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Ethnic differences in the expression of blood group antigens in the salivary gland secretory cells from German and Japanese non-secretor individuals

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Type 1 ABO blood group antigens (peripheral core structure: Galβ1-3GlcNAcβ1-R) are expressed mainly in endodermally-derived tissues, but are not synthesized in mesodermally-derived tissues. In the former tissues, H type 1 antigen is generated largely by α-2-L-fucosyltransferase encoded by secretor (*Se*) gene and acting on the terminal galactose of the type 1 precursor chain. This theory has been generally accepted, and it seems that the expression of ABO blood group antigens is absent, or expressed at a low level, in these tissues from non-secretor individuals. In this immunohistochemical study on the secretory cells of salivary glands, we found ethnic difference between German and Japanese non-secretor individuals in the expression of blood group antigens: i.e. the expression of the type 1 blood group antigens is present in these cells from Japanese non-secretor individuals but absent from German. A possible explanation is that another α-2-L-fucosyltransferase, independent of the secretor gene, is present in Japanese non-secretor individuals.

Keywords: ABO blood-group, immunohistochemistry, salivary gland, ethnic difference, fucosyltransferase

Introduction

In a previous study [1], we compared the staining properties of several blood group A specific lectins in different human tissues and found that in submandibular glands from blood group A non-secretors, Dolichos biflorus agglutinin (DBA), Griffonis simplicifolia agglutinin I (GSA-I), and Sophora japonica agglutinin (SJA) did not react with mucous cells, whereas Helix pomatia agglutinin (HPA) and Helix aspersa agglutinin (HAA) did react. In a preliminary study using German subjects, however, we found that the two snail lectins did not react with mucous cells of salivary glands from blood group A non-secretors, suggesting the existence of ethnic differences in the expression of blood group antigens. It has been reported that the H type 1 antigenicity was clearly detected in saliva from Japanese blood group O non-secretor individuals [2]. Gibbs *et al.* [3] reported that the reactivity of blood group B erythrocytes with anti-B serum was the strongest among Blacks, weakest among Mongoloids and intermediate among Caucasians. Henry *et al.* [4] showed in their study of the expression of Lewis blood group antigens in the human plasma, that ethnic differences are present in the phenotypical expression of Le antigens in plasma of some populations. They presumed that the differences were caused by an inefficient type α-2-L-fucosyltransferase appearing in the Le^{b}+ non-secretor phenotypes of a certain population.

However, ethnic differences in blood group antigen expression in tissue sections have been dealt with in only a few studies.

In the present study, we systematically compared the histochemical properties of secretory cells of various salivary glands obtained from German blood group A,

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AB and O non-secretor individuals with those from Japanese non-secretors for the purpose of analysing the mechanism causing the ethnic difference.

Materials and methods

Tissue specimens of the submandibular glands, sublingual glands and tongues were collected at autopsies in the Institüt für Rechtsmedizin, Münster University, Department of Legal Medicine, Shiga University of Medical Science and Osaka Medical Examiners Office. ABO and Lewis blood grouping of the donors were performed by routine haemagglutination testing, using the blood samples obtained at autopsies. The secretor status of the donors was determined by the Lewis blood type or histochemically deduced from the presence (secretor) or absence (non-secretor) of H antigen in the serous cells of submandibular glands. The distribution of the blood groups of German and Japanese samples examined is listed in Table 1.

Tissue specimens were fixed in 10%-formalin at room temperature for 3–6 days and embedded in paraffin. Serial sections were sliced at a thickness of 4 μm and stained with monoclonal antibodies, labelled lectins, and conventional carbohydrate staining methods such as periodic acid Schiff (PAS), Alcian blue at pH 2.5, and aldehyde pararosanilin methods. Staining procedures with labelled lectins and monoclonal antibodies as well as conventional histochemical methods were described in the previous papers [5–7].

Digestion with α-L-fucosidase was carried out by incubating tissue sections in a solution containing the enzyme at a concentration of 1 U ml^{-1} in 0.1 M citrate phosphate buffer, pH 5.2, at 37 °C for 20 h [8]. As controls for this enzyme digestion experiment, tissue sections were incubated in the same buffer solution without enzyme under each incubation condition.

The following blood group A, B or AB specific lectins, conjugated with horseradish peroxidase (HRP) or with biotin were used: DBA, GSA-I, HAA, HPA, SJA and Vicia villosa agglutinin (VVA). In addition, Ulex europaeus agglutinin (UEA) and Lotus tetragonolobus agglutinin (LTA) which are specific for H type 2 antigen, and soy bean agglutinin (SBA) and peanut agglutinin (PNA) which are specific for type 2 and 3 precursor chain, respectively, were also used. HAA and VVA were provided as biotin labelled lectins and the others as HRP labelled lectins and were purchased from Sigma Chemical Co., St Louis, Mo, USA (DBA, GSA-I, HAA, VVA, GSAI-B4, LTA, SBA and PNA) or E. Y. Laboratories, San Mateo, CA, USA (SJA and UEA).

