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Comparative study on the expression of the blood group antigens Le a, Le b, Le x, Le y and the carbohydrate antigens CA 19-9 and CA-50 in chronic pancreatitis and pancreatic carcinoma *

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Summary. The expression of the blood group antigens Le a, Le b, Le x, Le y and the carbohydrate antigens CA 19-9 and CA-50 was studied in 20 ductal pancreatic carcinomas, 24 pancreases with chronic pancreatitis and 10 normal fetal and adult pancreases. CA 19-9, CA-50 and Le a showed the strongest staining intensity, the highest percentage of labelled cells, and a membrane-bound expression pattern in epithelial cells of normal pancreas, chronic pancreatitis and well differentiated (G1) carcinoma; in moderately and poorly differentiated carcinomas (G2/3) it was predominantly cytoplasmic. The staining pattern of Le b and Le x was less clearly membrane-bound but varied with cytoplasmic and Golgi-located distributions in all pancreatic specimens. Le y revealed a consistent granular antigen expression in the Golgi-region of ductal epithelial, acinar and carcinoma cells.

None of the antibodies allowed a morphological differentiation by their expression pattern between hyperplastic, metaplastic and dysplastic or neoplastic cells. The differences in their staining patterns were quantitative and did not allow a qualitative differentiation between chronic pancreatitis and pancreatic carcinoma.

We found coexpression of Le a and Le b antigens in 46/54 pancreatic specimens. All but 7 pancreata were CA 19-9 positive. An association between Le x, y and Le a, b antigen expression could not be noted in our material.

Key words: Le a – Le b – Le x – Le y – CA 19-9 – CA-50 – Chronic pancreatitis – Pancreatic carcinoma – Immunohistochemistry

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Introduction

An association between blood group antigenicity and predisposition to gastrointestinal cancer has been discussed for many years in the medical literature. It has been suggested that pancreatic carcinoma occurs more often in patients with blood type A (Aird et al. 1960). Sialylated Le a and Le b epitopes have been noted on circulating mucin-type glykoproteins in sera from patients with pancreatic cancer (Magnani et al. 1983). The Lewis-related antigens CA 19-9 and CA-50 are tumour markers with the highest sensitivity (up to 82%) and specificity (up to 98%) for pancreatic carcinoma (Dienst et al. 1987; Farini et al. 1985; Heptner et al. 1986; Holmgren et al. 1984; Schmiegel et al. 1985). In a previous study (Schwenk and Makovitzky, unpublished work) we examined the CA 19-9 and CA-50 expressions in pancreatic tissues; we found a change in the cellular antigen localization pattern between normal, chronically inflamed and well differentiated (G1) neoplastic cells on the one hand and moderately to poorly differentiated (G 2/3) carcinoma cells on the other.

Little information is available about the expression of the Le x and Le y antigens by the pancreas (Brown et al. 1984; Combs et al. 1984; Fukushi et al. 1984; Fukushi et al. 1985; Fukushima et al. 1984; Kim et al. 1988; Pour et al. 1986; Pour et al. 1987; Rettig et al. 1985; Uchida et al. 1986). For Le x antigen sensitivities of 22%, for Le y of 41% have been noted in sera of patients with pancreatic cancer (Kannagi et al. 1986).

The present study is the first to examine all 6 related antigens CA 19-9, CA-50, Le a, Le b, Le x and Le y simultaneously in a comparison of normal pancreatic tissues, chronic pancreatitis and pancreatic carcinoma tissues.

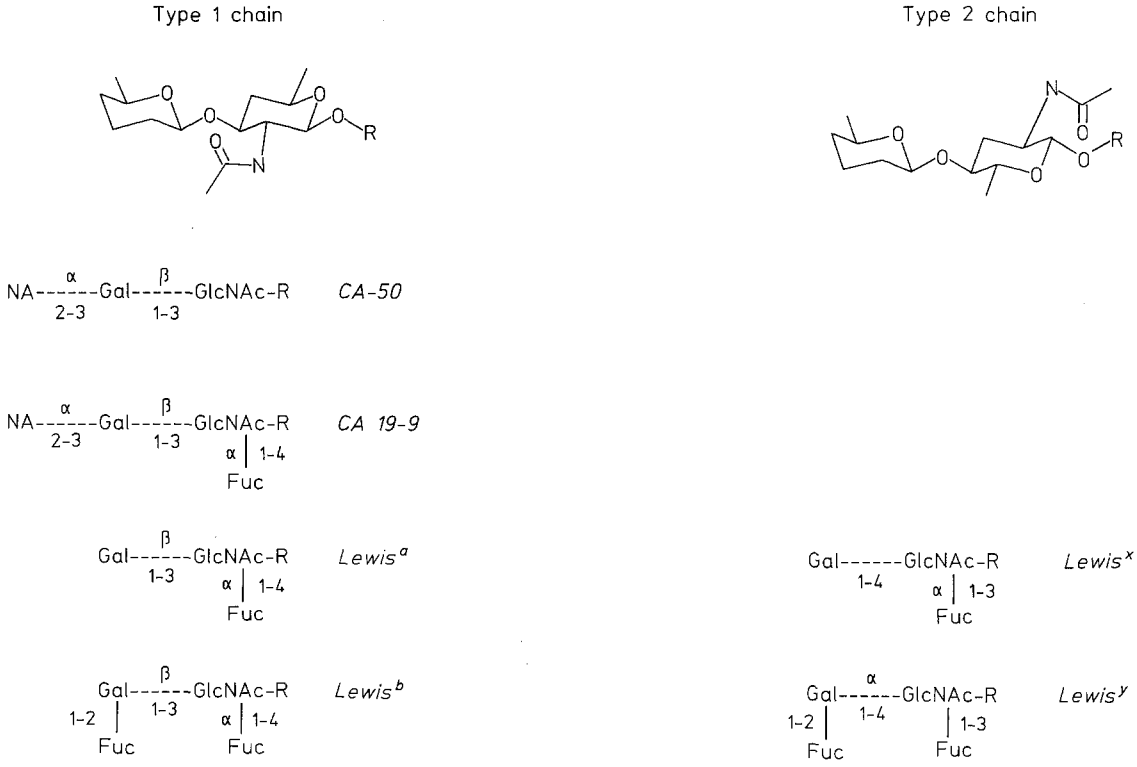


Fig. 1. Biochemical relationship of the carbohydrate antigens CA 19-9 and CA-50 and the blood group antigens Le a, Le b, Le x, Le y (modified from Mollicone et al. 1985). NA, N-acetyl-neuraminic acid; Gal, D-galactose; GlcNAc, N-acetyl-D-glucosamine; Fuc, L-fucose; R, remainder of chain

Of special interest to us was the question whether we could identify alterations in cellular antigen expression between ductal dysplastic cells in chronic pancreatitis and pancreatic carcinoma cells. According to Stolte (1979) and Volkholz (1982) dysplastic cells occuring in chronic pancreatitis cannot be distinguished, morphologically, from dysplasia found in the vicinity of pancreatic carcinoma – a finding which implies the possibility of a transition of chronic pancreatitis to pancreatic carcinoma. Immunohistochemical labeling of cellular dysplasia would help to elucidate this question.

