(1 - U_{max}) \cdot C_a$$

Pancreata were perfused for 4 min with six concentrations of L-phenylalanine (1–24 mM, Sigma) or L-lysine (0.05–10 mM, Sigma) before measuring L-[^{3}H]amino acid uptake in the continued presence of substrate. As in our previous studies [16,25], Michaelis-Menten kinetic constants were calculated using a single entry site analysis which revealed the lowest weighted standard deviation of residuals [29].

Statistical analysis

Results are presented as means ± standard error of the mean. Group differences in K_t and V_{max} were evaluated using a one-way analysis of variance. Subsequently, an unpaired Student t-test using the residual error of the analysis of variance was employed to assess significance of differences in K_t and V_{max}.

Radioactive molecules

L-[4-^{3}H]Phenylalanine (23.5 Ci/mmol) was purchased from Amersham International p.l.c. (U.K.) and L-[4,5-^{3}H]lysine (97 Ci/mmol) and D-[1-^{14}C]mannitol (53.4 mCi/mmol) from NEN, Dreieich, F.R.G.

Results

Animals consumed between 8 and 14 g diet per 100 g body weight/day (Table II) during adaptation (14 days) to each of the isocaloric diets (Table I). With exception of the animals adapted to a 0% casein diet, all other groups of animals gained weight.

Unidirectional uptake and efflux of L-phenylalanine

In pancreata isolated from 20% casein adapted rats L-[^{3}H]phenylalanine uptake was high (57 ± 4%, $n = 6$) during perfusion with 1 mM substrate. Unidirectional uptake was followed by rapid efflux of ^{3}H-labelled substrate (see Fig. 1 in Ref. 25), and in kinetic experiments tracer uptake was

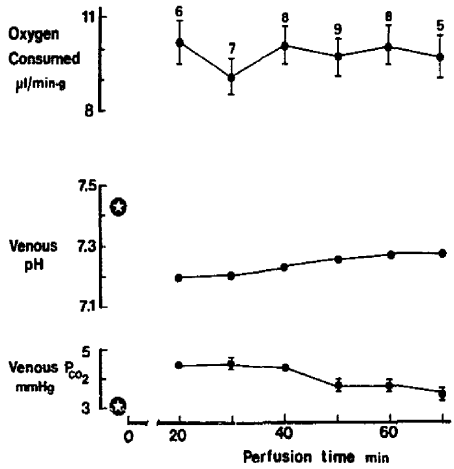

Fig. 1. Oxygen consumption by the isolated perfused rat pancreas. P_{O_2}, P_{CO_2} and pH levels in the arterial perfusate and venous effluent were measured over a 70 min perfusion interval using an ABL2 Acid-Base Laboratory. Mean arterial pH and P_{CO_2} levels ($n = 13$) are indicated by star symbols, and all other values denote the mean ± S.E. of measurements in 5–9 different preparations.

inhibited by increasing concentrations (1–24 mM) of phenylalanine (data not shown).

Adaptation of phenylalanine transport to altered carbohydrate content

Influx of phenylalanine conformed to Michaelis-Menten kinetics and was best described by a single entry site analysis (Fig. 2). The kinetic data from animals adapted to a 20% casein diet revealed a $K_t = 9.4 \pm 1.1$ mM and $V_{max} = 14.8 \pm 0.9$ µmol/min per g (mean ± S.E., $n = 6$ rats). An Eadie-Hofstee transformation confirmed that influx occurred via a single entry site (Fig. 2B). After adaptation to a diet low in carbohydrate and high in fat, both the K_t (4.2 mM) and V_{max} (6.8 µmol/min per g) for phenylalanine transport were reduced. In rats adapted to a diet rich in carbohydrate, the K_t (3.6 mM) and V_{max} (8.2 µmol/min per g) for phenylalanine transport were also decreased relative to values measured in rats fed a 20% casein diet (Table III). A one-way analysis of variance using all six groups of data revealed significant group differences for both K_t and V_{max}. Subsequent unpaired t-tests using the residual error of the analysis of variance confirmed that the characteristics of phenylalanine transport measured in rats adapted to a 20% casein diet were significantly altered following adaptation to either a high or low carbohydrate diet (Table III).

