ImmunoTools *special* Award 2014

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Immune response against bladder cancer after BCG treatment

The idea that the immune system could be harnessed to attack cancer is not new, but despite years of research, and some genuine progress, tools for effective use of the immune system to fight cancer effectively are still lacking.

However, one form of immunotherapy, based on intravesical instillation with Bacillus Calmette-Guérin (BCG), an attenuated strain of *Mycobacterium bovis*, is the current gold standard for treatment of superficial bladder cancer, since 1976. This therapy has been demonstrated to reduce the recurrence rate and the risk of progression to muscle-invasive disease in about 70% of the patients. Unfortunately, the mechanisms underlying the effectiveness of this therapy are still largely unknown. Data in the literature and preliminary results in our laboratory suggest that NK cells and myeloid cells could be playing an important role in the process, and the communication between these cells seems to be very important in order to mount an effective immune response. Further investigation will be necessary to gain a deeper understanding of this process.

With this aim, I propose to study the interaction between BCG, the immune system and bladder cancer from molecular, cellular and systemic perspectives, integrating data obtained through each one of these strategies to obtain a complete picture of the interactions between the immune system and the tumour in bladder cancer patients. A large variety of parameters that might contribute to tumour clearance are being monitored, including detection of cellular markers and soluble factors in blood and urine samples from patients treated with BCG. In this context, ImmunoTools anti-human conjugated antibodies for flow cytometry would be very useful to characterize better both the populations that play a role in the response to the treatment as well as the changes that happen on each population due to the treatment. With the ELISA-sets, we would analyse different cytokines in samples of serum and urine to determine if

the developing patient response is more Th1, Th2 or Th17-like. Comparison of these sets of data between responder and non-responder patients should facilitate the identification of possible biomarkers of therapy success or treatment failure.

Additionally, we have developed an *in vitro* system, in which immune cells are exposed to BCG, to explore in detail their changes in phenotype–studying the expression of different surface molecules or receptors- and in function, coincubating untreated and BCG-treated immune cells with bladder tumour cells and testing their capacity to respond against bladder tumour cells. The study of changes in the expression of surface molecules on the bladder tumour cell after BCG exposure is also very interesting, because it could allow us to predict changes that would make them more or less recognizable by immune cells. With this aim, the anti-human conjugated antibodies for flow cytometry would also be very useful to characterize in detail this *in vitro* model. Moreover, some different cytokines (such as IL-6, IL-8 or MIP-1α) have been found in the urine of bladder cancer patients that were treated with BCG. It would be interesting to study the effect of each one of these cytokines in the different immune cell populations *in vitro* and, for this reason the use of ImmunoTools recombinant cytokines would be very helpful.