Tumori, 96: 999-1003, 2010

Influence of normal mammary epithelium on breast cancer progression: the protective role of early pregnancy

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ABSTRACT

Aims and background. The microenvironment has a well recognized role in breast cancer progression. Despite different theories, the mechanism of early pregnancy protection in mammary carcinogenesis is unknown. Since pregnancy is responsible for mammary gland differentiation, we tested the hypothesis that differentiated mammary epithelial cells may inhibit breast cancer progression. In other words, the protective role of early pregnancy could be due to the inhibitory influences of the more differentiated mammary tissue.

Methods. In order to test our hypothesis, we used 30 female Balb/c nude mice and MCF-7 cells of breast adenocarcinoma. The female mice were divided into two test groups, group I (GI) and group II (GII), and a control group. In GII, the animals were submitted to epithelial removal in the left fourth inguinal mammary gland at 3 weeks of age. Both groups were given continuous hormonal treatment to simulate the pregnancy development of the mammary gland. Two million MCF-7 cells were then injected into the fourth inguinal mammary gland (GI) or in the respective cleared mammary fat pad (GII). Five weeks later the mice were sacrificed and their tumors removed. Tumor development rates and tumor volumes were determined and proliferation and apoptosis were evaluated by immunohistochemistry.

Results. Tumors of GII mice had a larger mean volume than those of GI mice (P = 0.001, Mann-Whitney U-test) and an apparent increase in proliferation, demonstrated by a higher staining intensity for proliferating cell nuclear antigen (PCNA). As tumors presented caspase 8 staining, there may be apoptotic activation involved in cell death, mainly through an extrinsic pathway.

Conclusions. These results suggest that a differentiated intact mammary gland may have an inhibitory influence on mammary tumor growth in mice. Free full text available at www.tumorionline.it

Key words: breast cancer, pregnancy, mammary epithelium.

Acknowledgments: We would like to thank Prof João Patrício and Prof José Luís Santos for their background support in microsurgery and statistical analysis of the results, respectively. We would also like to thank Dr Hanna Guimarães for careful reading and language revision of the manuscript, and Mrs Margarida Menezes, Mrs Elisa França, Dr Pedro Peça, Dr Margarida Abrantes and Dr Mafalda Laranjo for other technical support.

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Received September 2, 2009;
accepted July 8, 2010.