ImmunoTools IT-Box-Cy55M-Award 2013

Ivana Campia

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Correlation between immune-tolerance and chemo-resistance

Chemo-resistance represents one of the major obstacles to cancer treatment because of the arising of multiple cross-resistance mechanisms towards anticancer drugs. Chemotherapy kills cancer cells in an apoptotic way, which is poorly immunogenic, but anthracyclines, in particular doxorubicin, are the only chemotherapeutic agents which elicit also an immunogenic death in tumours.

Previous findings from our group showed that doxorubicin-resistant cancer cells are barely recognized by the immune system and thus, they may also show immune-resistant like features [*De Boo S et al, Mol Cancer, 2009; Kopecka J et al, J Cell Mol Med, 2011*].

It is currently emerging that tumours are able to induce immune-tolerance by escaping host immune-surveillance, generating condition of immunological unresponsiveness towards their own antigens.

Aim of my PhD project is to investigate whether chemoresistant cells are also immune-tolerogenic, and which are the metabolic and immunological basis linking chemo-resistance and immune-tolerance in tumours.

I am studying a murine model of mammary adenocarcinoma (CRL-2116 cells), known for its high chemoresistance [*Lee BD et al, Oncol Res, 2003*].

More specifically, I am focusing on the immune-tolerogenic enzyme called indoleamine 2,3-dioxygenase (IDO) and I am investigating whether it could play a role in generating a “chemoresistant and immune-tolerogenic” phenotype. If yes, compounds targeting IDO, actually in use for the treatment of autoimmune diseases, may represent potential therapeutic tools in cancer treatment. Since IDO is up-regulated by several cytokines and chemokines via JAK/STAT pathway, I am evaluating the panel of cytokines and chemokines produced by CRL-2116 cells, to unravel the putative inducers of IDO in my chemoresistant model. I found that IDO is more expressed in CRL-2116 cells than in non transformed cells.

My preliminary highthroughput PCR screenings suggested that IL4, IL6 and other cytokines, are noteworthy of further investigations as putative inducers of JAK/STAT/IDO axis in my model. I plan to measure the levels of specific cytokines by ELISA and to evaluate IDO expression/activity in cytokine-treated cells.

The ImmunoTools *IT-Box-Cy55M* will greatly help me to define which cytokines, involved in such autocrine activation of IDO, may be amenable of therapeutic interventions for the treatment of resistant tumours.

ImmunoTools IT-Box-Cy55M for **Ivana Campia**
includes 55 recombinant mouse cytokines

rm EGF, rm Eotaxin / CCL11, rm FGF-a / FGF-1, rm FGF-b / FGF-2, rm FGF-8, rm Flt3L / CD135, rm G-CSF, rm GM-CSF, rm GRO-a / CXCL1, rm GRO-b / CXCL2, rm IFNgamma, rm IL-1alpha, rm IL-1beta, rm IL-2, rmIL-3, rm IL-4, rm IL-5, rm IL-6, rm IL-7, rm IL-9, rm IL-10, rm IL-11, rm IL-13, rm IL-15, rm IL-16, rm IL-17A, rm IL-17C, rm IL-17F, rm IL-19, rm IL-20, rm IL-21, rm IL-22, rm IL-25 / IL-17E, rm IL-27, rm IL-31, rm IL-33, rm IP-10 / CXCL10, rm LIF, rm MCP1 / CCL2, rm M-CSF, rm MIP-1α/ CCL3, rm MIP-1β / CCL4, rm MIP3α / CCL20, rm MIP3β / CCL19, rm NGF-beta, rm PDGF-AA, rm PDGF-BB, rm RANTES / CCL5, rm sCD40L / CD154, rm SCF, rm SDF-1α / CXCL12a, rm SDF-1β / CXCL12b, rm TNFα, rm TPO, rm VEGF DETAILS