19

EXPRESSION OF O-LINKED(mucin type) Tn AND SIALOSYL Tn ANTIGENS IN 22 COLORECTAL CARCINOMAS AND FETAL COLON TISSUE.

N.Harving, T.F.Ørntoft. The Danish Cancer Society, Dep. Exp. Clin. Oncology, Aarhus,DK.

The accumulation of O-linked glycoprotein core-structures has been suggested to be a general event in carcinomas. We have studied these structures during development and differentiation of the colon mucosa, by the use of monoclonal antibodies specific for Tn(GalNAcα1-O), SATn(SA2-6α GalNAcα1-O),T(Galβ1-3GalNAcα1-O),M/N(SA2-3Galβ1-3(SAα2-6)GalNAcα1-O), and A type 3(GalNAcα1-3(Fu cα1-2)Galβ1-3GalNAcα1-O).Immunolabelling of Western blots showed Tn and SATn antigens to be expressed on identical molecules with Mw 230.000, 210.000, and 170.000,whereas the other antigens could not be detected.Immunohistochemistry demon strated Tn antigens but not SATn and T antigens during fetal development of the colon, and SATn expression at 3 months of age, whereas adult colon was negative.In colon carcinomas Tn(82%) and SATn(73%)antigens were expressed. T and MN antigens were absent, but A type 3 was present in A individuals.Normal mucosa from carcinoma patients expressed Tn(40%) and SATn(40%)antigens, but none of the other antigens. The present data indicate coexpression in carcinomas of O-linked core - structures and extended structures with blood group active terminals.

Sponsored by the Danish Cancer Society.

21

THE IMPACT OF CIS-DPP ON EARLY RADIATION DAMAGE TO THE URINARY BLADDER

Finn Lundbeck and Jens Overgaard: Danish Cancer Society, Dept. of Experimental Clinical Oncology, Radiumstationen, DK-8000 Aarhus C, Denmark.

Aim: To compare the impact of Cis-DPP in combination with irradiation alone on the acute damage to the reservoir function of the urinary bladder.
Method: Fifteen minutes after intraperitoneally injected Cis-DPP (100 mg/kg) the urinary bladder of mebumal anaesthetized female mice were irradiated to a dose of 5-20 Gy. The same irradiation doses were delivered to a matched group of female mice and finally a group of mice were treated with Cis-DPP alone. The reservoir function of the bladder was repeatedly investigated during the following 25 days by inserting a catheter through the urethra, emptying the bladder, and infusing 0.1 ml/min of saline while simultaneously recording the intravesical pressure.
Results: The endpoint was a 50% reduction in the bladder volume at an intravesical pressure of 20 mmHg relative to control. In the group treated with Cis-DPP and irradiation the bladder volume was significantly lower than in the group treated with irradiation alone ($\chi^2 = 5.28$). There were no responders in the group treated with Cis-DPP alone (0/11).
Conclusion: Cis-DPP treatment 15 minutes before irradiation appears to enhance significantly the acute damage to the urinary bladder as opposed to irradiation alone.

Supported by the Danish Cancer Society.

20

DUAL-PARAMETER FLOW CYTOMETRY OF TRANSITIONAL CELL CARCINOMAS

T.F. Ørntoft, S.E. Petersen & H. Wolf. Danish Cancer Society, Dept. Exp. Clin. Oncology, Radiumstationen, Aarhus C, and Dept. Surgery I, Aarhus County Hospital, Aarhus C, Denmark.

To obtain an accurate quantitative characterization of cellular subpopulations on the basis of carbohydrate antigens, the authors have developed a dual-parameter flow cytometric method using a fluorescence-activated cell sorter. With this method single-cell suspensions from 26 transitional cell carcinomas were analyzed by means of propidium iodide (red fluorescence) as DNA ligand, and peanut agglutinin (PNA), wheat germ agglutinin (WGA), and anti-blood group A antibody (aBGA) as FITC-bound carbohydrate ligands. The carbohydrate ligand binding was correlated to the DNA content of cell populations in the way that aneuploid populations showed a higher PNA binding ($P<0.0002$) and a lower WGA ($P<0.01$) and aBGA ($P<0.04$) binding than did diploid cell populations. The binding of PNA to aneuploid populations could be further increased ($P<0.004$) by neuraminidase treatments. The carbohydrate ligand binding was cell cycle-dependent, as it was reduced (<0.008) in the G2-M phase. A low WGA ($P<0.004$) or aBGA ($P<0.02$) binding was correlated to tissue invasion. Immunohistochemistry showed a good correlation between aBGA ($P<0.0005$) and PNA ($P<0.004$) binding to tumor cells and flow cytometric assay of these, as well as a correlation ($P<0.003$) between cellular location of WGA receptors and flow cytometric assay of these.

22

HYDRALAZINE INDUCED CHANGES IN THE RADIATION RESPONSE OF TUMOURS AND NORMAL TISSUES.

R.V. Fisker, M.R. Horsman and J. Overgaard. Danish Cancer Society, Department of Experimental Clinical Oncology, DK-8000 Aarhus C, Denmark.

Hydralazine is an anti-hypertensive agent which has been reported to specifically reduce tumour blood flow. This is believed to produce an increase in tumour hypoxia, with a subsequent sensitization of tumours to certain drugs and hyperthermia. We have investigated the potential of hydralazine to change the oxygenation status of tumours and normal tissues using the response to radiation damage as the end point. Preliminary experiments were carried out on a C3H mammary carcinoma grown in the foot of CDF1 mice. Tumour response was assayed by percent local tumour control measured 90 days after treatment. Our results show that a single intravenous injection of hydralazine (5 mg/kg) produces a decrease in radiation damage. This was consistent with an increase in tumour hypoxia. The effect was dependent on the time of irradiation after drug injection with the greatest protection occurring when tumours were irradiated one hour after hydralazine administration. At longer time intervals this effect was diminished, and completely lost if radiation was delayed by about 6 hours after drug injection. Additional data will be presented on radiation damage in normal tissues and the results correlated with hydralazine induced changes in tissue blood flow.

Supported by the Danish Cancer Society.