LÍNEA DE INVESTIGACIÓN: Gene Therapy in Targeting MHC class I Expression to Increase Tumor Immunogenicity

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Recognition of tumor-associated antigens (TAA) by self-MHC (Major Histocompatibility Antigens) class I-restricted CD8+ T cells is a main feature in the detection and destruction of malignant cells. Currently, much work in tumor immunology and oncology has focused on targeting ‘tumor escape phase’ to increase tumor immunogenicity and on developing new therapeutic modalities. The discovery and molecular characterization of TAA has changed the field of cancer treatment and introduced a new era of cancer immunotherapy aimed at increasing tumor immunogenicity and T-cell-mediated anti-tumor immunity. Unfortunately, while these new protocols of cancer immunotherapy are mediating induction of tumor-specific T lymphocytes in patients with certain malignancies, they have not yet delivered substantial clinical benefits, such as induction of tumor regression or increased disease-free survival. It has become apparent that lack of tumor rejection is the result of immune selection and escape by tumor cells that develop low immunogenic phenotypes. Substantial experimental data support the existence of a variety of different mechanisms involved in the tumor escape phase, including loss or downregulation of MHC class I antigens. Malignant behavior of a tumor cell may depend on the level of MHC class I expression and alterations in tumor MHC class I antigens may be a factor in escape from immune surveillance. These alterations could be caused by reversible/regulatory changes or by structural/irreversible genetic defects, including mutations/deletions and chromosomal aberrations in genes coding for MHC molecules. Different mechanisms underlie these alterations and might require different therapeutic approach. On the basis of the evidence obtained from experimental mouse cancer models and metastatic human tumors, the structural defects underlying MHC class I loss may have more profound implications on T-cell-mediated tumor rejection and ultimately on the outcome of cancer immunotherapy. It may lead to resistance to immunomodulatory therapy and generation of dangerous MHC class I-negative tumor escape variants. Strategies to overcome this obstacle, including gene therapy to recover normal expression of MHC class I genes, could increase tumor immunogenicity and improve the efficacy of immunotherapeutic modalities.

Publicaciones Recientes


Tesis DIRIGIDAS RECENTEMENTE (5 ÚLTIMOS AÑOS).

1) Ana Belén del Campo – “Beta-2-microglobulin gene transfer in HLA class I deficient tumor cells using recombinant adenovirus"

Doctorado Internacional, Universidad de Granada, Febrero 2014

2) Javier Carretero Coca – “Analysis of the molecular mechanism of HLA altered expression in prostate cancer and its recuperation using viral vectors" (defenderá próximamente), Universidad de Granada.

TRABAJOS FIN DE MÁSTER REALIZADOS (5 ÚLTIMOS AÑOS).

Miguela Mendez Garcia - “Estudio de la relación entre la expresión de HLA de tipo I y de distintos receptores “inmune checkpoints”. 2014-2015

PROYECTOS Y AYUDAS DE INVESTIGACIÓN

TITULO: Incremento de la inmunogenicidad en células tumorales tras la restauración de la expresión de HLA de clase I mediante vectores adenovirales.

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