In vivo experiments showed that EGF immunization modified biodistribution of injected 125I-EGF. Mice with titers of anti-EGF antibodies accumulated more EGF in liver and less EGF in kidneys as compared with non-immunized, that could indicate a different way of elimination of immunocomplexes between EGF and anti-EGF antibodies. It was also shown a lesser content of EGF in ascites of immunized mice. These results point to the *in vivo* "EGF deprivation" by specific autoantibodies.

The effect of anti-EGF antibodies on tumor development was studied in mice trasplanted with Ehrlich Ascites Tumor (EAT), a trasplantable tumor with content of EGF-R. In 20 consecutive and independent experiments we observed increased survival times in EGF immunized mice trasplanted with EAT as compared with mice treated only with adjuvant.

The values of increase life span (ILS) in these experiments were in a range bewtween 10 % and 99 %. In the 85 % of the experiments the differences in survival times between immunized mice and controls were statistical significative, according to Wilcoxon and Mantel Haenszel tests.

We did not observe any effect over functional hepatic parameters of immunized mice compared with controls. Neither was observed any histological damage. In 19 monkeys immunized with hu-EGF coupled to different carrier proteins and using different immunization protocols we did not observe any sign of toxicity of the treatment.

These results support the idea of an "EGF-vaccine" for the treatment of EGF-dependent malignant tumors.

THE INHIBITORY EFFECT OF TUMOR-SHED GANGLIOSIDES ON THE PRODUCTION OF IL-1BETA BY MONOCYTES AS WELL AS ON THE PROLIFERATIVE ACTIVITY OF THIS LYMPHOKINE ON THYMOCYTES DEPENDS ON THE STRUCTURES OF BOTH OLIGOSACCHARIDE AND CERAMIDE MOIETIES OF THE GANGLIOSIDES

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Gangliosides are sialic acid-containing glycosphingolipids made of an oligosaccharide bound to a ceramide moiety. These molecules are highly exposed at the cell surface of tumor cells and one of the mechanisms by which the tumors escape the immune system is thought to involve shedding of gangliosides from the cell surface into the extracellular medium and the subsequent uptake of shed gangliosides by lymphocytes. Shedding is an active phenomenon closely related to the rate of proliferation and the amount of gangliosides released by tumor cells is equal after three to four days to the total cellular ganglioside content. At concentrations frequently found in the sera of tumor-bearing patients, the *in vitro* uptake of tumor-associated gangliosides during three days by monocytes leads to the insertion of these gangliosides in their plasma membrane. Such an enrichment of gangliosides results in a dramatic decrease in the production of IL-1β upon activation of monocytes by LPS. A study was carried out using several gangliosides known to be major components of various tumors and their effects were widely different. The production of IL-1β by LPS-activated monocytes was highly sensitive to gangliosides and GM2 had the most inhibitory effect whereas it had a very weak influence on the proliferative activity of IL-1β on thymocytes. At the opposite, GM3 showed a much more potent inhibition on the activity of IL-1β than on its production.

The potency of gangliosides as inhibitors of IL-1β production was in the decreasing order: GM2 > GD1a > 9-OAcGD3 > GD2 >> GT1b > GM3 > GD3 > GD1b. The study of these gangliosides as inhibitors of IL-1β dependent thymoproliferation showed quite different effects and the order of potency was the following: 9-OAcGD3 > GM3 > GD2 > GD1b > GT1b > GD3 > GD1a > GM2. These results suggest that the extent of immunomodulation by tumor-shed gangliosides depends greatly on the ganglioside pattern of the tumors.