

SELECTION OF TUMOR CELLS WITH BETA2-MICROGLOBULIN LOSS OVER THE COURSE OF METASTATIC MELANOMA: IMMUNE ESCAPE AND RESISTANCE TO IMMUNOTHERAPY

Abstract

One Andalusian research group has developed this invention that tracks the evolution of tumor HLA class expression in successive cancer lesions in metastatic melanoma treated with dendritic cells transfected with autologous tumor-mRNA.

Description

This discovery shows a successful use of a non-replicating adenovirus expressing the wild-type human b2m gene in recovery of normal human leucocyte antigen (HLA) class I expression in b2m-null cancer cells. Total loss of HLA class I expression in these cell lines is caused by a mutation in b2m gene and a loss of heterozygosity in chromosome 15 carrying another copy of that gene. Normal HLA class I expression on the tumour cell surface is critical for the successful outcome of cancer immunotherapy as T cells can only recognize tumour-derived peptides in a complex with self-HLA class I molecules. In this report we characterize the newly generated adenoviral vector AdCMVb2m and demonstrate an efficient b2m gene transfer in tumour cell lines of different histological origin, including melanoma, prostate and colorectal carcinoma.

Advantages

Advances in our understanding of the relationship between the immune system and tumor cells has given rise to new prospects for immunological treatment and the prevention of cancer. Clinical trials report so far only limited efficacy of cancer immunotherapy.

As T-cell recognition of malignant cells depends on tumor antigen presentation, in the absence of a suitable HLA-peptide target on the cell surface, peptidebased immunotherapy is unlikely to improve the anti-tumor CTL response. We favor the idea that the primary tumor is composed of tumor cells with a large diversity in HLA class I expression which therefore present tumor antigens with a different efficiency. Analysis of the correlation of impaired HLA expression with metastatic progression is important for the improvement of existing protocols of cancer immunotherapy.

Application domain

The present invention generally falls within the technical field of pharmaceuticals

What we looking for?

This research group is looking to establish a license agreement or agreement for public-private partnership for the development of technology.

