Interleukin 15 (IL-15) has been evaluated as a potential treatment for solid tumors in clinical trials, but the effectiveness of systemic IL-15 administration as a monotherapy has not been realized. IL-15 receptor alpha (IL-15Rα) can stabilize IL-15 and enhance its bioactivity. The goal of this study was to examine the activity of IL-15/IL-15Rα complex (IL-15cx) to CD8+ T cells and evaluate its potential efficacy in murine breast cancer models.

Methods

The bioactivity of IL-15cx to CD8 T cells was assessed by ex vivo and in vivo cell proliferation assays. The antitumor efficacy was studied in mouse mammary carcinoma models (Her2/neu transgenic and 4T1-luc mammary cancers) treated with systemic recombinant protein with/without the depletion of myeloid-derived suppressor cells (MDSCs) has no impact on mouse breast cancer growth. Intraperitoneal administration of IL-15cx results in a moderate inhibition of breast cancer growth that is associated with an increase in the frequency of cytotoxic CD8 T cells and the improvement of their function. The depletion of myeloid-derived suppressor cells (MDSCs) has no impact on mouse breast cancer growth. IL-15cx treatment diminishes MDSCs in murine tumors. However, it also antagonizes the effects of depleting antibody. Intratumoral GET with plasmid IL-15/IL-15Rα leads to a long-term survival benefit in 4T1 mammary carcinoma model. An early increase of local cytotoxic cells correlates with GET treatment and an increase of long-term memory T cells results from animals with complete tumor regression.

Conclusions

Systemic and local administration of IL-15cx shows two distinct therapeutic responses, a moderate tumor growth inhibition or heterogenous tumor regressions with survival improvement. Further studies are warranted to improve the efficacy of IL-15cx as an immunotherapy for breast cancer.

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Trial Registration

N/A

Ethics Approval

Experimental procedures were approved by the Institutional Animal Care and Use Committee (IACUC) at Old Dominion University (S. Guo) and by the IACUC at Virginia Commonwealth University (R.B. Smeltz).

References

N/A