

Simultaneous injection of recombinant vaccinia virus strain expressing interleukin-15 and the strain expressing interleukin-15 Receptor alpha has synergetic oncolytic effects on solid tumors

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Using Interleukin (IL)-15 as a cancer therapeutic agent has shown to promote T- and Natural Killer (NK) cell maturation and enhance cytotoxic functions resulting in significant tumor regression [1]. Combining IL-15 with its α -moiety receptor (IL-15R α), which is also called IL-15 transpresentation, increases the half-life of IL-15 and enhances its binding with cells expressing the IL-15R $\beta\gamma$ like NK cells and CD8 $^+$ T cells, leading to improve oncolysis [2]. We constructed recombinant vaccinia virus strains expressing IL-15 (VV- IL-15) or IL-15R α (VV- IL-15R α). In xenografts mice models of breast adenocarcinoma (4T1), melanoma (B16), and colon carcinoma (CT26), oncolytic activity of VV-IL-15 with or without VV- IL-15R α have been assessed. Our data suggest simultaneous injection of these two types of recombinant viruses enhance tumor regression and increase survival of the mice rather than injection of VV-IL-15 solely.

[1] C. Berger *et al.*, "Safety and immunologic effects of IL-15 administration in nonhuman primates," (in eng), *Blood*, vol. 114, no. 12, pp. 2417-26, Sep 17 2009, doi: 10.1182/blood-2008-12-189266.

[2] J. M. Van den Bergh, E. Lion, V. F. Van Tendeloo, and E. L. Smits, "IL-15 receptor alpha as the magic wand to boost the success of IL-15 antitumor therapies: The upswing of IL-15 transpresentation," (in eng), *Pharmacol Ther*, vol. 170, pp. 73-79, 02 2017, doi: 10.1016/j.pharmthera.2016.10.012.