The Le antigens are built up by a sequential addition of specific sugars on two main types of precursor chains (see Fig. 1): with type 1 precursor (β-D-Gal[1–3]D-GlcNAc-R) the Le a and Le b antigens are formed, type 2 precursor (Gal[1–4]-linkage) gives the Le x and Le y variants. The carbohydrate antigens CA 19-9 and CA-50 are related to the Lewis antigens by CA 19-9 being a sialytated Le a antigen.

Materials and methods

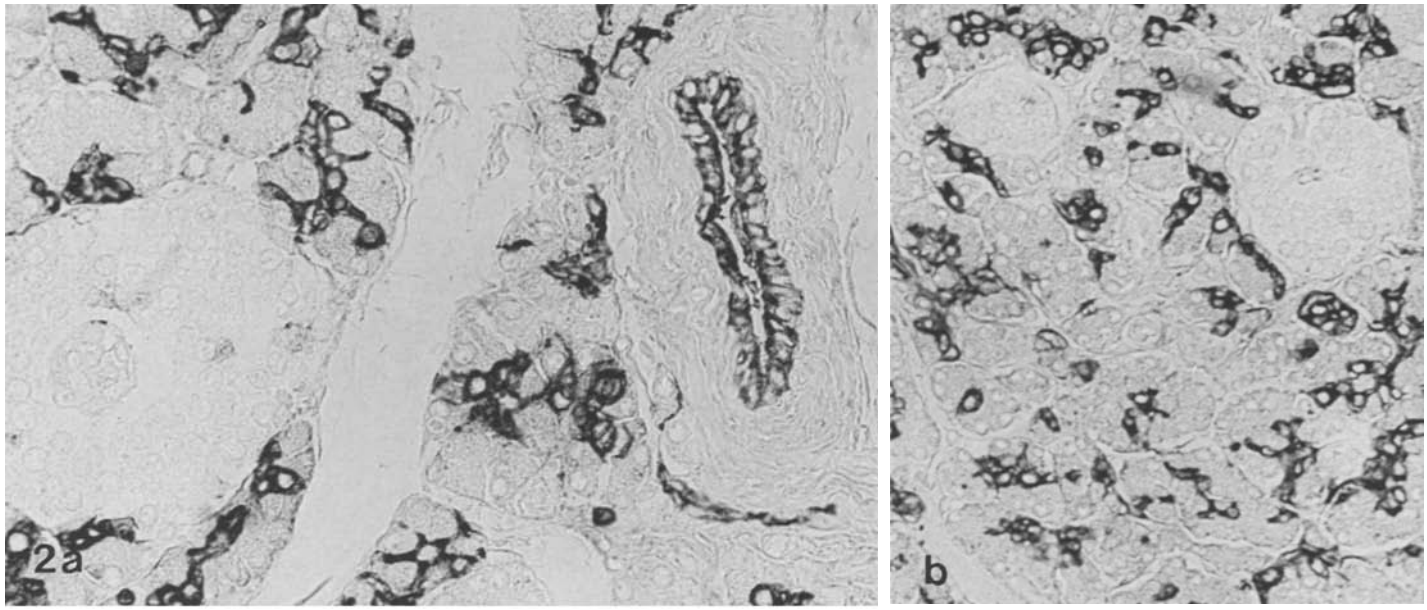
Specimens were studied from 20 samples of exocrine pancreatic adenocarcinoma, 24 samples of chronic pancreatitis and 10 samples of fetal and adult pancreas without pathological changes. The samples were formalin-fixed, paraffin-embedded surgical specimens; except for the normal pancreas which was from autopsy cases.

5 adenocarcinomas were well (G1), 10 moderately (G2) and 5 poorly (G3) differentiated. 12 had a predominantly papillary, tubular or tubulopapillary growth pattern, 7 were partially cribrous or solid and 1 was the mucinous type. 9 of the pancreatic carcinomas presented additional chronic obstructive pancreatitis due to duct obstruction by the tumour.

The chronically inflamed pancreases belonged to different stages of chronic pancreatitis (according to Becker [1984]): 2 samples belonged to stage I, 10 to stage II and 12 to stage III. In this group, we excluded cases with chronic pancreatitis due to obstruction, as this type may result from but never transforms to carcinoma (Becker 1984). Referring to Volkholz et al. (1982) we differentiated reactive epithelial changes (papillary and pseudopapillary hyperplasia, mucoid transformation and squamous metaplasia) from true cellular dysplasia (characterized by altered relationship of nuclear size and cytoplasm, moderate hyperchromatic and polyploid changes of the nuclei).

We used the commercially available monoclonal antibodies against CA 19-9 (CA 19-9, Isotopen-Diagnostik CIS GmbH, Dreieich, Germany), against CA-50 (Can AG CA-50, Stena Diagnostics AB, Gothenburg, Sweden), against Le a (Seraclone Anti-Le a (Lewis a)) and Le b (Seraclone Le b (Lewis b), Biotest GmbH, Dreieich, Germany). The monoclonal antibodies against Le x and Le y were kindly provided to us by Dr. Steplewski (The Wistar Institute, Philadelphia, Pennsylvania, USA).

