ImmunoTools *special* Award 2021

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Functionalization of macrophages with superparamagnetic iron oxide nanoparticles for use in magnetically targeted adoptive cell therapy

Tumor-associated macrophages play a major part in the growth and immune escape of advanced tumors by modulating the tumor microenvironment. This modulation is achieved by the expression and secretion of agents influencing cell proliferation, angiogenesis or immunosuppression leading to tumor progression and the inhibition of T cell infiltration. By administration of either pro-inflammatory cytokines, microbial molecules, or *ex vivo*-activated macrophages, it has been attempted to circumvent tumor immune escape by tumor-associated macrophages [1, 2]. Tumor therapy via macrophages enables interesting therapeutic options due to their ability to recruit and activate tumor infiltrating lymphocytes. While the administration of autologous macrophages resulted in increased cytokine levels and sometimes even tumor shrinkage, however the systemic, non-specific nature of the administration reduces the efficacy of this type of therapy. Therefore, additional strategies are needed to increase site specific macrophages, which are still able to mount an anti-tumor immune response.

Magnetically targeted adoptive macrophage cell therapy is an approach which we want to develop in the Section of Experimental Oncology and Nanomedicine (SEON) at the Department of Otorhinolaryngology, Head and Neck Surgery of the University Hospital Erlangen. To achieve this, monocytes will be isolated from whole blood and cultured and differentiated into mature and activated M1 macrophages. These macrophages will be loaded with citrate coated superparamagnetic iron oxide nanoparticles (SPIONs) and then re-administered into the patient via the vascular system and enriched in the region of interest by an external magnetic field. There, the M1 macrophages will locally alter the tumor microenvironment.

Therefore, we want to first analyze the biocompatibility of SPIONs with macrophages in vitro and ensure that they are still viable and capable of performing their effector functions. Reagents from the **ImmunoTools** special award will be used to analyze the impact of SPION-loading on macrophages by flow cytometry and ELISA.

- The differentiation of macrophages into distinct subclasses and their subsequent role in the immune response is determined by various cytokines [3-5]. Therefore, to analyze the impact of SPION-loading on the polarization of macrophages, cytokines by **ImmunoTools** (rh M-CSF, rh GM-CSF, rh IFN-gamma, rh IL-4, rh IL-13, rh IL-10, rh TGF-beta) will be needed.

- The uptake of SPIONs by macrophages can be estimated by the increased side scatter in flow cytometry. However, for the identification of macrophages and their subclasses, various **ImmunoTools** antibodies will be required (CD14-PerCP, TNF-alpha-PE, CD80-FITC, CD86-APC).

The **ImmunoTools** award would support us in our research concerning the anti-tumor properties of a locally targeted, SPION-loaded macrophage cell therapy and would give insights about possible future treatment possibilities.

References:

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ImmunoTools *special* AWARD for **Felix Pfister** includes 10 reagents

FITC - conjugated anti-human CD80

PE - conjugated anti-human TNF-alpha

PerCP - conjugated anti-human CD14

APC - conjugated anti-human CD86

recombinant human rh M-CSF, rh GM-CSF, rh IFN-gamma, rh IL-4, rh IL-13, rh IL-10, rh TGF-beta

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