Effects of altered dietary protein content on phenylalanine transport

In the present study adaptation to reduced dietary protein gradually lowered the K_t for phenylalanine transport without significantly altering the maximal transport capacity (Table III). Although an analysis of variance revealed no significant alterations, a weighted regression analysis indicated that increases in dietary casein (0%–45%) resulted in higher K_t values for phenyalanine transport ($r = 0.94$, $P < 0.05$). Moreover, the rate constant (V_{max}/K_t) for phenylalanine transport decreased from 2.15 (0% casein) to 1.47 following

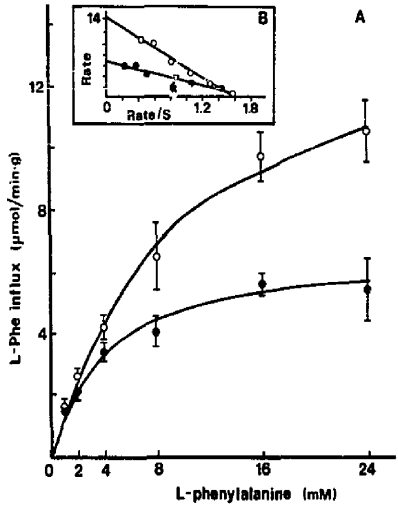

Fig. 2. Adaptation of pancreatic L-phenylalanine transport to a low carbohydrate diet. Preparations were isolated from rats adapted for 14 days to either a 20% casein (○——○) or low carbohydrate diet (●——●) and perfused in vitro with six different concentrations of L-phenylalanine (1–24 mM). (A) Michaelis-Menten kinetic curves were obtained by a direct fit to the mean influx values weighted for the reciprocal of their respective standard errors. Values denote the mean ± S.E. of measurements in 3–6 animals. (B) Eadie-Hofstee analysis of phenylalanine transport. Data denote mean values and lines were obtained using a linear regression analysis.

adaptation to a 45% casein diet (Table III). When compared with the 20% casein diet, adaptation to 45% casein had negligible effects on the V_{max} or V_{max}/K_t ratio for phenylalanine transport.

Adaptation of L-lysine transport to a 0% casein diet

Influx of the essential basic amino acid L-lysine was saturable at lower substrate concentrations, and a weighted Michaelis-Menten analysis (Fig. 3A) revealed a $K_t = 2.44 \pm 0.18$ mM, $V_{max} = 2.40 \pm 0.09$ μmol/min · g and $V_{max}/K_t = 0.98$ ($n = 6$). An Eadie-Hofstee transformation of the control influx measurements confirmed that uptake occurred via a single entry site (Fig. 3B). Our previous studies in the perfused rat pancreas [23] suggested that influx of lysine and other basic amino acids was mediated largely by a cationic amino acid transporter resembling System y^+ described in hepatocytes [30].

Lysine transport was also measured in rats adapted to a 0% casein diet. As shown in Fig. 3, adaptation to a 0% casein diet had no effect on the K_t (2.54 ± 0.23 mM, $n = 4$) for lysine transport but doubled the transport capacity ($V_{max} = 4.82 \pm 0.21$ μmol/min.g) and the V_{max}/K_t ratio. Moreover, lysine transport was still mediated by a single entry site. We have not yet examined the effects of altered carbohydrate intake on lysine uptake nor the reversibility of dietary-induced changes in lysine (0% casein diet) or phenylalanine (high and low carbohydrate diets) transport.

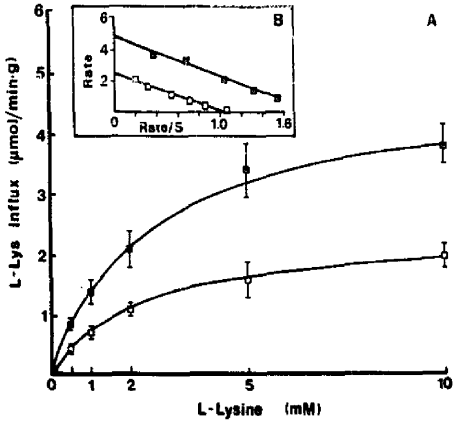

Fig. 3. Adaptation of pancreatic lysine transport to a 0% casein diet. Kinetics of L-lysine transport was measured during perfusion of isolated preparations with six substrate concentrations (0.5–10 mM). Control diet (□——□), 0% casein diet (■——■). (A) Michaelis-Menten kinetic curves were obtained as described in the legend to Fig. 2. Values denote the mean ± S.E. of measurements in 4–6 animals. (B) Eadie-Hofstee analysis of lysine transport. Data denote mean values and lines were obtained using a linear regression analysis.

