Mem. Inst. Oswaldo Cruz, Rio de Janeiro, Vol. *86*, Suppl. III, 127-128, 1991

LOCAL RESPONSE IN MOUSE TUMOR TREATED WITH *SCHISTOSOMA MANSONI* ANTIGEN

MARIA APARECIDA LIMONGI LOURES/*; ADRIANA ANDRADE**; & JOSÉ MAURO PERALTA*

Centro de Pesquisa Básica, Instituto Nacional do Câncer, Praça da Cruz Vermelha 23, 20230 Rio de Janeiro, RJ, Brasil *Instituto de Microbologia UFRJ, **Departamento de Bioquímica, CCS, UFRJ, Ilha do Fundão, 21941 Rio de Janeiro, RJ, Brasil

Proteoglycans of heparan sulphate, dermatan sulphate and condroitin sulphate are ubiquitous compounds of mammalian cells (C. P. Dietrich & H. Montes de Oca, 1978, ***Biochem. Biophys. Res. Com.***, *80*: 805-812). They are the main compounds of extra-cellular matrix and are associated to collagen. Those compounds are present in relatively small amounts in most of the tissue but are of great importance in the relationship among cells (C. P. Dietrich, 1984, ***Bras. J. Med. Biol. Res.***, *17*: 5-15).

Condroitin sulphate is found only in trace amounts in most normal adult animal cells. However it is detected in a variety of mesenchymal and epithelial neoplastic cells (R. V. Iozzo, 1988, ***Cancer Metastasis Rev.***, *0:* 39-50) suggesting a correlation with stimulation of cell proliferation. Heparan sulphate binds to several matrix constituents including various types of collagen, fibronectin and laminin (R. V. Iozzo, *loc. cit.*) Heparan sulphate isolated from liver inhibits the growth of hepatoma cells *in vitro* (H. Kawakami & H. Terayama, 1981, ***Biochim. Biophys. Acta***, *646*: 161-168). Abnormality in heparan sulphate structure may interfere with attachment of cells to the substratum and may contribute to the lack of cohesiveness, a well-know property of transformed cells (R. V. Iozzo, 1988, *loc. cit.*). Dermatan sulphate is sinthetized in high levels by normal fibroblasts and it is related to surface of resting cells (C. P. Dietrich et al., 1982, ***Biochim. Biophys. Acta***, *717*: 387-397).

Some helmintic infections seem to be involved in the decreasing of tumor growth. The incidence of spontaneous breast cancer in C3H mice decrease when they were infected with ***Trichnella spiralis*** (N. F. Wheatherly, 1970, ***J. Parasitol.***, *56*: 748-752). ***Schistosoma mansoni*** infection affect the development of sarcoma 180 in mice (F. L. Pereira et al., 1986, ***Rev. Soc. Bras. Med. Trop.***, *19*: 39-42).

This work was supported by CNCC and CNPq, Brazil.

