CONTINUOUS RELEASE OF ENDOSTATIN FROM ENCAPSULATED ENGINEERED CELLS FOR TUMOR THERAPY

Rodrigues, D.B.[1], Malavasi, N.V.[1] Chura-Chambi R. M.[1], Barbuto, J.A.M.[2],Morganti, L.[1]; [1]Centro de Biotecnologia, IPEN, São Paulo, Brazil; [2]Instituto de Ciências Biomédicas, Universidade de São Paulo, São Paulo, Brazil.

Endostatin, a 20 kDa COOH-terminal fragment of collagen-XVIII, has been shown to act as an antiangiogenic agent which specifically inhibits the proliferation of endothelial cells and growth of various primary tumors. The following work aimed to study the endostatin effect in the growth of Ehrlich tumors in mice by treatment using engineered murine fibroblast cells encapsulated within macroimmunoisolation devices. The TheraCyte® immunoisolation system is a membrane encapsulation system developed for implantation of cells for therapeutic protein delivery *in vivo* and which protect allogeneic cells from rejection. The devices were implanted subcutaneously in the mice. After the healing and when the tumors reached a thickness of approximately 0,5 mm, the treatment began by the injection of 10^7LM cells which presents a continuous production 70ng endostatin/day (+/- 2,3) inside the devices. After 17 days, we observed a reduction of 50% in the thickness of the tumors compared to the control animals, indicating that the treatment is efficient due to the continuous liberation of endostatin. Treatment with the same amount of free LM cells, which are tumorigenic, also inhibits the growth of the tumors. We did not observe the presence of local tumors when the cells were enclosed into the device. Immunohistochemistry of tumors and studies with other tumors are underway.

Key words: Tumor, Endostatin, Antiangiogenic, therapy, immunoisolation device.

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