The ABC method of immunoperoxidase histochemistry was performed as described elsewhere (Haglund et al. 1986a) using the following dilutions of primary antibodies: Le a 1:30,



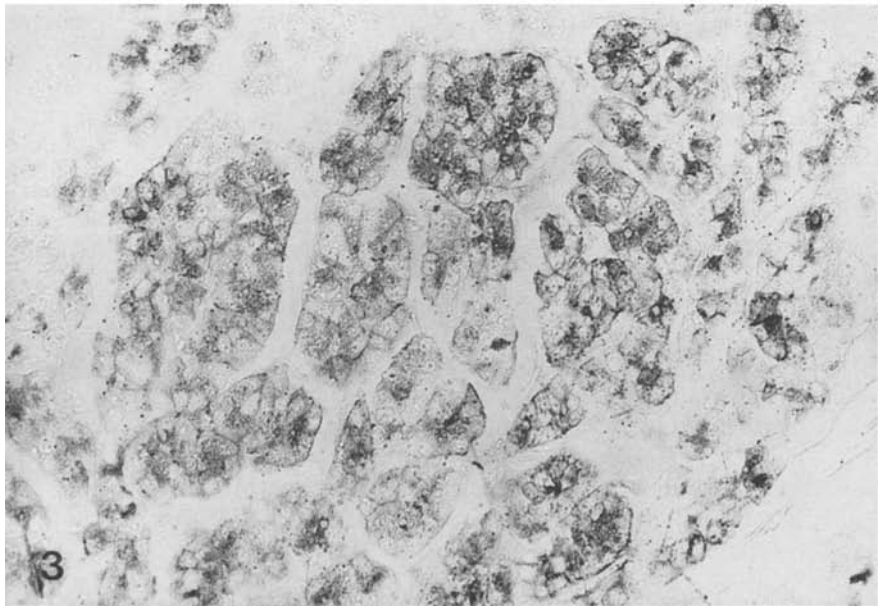


Fig. 2. Membrane-bound antigen expression in centroacinar and ductal cells of normal adult pancreas. Anti-CA-50, 250× (**a**), 400× (**b**)

Fig. 3. Cytoplasmic Le b expression in acinar cells of normal adult pancreas. 400×

Le b 1:50, Le x 1:1000, CA 19-9 1:5000; CA-50 was used undiluted.

As second (bridge) antibody horse anti-mouse IgG was used for Le y and CA 19-9, the other secondary antibodies were of the IgM type. Negative controls were performed by substituting PBS buffer for specific antibodies.

The glycoprotein nature of the carbohydrate antigens was tested by sialidase digestion (according to Romhanyi 1972) and chemical desialylation, i.e. acid and alkaline hydrolysis (according to Quintarelli et al. 1960, and Geyer et al. 1970). After enzymatic digestion and chemical desialylation all specimens gave negative immunohistochemical reactions with anti-CA 19-9 and anti-CA-50, thus proving the glykoprotein form of both antigens in our routinely fixed paraffin-embedded material.

Cellular localization of antigen was classified as membrane-bound (M), cytoplasmic (C), or bound to the apical (a), luminal (l) or basal (b) cell borders, or situated in the Golgi-region (G) of the cell. Staining intensity was scored as: $-/+/++/+++$. The percentage of positively stained cells over the slide was roughly estimated (in %) by each of the authors separately.

Results

The results are summarized in Tables 1–3.

Fetal and adult ductular epithelial cells were labeled with anti-Le a, -Le b, -CA 19-9 and -CA-50 in a membrane-bound pattern (Fig. 2); Le x antigen was positive in adult ducts only, while Le y gave completely negative results in fetal and adult ducts.

Tabelle 1. Intensity, localization pattern and percentage of antigen expression in normal fetal and adult pancreas for Le a, Le b, Le x, Le y, CA 19-9 and CA-50 antigens

	Fetal pancreas				Adult pancreas				
	ductal epithelial cells	centro-acinar cells	acinar cells	islet cells	ductal epithelial cells	centro-acinar cells	acinar cells	islet cells	(10 cases) staining
Le a	+++	+++	–	–	+++	+++	–	–	intensity
	M/C, M	M	–	–	M	M	–	–	localization
	100%	100%	–	–	100%	100%	–	–	percentage
Le b	++	–	++/+++	–	++/+++	–	++/+++	–	
	M	–	G	–	M	–	G/C	–	
	100%	–	70–100%	–	100%	–	20–40%	–	
Le x	++	–	–	–	–	–	++	– (++)*	* (2 cases)
	M, l/M, a	–	–	–	–	–	C	– (C)*	
	90–100%	–	–	–	–	–	20–50%	– (10–20%)*	
Le y	–	–	–	–	–	–	+	– (+)	* (1 case)
	–	–	–	–	–	–	G	– (G)*	
	–	–	–	–	–	–	10–30%	– (100%)*	
CA 19-9	+++	–	–	–	++	++	–	–	
	M, l	–	–	–	M/M, C	M	–	–	
	100%	–	–	–	20–50%	100%	–	–	
CA-50	++	++	–	–	++/+++	++/+++	–	–	
	M	M	–	–	M	M	–	–	
	100%	100%	–	–	100%	100%	–	–	

Abbreviations used: M – membrane-bound, c – cytoplasmic, G – Golgi-region, l – luminal, a – apical, M, a – membrane-bound and apical, M/a – membrane-bound or apical

Centroacinar cells of terminal ductules in normal fetal and adult pancreata expressed Le a and CA-50 antigen (Fig. 2); CA 19-9 was positive only in adult samples. Anti-Le b, -Le x and -Le y did not stain centroacinar cells either in fetal or in adult pancreata.

Acinar cells expressed Le b in fetal and adult pancreata (Fig. 3), but expressed Le x and Le y in adult samples only. The percentage of labeled cells was usually very low (see Table 1). The other antibodies did not stain acinar cells at all.

Langerhans' islets almost always stained negatively; only 2 and 3 cases showed a weak positivity of islet cells for Le x and Le y, respectively (Fig. 4). The cellular localization of the antigens was predominantly membrane-bound in ductular epithelia and in centroacinar cells (see Table 1), and cytoplasmic in acinar and islet cells. Only Le y showed a characteristic granular antigen accumulation in the Golgi-region of cells (Fig. 4). Staining intensity was strongest with anti-Le a, -Le b, -CA 19-9 and -CA-50.

