S.16 TISSUE EXPRESSION OF BLOOD GROUP ANTIGENS

S16.1
ABO and Lewis Antigens in Bladder Epithelium

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In normal urothelium one would expect an ABO and Lewis antigen expression corresponding to erythrocyte and saliva status. However, in urothelium Lewis b is expressed in non-secretors who have α1-2fucosyltransferase activity (LNBI acceptor),[1] and in Le(a-b-) individuals we do find Lewis antigens as well as α1-4 fucosyltransferase activity.[2]

In urothelial carcinomas there exist a sequence of changes from low grade to high grade tumors: (1) disruption of stratification of antigen expression (2) loss of secretor/non-secretor difference (3) Golgi-restricted precursors occur at membrane (4) gradual deletion of ABH antigens (5) uniform expression of difucosylated Le^b, and Le^y.[3] DNA/RNA studies have demonstrated that the loss of ABH antigen expression is not due to allelic loss (monosomy 9) but seems to be associated with lack of transcription of the ABO gene-complex, as evidenced by lack of mRNA in RT-PCR techniques, lack of transferase protein, and lack of enzyme activity. Studies on fucosyltransferase genes are currently being carried out.

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2. Ørntoft, T. F., Holmes, E., Johnson, P., Hakomori, S., Clausen, H. *Blood*, **77**: 1389, 1991.
3. Ørntoft, T. F., Review, APMIS, "Carbohydrate Pathology", suppl. **27**, 100: 181, 1992.

S16.2
Tissue Distribution of the Sd^a Antigen and its Biosynthetic Enzyme

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Sd^a character has been originally described as an inherited human blood group present on erythrocytes of over 90% of Caucasian population. The Sd^a determinant also occurs in tissues and body fluids, particularly in urine associated with Tamm-Horsfall glycoprotein. In human tissues the Sd^a antigen has been localized on renal cells and on brush border and goblet cells of colon. This antigen is not restricted to human species and many mammals express it at a very high level in the kidney, in the large intestine and in some functionally defined T-cell ciones. As many other isto-blood determinants, the Sd^a antigen has a carbohydrate structure and the GalNAcβ1,4-(NeuAcα2,3)Galβ1,4GlcNAc sequence has been found responsible for the immunological specificity. The GalNAc-transferase responsible for the addition of the immunodominant sugar, in β1,4 linkage to the Gal residue, requires for its activity the presence of NeuAc (not NeuGc) α2,3-linked to Gal. This enzyme also referred to as Sd^a-transferase acts towards *N*- and *O*-linked chains of glycoproteins as well as NeuAcα2,3Galβ1,4GlcNAc/Glc glycans but not towards GM_3. The tissue distribution of Sd^a-transferase correlates with the tissue localization of Sd^a antigen and a soluble form has been described in plasma and urine of Sd(a+) individuals as well as in culture medium of differentiated human colon carcinoma CaCo-2 cells. The Sd^a-transferase is practically absent in neonatal guinea-pig kidney and in sucking rat colon, and is dramatically reduced in human colon carcinomas. In CaCo-2 cells, Sd^a-transferase activity increases with the degree of enterocytic differentiation. Therefore the expression appears to be onco-developmentally regulated as it is for other blood-group related glycosyltransferases. We postulated that a reduced susceptibility to enterotoxigenic and pyelonephritogenic *E. coli* strains which specifically bind the NeuAcα2,3Gal unit has been the selective agent responsible for the dominant expression of the Sd^a glycosyltransferase in distal kidney and colon. Supported by A.I.R.C, CNR Progetto finalizzato A.C.R.O. and Regione Emilia-Romagna, Ricerca sanitaria finalizzata (DGR n. 4243 dated October 8, 1991).

S16.3
Carbohydrate Antigen Expression in Pig Tissues and Possible Relevance in Human Xenotransplantation

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The lack of donor organs in human transplantation is a major medical problem throughout the world. To use animals as resource for donor organs is today a challenging possibility. Pigs are by many considered the most probable donor species for reasons related to ethics, physiology, breeding, viral infectivity and immunology. A pig to human xenotransplantation is a discordant one as humans have preformed IgM antibodies against pigs causing a hyper acute rejection. Carbohydrate antigens are considered the main target for these antibodies.

We have characterised the carbohydrate antigen expression in pig aorta as a crude way to study the target endothelial cell expression. We have also studied the expression in a number of different organs from a semi inbred pig line, this being a possible future organ donor candidate. By means of MS, MS/MS, NMR, thin-layer chromatography (HPTLC) with immunostaining and immunofluorescence methods, we have identified the "straight chain B antigen", Galα1-3Galβ1-4GlcNAcβ1-3Galβ1-4Glcβ1-1 Ceramide in pig endothelial cells. All human beings have so far been shown to have antibodies against this antigen.

Glycolipid antigen fractions from pig aorta have been used to screen for binding epitopes of antibodies produced after pig islet cell to human xenotransplantations. Both IgG and IgM antibodies against the "straight chain B antigen" have been found in sera from patients being transplanted with pig islet cells. Other epitopes were also identified. Glycolipid fractions from kidney, liver, heart, lung, intestine, skin, salivary gland from the semi in-bred pig line have been characterised by HPTLC with immunostaining and GC/MS of ceramidase-released oligosaccharides. Data indicate qualitative different