TABLE III

DIETARY REGULATION OF PANCREATIC L-PHENYLALANINE TRANSPORT

The kinetics of rapid (approx. 15 s) phenylalanine influx were quantified using a single weighted Michaelis-Menten analysis (see Methods). The V_{max}/K_t ratios for each experimental condition are tabulated for comparison. Values denote the mean ± S.E. of between 18 and 31 measurements in 3–6 animals. An unpaired *t*-test using the residual error from an analysis of variance was applied to assess the differences in K_t or V_{max} with respect to the group fed a 20% casein diet.

Condition	*n*	K_t (mM)	V_{max} (μmol/min per g)	V_{max}/K_t
0% Casein	4	6.9 ± 1.2	14.9 ± 1.2	2.15
10% Casein	6	9.2 ± 1.4	18.0 ± 1.5	1.96
20% Casein	6	9.4 ± 1.1	14.8 ± 0.9	1.57
45% Casein	5	11.3 ± 1.8	16.7 ± 1.5	1.47
Low CHO	3	4.2 ± 0.9	6.8 ± 0.5 [c]	1.62
High CHO	3	3.6 ± 1.0 [a]	8.2 ± 0.9 [b]	2.27

Comparison with 20% casein diet: [a] $P < 0.05$, [b] $P < 0.01$, [c] $P < 0.001$.

Discussion

The present findings indicate that amino acid transporters in the basolateral membrane of the pancreatic epithelium are modulated differently by altered dietary intake. The maximal transport rate of System L (phenylalanine) appeared to be inhibited after adaptation to diets of high carbohydrate (Table III) and low carbohydrate (high fat) content (Fig. 2). Depletion of dietary protein appears to have selectively reduced the K_t for phenylalanine transport (Table III) and doubled the V_{max} for lysine transport via the cationic System y^+ (Fig. 3).

Adaptation to changes in dietary carbohydrate

An increased intake of dietary carbohydrate results in adaptive changes in the pancreatic con-

tent of active cytoplasmic mRNA levels and enzyme synthesis [9]. A 3.6-fold increase in the ratio of amylase:serine proteinases was measured by these authors in isolated rat pancreatic lobules. By contrast, mRNAs coding for lipase and procarboxypeptidases were unaffected by these nutritional manipulations. Further studies are required to establish whether the observed reduction in the V_{max} for phenylalanine transport (Table III) is correlated with decreased levels of serine proteinases or altered amino acid metabolism.

A high carbohydrate diet induced complex changes in phenylalanine transport. Although the K_t and V_{max} decreased following adaptation to a high carbohydrate diet (Table III), the more significant index of rate (V_{max}/K_t) increased 1.4-fold with respect to the 20% casein diet. In intestinal brush-border membrane vesicles prepared from rats adapted to a high carbohydrate diet K_t and V_{max} values for leucine transport were also reduced when compared with values from rats adapted to a high protein diet [31]. As our experimental protocols utilized isocaloric diets, it is difficult to assess whether the reductions in protein and fat in the high carbohydrate diet also affected transport. Elevated carbohydrate intake is known to stimulate insulin secretion [32], however, pancreatic phenylalanine transport was previously shown to be insulin-insensitive [16].

In the low carbohydrate diet corn starch was replaced by enhanced amounts of corn oil and cellulose (Table I). Under these conditions only the V_{max} for phenylalanine transport was significantly reduced compared to animals fed a 20% casein diet (Table III). In contrast to the high carbohydrate diet the transport index V_{max}/K_t remained unchanged. Concurrent chromatographic studies in the pancreas in vivo have revealed that essential and non-essential intracellular amino acid levels are markedly reduced following adaptation to either low or high carbohydrate diets (Muñoz, M., Emery, P.W. and Mann, G.E., unpublished data). Under these conditions exchange diffusion of phenylalanine would be inhibited.

