NEW THERAPEUTICAL APPROACHES FOR THE TREATMENT OF MALIGNANT MELANOMA

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Gene therapy approaches for the successful combat of cancer include several conceptually different strategies: (i) enhancement of the tumor's immunogenicity; (ii) modification of the host immune system, e.g. by transducing tumor-infiltrating lymphocytes with TNE or IL - 2 genes; (iii) midification of other host tissues, e.g. by transfer of cytotoxic drug resistance genes into hematopoetic progenitor cells; (iv) introduction of corrective genes (e.g. wild type p 53) into tumors: (v) transfer of enzymes for prodrug therapy, e.g. introduction of the viral thymidine kinase gene into tumor cells which then become sensitive to gancyclovif.

In the case of melanoma, most gene therapy trials are conducted with melanoma cells the immunogenicity of which has been augmented by transfection with genes encoding cytokines (e.g. IL-2-IL-7, GM-CSF) and costimulatory molecules (e.g.CD80).

We have shown (i) that highly tumorigenic mouse melanoma cell lines lose their tumorigenicity upon transfection with IL-2, (ii) that mice injected with IL-2 transduced melanoma cells are protected when challenged with wild type tumor cells, and (iii) that administration of IL-2 transfected melanoma cells into mice can induce elimination of preexisting cancer cell deposits. Thus, we have developed the methodology for the production of IL-2-based, autologous melanoma vaccines which are currently being tested for safety and immunstimulatory efficacy in patients with stage IV disease.