Monoclonal anti-A and anti-B antibodies were purchased from Biotest-Serum-Inst. (Frankfurt, Germany), Ortho Diagnostic System (Raritan, NJ, USA), Dako Co. (Santa Barbara, CA, USA), Biocarb Chemicals (Lund, Sweden) and Cromatest Laboratories (Knickerbocker Co., Spain). Monoclonal anti-A_1 antibody specific for A type 3 or 4 chain antigens was purchased from Biotest-Serum-Inst. Monoclonal anti-H antibody which is specific for type 2 chain was purchased from Dako Co. Monoclonal anti-Le^a and anti-Le^b antibodies were purchased from Biotest-Serum-Inst. Monoclonal anti-Le^x and anti-Le^y antibodies were purchased from Seikagaku Co. (Tokyo, Japan). Monoclonal anti-type 1 precursor antibody (BG-1) was purchased from Signet Laboratories (Cambridge, MA, USA).

α-L-fucosidase (bovine kidney) was purchased from Boehringer-Mannheim (Indianapolis, IN, USA).

Table 1. Distribution of ABO and Lewis blood groups of German (a) and Japanese (b) samples tested in this study.

(a)	*Le(a+b−)*		*Le(a−b−)*	*Le(a−b+)*	
	non-secretor		*secretor*		*total*
A_1	4	1	2	8	15
A_2	2	0	0	4	6
A_1B	2	0	2	2	6
A_2B	1	1	1	2	5
B	1	0	0	1	2
O	4	1	3	11	19
	14	3	8	28	53

(b)	*Le(a+b−)*		*Le(a−b−)*	*Le(a−b+)*	
	non-secretor		*secretor*		*total*
A_1	9	2	2	6	19
A_1B	5	1	2	4	12
B	3	0	0	2	5
O	4	2	1	4	11
	21	5	5	16	47

Results

The conventional histochemical staining method showed no observable difference in the staining patterns of the secretory cells between German and Japanese individuals irrespective of blood group and secretor status of the donors.

Expression of A antigen

In all Japanese blood group A and AB non-secretors examined, HPA (Fig. 1B; Table 2) and HAA reacted moderately or strongly with the mucous cells of submandibular glands, sublingual glands, anterior and posterior lingual glands and with the serous cells of von

