# ImmunoTools *special* Award 2017

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## Therapeutic effects of monoclonal antibodies

Monoclonal antibodies (mAbs) are a major medical tool, as they constitute the main class of biotherapeutics. More than 50 mAbs have been approved or are under review for human use, and several hundred are currently being tested in the clinic *(1,2)*.

Currently, they are used successfully mainly in patients suffering from different types of cancer and, to a lesser extent, inflammatory diseases. Conversely, until recently, the possibility of using mAbs as antiviral molecules has rarely been considered and investigated. However, probably to the success of anticancer mAb-based immunotherapies this situation has been reversed, as judged from the flurry of anti-H5N1, -HIV, -HCV, -Ebola, -SARS, -West Nile, Zika virus mAbs described these last few years, some of which are currently tested in clinical trials *(3,4)*. Curiously, only the direct effects of antiviral mAbs on their targets have been well studied while their indirect effects on the immunity of treated patients have, mostly overlooked by the scientific and medical communities.

By using an immunocompetent mouse model of retroviral chronic infection, our group has proven the concept that short "one shot" passive mAb-based therapies (with a neutralizing mAb), in addition to viral propagation blunting, can lead to the induction of a long-lasting and strong endogenous antiviral response. This strong response protect mice from disease and is characterized by a Th1 profile, with a endogenous neutralizing humoral response and a cytotoxic T lymphocyte (CTL) arm (4). This original observation might constitute a major breakthrough in the conception of future antiviral immunotherapies.

Although our previous work has led to the proof of concept that mAb-based immunotherapies induce vaccine-like effects, the identification of the molecular and cellular mechanisms involved in this effect still require intensive investigations. This is crucial to improve future anti-viral immunotherapies. So, the overall goal of our

project is to establish how different immune system cells and cell signaling events contribute to the induction of protective effects by mAb.

In this regard, it is important to stress the fact that the immune system is a highly complex system, with different soluble and cellular components that can interact among them and that immunological outcomes depend on the nature of such interactions. In this frame, I will perform an extensive immunophenotyping of different populations of immune system and a deeply evaluation of soluble factors produced by different immune cells to dissect the main mechanisms involved in the induction of vaccine-like effects by mAbs in our mouse model. Notably, I will study the mobilization and the activation of the main actors of innate (macrophages, NK, DCs, etc) and adaptive immune cells (B cell subsets, CD4 T cell subsets and CD8 T cells) at different immunological time-points post infection and treatment. The ImmunoTools reagents such as recombinant cytokines and flow cytometry antibodies selected here below will be essential to better understand the mechanisms involved in induction of the protective immunity.

References:

*1 Irani V, Guy AJ, Andrew D, Beeson JG, Ramsland PA, Richards JS. Molecular properties of human IgG subclasses and their implications for designing therapeutic monoclonal antibodies against infectious diseases. Mol Immunol 2015; 67: 171–182.*

*2 Vacchelli E, Eggermont A, Galon J et al. Trial watch: monoclonal antibodies in cancer therapy. Oncoimmunology 2013; 2: e22789.*

*3. Corti, D., and Lanzavecchia, A. 2013. Annu Rev Immunol 31:705-742.*

*4. Pelegrin M, Naranjo-Gomez M, Piechaczyk M. Antiviral Monoclonal Antibodies: Can They Be More Than Simple Neutralizing Agents? Trends Microbiol. 2015 Oct;23(10):653-65*

**ImmunoTools** *special* AWARD for **M.Mar NARANJO-GOMEZ**

includes 20 reagents

ImmunoTools recombinant mouse cytokines
rm IL-2, rm IL-15, rm IFNgamma, rm TNFa, rm MCP1 / CCL2

ImmunoTools anti-mouse antibodies for flow cytometry
FITC - conjugated anti-mouse CD3e, CD9, CD18, CD19, a/b TCR
PE - conjugated anti-mouse CD8a, CD29, CD49d, CD62L, Gr-1, g/d TCR
APC - conjugated anti-mouse CD4, CD44, CD62L, Gr-1

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