Nanomedicine for immunotherapy

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The starting point for this special volume was discussions parallel to the meeting with the title: “Quo Vadis Nanomedicine?” organized in 2014 in Exeter, UK by M Barz, R Luxenhofer and M Schillmeier, which led to a special volume with the same title in this journal [1].

While most of the work with nanomedicines tries to target the tumor directly, there are definitely much more opportunities for nanoparticulate carrier systems to improve therapeutic outcome of conventional interventions. One example is immune therapies, which can be used to fight either chronic infections, allergies or even cancer. Especially in cancer therapy the use of immune therapy seems highly promising following the old idea of a vaccination against tumor associated antigens. The immune system, however, is equipped with different levels of self-control to avoid autoimmune responses. Tumors, for example, exploit these tolerance mechanism (or at least any successfully expanding tumor has found a way to induce tolerance). Thus, it is not sufficient to only activate the immune system against a tumor associated antigen, but the elimination of immune tolerance is of equal importance (see the Editorial by Grabbe *et al.* [2] and the contribution by Jonuleit *et al.* [3]).

In this respect, we combined in this special volume Research Papers, Perspectives and Reviews, which address different aspects of

cancer immune therapies, from the elimination of immune tolerance to antigen-selective activation. These contributions are completed by a report about concepts for immune-imaging and a case study about RNA-Lipoplexes for the treatment of melanoma.

At first Mailänder and Tonigold underline differences in cellular uptake mechanisms for nanoparticles in dendritic cells, which determine the intracellular fate of nanoparticle and cargo and are thus highly relevant for the effective delivery of nanosized therapeutics [4].

Next Foerster *et al.* evaluate a new carrier system with minimal toxicity, which is based on cross-linked dextran for hepatic drug delivery and the addressing of liver macrophages [5].

De Geest and coworkers present a new synthetic route to core cross-linked polymer micelles, which can be used as well-defined vaccines co-delivering antigen and adjuvant [6].

Bros, Zentel and coworkers describe the synthesis of micelles from block copolymers with pHPMA as the hydrophilic corona and their functionalization with mannose [7]. These micelles bind DC only when conjugated with mannose, and in a mannose receptor-specific manner leading to internalization. This allows a selective DC activation by loading of the micelles with hydrophobic L18-MDP.

Shen *et al.* study dextran-coated colloidal superparamagnetic nanoparticles, which are triple functionalized with immunostimulatory CpG-ODN, anti-DEC205 antibody (targeting to DCs) and ovalbumin as a model antigen to induce antigen-specific T-cell responses and antitumor responses in *in vitro* and *in vivo* experiments [8]. These particles induce a strong activation of the immune system *in vitro* and lead to a tumor growth arrest *in vivo*.

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Tüttenberg, Steinbrink and Schuppan review the role of myeloid cells as orchestrators of the tumor microenvironment. Due to their role in immunosuppression they are new targets for nanoparticle cancer therapy [9].

Jonuleit, Bopp and Becker review the role of regulatory T cells – another class of cells controlling

immune suppression – as potential cellular targets for functionalized nanoparticles in cancer therapy [3].

Diken, Miederer *et al.* present concepts for immunosensing as a noninvasive *in vivo* preclinical method for imaging of the status of the immune system [10].

Finally, Grabbe, Langguth, Sahin and coworkers report a case study of RNA-Lipoplexes for the treatment of melanoma as personalized nano-sized cancer vaccines [11].

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