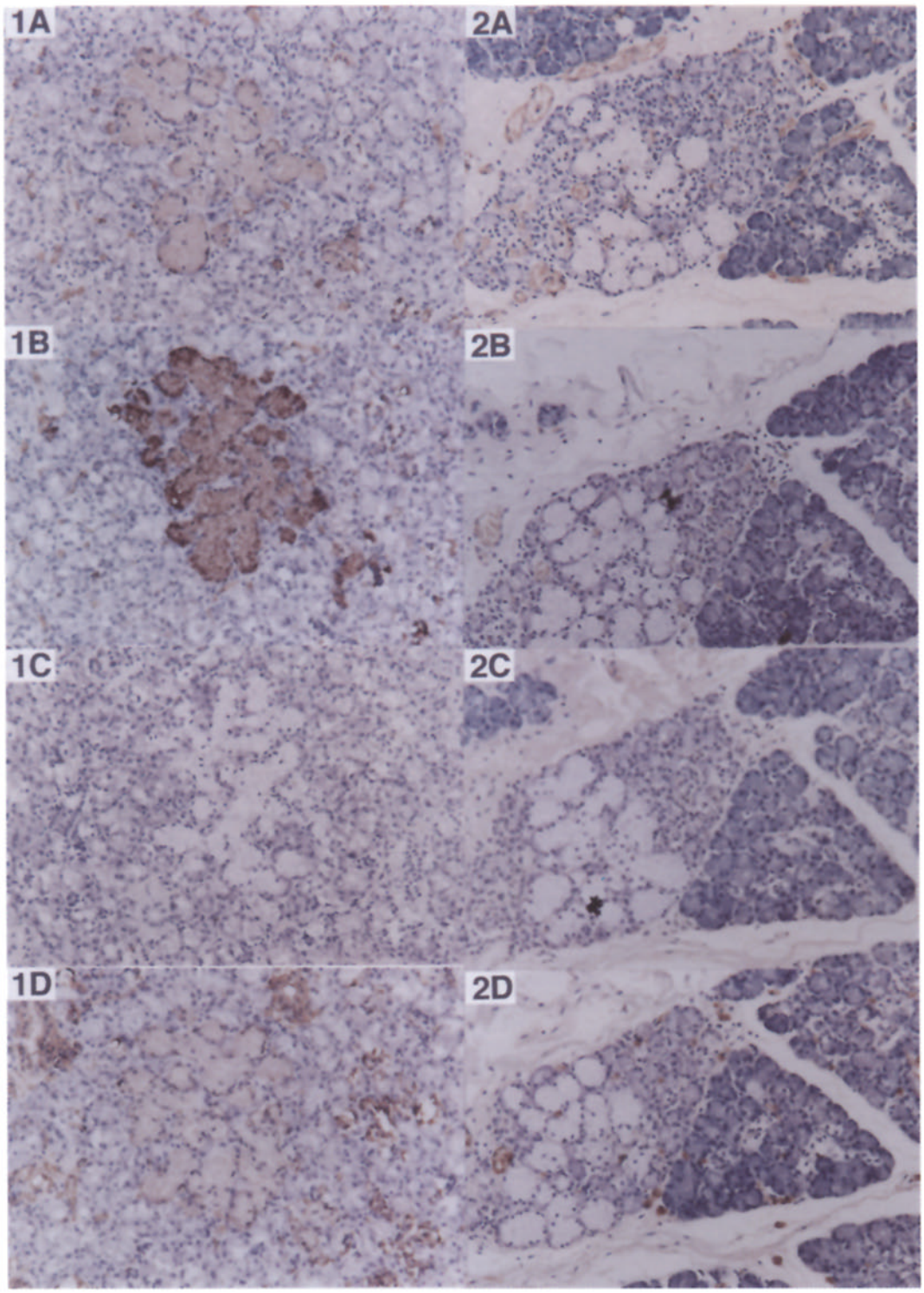

Figure 1. Sections of submandiblar gland from a Japanese blood group AB non-secretor stained with: A, monoclonal anti-A antibody; B, HPA; C, DBA; D, monoclonal anti-B antibody. The mucous cells and the endothelial cells of blood vessels were stained with monoclonal anti-A antibody (1A), HPA (1B), and monoclonal anti-B antibody (1D). No staining with DBA was detected (1C).

Figure 2. Sections of submandiblar gland from a German blood group A_2B non-secretor stained with: A, monoclonal anti-A antibody; B, HPA; C, DBA; D, monoclonal anti-B antibody. The endothelial cells of blood vessels were well stained with monoclonal anti-A antibody (2A), HPA (2B), and monoclonal anti-B antibody (2D), but the mucous cells showed no reactivities with these antibodies and lectin. No staining with DBA was detected (2C).

