Tumor-associated antigens

Description

The importance of choosing the right antigen to develop anticancer vaccines represents a first, important challenge, which also prompted the understanding towards other key aspects.

Following the achievements obtained by employing live attenuated pathogens vaccines, and because of the initial absence of defined tumor-associated antigens (TAAs), the first anticancer vaccines were constituted by whole tumor cells, previously inactivated.Ward et al., 2002 As this approach was tested in models able to better mimic human tumors, its resulting weak or absent immunogenicity led immunologists to decipher additional co-stimulatory signals required to activate T cells.Jaffee et al., 2001 In the case of whole tumor cell, TAAs are expected to be captured and processed along with auto-antigens. If activated DCs succeed in eliciting strong immune responses against the entire collection of epitopes, autoimmunity reactions will imply unwanted, detrimental and life-threatening consequences.Dudley et al., 2002 Moreover, the use of whole tumor cells, or complex mixtures of tumor-derived material, neutralizes the specificity of the vaccination approach.

A desirable immune response should promote the destruction of cancer cells, without harming normal tissue. Therefore, many efforts have been made to identify tumor-specific antigens, which have been used for the realization of cancer vaccines which demonstrated its ability to generate tumor-specific immunity and a memory effect, without giving rise to autoimmunity.Soares, Mehta, & Finn, 2001 Antigen-specific active immunization represents an adequate approach not only in terms of safety, but also regarding reproducibility and scale-up production. A variety of epitopes derived from mucin 1 (MUC1),Tang & Apostolopoulos, 2008 HER/NEU,Disis et al., 2002 melanoma-associated antigen 3 (MAGE3),Chomez et al., 2001 and many others, have been already subjected to extensive studies. In principle, antigen-specific immunotherapies which exploit narrow epitope specificity might lead to a less effective immune response ; on the other hand, many of these antigens fall within the category of shared antigens, enclosing molecules that are expressed by many tumors and not normal tissues, or expressed also by normal tissues but in a different quantitative and qualitative manner (*vide infra*). Therefore, vaccines that include shared antigens can be envisaged for use in a large number of patients. Intriguingly, it has been shown in animal models and clinical trials that a vaccination against a single shared antigen is able to elicit an immune response which spreads towards other antigens on that tumor, a process known as epitope spreading.Hardwick & Chain, 2011

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1. News