In vivo pre-treatment of tumour-derived dendritic cells with anti-CD40 agonist mAb results in therapeutic responses in resistant tumour models when used as vaccination strategies

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90% of all cancer related deaths result from the development of metastasis or relapse and treatments specifically targeting these phenomena are currently lacking. However, the rise of immunotherapy has opened new avenues for treatments capable of not only treating existing lesions in patients, but also generating immune memory against tumours, reducing the incidence of metastasis and relapse.
Dendritic cells (DCs) are crucial for the generation of antitumor immune responses and we recently demonstrated the presence of two strongly immunostimulatory conventional DC (cDC) populations within the tumour microenvironment (TME) of multiple mouse as well as human tumours. Importantly, prophylactic and therapeutic vaccinations with tumour-derived cDC subpopulations reached significant therapeutic effects in several, but not all, pre-clinical tumour models. To increase the efficacy of tumour-derived cDC vaccinations, these were combined with different existing immunotherapies. In this respect, anti-CD40 agonist mAb could increase the activation status and the migration capacity to the tumour-draining lymph nodes of both cDC1 and cDC2s. This treatment resulted in an increased activation of cytotoxic T-cells in the tumour and lymph nodes and a was accompanied with a reduction in tumour growth, in a B-cell independent manner. Moreover, vaccinations using tumour-derived cDCs subsets that were pre-treated in vivo with anti-CD40 agonist mAb induced responses in resistant tumour models.
Overall, our results demonstrate the potential of tumour-derived cDCs strategies to generate anti-tumour immune memory responses in models that are resistant against the commonly used (immuno)therapies.

Keywords : Tumor, Dendritic Cell, Vaccination, Immunotherapy, CD40
Authors :
References : , , ,

Authors

Aleks Murgaski 1, Emile J. Clappaert 1, Mate Kiss 1, Helena Van Damme 1, Jiri Keirsse 1, Maryse Schmoetten 1, Yvon Elkrim 1, Sabine Hoves 2, Cleo Goyvaerts 3, Martina Schmittnaegel 2, Carola H. Ries 2, Jo A. Van Ginderachter 1, Damya Laoui 1,

1. CMIM, VUB, Brussels, BELGIUM
2. Roche Pharmaceutical Research and Early Development, Roche, Penzberg, GERMANY
3. LMCT, VUB, Brussels, BELGIUM