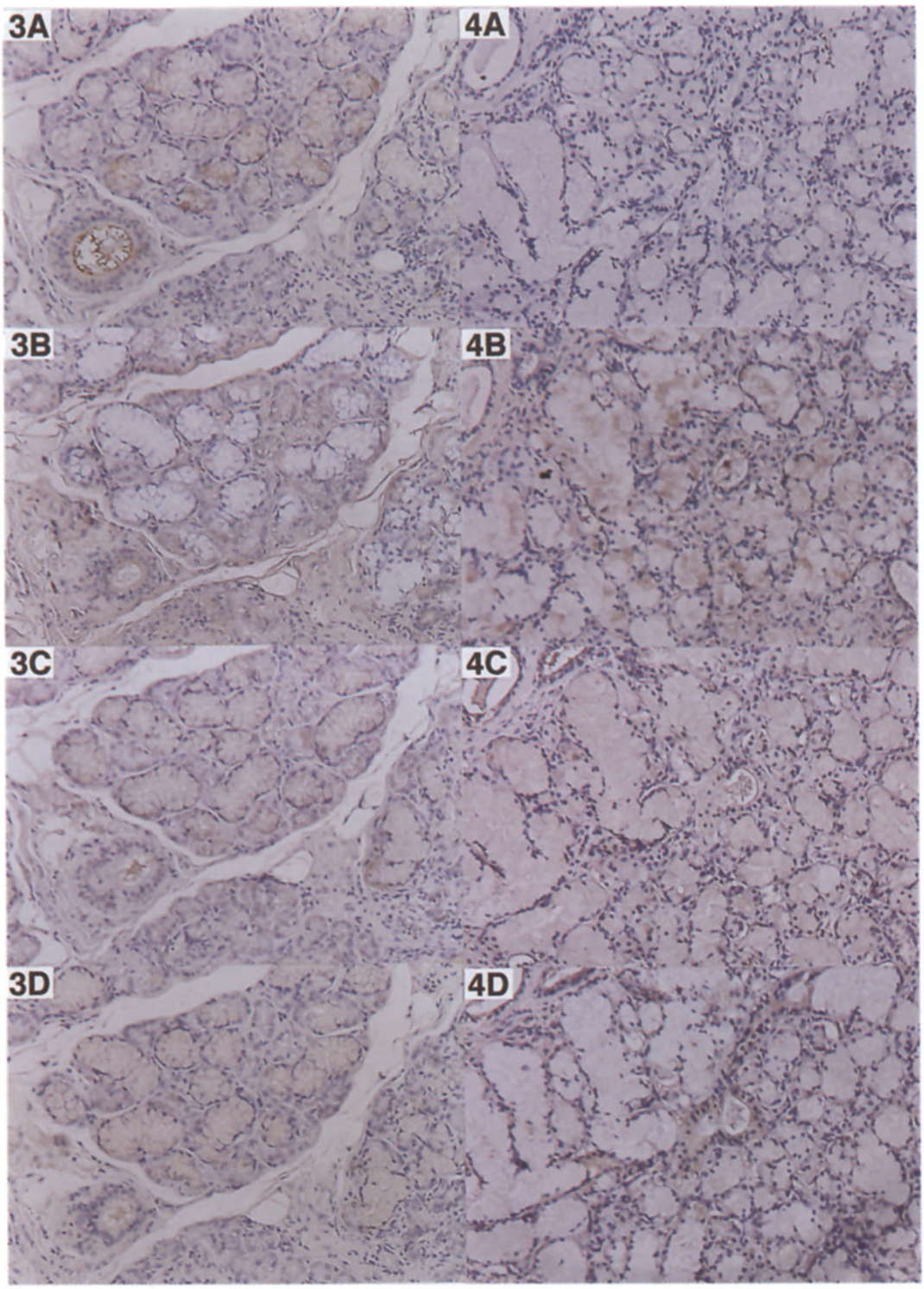

Figure 3. Sections of sublingual gland from a Japanese blood group O non-secretor stained with: A, UEA; B, monoclonal anti-type 1 precursor antibody; C, monoclonal anti-Le^a antibody; D, monoclonal anti-Le^b antibody. The mucous cells showed good reactivity with UEA (3A), but no reactivity with anti-type 1 precursor antibody could be detected (3B). Not only Le^a (3C) antigenicity but also Le^b (3D) antigenicity were detected in the mucous cells.

Figure 4. Sections of sublingual gland from a German blood group O non-secretor stained with: A, UEA; B, monoclonal anti-type 1 precursor antibody; C, monoclonal anti-Le^a antibody; D, monoclonal anti-Le^b antibody. In contrast to Japanese O non-secretor individuals, the mucous cells showed no reactivity with UEA (4A), but weak reactivity with anti-type 1 precursor antibody (4B). These cells showed good reactivity with anti-Le^a antibody (4C), while Le^b antigenicity could not be detected in the mucous cells (4D).

Table 2. Staining with blood group-specific monoclonal antibodies and lectins in salivary glands from German and Japanese blood group AB non-secretor individuals.

German AB Le(a+b-)

	SM muc.	*SM ser.*	*SL muc.*	*Lin. gl.*	*Duct*	*Eb. gl.*	*Endo.*
MoAB-A	−	−	−	−	+		+++
HPA	−	−	−	−	−		+++
DBA	−	−	−	−	−		−
MoAB-B	−	−	−	−	++*		+++
Le^a	++	++*	++	++	++		−
Le^b	−	−	−	−	−		−
Le^x	+++*	+++*	+++*	+++*	++		−
Le^y	−	−	−	−	+		−

Japanese AB Le(a+b−)

	SM muc.	*SM ser.*	*SL muc.*	*Lin. gl.*	*Duct*	*Eb. gl.*	*Endo.*
MoAB-A	+++	−	+++	+++	+*	++*	+++
HPA	+++	+*	+++	+++	−	++*	+++
DBA	−	−	−	−	+**	−	−
MoAB-B	++	++*	++	++	+++	++*	+++
Le^a	++	++*	++	++	+	++	−
Le^b	+	+*	+*	+*	+	+*	−
Le^x	+++*	+++*	++*	++*	++	+++	−
Le^y	−	+*	−	−	+++	+*	−

−: negative, +: weak, ++: moderate, +++: strong. MoAB-A, B, and Le^{abxy}: monoclonal anti-A, -B, -Le^{abxy} antibody, respectively. Monoclonal anti-B antibody made by Nickerbocker Co. was used. SM: submandiblar gland, SL: sublingal gland, Lin. gl.: lingual gland, Eb. gl.: von Ebner gland, Endo.: endothelial cell, Duct: duct cell in all salivary glands. muc.: mucous cell, ser.: serous cell.
*: some of all cells were positive. **: only supranuclear area was positive.