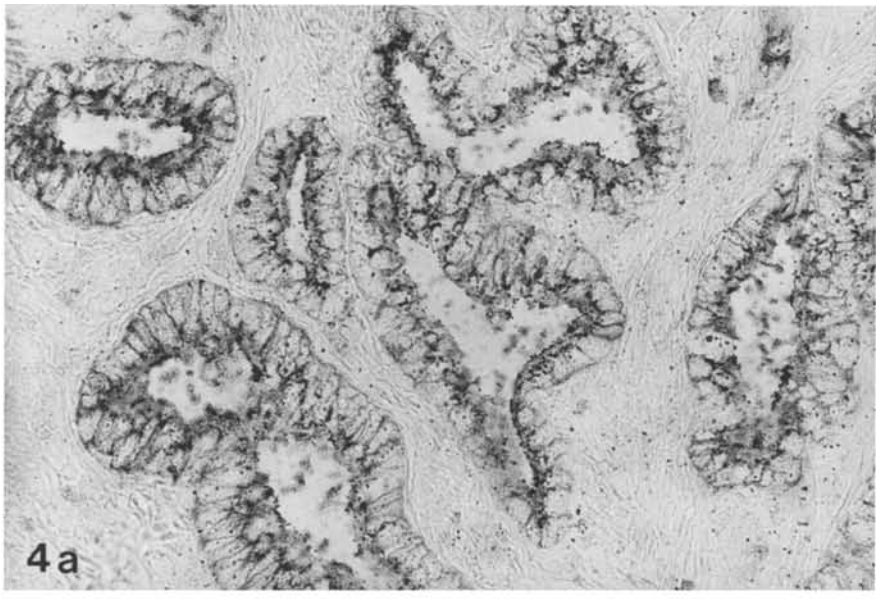
In chronic pancreatitis the staining pattern of Le a-, Le b-, CA 19-9- and CA-50-antigens did not differ from that in normal pancreas; half of the cases, however, presented additional centroacinar cell positivity with anti-Le b. Le x- and Le y-antigen expression differed from that in normal pancreas in that ductular epithelia stained positively in chronic pancreatitis (Fig. 5); anti-Le x showed an additional labeling of centroacinar cells.

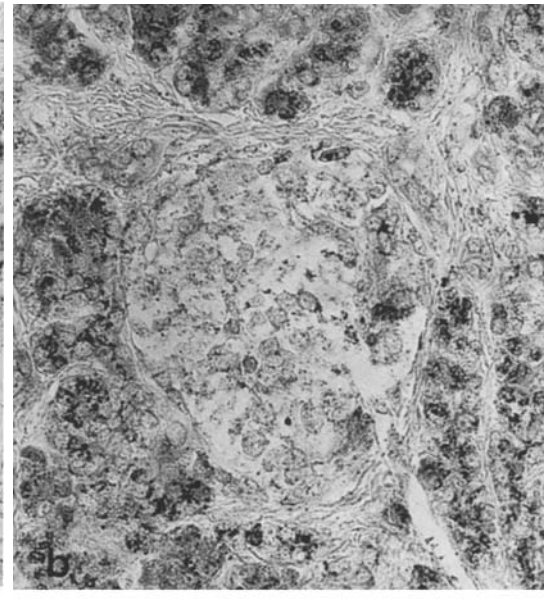
Reactive ductal epithelial changes such as papillary or pseudo-papillary hyperplasia (Fig. 6), squamous metaplasia, mucoid transformation (Fig. 7) and slight or moderate dysplasia (Fig. 8) did not differ from unaltered epithelial cells in their staining patterns (see Table 2); dysplastic cells, therefore, could not be differentiated from hyperplastic or metaplastic epithelial cells by their expression pattern with either antibody. Squamous metaplasia reacted slightly positive with anti-Le a and -Le b only. Staining intensity was strongest with both carbohydrate antibodies (see Table 2).

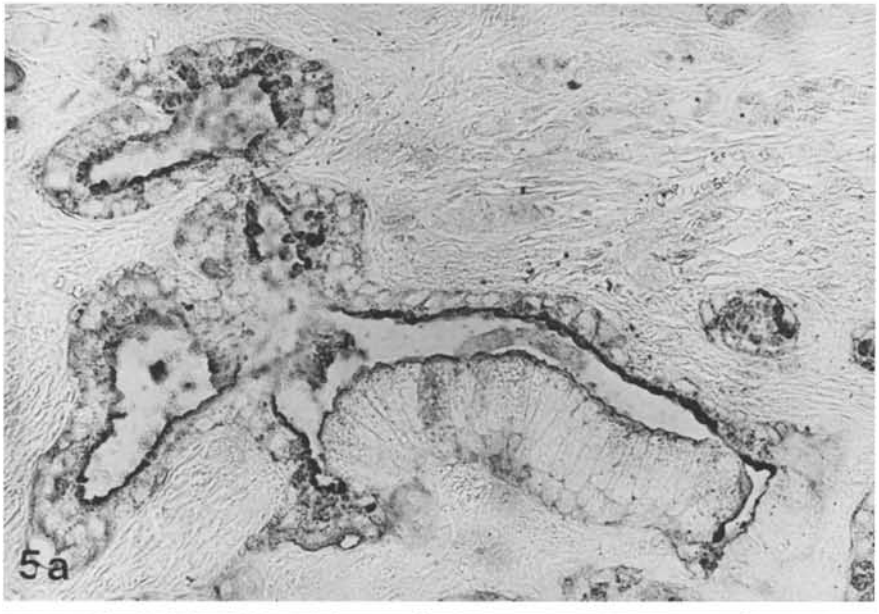
The percentage of labeled cells was highest with anti-CA-50 and Le a, and lowest with anti- Le x and -Le y (see Table 2).

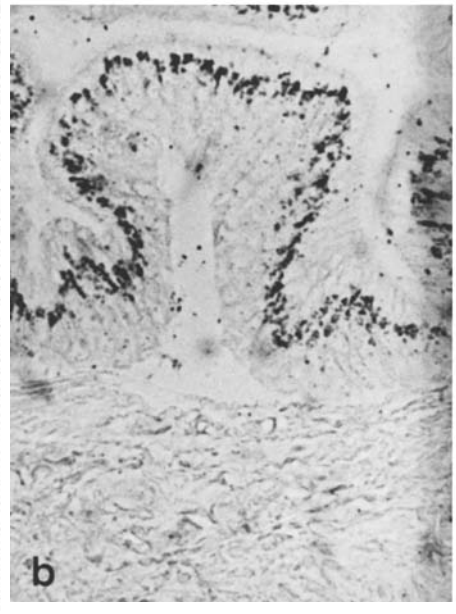
In pancreatic carcinoma the staining patterns of all 6 antibodies in ductular, centroacinar and acinar cells adjacent to exocrine pancreatic carcinoma did not differ from the findings in chronic pancreatitis.

