IFNγ-armed oncolytic virus for cancer treatment

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Oncolytic viruses are known to stimulate the immune system but the extent by which they revert tumor-induced immune suppression is not well characterized. By specifically replicating in tumor cells, they are believed to trigger immune activation through the release of tumor-specific antigens in the context of viral pathogen associated molecular patterns to allow for simultaneous TLR co-stimulation. In this study, we used 4T1 mammary adenocarcinoma and CT26 colon carcinoma murine tumor models to demonstrate the general activation of immune cells by treatment with vesicular stomatitis virus. We observed a rapid and sustained upregulation of the pro-inflammatory cytokines IFNγ, IL-6 and TNFα in the blood following treatment. Also, flow cytometry analysis showed a greater activation of dendritic cells, natural killer cells and T cells in the blood and the spleen of VSV-treated animals. Moreover, an ELISPOT assay allowed us to demonstrate the presence of an increased number of IFNγ-secreting splenocytes following virus treatment. As a further means to activate immune responses, an oncolytic virus was engineered to encode the pro-inflammatory cytokine IFNγ. This virus demonstrated greater activation of dendritic cells and secretion of proinflammatory cytokines. The VSV-IFNγ virus treatment slowed tumor growth, minimized lung tumors and prolonged survival in both tumor models. Taken together, these results show the great potential of oncolytic viruses as immune stimulators to generate a tumor-specific immune response as well as their potential in targeted gene therapy by expression of beneficial genes specifically within the tumor.