ImmunoTools *special* Award 2015

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Evaluation of immunomodulatory potential of natural products

Currently, cancer has become a major public health problem worldwide, accounting for about six million deaths each year, representing 12% of all deaths worldwide. The World Health Organization estimated for the year 2030, about 27 million cases of cancer, 17 million deaths from cancer and 75 million people living annually with cancer. Modern medicine has a variety of methods for the treatment of different diseases, such as the administration of medication and surgical interventions. Despite technological advances, adverse effects related to treatment, and the very inefficiency of these therapies in some cases, has led a growing number of patients to look for "alternative methods" of treatment. The use of biological response modifiers to stimulate the host immune response is one of the most recent and promising strategies for alternative treatment of human diseases. Recent studies show that a variety of active principles isolated from natural sources such as mushrooms, plants and algae have therapeutic properties, particularly immunostimulating. The participation of the immune response in combating the development of malignant tumors can be demonstrated by the presence of immune effector cells able to recognize and kill cancer cells directly in tumor microenvironment and also to promote the destruction of their stroma and inhibition of angiogenesis. However, the pressure exerted by the antitumor immune response often favors the development of strategies for the exhaust tumor cells resulting in the induction of an immunosuppressive microenvironment. In previous studies by the group, we found that extracts of the medicinal mushroom Agaricus brasiliensis are able to reverse the immunosuppressive state induced by the development of subcutaneously Ehrlich carcinoma. Studies with acid-treated fraction showed that the mushroom extract was able to increase the phagocytic activity of human monocytes challenged with Candida albicans, the tumor necrosis factor (TNF) and IL-1 cytokine production and the Toll-like receptor expression (TLR 2 and TLR-4). The Amazon region is the largest natural products reserve with herbal effects on the planet and its

population utilizes them empirically for these purposes. The goal of this project is to evaluate the immunomodulatory potential of bioactive compounds extracted of native plants to the north of the Mato Grosso State, a region that is part of the Amazonia Legal. This project was started in 2010, with initial studies with jatobá, aveloz and copaiba. Initially, we evaluated the *in vitro* cytotoxic effect of the extracts in mice spleen cell cultures and Ehrlich tumor cells. Thereafter, i*n vivo* experiments were performed in two stages. In the first phase, the Ehrlich tumor bearing mice (swiss, n= 10; 45g; 90 days) are treated daily for 30 days with different concentrations of the extract for selecting the dose able to induce a reduction of tumor growth. The animals were treated by gavage and after the treatment period, the animals were euthanized and the tumor mass was excised and weighed to assess tumor development. According to the obtained results in the 1st phase experiments, the best dose was selected for immune modulator effects evaluation in the subsequent phase. In the 2nd phase experiment, animals (n = 8), tumor bearing or not, were treated daily by gavage with plants extracts or diluent vehicle for 7 and 14 days. After this period, the animals were sacrificed to *in vitro* evaluation of lymphoproliferation, natural killer activity and *in vitro* cytokine production. ImmunoTools products are important in the selection and quantification of immune effector cells, as well as the dosage of cytokines.

ImmunoTools *special* AWARD for **Lindsey Castoldi** includes 25 reagents

FITC - conjugated anti-mouse CD3e, CD11a, CD18, isotype control IgG2b

PE - conjugated anti-mouse CD11c, CD19, CD25, CD45R, CD45RC, CD49d, isotype control IgG2b

APC - conjugated anti-mouse CD4, CD8a, NK-cells, isotype control IgG2b

recombinant mouse cytokines: rm IFNgamma, rm IL-2, rm IL-4, rm IL-5, rm IL-6, rm IL-10 rm IL-15, rm IL-17A, rm IL-21, rm TNFa DETAILS more AWARDS