Release of cholecystokinin from the duodenum in response to increased dietary fat (LHCO diet) and protein intake stimulates pancreatic enzyme secretion [33] and may modulate pancreatic amino acid transport. We recently reported that carbachol, a cholinergic secretagogue with similar actions to cholecystokinin, rapidly inhibited influx and accelerated efflux of System A amino acids in the exocrine pancreatic epithelium [34].

Adaptation to changes in dietary protein

In rats adapted for 12 days to a protein-free diet total pancreatic enzyme synthesis has been reported to decrease by 30%, and yet synthesis of acidic proteinase zymogens such as trysinogen 1 and 2, chymotrypsinogen 1, proelastase 1 and procarboxypeptidases A and B is markedly enhanced [8]. These authors concluded that dietary adaptation to zero protein was under genetic control and prepared the animal for survival during periods of protein deprivation. Decreases in dietary casein has no significant effects on the V_{max} or K_t for phenylalanine transport in the pancreas (Table III), although the value of V_{max}/K_t increased 1.5-fold as dietary casein intake was reduced from 45% to 0%. The observed changes in V_{max}/K_t appeared to be mediated by an increase in the substrate affinity of the transport system. Such an adaptation would facilitate substrate uptake at lowered plasma amino acid concentrations. In contrast to phenylalanine, the V_{max} for lysine doubled (Fig. 3) after adaptation to a 0% casein diet suggesting an increase in the number of functional memrane carriers.

During development amino transport in the rat pancreas undergoes significant changes, and subsequent to birth there is a rapid increase in transport associated with food intake [35]. This increased rate of amino acid transport may be related to dietary-induced changes in the synthesis of pancreatic digestive enzymes [3]. In hepatocytes leucine and alanine transport were shown to increase markedly in rats fed a high protein (90% casein) diet [36]. It was suggested that adaptation to the 90% casein diet enhanced the transport activity of the small neutral amino acid carrier System A, since neither System L nor System ASC exhibited any significant changes. The adaptative response for leucine, normally transported by a large neutral System L, was partly attributed to an adaptation of enzymes of leucine catabolism [36].

The present findings suggest that System L transport activity in the exocrine pancreas is in-

fluenced not only by fasting and refeeding [16] but also by alterations in dietary protein and carbohydrate intake. Unlike phenylalanine, lysine transport via a cationic membrane carrier resembling System y^+ (see Ref. 30) is stimulated after adaptation to a 0% casein diet. We have yet not determined whether these dietary-induced changes in precursor amino acid uptake are the consequence of altered pancreatic amino metabolism and/or digestive enzyme synthesis.

As reviewed by Dagorn [37], pancreatic adaptation to dietary changes occurs at the level of expression of genes coding for different pancreatic proteins. Changes in the relative rates of protein synthesis occur within 2–4 h [5] and moreover, different mechanisms may be involved in regulating adaptation of pancreatic protein synthesis to high carbohydrate or high protein diets [6]. It is interesting that changes in pancreatic enzyme activities identified in rats adapted to a high fat diet appear to be associated with a depressed acinar cell transport and metabolism of glucose [38] and a decreased intracellular pool size for phenylalanine [39]. As amino acid availability and fasting appear to modulate amino acid transport [16,18–21,36], nutritionally-induced changes in the characteristics of basolateral amino acid transporters may influence the synthesis of pancreatic digestive enzymes.