Ebner gland in tongues. Similar results were obtained from the Japanese secretor individuals (data not shown). In contrast, other blood group A or AB specific lectins such as DBA (Fig. 1C), VVA, GSA-I and SJA did not bind to these cells from Japanese non-secretors, although these reagents reacted well with the cells from secretor individuals (data not shown). Monoclonal anti-A antibodies used in this study showed good reactivity with these secretory cells of salivary glands (Fig. 1A). No differences were observed in the staining specificities among the monoclonal anti-A antibodies from the five different sources.

In the German non-secretors, however, the mucous cells of salivary glands and serous cells of the von Ebner glands showed no reaction or only feeble reactivity with HPA and HAA as well as other blood group A or AB specific lectins (Fig. 2B, C; Table 2). The majority of these cells likewise showed no or feeble reactivity with the monoclonal anti-A antibodies (Fig. 2A). Among the specimens examined in the present study, the secretory cells from A_2 non-secretor individuals showed the lowest reactivity with these reagents. In fact, it was difficult to find any such cells reactive with these reagents, although erythrocytes and vascular endothelium showed good reactivity with anti-A and H antibodies.

The secretory cells from blood group A_2 secretor individuals reacted strongly both with monoclonal anti-A and H antibodies, although the secretory cells from blood group A_1 secretor individuals showed good reactivity with anti-A antibody and relatively weak reactivity with anti-H antibody.

Anti-A_1 antibody showed no reactivity with the mucous cells of salivary glands and lingual glands from Japanese and German blood group A and AB non-secretor individuals, and weak reactivity with the supranuclear area of some duct cells of von Ebner glands. PNA also showed no reactivity with mucous acinar cells. On the other hand anti-A_1 antibody showed weak reactivity with the mucous cells of the salivary glands and strong staining with the supranuclear region in the duct cells of salivary glands from blood group A_1 secretor individuals. No staining with anti-A_1 was found on vascular endothelium or erythrocytes.

Expression of B antigen

Although the secretory cells from Japanese blood group B non-secretor individuals showed no reactivity with four out of five monoclonal anti-B antibodies used in the present study, the antibody purchased from Knickerbocker did react with the secretory cells of salivary gland from Japanese non-secretors (Fig. 1D). In contrast, the secretory cells from German blood group B non-secretors showed no reactivity with any of 5 blood group B antibodies, including the antibody from the Knickerbocker Co. (Fig. 2D), as well as antibodies obtained from the sera of blood group A individuals.

The results obtained with blood group AB non-secretor individuals are summarized in Table 2.

Expression of H and Le antigens

The secretory cells from blood group O secretor individuals showed good reactivity with anti-H antibody and UEA-I (an H antigen-specific lectin), as did their erythrocytes and endothelial cells. In the salivary glands from Japanese blood group O non-secretor individuals, the mucous cells showed no reactivity with anti-H antibody, although the serous cells and endothelial cells showed good reactivity (Table 3). Their mucous cells as well as serous cells and endothelial cells showed good reactivity with UEA-I (Fig. 3A; Table 3). In the salivary glands from German blood group O non-secretors, however, only endothelial cells showed reactivity with anti-H antibody and UEA-I, and secretory cells showed no reactivity (Fig. 4A; Table 3).

Although the secretory cells from Japanese blood group O non-secretor individuals expressed a small amount of blood group Le^b antigen and large amounts of blood group Le^a antigens (Fig. 3C, D; Table 3), the

Table 3. Staining with blood group-specific monoclonal antibodies and lectins in salivary glands from German and Japanese blood group O non-secretor individuals.

German O Le(a+b−)

	SM muc.	*SM ser.*	*SL muc.*	*Lin. gl.*	*Duct*	*Eb. gl.*	*Endo.*
MoAB-H	−	−	−	−	−		++
UEA	−	−	−	−	−		+
Type 1	+*	++*	++*	++*	+		−
Le^a	+	+	+	+	−		−
Le^b	−	−	−	−	+		−
Le^x	++*	++*	++*	++*	+*		−
Le^y	−	+*	−	−	++		−

Japanese O Le(a+b−)

	SM muc.	*SM ser.*	*SL muc.*	*Lin. gl.*	*Duct*	*Eb. gl.*	*Endo.*
MoAB-H	−	+*	−	−	+		++
UEA	++*	++*	++*	++*	+		++
Type 1	+*	++*	−	−	+*		−
Le^a	++	+*	++	++	+		−
Le^b	+	+*	+	+	++		−
Le^x	++*	++*	++*	++*	+		−
Le^y	−	+*	−	−	++		−

−: negative, +: weak, ++: moderate, +++: strong. MoAB-H Type 1 and Le^{abxy}: monoclonal anti-H, -type 1 precursor, -Le^{abxy} antibody, respectively. SM: submandibular gland, SL: sublingal gland, Lin. gl.: lingual gland, Eb. gl.: von Ebner gland, Endo.: endothelial cell, Duct: duct cell in all salivary glands. muc.: mucous cell, ser.: serous cells.
*: some of all cells were positive.

secretory cells from German blood group O non-secretor individuals expressed only Le^a antigens (Fig. 4C, D; Table 3).