With none of the antibodies ductular epithelial









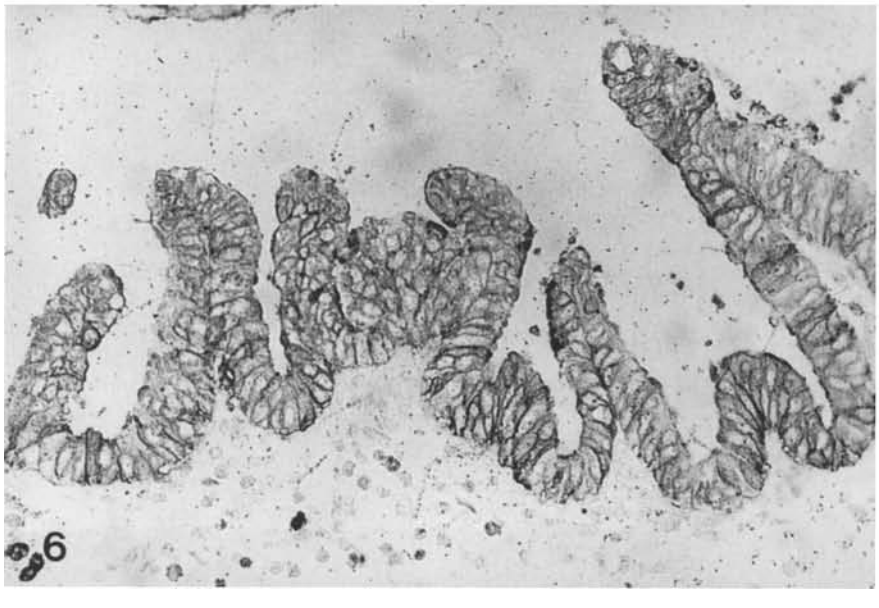
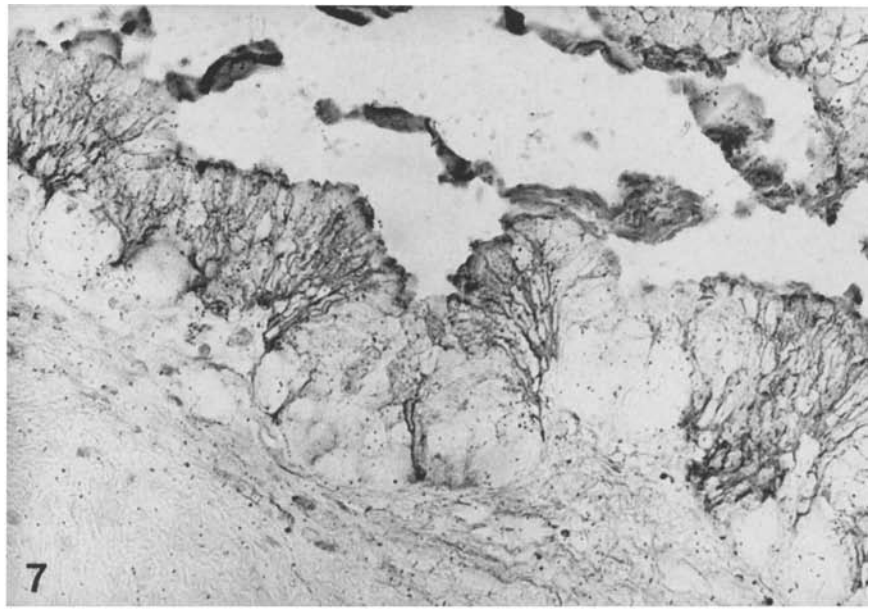
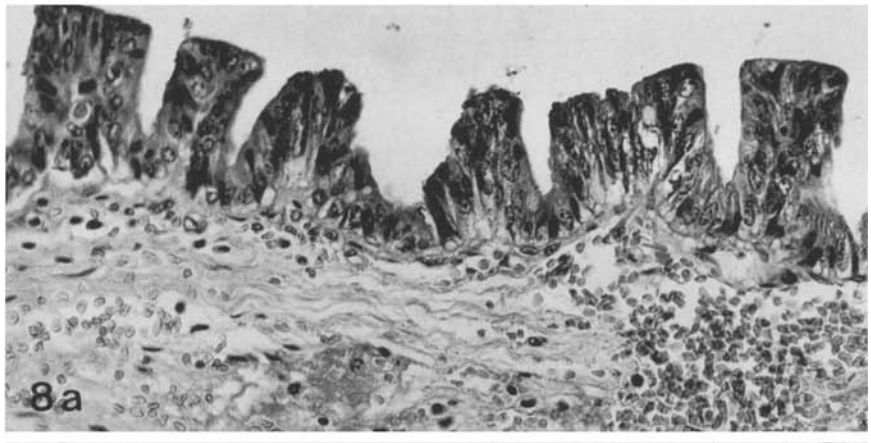


Fig. 4. Granular Le y expression in the Golgi-region of ductal (**a**) and acinar (**b**) cells of normal adult pancreas. Note scarce antigen accumulation in islet cells. 250 × (**a**), 400 × (**b**)

Fig. 5. (**a**) Membrane-bound Le x expression by ductal epithelia in chronic pancreatitis. The apical cell borders are stained intensely; 250 ×. (**b**) Granular Le y expression in the Golgi-region of ductal cells in chronic pancreatitis; 400 ×

Fig. 6. Membrane-bound Le a expression in papillary and pseudo-papillary ductal hyperplasia; 250 ×





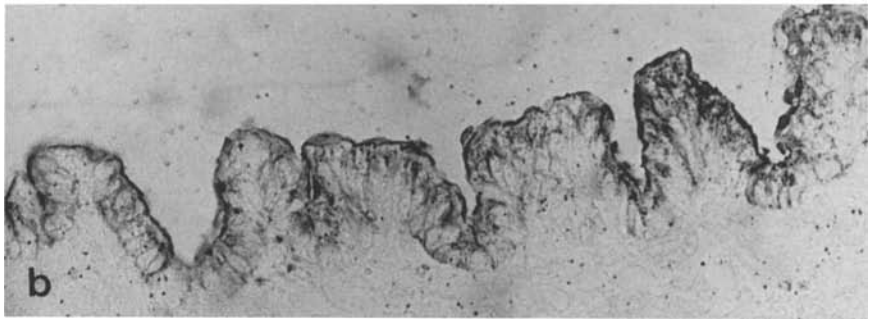


Fig. 7. Mucoid transformation staining negatively with anti-CA-50. The hyperplastic epithelia show a membrane-bound antigen expression; 250×

Fig. 8. Moderate dysplasia in chronic pancreatitis; **(a)** H &E, 250×; **(b)** Anti-CA 19-9, 250×

dysplasias in the vicinity of adenocarcinoma showed a characteristic antigen expression that would allow us to differentiate them from dysplasias in chronic pancreatitis.

