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Poster presentation

The immunological basis of tumor therapy by targeted delivery of TNFa to tumor vessels

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L19mTNFa is a fusion protein constituted by the scFv L19 specific for the oncofetal ED-B domain of fibronectin and TNFa. Treatment with L19mTNFa, in combination with melphalan, induced complete tumor regression in 83% of BALB/c mice with WEHI-164 fibrosarcoma and 33% of animals with C51 colon carcinoma. All cured mice rejected challenges with the same tumor cells and, in a very high percentage of animals, also challenges with syngeneic tumor cells of different histological origin. In adoptive immunity transfer experiments the splenocytes from C51-cured mice protected 100% of naive mice both from C51 colon carcinoma and from WEHI-164 fibrosarcoma. The splenocytes from WEHI-164-cured mice protected 100% of mice from the fibrosarcoma and 80% from the C51 colon carcinoma. Similar results were also obtained in adoptive immunity transfer experiments using severely immunodepressed SCID mice. Experiments using depleted splenocytes showed that T cells play a major role in tumor rejection. These data demonstrate that the selective targeting of mTNFa to the tumor enhances its immunostimulatory properties to the point of generating a therapeutic immune response against different histologically unrelated syngeneic tumors. These findings predicate treatment approaches for cancer patients based on the targeted delivery of TNFa to tumor vasculature.