

Wei Geng
Dr.med.

Selective Expression of Tumor Specific Antigens by Samples derived from human Pancreatic Cancer

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Doktorvater: Prof. Dr. med. Jürgen Weitz

To be effective and selective, immunotherapy ideally targets specifically tumor cells and spares normal tissues. Identification of tumor specific antigens is a prerequisite to establish an effective immunotherapy. Still very little is known about the expression of tumor-related antigens in pancreatic neoplasms. Cancer Testis antigens (CT) are antigens shared by a variety of malignant tumors, but not by normal tissues with the exception of germ cells in testis. Restricted expression in neoplastic tissues and inherent immunogenic features make CT antigens ideal for use in immunotherapy. We analysed the expression of a selected panel of ten CT antigens that have been proven to elicit an efficient immunogenic response in other malignancies. In addition we analyzed the expression of HERV-K-MEL, an immunogenic antigen of viral origin.

Pancreatic adenocarcinoma tumor samples (n=130) were obtained intraoperatively, control tissues (n=24) were collected from cadaveric donor and from patients with chronic pancreatitis. Tumor-associated antigen expression of MAGE-A1, MAGE-A3, MAGE-A4, MAGE-A10, LAGE-1, NA-17A, NY-ESO-1, PRAME, SCP-1, SSX-2, SSX-4 and HERV-K-MEL was assessed by PCR. Sequencing of PCR products were performed to assess the expression of SSX-4 in neoplastic and normal pancreatic tissues.

Three of twelve tested antigens were expressed in over 10% of malignant pancreatic tissue samples. SSX-4 was found positive in 30 % of cases, SCP-1 in 19% and HERV-K-MEL in 23% of cases. No expression of CT antigens was found in healthy pancreatic tissue with the exception of SSX-4 and SSX-2.

52% of the analyzed tissues expressed at least one CT antigen. The concomitant expression of SSX-4 in both malignant and normal pancreatic tissue is a new finding which may raise concerns for immunotherapy. However, HERV-K-MEL is expressed with a relatively high prevalence and may be a candidate for specific immunotherapy in a large subgroup of pancreatic cancer patients. This study advocates the analysis of patients with regard to their immunogenic profile before the onset of antigen-specific immunotherapy.