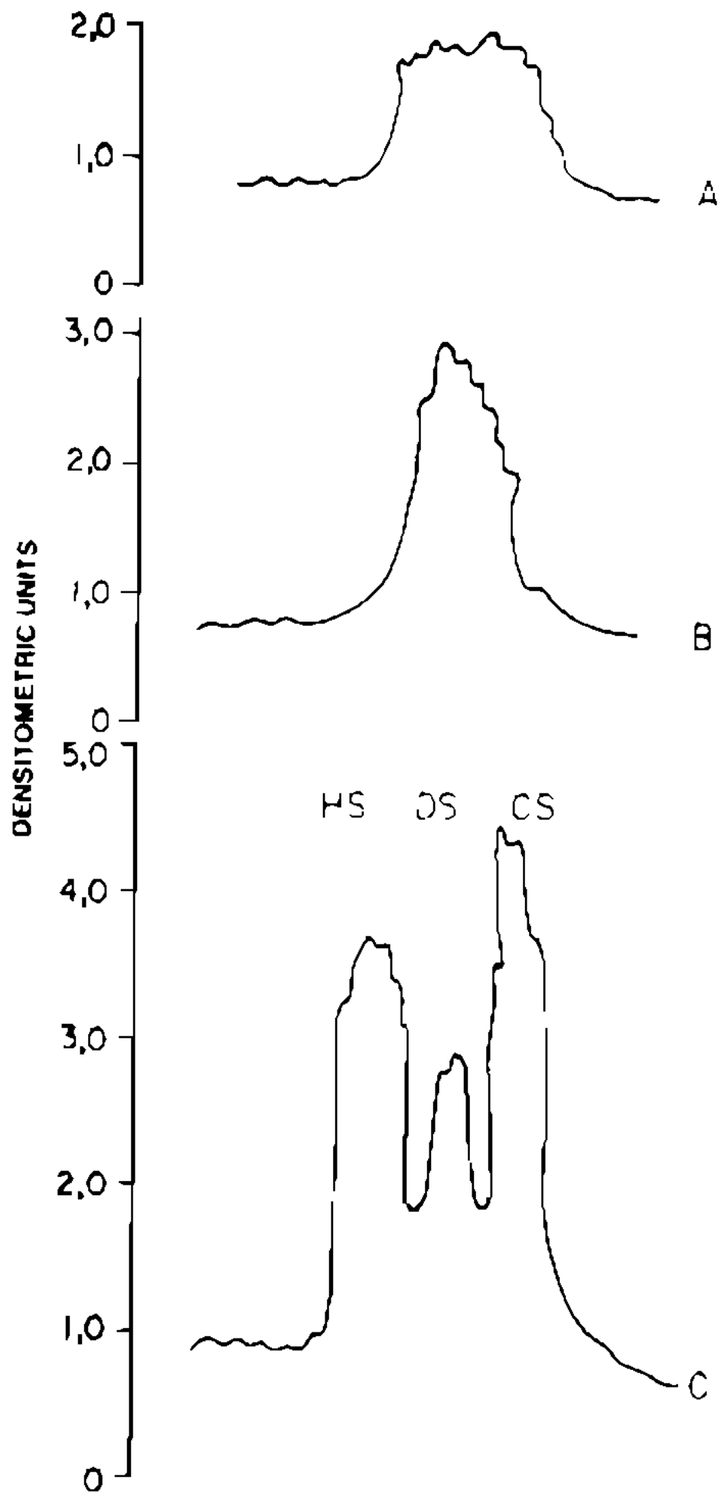

Fig. 1: electrophorese in agarose gel (A) non treated tumor, (B) SMA treated tumor and (C) glycosaminoglycan pattern. HS, heparan sulphate, DS dermatan sulphate e CS condroitin sulphate.

The purpose of this study was to analyse the production of glycosaminoglycans by tumor cells submitted or not to treatment with ***Schistosoma mansoni*** antigens.

Groups of mice were infected subcutaneously, in the back, with 10^6 cells of histiocytoma B10MC2 and treated as follow: A, saline was injected around tumor 3 times a week; B, *S. mansoni* adult worms (4 couples) were implanted in the back on day 7 and crude extracts of *S. mansoni* worms (SMA) (100 μg of protein) were injected 3 times a week from day 7 during 3 weeks. Tumors were measured 3 times a week and areas were calculated. The animals were sacrified 4 weeks after tumor implantation.

Tumor were removed, immersed immediatelly in 10 Vol of acetone, incubated for 24 h at 4°C and processed as described (L. C. F. da Silva et al., 1989, ***Exp. Mol. Pathol., 50***: 411-420). Briefly, dried tumors were suspended in 2,0 ml sodium acetate buffer, pH 5.5, containing 40 mg papain, 5 mM EDTA and 5 mM cystein (Sigma Chemical Co. St. Louis, MO) and incubated at 60°C 24 h. The suspension was centrifuged at 2000 g for 10 min and supernatant was precipitated with 2 vol of 95% ethanol and vacum dried. Agarose gel analysis was carried out applying tumor extract and standars to 0.5% agarose gel in 0.05M 1,3-diamino propanoacetate buffer (pH 9.0). After electrophoresis, glycosaminoglycans were fixed to the gel with 0.1% cetavlon (N-cetyl-N-N-N-trimethylamonium bromide) in water and stained with 0.1% Toluidine blue in acetic acid: water (0.1:5:5, V/V). Glycosaminoglycans were quantified in the gel by densitometry using a quick scan densitometer (Helena Laboratories, Beaumont, Tx).

Tumors growth among animals from group A (non treated) showed an exponential growth curve reaching a maximal tumor size at the end of experiment (1.3 cm^2). Tumors of group A (SMA treated animals) were significantly reduced at this time (0.25 cm^2).

The patterns of glycosaminoglycan contents in tumors from treated and non treated animals are shown in Figure. The mouse histiocytoma B10MC2 was showed to have very low concetration of glycosaminoglycans (Fig. 1A). However, a significant increasing in glycosaminoglycans content was found in the tumor from *S. mansoni* antigen treated animals, being dermatan sulphate the major one (Fig. 1B). This increase seems to be related with the decrease in the process of celular division and could be envolved in the process of the tumor regression. The distribuition of this proteoglycan in tumoral tissues has to be better understood in order to conclude on their role in tumoral regression. The point is that there is a disturbance in the balance between extra-celular matrix and cells in tumor tissues. Studies applying other mouse tumor types, and different antigenic preparations of *S. mansoni* have been performed to assess if similar results can occur in other situations.

ACKNOWLEDGEMENTS

To Dr Ligia R. Corrêa from Instuto Oswaldo Cruz for providing *Schistosoma mansoni* adult worms.