Combination therapy with reovirus and PD-1 blockade effectively establishes tumor control via innate and adaptive immune responses

Introduction

Previous work from our group and others has developed the use of reovirus, a naturally occurring oncolytic virus, as a systemically delivered anti-cancer agent. Our studies have shown that reovirus can induce innate and adaptive immune responses in vivo, which reovirus is injected into B16 melanomas growing subcutaneously (SC). This hypothesis was tested using our immune experimental schema.

Key result: Combination therapy of reovirus with PD-1 blockade establishes tumor control via innate and adaptive immune responses.

Figure 1: Reovirus plus PD-1 blockade prolongs survival of mice with melanomas.

Figure 2: Reovirus plus PD-1 blockade induces robust IFNγ memory T cell responses.

Figure 3: PD-1 blockade augments reovirus-induced NK cytokine production and killing.

Figure 4: PD-1 blockade ablates tumor-specific immune suppression by Treg.

Figure 5: Both innate and adaptive immunity mediate in vivo efficacy of Reovirus + αPD-1

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Summary

• Combining reovirus with αPD-1 therapy induces durable anti-tumor responses in established tumors.
• Combined therapy results in augmented T cell recall responses against both reovirus-tumor-saturated and specific tumor-associated antigens.
• Antibodies against CD4, CD8 or NK are sufficient to deplete these cells.
• In vivo depletion of CD4 or CD8 cells reduced the efficacy of the reovirus-αPD-1 combination. However, NK cell depletion had an even more marked effect, confirming the central role of NK cell-mediated cell death in tumor control.

Keywords: reovirus; PD-1; tumor control; innate and adaptive immunity.