The Le a-, CA 19-9- and CA-50-antigens exhibited a change in cellular expression pattern between well (G1) differentiated carcinomas on the one side and moderately (G2) to poorly (G3) differentiated carcinomas on the other side (see Table 3): their antigen localization was predominantly membrane-bound in G1-carcinomas (Fig. 9) and more cytoplasmic in G2/3-carcinomas (Fig. 10). Anti-Le b, -Le x and -Le y did not allow us to distinguish different antigen expression patterns in pancreatic cancer (Figs. 11, 12).

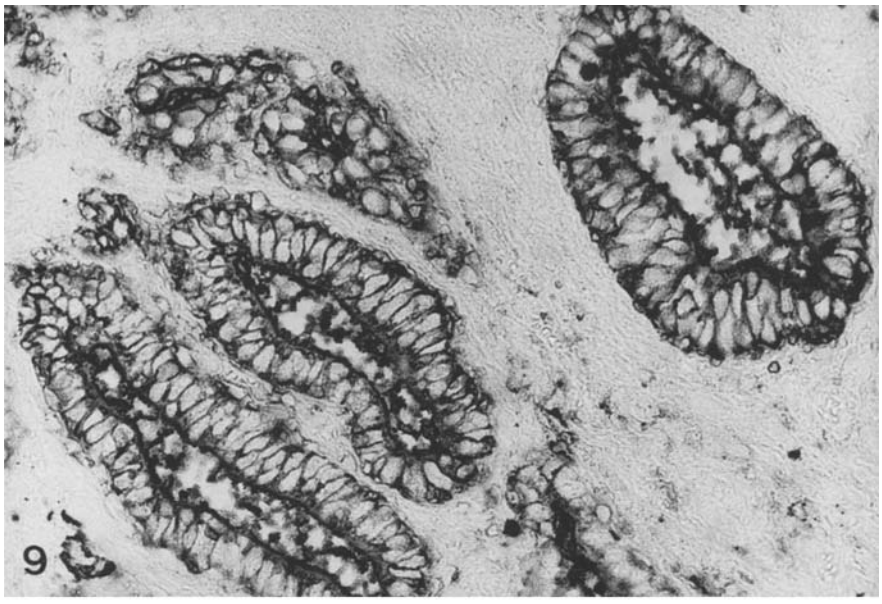
Staining intensity and percentage revealed no marked differences between well, moderately and poorly differentiated carcinomas. In G2- and G3-

Table 2. Intensity, localization pattern and percentage of antigen expression in chronic pancreatitis of Le a, Le b, Le x, Le y, CA 19-9 and CA-50 antigens. (For abbreviations see Table 1)

	Chronic pancreatitis (24 cases)								
	ductal epithelial cells	centro-acinar cells	acinar cells	islet cells	mucoid trans-formation	squamous meta-plasia	(pseudo-) papillary hyperplasia	epithelial dysplasia	staining
Le a	+/++ M/C, a 100%	+/++ M 100%	– – –	– – –	+/++ M 100%	+ M 100%	+/++ C, a 100%	+/++ C,a 100%	intensity localization percentage
Le b	+/++ M/C 60–100%	–/++ M/G 50%	+ G 100%	– – –	+ M 70–100%	+ C/C, a 100%	+/++ M/C 60–100%	+/++ M 60–100%	
Le x	+/++ M 10–100%	–/+ M 50%	– (+)* – (G)* – (50%)*	– – –	+ C/M 40–60%	– – –	+ a/M 40–100%	+ M, l 40–100%	* (4 cases)
Le y	+ G/C 20–80%	– – –	+ G 70–100%	– – –	+/++ l, a 10–100%	– – –	+ G/C 50–80%	+ G/C 70–90%	
CA 19-9	++/+++ M/M, l, a 60–70%	++ M 100%	– – –	– – –	+ C, l/l 60–70%	– – –	++/+++ M, l, a/l 70–80%	++/+++ M, l, a 60–80%	
CA-50	++/+++ M/C 100%	+++ M 100%	– – –	– – –	–/+++ C, M, l 50%	– – –	++/+++ M/C, l, a 100%	++/+++ M/C, l, a 100%	

Table 3. Intensity, localization and percentage of antigen expression in pancreatic carcinoma of Le a, Le b, Le x, Le y, CA 19-9 and CA-50 antigens. (For abbreviations see Table 1)

	Pancreatic carcinoma (20 cases)				
	G1-carcinoma	G2-carcinoma	G3-carcinoma	ductal dysplasia	staining
Le a	+ M/M, a/C/C, a 60–90%	+ C 10–90%	+ C 50–90%	+ C/M 50–80%	intensity localization percentage
Le b	+ C, a 60–100%	+ C 60–100%	+ C 70–80%	+ M/C/M, a 80–100%	
Le x	+ M, a 60–100%	+ M, a/C, a 60–90%	+ C/C, a 80–90%	+ M, a 70–80%	
Le y	+ G 60–80%	+ G 10–80%	+ G 10–100%	+ G/C 50–80%	
CA 19-9	+ M, a 80–90%	++ C, a 40–100%	+ C 60–70%	+ a/C/M 40–90%	
CA-50	++ M 50–90%	++ C, a 50–90%	+ C/C, a 70–90%	++ M, a/M, l, a/C, a 60–100%	