Weak or moderate reactivity with monoclonal anti-type 1 precursor antibody was seen in the mucous cells of the sublingual glands from blood group O non-secretors from Germany (Fig. 4B) but none from the corresponding Japanese samples (Fig. 3B).

The results obtained with blood group O non-secretor individuals are summarized in Table 3.

After α-L-fucosidase digestion, monoclonal anti-type 1 precursor antibody could detect small amounts of type 1 precursor antigen in the sublingual gland mucous cells from Japanese non-secretor individuals (Fig. 5).

Some salivary gland mucous cells from all non-secretors including Le(a+b−) and Le(a−b−) individuals, both Japanese and German, showed reactivity with anti-Le^x antibody (Tables 2 and 3). In contrast, no reactivity was found between anti-Le^x antibody and salivary gland mucous cells from both Japanese and German secretor individuals.

The anti-Le^y antibody showed good reactivity with salivary gland duct cells from all individuals independent of secretor status or ethnic origin. In addition, this antibody showed good reactivity with the salivary gland mucous cells from secretor individuals.

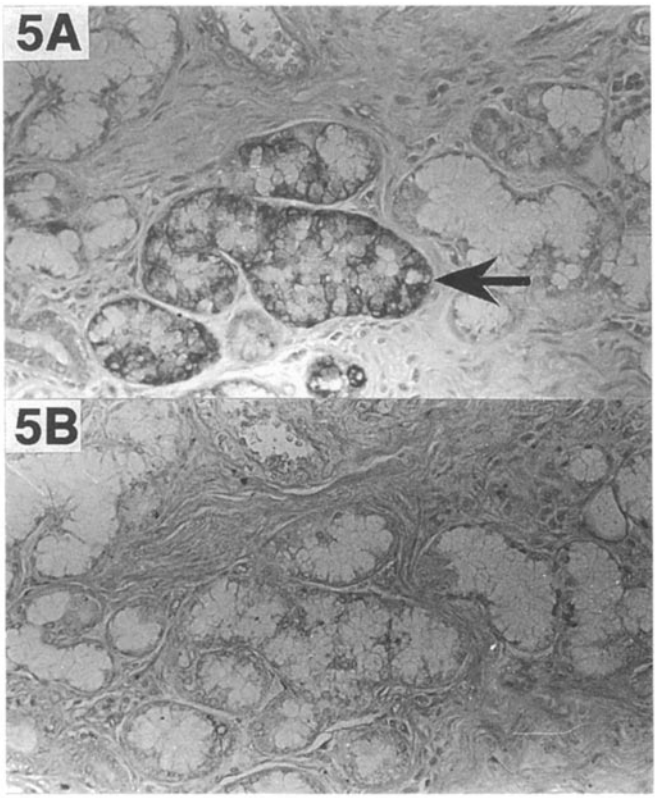

Figure 5. Effect of α-L-fucosidase digestion on anti-type 1 precursor antibody staining to sublingual gland from a Japanese non-secretor individual. A, after enzyme digestion; B, control. After this enzyme digestion, staining with anti-type 1 precursor antibody was observed in some mucous cells (arrow). This observation suggests that the 1-2-fucosylation of type 1 precursor chain, which is the reverse pathway to this enzyme digestion, may occur in these cells from Japanese O non-secretor individuals.

Discussion

Recent developments in biochemical methods for analysing blood group substances have provided definite information as to the complexity and heterogeneity of the basic structures of the blood group determinants [9]. The blood group A determinant is a well characterized trisaccharide, and 4 types of precursor chains, types 1, 2, 3 and 4, have been recognized.

The mucous cells of salivary glands and serous cells of von Ebner gland from Japanese blood group A non-secretor individuals expressed A antigen when monoclonal anti-A antibodies and HPA and VVA lectins were used. DBA and other A or AB specific lectins did not react with the cells from non-secretor individuals, therefore it was concluded that the expression of A antigen detected by DBA in the salivary glands was controlled by the secretor gene. This discrepancy is most likely to be due to the difference in binding specificity of the lectin used in the present study and in the structure or number of A antigens expressed in the cells.

