ImmunoTools *special* Award 2013

Jorrit De Waele, PhD student

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Shifting the balance towards immune-mediated elimination of residual glioblastoma cells: combining immune stimulation with inhibition of the immunosuppressive tumor microenvironment

Glioblastoma multiforme (GBM) is the most common malignant primary brain tumor characterized by an extremely poor prognosis. The current standard of care consists of maximal surgical resection followed by chemo- and radiotherapy. However, due to its aggressive nature, nearly all GBM patients quickly show locoregional recurrence, contributing to a median survival of only 14.6 months and a five year survival of less than 5%. GBM cancer stem cells contribute to the tumor's aggressiveness and recurrence, because of their resistance to chemo- and radiotherapy. New treatment options that focus on locoregional control or eradication of GBM (stem) cells would significantly improve clinical outcome. Immunotherapy is in the center of attention as adjuvant cancer therapy, because of its potential to specifically target cancer cells and to mediate long-term surveillance. For GBM, early clinical trials suggest immunotherapy is safe and beneficial in a subset of patients. However, GBM is still one of the most aggressive cancers, requiring further development of multimodal cytotoxic treatment methods that treat (residual) GBM stem cells and their niche.

The innate immune system forms the first line of defense against tumors with microglia and natural killer (NK) cells being GBM-infiltrating innate immune cells with the potential to exert antitumor effects. An important mediator in GBM is the hypoxic microenvironment, supporting the stemness of GBM stem cells and enhancing resistance of tumor cells to therapies. In my PhD project, I strive to tackle GBM-mediated immune suppression by stimulating the innate immune system and targeting the tumor microenvironment.

Therefore, bi- and tripartite *in vitro* cocultures of GBM (stem) cells, microglia and NK cells will be carried out. Different combinations of agents which affect the tumor microenvironment and/or activate innate immune cells will be tested for their capacity to break GBM immune evasion. I will generate monocyte-derived microglia using a differentiation cocktail with cytokines from ImmunoTools. The growth factors fibroblast growth factor 2 and epidermal growth factor from ImmunoTools will be essential to maintain the stemness of the GBM stem cells and prevent them from differentiating.

Effector functions of the innate immune cells will be detected by flow cytometry and enzyme-linked immunosorbent assay (ELISA), using fluorochrome-conjugated

antibodies and pro- and anti-inflammatory cytokine ELISA-sets from ImmunoTools in order to assess phenotypic and functional changes of the cell types involved.

This study will contribute to the elucidation of GBM-mediated immune suppression and will generate valuable new insights for the development of a new efficacious immunotherapeutic strategy to treat GBM. Reagents of ImmunoTools will be valuable assets to perform this research project.

ImmunoTools *special* AWARD for **Jorrit De Waele** includes 20 reagents

FITC - conjugated anti-human CD11b (IgG1); HLA-DP; Control-IgG1

PE - conjugated anti-human CD44; IL-6; Control-IgG2b,

APC -conjugated anti-human CD44; IL-6; Control-IgG2b

recombinant human cytokines rh beta NGF; rh EGF; rh FGF-b/(FGF-2; rh GM-CSF; rhMCP1 (CCL2); rh M-CSF,

human IL-4 ELISA-set, human IL-6 ELISA-set, human IL-8 ELISA-set, human IL-12p40 ELISA-set, human TNFa ELISA-set,

DETAILS