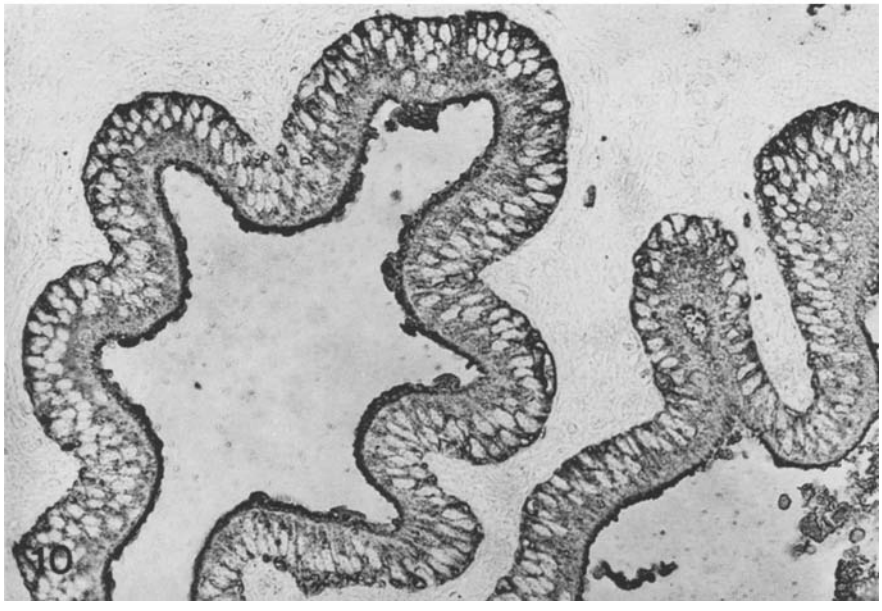


Fig. 9. Membrane-bound Le a expression in well differentiated pancreatic carcinoma; 250 × /160 ×

Fig. 10. Cytoplasmic Le a expression in moderately differentiated pancreatic carcinoma; 250 × /160 ×

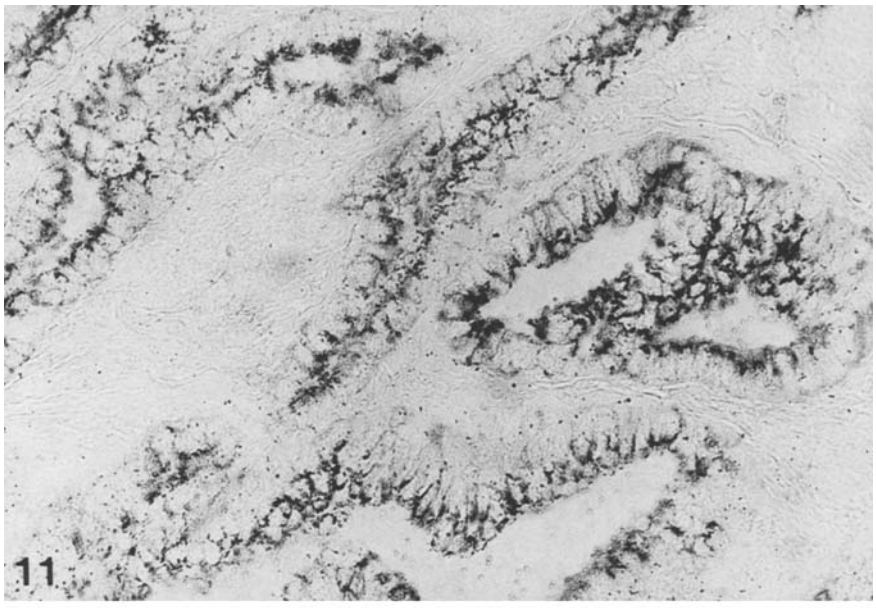
carcinomas a focal positivity of the tumor stroma was seen with all of the 6 antibodies.

Lymph node metastases reacted with all 6 antibodies in the same fashion as the primary lesions.

In pancreases with negative antigen expression all but 1 expressed Le b- and all but 7 expressed Le a-antigen; 7 samples were CA 19-9 negative, 2 cases did not express CA-50 antigen. Le x stained negatively in 7, Le y in 13 cases (see Table 4).

Discussion

Although the applied antibodies anti-CA 19-9, -CA-50, -Le a, -Le b, -Le x and -Le y are biochemically closely related, they revealed different marker qualities: Anti-CA 19-9, -CA-50 and -Le a showed the strongest staining intensities, the highest percentage of labelled cells, and a predominantly membrane-bound expression pattern in normal pancreas, chronic pancreatitis and well differentiated (G1-) carcinoma; in moderately and poorly differentiated (G2/3-) carcinomas the antigen expression was predominantly cytoplasmic. Anti-Le b and -Le x displayed moderate staining intensities and a high percentage of labeled cells; their staining pattern was less clearly membrane-bound and varied with cytoplasmic and Golgi-located distributions in all pancreatic specimens. Le y showed



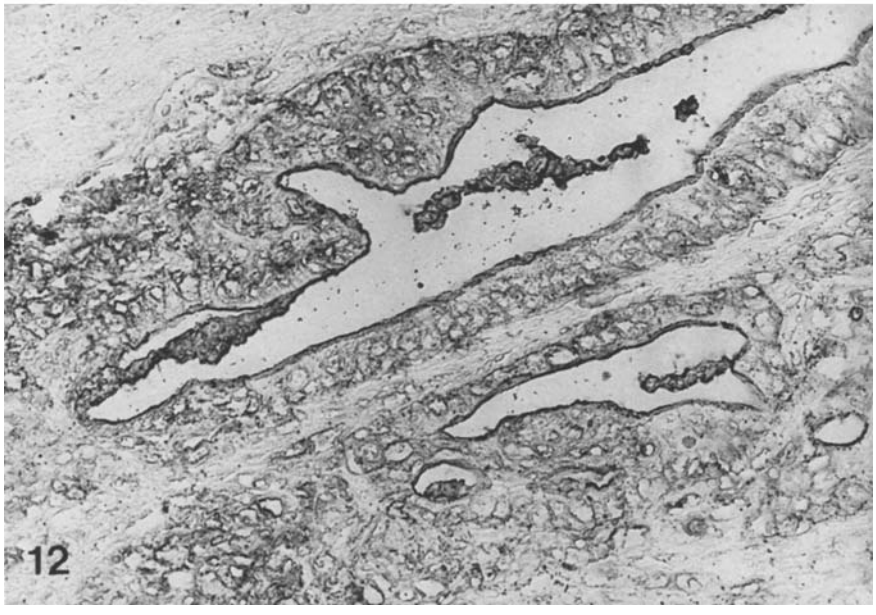


Fig. 11. Granular Le y expression in the Golgi-region of well to moderately differentiated pancreatic carcinoma cells; 250 ×

Fig. 12. Moderately to poorly differentiated pancreatic carcinoma with partly membrane-bound, partly cytoplasmic Le b antigen expression; 250 ×

the weakest staining intensity and the lowest number of labeled cells; its expression pattern was a granular antigen accumulation in the Golgi-region of ductal epithelial, acinar and carcinoma cells.

