ImmunoTools *special* Award 2014

Angel Miguel Garcia Lora
PhD, Principal Investigator, Group Leader

Tumor Immunology: Preclinical animal models,
Servicio de Analisis Clinicos e Inmunologia,
UGC Laboratorio Clinico, Hospital Universitario
Virgen de las Nieves, Av de las Fuerzas Armadas, 2
18014 Granada, Spain

Immune mechanisms involved in the latency of dormant metastases

One of the most important problems in cancer is the progression from primary tumour to metastases. In the great majority of cases, the metastases cause the death of the patient. When a tumour is clinically detected in a patient, this is removed and diagnostic tests are performed to detect any presence of metastases. In many cases, however, the metastatic cells are not detected and the patient eventually develops metastases after a long latency period. These micrometastases are in latency and they are known as “dormant metastases”. These metastases cannot be analysed or studied in the patient because they are not detectable. The mechanisms underlying cancer dormancy remain poorly understood, due to difficulties in isolating dormant human metastatic cells and constructing preclinical models of dormant metastases. Our group has developed a novel non-transgenic murine cancer model, in which spontaneous metastases are permanently kept in dormancy by the immune system of the hosts (Romero, et al, 2014). Furthermore, disseminated metastatic cells were awoken after depletion of T or NK cells in the hosts, originating overt lung metastases. This metastatic tumour murine model mimics the progression of human cancers in which disseminated metastatic cells remain in dormancy for a long latency period or indefinitely. The study of the genes, the mechanisms and immune cells involved in this process may improve knowledge of the phenomenon of metastatic dormancy and how the immune system may control dormant disseminated metastatic cells. The GR9-B11 metastatic tumour model is a unique and reproducible experimental system for detailed analysis of the phenomenon of immune-mediated metastatic dormancy. The results may open up new possibilities for the development of anticancer treatments directed at the immune control of metastatic disease. These data could help us to understand how cancer might become a chronic disease that persists in non-fatal form in a clinically healthy individual.

The specific aim of this project is to analyse and in detail characterize the local and systemic immune response promoted by GR9-B11 in tumour-bearing mice. We will perform spontaneous metastasis assays using GR9-B11 tumor cells. GR9-B11 fibrosarcoma cells will be injected subcutaneously in BALB/c mice. When the largest diameter of primary tumor reaches 10 mm, the local tumor will be removal, and the mice will be left to apparition of spontaneous metastases. Leukocytes from spleen and from the lungs will be isolated 25, 50 and 100 days after tumor injection. We will perform a detailed analysis of leukocyte subpopulations and the expression of markers and surface receptors involved in tumour immunosurveillance of dormant metastases in this metastatic model by flow cytometry. We previously found that the growth and metastatic dissemination of GR9-B11 cells generates an increase in different leukocyte subpopulations at local and systemic level. Thus, T cells, dendritic cells and macrophages were found to be increased in GR9-B11-tumour-bearing mice. We shall now characterize this immune response in detail. Lungs and spleen leukocytes will be isolated from the animals and be analysed by immunofluorescence and flow cytometry using antibodies against specific surface markers selected from ImmunoTools.

Romero I, Garrido C, Algarra I, Collado A, Garrido F, Garcia-Lora AM: **T lymphocytes restrain spontaneous metastases in permanent dormancy**. 2014. *Cancer Research*, 74(7):1958-68.

ImmunoTools *special* AWARD for **Angel Miguel Garcia Lora**

includes 25 reagents

FITC - conjugated anti-mouse CD9, CD11b, CD19, CD29, CD44, CD45, CD45R, CD45RC, CD62L, CD81, CD90, CD134, CD247, NK-cells, a/b TCR, g/d TCR, isotype control IgG2b,

PE - conjugated anti-mouse CD3e, CD34, CD55, CD117, Gr-1, g/d TCR, isotype control IgG2b,

APC - conjugated anti-mouse CD8a, CD11a, CD25, CD49d, isotype control IgG2b

DETAILS more AWARDS