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Interferon gamma induces MHC class I/II expression on Primary Pancreatic Cancer Cells and enhances their recognition by autologous cytotoxic and helper T cells

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Pancreatic cancer is an aggressive disease with a poor prognosis. Immunotherapeutic strategies aim to enhance autologous T cells responses against tumor associated antigens. Up to date spontaneously induced functional anti tumor effector T cells in pancreatic cancer have hardly been reported. Immunotherapeutic treatment strategies may fail due to inefficient antigen presentation by the neoplastic cell. IFN-gamma treatment enhances the immunogenicity of several cancers through induction of MHC-I, MHC-II. We here tested the presence of spontaneously induced functional CD4⁺ and CD8⁺ memory/effector T cells reactive to autologous primary cultured pancreatic cancer cells stimulated with IFN-gamma. The effect of IFN-gamma stimulation on the expression of MHC-I and MHC-II in primary pancreatic cancer cell cultures was analyzed by immunohistochemistry and flow cytometry staining both surface molecules. Subsequently, the capacity of *ex vivo* isolated cancer reactive autologous PBMCs, CD8⁺ and CD4⁺ T cells was tested for reactivity against pancreatic cancer cells with and without IFN-gamma stimulation by ELISPOT-cytokine release assays and cytotoxicity assays.

The MHC restriction of the T cell response was evaluated by MHC class I and -II blockade with specific monoclonal antibodies. Immunohistochemistry and flow cytometry was performed to characterize the expression of MHC class I and -II molecules on primary pancreatic cancer cell cultures before and after IFN- gamma stimulation.

Spontaneously induced CD4⁺ and CD8⁺ T cells with specificity for autologous cancer cells and defined cancer antigens were present at low frequencies in peripheral blood of most tested patients. Low dose stimulation with 500 IU/ml IFN-gamma for 72 hours enhanced MHC-I expression and induced a strong expression of MHC-II in primary pancreatic cancer cell cultures. IFN-gamma stimulated pancreatic cancer cells significantly enhanced the reactivity and cytotoxicity of cancer -reactive MHC-I restricted and purified CD8⁺ T cells and were directly recognized by MHC II restricted purified CD4⁺ T helper cells.

We concluded that low dose IFN-gamma treatment may be useful as a systemic and local adjuvant in immunotherapy to enhance the immunogenicity of, and spontaneous as well as induced immune responses against, residual cancer cells.