Similar Le a, b, x, y-expression patterns have been described by a number of investigators (Ernst et al. 1984; Itzkowitz et al. 1987; Rouger et al. 1981; Uchida et al. 1986); others reported different results. Ernst et al. (1984), Okada et al. (1987) and Pour et al. (1987) found Le a expression primarily in centroacinar and ductal cells of medium-sized but not in large ducts, whereas Le b-antigen was present in epithelial cells of small and large ducts. Kim et al. (1988) found Le y-expression in 32–77% of normal pancreatic epithelial cells, similar to our own results. However, they found no Le x-expression in their normal pancreases and determined the "pancreatic phenotype" therefore as Le x− y+. In chronic pancreatitis and in pancreatic cancer tissues, however, they detected Le x antigen in 10–20% and 50–70% of cells, respectively; they concluded that Le x-related antigens are cancer-associated determinants in the human pancreas. These findings are in total contrast to ours.

Several factors might explain the reported discrepancies in antigen expression patterns: differences in antigenic specificity between the anti-

Table 4. Pancreatic specimens with negative (−), weak ((+)) or positive (+) blood group antigen expression

Le a	Le b	Le x	Le y	CA 19-9	CA-50	Case
Normal adult pancreas						
+	+	+	+	−	+	1
Chronic pancreatitis						
−	+	−	+	−	−	2
−	+	(+)	+	−	(+)	3
−	+	−	+	−	(+)	4
−	+	+	−	−	+	5
−	+	+	−	−	+	6
+	+	+	−	+	−	7
+	+	+	−	+	+	8
+	+	(+)	−	+	+	9
+	+	+	−	(+)	+	10
+	+	+	−	+	+	11
+	+	(+)	−	+	+	12
+	+	−	+	+	+	13
+	+	−	+	+	+	14
Pancreatic carcinoma						
−	(+)	−	−	+	+	15
(+)	−	−	+	(+)	+	16
−	(+)	(+)	+	+	(+)	17
+	+	(+)	−	+	+	18
+	+	(+)	−	(+)	+	19
+	+	+	−	+	+	20
+	+	+	−	+	+	21
+	+	−	+	+	(+)	22
+	+	+	+	−	−	23

bodies used by the authors; some antibodies might recognize also the extended (sialylated) Le-determinants. In addition, technical factors might play a role in interstudy variations. A surprising result was the negativity of ductal epithelial and centroacinar cells for Le x and Le y in the normal pancreatic specimens, whereas both cell types stained positively in fetal pancreas, in chronic pancreatitis and in pancreatic carcinoma tissues with one or both antibodies. Pour et al. (1987) reported on corresponding findings for Le x, but not for Le y.

Le x and Le y are considered to be embryological antigens and seem to be involved in cell differentiation processes (Cooper et al. 1987); this may explain their presence in chronic pancreatitis and pancreatic carcinoma cells as well as in fetal tissues and their absence in normal adult pancreas.

A membrane-bound staining pattern by anti-CA 19-9 and anti-CA-50 in chronic pancreatitis and G1-carcinoma and a predominantly cytoplasmic antigen expression in G2/3-carcinoma has been documented before (Haglund et al. 1986a; Schwenk and Makovitzky, unpublished work); it has not yet been described, however, for anti-Le a. This finding reflects a severe loss of cellular polarization and cell function during neoplastic dedifferentiation. None of the neoplastic pancreases, however, displayed a general loss of blood group substances as it has been shown for poorly differentiated malignant salivary gland tumours (Hamper et al. 1986).

In our experience, the differences in antigen expression are merely quantitative; the expression patterns do not allow a qualitative discrimination between chronically inflamed, dysplastic and neoplastic cells. A transition from chronic pancreatitis to pancreatic carcinoma, therefore, cannot be demonstrated by the applied antibodies.

The patients' serum- or red blood cell-phenotypes have not been determined in this study. It is known that 70% of the population belong to the Le a−b+ blood group type and 30% are either Le a+b−, Le a+b+ or Le a−b− (Brockhaus et al. 1981). According to Dienst et al. (1987) 7–10% of the population lack the α 1–4 fucosyltransferase and therefore belong to the Le a−b− phenotype. These individuals cannot synthesize CA 19-9 either. (Dienst et al. 1987; Hirano et al. 1987; Magnani et al. 1982). However, they have been shown to express CA-50 antigen in their tissues, even if in a weaker and more focal distribution (Dienst et al. 1987; Haglund et al. 1986a; Haglund et al. 1986b; Haglund et al. 1987; Schwenk and Makovitzky, unpublished observations).

None of our pancreases was Le a, Le b and CA 19-9 negative. Several explanations are possible: our patients could, accidentally, all belong to the Le a and/or Le b positive population. However, co-expression of Le a and Le b antigens in pancreatic tissues, regardless of the individuals' Lewis-blood group phenotypes has also been reported by Itzkowitz et al. (1987); Ernst et al. (1984) and Hirano et al. (1987). "Inappropriate" expression of Le-antigens in cancerous tissues of Lewis negative patients is another well-known finding in pancreatic, gastric or colonic carcinomas (Itzkowitz et al. 1986; Itzkowitz et al. 1987; Tempero et al. 1987; Yokota et al. 1981; Yuan et al. 1985). A possible explanation for this phenomenon is the existence of tumour-associated variants of the normal fucosyl- and sialyl-transferases (Uhlenbruck 1986) with altered enzyme specificity (Itzkowitz et al. 1987) or the production by the tumour of blood group antigen-"like" substances with similar immunodeterminants. Most probably, more than one factor is involved in this process.

Very little information is available about the co-expression of Le x, y and Le a, b antigens in human tissues. Le a+b− individuals who lack the

α 1–2 fucosyltransferase should not be able to synthesize Le y antigen (see Fig. 1). Our only Le a+ b− pancreas, however, was negative with anti Le x, but positive with anti-Le y. We cannot explain this finding. It is not known, however, whether the α 1–2 fucosyltransferases responsible for Le b and Le y synthesis are similar.

Our data do not reveal any association between Le a, b, and Le x, y antigen expression. Hanisch et al. (1985) demonstrated that the synthesis of sugars with the Le x determinant is partly dependent on the donor's Le a, b status. The sialyl-Le x antigen expression, on the other hand, has been shown to be independent of the patient's Le a, b blood group (Hakomori 1985).

Much further investigation is still required to elucidate these issues.

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