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Exploiting defects of type I interferon response in tumor cells for oncolytic immunotherapy with attenuated measles virus

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We studied oncolytic immunotherapy using the live attenuated Schwarz strain of measles virus (MV) in collaboration with Dr. Frédéric Tangy from Institut Pasteur. This oncolytic virus preferentially infects and replicates in tumor cells and triggers their cell death while sparing healthy cells. Recently we characterized what make melanoma or mesothelioma tumor cells sensitive to this virus. We show that 70% of tumor cell lines are sensitive to the oncolytic activity of MV, whereas the different types of healthy cells and the other tumor cell lines exhibit no or low sensitivity. We observed overexpression of the MV entry receptor CD46 on the surface of the majority of tumor cell lines compared to healthy cells. However, the sensitivity of tumor cell lines to the oncolytic activity of MV cannot be explained by the expression level of the CD46 molecules. Thus, we studied the type I IFN response of tumor cell lines exposed to MV or type I IFN by a transcriptomic study. We found that the tumor cell lines that are sensitive to MV oncolytic activity develop a partial type I IFN response in presence of MV and are thus unable to control the viral replication. On the contrary, the four types of healthy cells and the resistant tumor cell lines develop a complete type I IFN response, preserving them from the viral replication and lysis. We then found that the most frequent defect of the type I IFN response in MPM cell lines that are sensitive to MV oncolytic activity is the deletion of both alleles of the genes encoding type I IFN (IFN-a and -b). Altogether, our results show that the sensitivity of tumor cells to MV oncolytic activity depends on defects of the type I IFN response that are frequent in cancer.

Biography

Jean-François Fonteneau has done his PhD degree from Nantes University, France, in 1999. During his thesis training in the INSERM Laboratory of Pr Francine Jotereau, Nantes, France, he studied human CD8+ T lymphocytes response against melanoma and how to induce such response. He joined Dr. Nina Bhardwaj's Group in Dr. Ralph Steinman Laboratory as a Post-doctoral Fellow at Rockefeller University, New York, USA, from 1999 to 2003, where he studied human dendritic cells (DC) biology, notably cross-presentation of viral and tumor antigens and interactions between virus, myeloid DC and plasmacytoid DC. In 2009, he joined Dr. Marc Gregoire's Laboratory, INSERM U892, Nantes, to study attenuated measles virus as an oncolytic virus for oncolytic immunotherapy of pleural mesothelioma to induce immunogenic cell death of tumor cells to initiate or increase the antitumor immune response.

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