ImmunoTools *special* Award 2014

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Study and characterization of innate CD8$^+$ T cells as possible therapeutic mediators in cancer models

In my lab, we are dedicated to study the role of interleukin 12 (IL-12) and IL-18 as antitumor agents in human and murine cancer models.

Due to its angiostatic capacity and to display a strong antitumor immune response, these cytokines are quite interesting since they are currently used as immunotherapy (mainly IL-12) in different type of cancers like T cell lymphoma, non-Hodgkin lymphoma, melanoma, ovarian cancer, Kaposi´s sarcoma, renal carcinoma, etc. Even when the results of clinical trials demonstrated not to as efficient as in murine models of cancer, the use of IL-12 still represents an important area of investigation in cancer immunotherapy when is administrated alone or with other antitumor mediators.

Our published data demonstrated that systemic expression of IL-12+IL-18 induces a strong cytotoxic activity against solid or metastatic tumors in murine models utilizing B16 and 3LL cell lines. Moreover, co-expression on both cytokines demonstrated less side effects than when IL-12 was administrated alone. These findings encouraged us to study in more detail the toxic mediators induced after systemic expression of IL-12+IL-18 in order to find strategies aimed to control its toxicity that are currently limiting is use in cancer patients. Based on this, we described the role of the cytokine TNFα as the responsible mediator of IL-12 undesirable side effects. Importantly, we demonstrated that TNFα neutralization does not affect IL-12-antitumoral capacity and highly increase the animal survival. Our data encourage the use of antagonists/blocking antibodies against TNFα in cancer patients under IL-12 treatment already approved for human use as infliximab, adalimumab, etc.

Since a while ago, it has been described a group of CD8$^+$ T cells, pre-existing in mice (and in humans), with the capacity to rapidly respond to the cytokines IL-12 and IL-18 similarly to NK cells, producing large amounts of IFNγ. Due to the mentioned characteristics, those cells were named as “innate CD8$^+$ T cells” and because they are able to act in different infectious processes as a first line of defense in a TCR-

independent way. Recent reports demonstrated that IL-12 e IL-18 can induce antitumoral immune responses by $CD8^+$ T cells similar to memory responses in the absence of any antigen stimulation. The number of papers that describe the role of innate $CD8^+$ T cells are still scarce then we consider that a deeper effort has to be made in studying the antitumor role of these cells since they can open a new door as a possible therapeutic tool in cancer immunotherapy.

The aim of our group is to continue with the study of the mechanisms that participate in tumors control by the immune system when it stimulated by IL-12 and IL-18 in murine models and also we wish to extend our work to develop xenographs models in SCID/NOD mice transplanted with human tumoral cell lines.

In this context, the ImmunoTools antibodies that we request will greatly help to initiate our studies evaluating the expression of the different immune population ($CD4^+$ and CD8 T cells, B cells, macrophages, etc) that invade the tumors from lymphatic immune tissues. Also to determine the expression of HLAs expressed by human cell lines. The recombinant protein requested is planned to be utilized to perform *in vitro* stimulations of immune cells and human cell lines. We will use the ELISA test to measure TNFα, a cytokine produced in the tumor microenvironment that has been reported as a pro-tumoral agent in the tumor site.

ImmunoTools *special* AWARD for

Maria Cecilia Rodriguez-Galán includes 25 reagents

FITC - conjugated anti-human CD4, CD24, HLA-ABC, HLA-DP, HLA-DR, Control-IgG1,

PE - conjugated anti-human CD8, CD19, Control-IgG1,

PerCP - conjugated anti-human CD3, CD45,

APC - conjugated anti-human CD44, Control-IgG1,

human TNFa ELISA-set for 96 wells (each 3 reagents),

recombinant human cytokines: rh IL-12, human TNF-a,

FITC - conjugated anti-mouse CD3e,

APC - conjugated anti-mouse CD3e, CD8a, CD19,

recombinant mouse cytokines: rm IL-4, rm IL-10, rm IFNgamma, rm IL-15, rm MCP1 / CCL2, rmCCL5

DETAILS more AWARDS