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Antitumor virotherapy based on attenuated measles virus: Consequences on the antitumor immune response

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Antitumor viro therapy consists in the use of oncolytic viruses able to infect and kill tumor cells without or with limited infection of healthy cells. Antitumor viro therapy is also able to induce or reinforce the antitumor immune response. Our group studies the Schwarz attenuated strain of measles virus (MV) for its oncolytic properties against various cancers, notably pleural mesothelioma. MV enters cells by the CD46 molecule that is often over expressed by numerous types of tumor cells. Recently, we studied how MV or MV-infected tumor cells can influence the antitumor immune response by studying their effects on myeloid and plasmacytoid dendritic cells (mDC and pDC) that are specialized in T cell response induction. We found that MV-infected tumor cells induced maturation of both types of DC, whereas tumor cells killed by UV-irradiation were not able to induce maturation. Then, we found that this maturation was mainly due to danger signals released by infected tumor cells for the activation of mDC and to MV ssRNA for the activation of pDC via TLR7. pDC maturation was accompanied by a strong production of IFN-α. In addition, we observed that MV-infected and UV-irradiated tumor cells were efficiently phagocytosed by mDC and pDC. Interestingly, we observed cross-presentation of the tumor antigen, NYESO-1, to a specific CD8+ T-cell clone only when mDC and pDC were cocultured with MV-infected tumor cells. Altogether, our results showed that the use of MV as an oncolytic virus induces immunogenic tumor cell death, allowing cross-presentation of tumor antigens by mDC and pDC. This phenomenon suggests that MV based antitumor virotherapy may strengthen the anti-tumor immune response by recruitment of DC.

Biography

Jean-Francois Fonteneau received the PhD degree from Nantes University, France, in 1999. During his thesis training, he studied CD8+ T lymphocytes response against melanoma in the INSERM Laboratory of Pr Francine Jotereau, Nantes, France. He then joined Dr. Nina Bhardwaj's group in Dr. Ralph Steinman Laboratory as a Postdoctoral Fellow at Rockefeller University, New York, USA, from 1999 to 2003, where he studied dendritic cells (DC) biology, notably cross-presentation of viral and tumor antigens and interactions between virus/myeloid DC/plasmacytoid DC. In 2003, he returned to Pr Francine Jotereau Laboratory, INSERM U892, Nantes to identify new melanoma epitopes recognized by patient's CD8+ and CD4+ T cells. In 2009, he joined Dr. Marc Gregoire's Laboratory, INSERM U892, Nantes, to study attenuated measles virus as an oncolytic virus for antitumor virotherapy of pleural mesothelioma to induce immunogenic cell death of tumor cells.

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