In a previous study, we employed 12 different labelled lectins and assessed their ability to recognize blood group antigens in tissue sections. The results showed that blood group A or AB specific lectins display marked differences in their recognition patterns in certain tissues, i.e. HPA and HAA recognized A antigens in the mucous cells of salivary glands from blood group A or AB non-secretor and secretor individuals, whereas DBA, SJA and GSA-I did not bind to these cells from non-secretors.

According to Baker *et al.* [10], HPA exhibits much broader specificity for terminal GalNAc than DBA. DBA is assumed to have restricted specificity for certain A antigen variants, since the lectin has been employed as blood group A_1 specific lectin. Among the monoclonal anti-A antibodies used in the present study, the antibody (A581) obtained from the Dako Co. reacted with all blood group A variants, including type 1, 2 and 4 chains, mono and difucosyl structures [11, 12]. The snail lectins can react with Tn determinants (GalNAc-Ser/Thr) as well as with A determinants. However, in this study, the recognition pattern of the snail lectins in the salivary gland mucous cells was similar to the anti-A antibodies which cannot detect the Tn determinants. This observation showed that the snail lectins probably do not detect the Tn determinants but do detect the A determinants in these cells. Our results showed at least two different types of A antigen variants were expressed in salivary glands from blood group A Japanese individuals; first, the HPA and monoclonal anti-A antibody reactive A antigen which cannot be recognized by other lectins and is not expressed in the glands from German blood group A non-secretors, and second, the A antigen which reacts with all the A-specific lectins. It is assumed that the latter but not former is under the control of the secretor gene. The monoclonal anti-A_1 antibody, which has a specificity for type 3 and type 4 chains, was found to react with the mucous cells and duct cells from both Japanese and German (blood group A_1) secretor individuals but not from non-secretors.

The monoclonal anti-H antibody purchased from the Dako Co. which has a specificity for type 2 chain oligosaccharide showed good reactivity with endothelial cells and erythrocytes in salivary glands from blood group O non-secretor individuals but not with mucous cells, although it reacted strongly with mucous cells from the corresponding secretor individuals.

UEA-I was reported as being specific for H type 2 structures [13]. In this study, however, UEA-I could react with the salivary gland mucous cells from Japanese blood group O non-secretors in which H type 2 antigens could not be detected by anti-H type 2 antibody from the Dako Co. This observation suggests that UEA-I lectin may detect the H type 1 precursor antigen, and showed ethnic differences, reacting well with salivary gland mucous cells from Japanese but not German blood group O non-secretor individuals. The type 1 precursor antigen, in contrast, was detected in the sublingual gland mucous cells of German but not Japanese blood group O non-secretors (Figs 3 and 4; Table 3).

The type 1 precursor chain could be detected in sublingual gland mucous cells from Japanese blood group O non-secretors, as a weak reaction to a monoclonal anti-type 1 precursor antibody, only after fucosidase digestion (Fig. 5) which can hydrolyse fucose residues of the H type 1 antigen to the type 1 precursor antigenic structure. This suggests that the cells in Japanese but not German blood group O non-secretors possess an enzyme to catalyse the addition of fucose to the type 1 precursor chain.

On the basis of these considerations, it is presumed that blood group A and B active type 1 chain is secreted in the secretory cells from Japanese blood group A non-secretor individuals, since type 3 and 4 chains which are recognized by anti-A_1 antibody are not secreted in those cells and the expression of type 2 chain is probably controlled by the secretor gene as in the case of blood group O individuals.

In German non-secretors, it is assumed that relatively small amounts of A and B active type 1 antigen are secreted as compared with those in Japanese. This conclusion may be supported by findings of the previous studies where the Le(a+b+) phenotype and partial secretory phenotypes are frequent in Polynesians and Asians [14–16] but they are absent or rare in adult Caucasians [17].

The expression of type 1 blood group antigens in salivary glands from Japanese could be explained by at least three hypotheses (Fig. 6). First, the *H* gene, which is normally expressed mainly in tissues of mesodermic origin and is one of two closely linked loci (*H* and *Se*) encoding an α-2-L-fucosyltransferase reacting with both type 1 and type 2 precursor chains [18–23], may be expressed weakly in the secretory glands of Japanese non-secretors thereby leading to the production of some H type 1 antigen. Second, another enzyme which is independent of both *H* and *Se* genes may be present in these glands. Third, Japanese non-secretors may have a mutant *Se*-encoded α-2-L-fucosyltransferase with low activity.

