# ImmunoTools *special* Award 2015

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## Development and Evaluation of Immunomodulatory Nanostructures for Cancer Treatment

Our project is focused on the development of new Immunomodulatory Nanostructures (INs) with the aim to manipulate the host's immune system for the tumour treatment.

The applicant is working as postdoctoral researcher, in the group of Prof. Paola Allavena (Laboratory of Cellular Immunology, Clinical and Research Institute HUMANITAS), studying the effects of INs on the immune system. In most cancer patients, chronic inflammation and immune suppression are the dominant effects in the tumour microenvironment. The infiltration of tumor associated macrophages (TAM) in tumour tissues supports tumour growth, invasion and metastasis. Indeed, high density of TAM in tumours is correlated with resistance to therapies and poor prognosis (*Mantovani A. et al. 2008*). These recent findings establish TAM as promising targets of future anti-tumour therapies. New drugs for killing or re-educating TAM towards a tumour-suppressing M1 phenotype have been recently investigated. However, the toxicity and secondary effects induced by these cytotoxic or immunomodulatory drugs are still one of the major causes of failure of therapies, particularly in the oncology field.

A broad nanocapsule-type delivery platform has been recently developed by the group of Prof. María José Alonso at "Universidade de Santiago de Compostela" (USC, Spain) consisting of polymeric nanocarriers which are combined with immunomodulatory properties (INs), but also with the aim to improve the drug stability and its presentation to immunocompetent cells (Garcia-Fuentes and Alonso, 2012).

We have recently established a key collaboration with Prof. Alonso with the aim to develop INs to reach and re-educate TAM. The INs will be tested using appropriate *in vitro* and *in vivo* preclinical tumour models, to verify their effectiveness in switching back the pro-tumoural properties of TAM, towards M1-macrophages with active

defensive activity (i.e. direct killing of tumour cells and eliciting of vascular damage and tissue destruction), and their effect on tumour growth.

I will assess the biocompatibility and efficacy of new INs. The immunomodulatory and/or cytotoxic effects of MINs will be evaluated *in vitro* on monocytes, M1 and M2-polarized and tumor-conditioned macrophages mimicking TAM. Phenotype and functional analysis will be performed by flow cytometry and ELISA assays. For this, we aim to use Immunotools antibodies which will allow us the proper evaluation of the phenotype of immune-competent cells exposed to INs. Also we will differentiate monocytes to proper macrophages (M1/M2) with ImmunoTools cytokines *in vitro* experiments.

Biodistribution and efficacy of INs *in vivo* will be tested on a transplantable fibrosarcoma mouse model, rich in macrophages. Weight of mice, effects on blood, bone marrow, lung, spleen and also tumour development will be tested upon intratumoral and intravenous administration of INs. TAM and other relevant populations of immune and cancer related cells (i.e. tumor derived mesenchymal stem cells) will also be analyzed by flow cytometry using Immunotools antibodies detailed below.

In summary, we provide an state-of-the-art approach for the treatment of cancer. The novel nanomedicines developed in our project must be able to reach and re-educate TAM, unleashing the patient immune system and improving anti-tumour responses. I expect that this approach will enable greater progress in the treatment of tumours and ultimately lead to improved outcomes for cancer patients.

**References:**

Garcia-Fuentes, Marcos, and Maria J Alonso. 2012. “Chitosan-Based Drug Nanocarriers: Where Do We Stand?” Journal of Controlled Release : Official Journal of the Controlled Release Society 161 (2): 496–504.

Mantovani A, Allavena P, Sica A, et al. 2008. Cancer-related inflammation. Nature, 454 (7203): 436–44.