MATWIN
MATURATION & ACCELERATING TRANSLATION **WITH INDUSTRY**

TECHNOLOGY OFFER

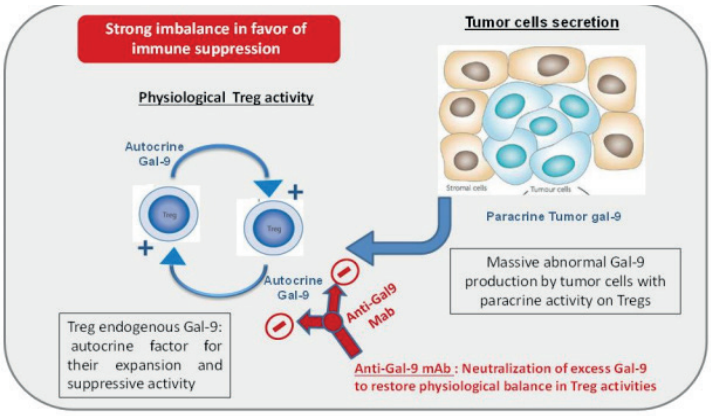
SUPPORTING INNOVATION AND TECHNOLOGY TRANSFER IN ONCOLOGY

GALIMAB

Proposition of a novel anti-tumoral immunotherapy based on the neutralization of regulatory t-cells activity with anti-galection 9 monoclonal antibodies

CONTEXT & BACKGROUND

In healthy people, Tregs have a beneficial role to prevent allergies and autoimmune diseases. However in patients bearing malignancies, they contribute to tumor growth by inhibiting local immune reactions. In a collaborative project, teams lead by Nadira Delhem (Institut de Biologie de Lille) and Pierre Busson (Gustave Roussy) have shown that a protein called galectin-9 enhances the expansion and suppressive activity of Tregs. This protein is secreted by the Tregs themselves and is involved in a positive feed-back mechanism. In several human malignancies, galectin-9 is abundantly secreted by tumor cells leading to exacerbation of local Treg activity. To take advantage of these observations for therapeutic applications, the two teams have developed monoclonal antibodies with the capacity to neutralize galectin-9. These antibodies have proven to have inhibitory effects on Treg activity and anti-tumor effects in murine models of several human malignancies.



Rationale of galectin-9 neutralization to inhibit expansion and suppressive activity of regulatory T-cells

INNOVATIVE COMPONENT & TECHNOLOGY

Several molecular targets have been proposed for Treg inhibition but one major limitation of these target molecules is their expression at the surface of activated effector T-cells. Our novel therapeutic tool targets an extra-cellular factor which is critical for Treg expansion and suppressive activity but which is not expressed by activated effector T-cells. These antibodies have been validated in a unique chimeric human-murine model of nasopharyngeal carcinoma. Their validation in other model of cancers Maj mai 2016 such as hepatocellular carcinoma and breast cancer are currently in course. Moreover their validation in syngenic murine tumor models is in progress. Chimeric human-murine antibodies have proven to have the same neutralizing potential as the wild-type antibody. Humanization of the lead antibodies is now finished and we are currently evaluating the effectiveness of 8 humanized antibody variants

SCOPE

Anti-Cancer Therapeutic action by immune system restoration

KEYWORDS

Cancer immunotherapy, humanized monoclonal antibodies, regulatory T-cells, galectin-9

OBJECTIVES

We seek industrial partnership for R&D collaborations and licensing.
Our general aim is to develop our antibodies until obtaining a product directly usable in a clinical trial. Intermediate goals are (i) to validate the neutralizing properties of the lead antibody on several cancer models (at least 3) (ii) to improve our syngeneic tumor models, (iii) to complete humanization of our lead antibodies, (iv) to develop toxicity studies and (v) to produce clinical batches in GMP conditions.

DEVELOPMENT & MATURATION STAGE

Two lead antibodies have proven to be efficient in vitro and in murine models. One of them is currently subjected to humanization. Fusions and cloning of hybridomas for additional murine antibodies are currently taking place.

INTELLECTUAL PROPERTY & PATIENT CO-OWNER(S)

The VH and VL sequences of our two main antibodies have been sequenced. They are protected by one international patent published on December 2015 (WO 2015/185875 A2).
Inventors: N. Delhem, P. Busson, O. Moralès, C. Barjon, R. Mustapha, C. Lhuillier
Co-owners : CNRS, Lille 1 university, Lille 2 University, Gustave Roussy, Pasteur Institute of Lille

We plan additional patent applications for the novel monoclonal antibodies that will result from current fusion and cloning.

TARGET POPULATION

Human malignancies with frequent Treg infiltration and poor prognosis related to this infiltration (liver, lung, breast, colorectal, prostate, ovarian carcinomas...).
Human malignancies with abundant production of galectin-9 and strong Treg infiltration (nasopharyngeal carcinomas, liver carcinomas associated to HBV or HCV).

TARGET PROFILE

The basis of our novel therapeutic tool is a series of monoclonal antibodies neutralizing extra-cellular human galectin-9 in order to specifically block Treg expansion and activity. They are expected to contribute to immune restoration in the periphery and in the tumor tissue, and to facilitate tumor eradication. We are in the mainstream of current research and development of novel antibodies for cancer immunotherapy but we have a molecular target which is distinct from check-point inhibitors.

STRENGHTS & COMPETITIVE ADVANTAGES

- Novel strategy: we target an extra-cellular immune-suppressive factor
- Promising in vitro and in vivo results (humanized animal testing)
- P. Busson and N. Delhem are both inventors in a patent filled for antibodies neutralizing galectin-9
- No published patents about neutralizing anti-galectin-9 antibodies
- The targeted pathologies are major public health problems through the world in developed and emerging countries

INDUSTRIAL APPLICATIONS & OPPORTUNITIES

We intend to design and validate humanized anti-galectin-9 antibodies to be used in combination with other modalities of primary treatment (for example classical chemotherapy) or as adjuvant treatment for consolidation of remissions. Antigalectin-9 antibodies are expected to take place among a second generation of agents for cancer immunotherapy beyond Ipilimumab and Nivolumab with distinct mechanisms of action and distinct secondary effects.

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