Delivery of TLR7 agonist to monocytes and dendritic cells by DCIR targeted liposomes induces robust production of anti-cancer cytokines

Tumor immune escape is today recognized as an important cancer hallmark and is therefore a major focus area in cancer therapy. Monocytes and dendritic cells (DCs), which are central to creating a robust anti-tumor immune response and establishing an anti-tumorogenic microenvironment, are directly targeted by the tumor escape mechanisms to develop immunosuppressive phenotypes. Providing activated monocytes and DCs to the tumor tissue is therefore an attractive way to break the tumor-derived immune suppression and reinstate cancer immune surveillance. To activate monocytes and DCs with high efficiency, we have investigated an immunotherapeutic Toll-Like Receptor (TLR) agonist delivery system comprising liposomes targeted to the dendritic cell immunoreceptor (DCIR). We formulated the immune stimulating TLR7 agonist TMX-202 in the liposomes and examined the targeting of the liposomes as well as their immune activating potential in blood-derived monocytes, myeloid DCs (mDCs), and plasmacytoid DCs (pDCs). Monocytes and mDCs were targeted with high specificity over lymphocytes, and exhibited potent TLR7-specific secretion of the anti-cancer cytokines IL-12p70, IFN-α 2a, and IFN-γ. This delivery system could be a way to improve cancer treatment either in the form of a vaccine with co-formulated antigen or as an immunotherapeutic vector to boost monocyte and DC activity in combination with other treatment protocols such as chemotherapy or radiotherapy. Cancer immunotherapy is a powerful new tool in the oncologist's therapeutic arsenal, with our increased knowledge of anti-tumor immunity providing many new targets for intervention. Monocytes and dendritic cells (DCs) are attractive targets for enhancing the anti-tumor immune response, but systemic delivery of immunomodulators has proven to be associated with a high risk of fatal adverse events due to the systemic activation of the immune system. We address this important obstacle by targeting the delivery of an immunomodulator, a Toll-like receptor agonist, to DCs and monocytes in the bloodstream. We thus focus the activation, potentially avoiding the above-mentioned adverse effects, and demonstrate greatly increased ability of the agonist to induce secretion of anti-cancer cytokines.

General information
Publication status: Published
Organisations: Department of Micro- and Nanotechnology, Colloids and Biological Interfaces, Department of Biotechnology and Biomedicine, Disease Systems Immunology
Number of pages: 11
Pages: 367-377
Publication date: 2017
Peer-reviewed: Yes

Publication information
Journal: Acta Biomaterialia
Volume: 53
ISSN (Print): 1742-7061
Ratings:
BFI (2017): BFI-level 2
Scopus rating (2017): CiteScore 6.97 SJR 1.967 SNIP 1.815
Web of Science (2017): Impact factor 6.383
Web of Science (2017): Indexed yes
Original language: English
Keywords: C-type lectin, Cancer immunotherapy, Liposome, Targeted drug delivery, Toll-like receptor
DOIs:
10.1016/j.actbio.2017.01.072
Source: FindIt
Source-ID: 2351947511
Research output: Contribution to journal › Journal article – Annual report year: 2017 › Research › peer-review