In the present study, it must be assumed that the expression of H type 2 is absent in salivary gland mucous cells from Japanese blood group O non-secretor individuals. Type 2 chain antigens are found mainly in ecto- or mesodermally derived tissues [9, 24, 25]. In a few endodermally derived tissues, they are expressed similarly to type 1 chain structures, but normally they are expressed only weakly or not at all [26, 27]. In our study, the observation of the strong expression of Le^x antigen in both Japanese and German non-secretors shows that type 2 precursor structures are synthesized in the salivary

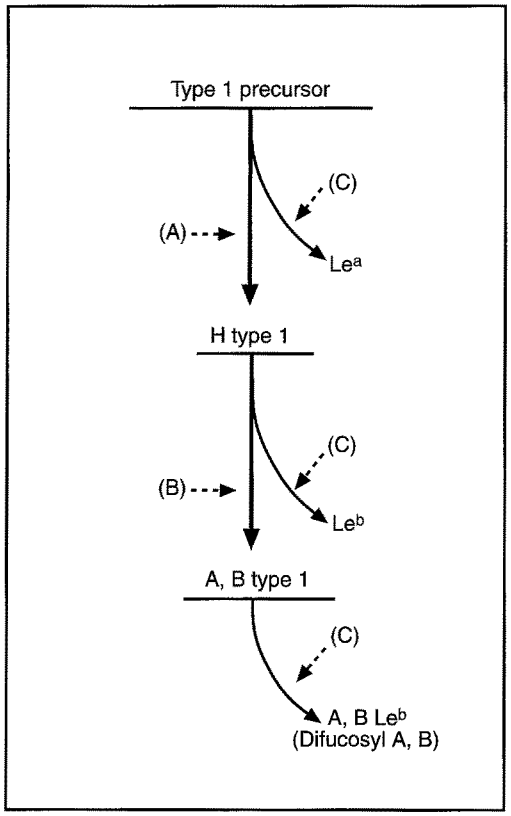

Figure 6. Biosynthesis of type 1 blood group antigens in secretory cells. Glycosyltransferases: A (1) Secretor individuals: synthesis of H type 1 chains is due primarily to an α-2-L-fucosyltransferase coded by the *Se* gene (*FUT* 2), (2) Japanese non-secretor individuals: synthesis of H type 1 chains may be due to a novel α-2-L-fucosyltransferase independent of the *H* and *Se* genes, or to weak expression of the *H*-gene encoded enzyme, or to a mutant *Se* gene (Henry *et al.* [4] have proposed an inefficient fucosyltransferase coded by the Se^w gene.) B, Blood group A, *N*-acetyl galactosaminyltransferase; blood group B, galactosyltransferase. C, α3/4L-fucosyltransferase coded by *Le* gene (*FUT 3*).

glands. The absence of H type 2 may indicate that the α-3-L-fucosyltransferase competes more effectively for the precursors than the α-2-L-fucosyltransferase with low activity.

This conclusion, furthermore, indicates that the expression of Le^x antigen in mucous cells of salivary glands could be a useful evidence for the immunohistochemical detection of secretory status.

In consideration of these above results, the second hypothesis, postulating the presence of another α-2-L-fucosyltransferase independent of both *H* gene and *Se* gene, cannot be excluded. In fact, it has been reported that a third distinct α-2-L-fucosyltransferase activity may be expressed by human cells [28].

Henry *et al.* [4] proposed a hypothesis that there may be a range of inefficient type fucosyltransferases coded by a mutant *Se* gene (Se^w), which consequently brought about the ethnic differences according to the ability of each transferase (third hypothesis).

In our study, it was found that only type 1 ABH antigens are expressed in the salivary gland mucous cells from Japanese non-secretor individuals. Because the type 2 chains may be utilized by the α-3-L-fucosyltransferase they are not available for conversion to H and then to A and B structures.

In conclusion, the difference in the expressions of blood group antigens in salivary glands from German and Japanese non-secretor individuals is assumed to be based on qualitative and/or quantitative variation in α-2-L-fucosyltransferase in the salivary gland. Recently, cDNA encoding the *H* gene-specified α-2-L-fucosyltransferase has been cloned and sequenced [29, 30].

Rouquier *et al.* [31] and Kelly *et al.* [32] reported the isolation of two human DNA segments that represent candidates for the *Se* gene-specified α-2-L-fucosyltransferase locus which cross-hybridize with the *H* gene and are in close physical proximity to this locus on chromosome 19. They presumed that one of these segments may correspond to the *Se* gene, and found that the non-secretor individuals in their study maintain homozygosity for an allele at this locus which contains an enzyme-inactivating translational termination codon. They also reported that the other segment is a pseudogene, which possibly associates with above-mentioned 'third distinct α-2-L-fucosyltransferase' expressed in human carcinoma cell line.

At the present time, it is not evident from what gene the α-2-L-fucosyltransferase, possibly causing the ethnic differences, is derived. It is, however, conceivable that the above two DNA segments may associate with this enzyme. Molecular analysis of the *Se* gene in Japanese non-secretors appears necessary to determine the exact mechanism responsible for the observed ethnic differences.

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