Acknowledgments

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References

1 Abdeljlil, A.B., Visani, A.M. and Desnuelle, P. (1963) Biochem. Biophys. Res. Commun. 10, 112–116.
2 Deschodt-Lanckman, M., Robberecht, P., Camus, H. and Christophe, J. (1971) Biochimie 53, 789–796.
3 Snook, J.T. (1971) Am. J. Physiol. 221, 1383–1387.
4 Keim, V. (1986) Ann. Nutr. Metab. 30, 113–119.
5 Dagorn, J.-C. and Lahaie, R.G. (1981) Biochim. Biophys. Acta 654, 111–118.
6 Lahaie, R.G. and Dagorn, J-C. (1981) Biochim. Biophys. Acta 654, 119–123.
7 Poort, S.R. and Poort, C. (1981) J. Nutr. 111, 1475–1479.
8 Schick, J., Verspohl, R., Kern, H. and Scheele, G.A. (1984) Am. J. Physiol. 247, G611–G616.
9 Wicker, C., Puigserver, A. and Scheele, G.A. (1984) Eur. J. Biochem. 139, 381–387.
10 Vandermeers-Piret, M.C., Vandermeers, A., Wiljns, W., Rathe, J. and Christophe, J. (1977) Am. J. Physiol. 232, E131–E135.
11 Saraux, B., Girad-Globa, A., Ouagued, M. and Vacher, D. (1982) Am. J. Physiol. 243, G10–G15.
12 Sabb, J.E., Godfrey, P.M. and Brannon, P.M. (1986) J. Nutr. 116, 892–899.
13 Wicker, C. and Puigserver, A. (1987) Eur. J. Biochem. 162, 25–30.
14 Giorgi, D., Renaud, W., Bernard, J.-P. and Dagorn, J.-C. (1985) Biochem. Biophys. Res. Commun. 127, 937–942.
15 Pitchumoni, C.S., Scheele, G., Lee, P.C. and Lebenthal, E. (1986) in The Exocrine Pancreas. Biology, Pathobiology and Diseases (Go, V.W.L., Brooks, F.P., DiMagno, E.P., Gardner, J.D., Lebenthal, E. and Scheele, G.A., eds.), pp. 387–406, Raven Press, New York.
16 Mann, G.E., Muñoz, M. and Peran, S. (1986) Biochim. Biophys. Acta 862, 119–126.
17 Mann, G.E., Smith, S.A., Norman, P.S.R. and Emery, P.W. (1988) Pancreas 3, 67–76.
18 Gazzola, G.C., Dall'Astra, V. and Guidotti, G.G. (1981) J. Biol. Chem. 256, 3191–3198.
19 Shotwell, M.A., Kilberg, M.S., Oxender, D.L. (1983) Biochim. Biophys. Acta 737, 267–284.
20 Kilberg, M.S. (1986) Fed. Proc. 45, 2438–2454.
21 Moreno, A., Lobaton, C.D. and Oxender, D.L. (1985) Biochim. Biophys. Acta 819, 271–274.
22 Clayman, S. and Scholefield, P.G. (1969) Biochim. Biophys. Acta 173, 277–289.
23 Mann, G.E., Muñoz, M. and Peran, S. (1987) J. Physiol. 396, 38P.
24 Muñoz, M., Peran, S. and Mann, G.E. (1987) Digestion 38, 104P.
25 Mann, G.E. and Peran, S. (1986) Biochim. Biophys. Acta 858, 263–274.
26 Norman, P.S.R. and Mann, G.E. (1987) J. Membr. Biol. 96, 153–163.
27 Kanno, T., Saito, A. and Ikei, N. (1983) Biomed. Res. 4, 175–186.
28 Yudilevich, D.L. and Mann, G.E. (1982) Fed. Proc. 41, 3045–3053.
29 Gardiner, M.L.G. and Atkins, G.L. (1982) Clin. Sci. 63, 405–414.
30 White, M.F. (1985) Biochim. Biophys. Acta 822, 355–374.
31 Wolffram, S. and Scharrer, E. (1984) Pflügers Arch. 400, 34–39.
32 Yokogoshi, H. and Wurtman, R.J. (1986) Metabolism 35, 837–842.
33 Stubbs, R.S. and Stabile, B.E. (1985) Am. J. Physiol. 248, G347–G352.
34 Norman, P.S.R. and Mann, G.E. (1988) Biochim. Biophys. Acta 943, 541–546.

35 Cheneval, J.P. and Johnstone, R.M. (1976) Biochim. Biophys. Acta 433, 630–637.
36 Fafournoux, P., Remesey, C. and Demigne, C. (1982) Biochem. J. 206, 13–18.
37 Dagorn, J.-C. (1986) Biochemie 68, 329–331.
38 Bazin, R. and Lavau, M. (1982) Am. J. Physiol. 243, G448–G454.
39 Brannon, P.M., Demarest, A.S., Sabb, J.F. and Kore, M. (1986) J. Nutr. 116, 1306–1315.