Assessment of IL13R2-dependent tumor aggression in an immunocompetent glioma animal model

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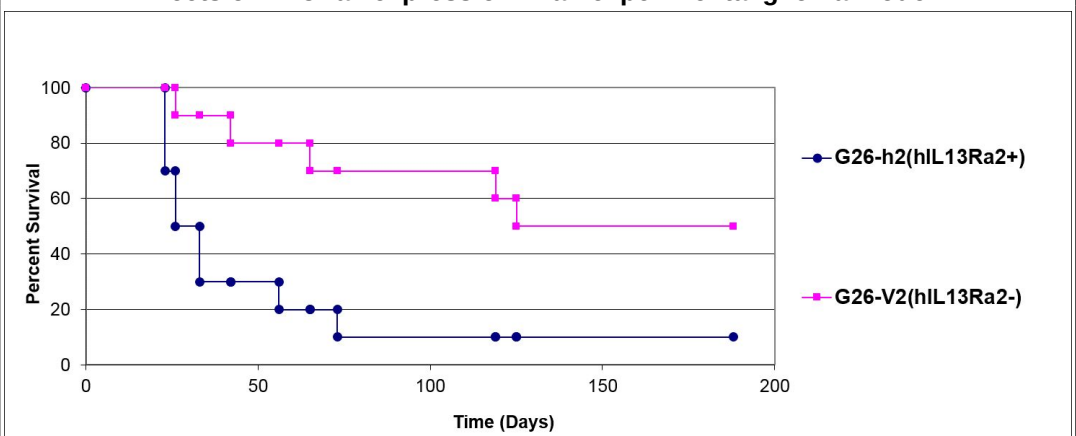
Introduction

IL13Ra2 is a well-established target for novel therapies in glioblastoma due to its overexpression on tumor cells as well as glioma-initiating cells. IL13Ra2-targeted GBM therapies have reached completion of several clinical trials, including a phase III trial. Recent studies have found that the expression of IL13Ra2, like other tumor-associated antigens, in GBM is heterogeneous and, therefore, better targeting strategies for its clinical application would be useful. This study investigated the effectiveness of different patterns of IL13Ra2 expression on the survival of syngeneic rodent glioma models. This study also aims to act as a blueprint for further tests of the level of immune response to the target immunotherapy in immunocompetent mice bearing gliomas with different levels of IL13Ra2 expression.

Methods

G26 murine glioma cell lines expressing hIL13Ra2 plasmid (G26-H2) or vector control (G26-V2) were used. Cells were FACS-sorted for IL13Ra2 expression. Ten C57Bl/6 mice were intracranially injected with G26-H2 cells (positive for hIL13Ra2) and ten received G26-V2 (negative for hIL13Ra2). The metric analyzed for outcome was survival.

Effects of IL13Ra2 expression in an experimental glioma model.



Effects of IL13Ra2 expression in an experimental glioma model. Kaplan–Meier curves show that the group that received G26-V2 cells (hIL13Ra2-) has a significantly better survival compared to the group that received G26-H2 cells (hIL13Ra2+), p=0.0006.

Results

Two populations of G26 glioma cell lines were established per hIL13Ra2 expression: the hIL13Ra2+ and the hIL13Ra2-. In vivo, the cell lines showed a significant difference in survival: the group that received intracranial injection of G26-H2 cells (100% positive for hIL13Ra2) had a median survival of 26 days compared to 188 days for group receiving G26-V2 cells (100% negative for h IL13Ra2), p=0.0006.

Conclusions

We assessed two different populations of G26 glioma cell lines: h IL13Ra2+ and h IL13Ra2-. In vivo, after intracranial implantation, the two populations showed a significant difference in survival. These results confirm the role of hIL13Ra2 overexpression in specific subtypes of glioblastomas, and most likely the most aggressive ones. Immunological characterization of the tumor -bearing animals is in progress.

Learning Objectives

Although several studies have highlighted the importance of IL13Ra2 and its positive correlation with poor prognosis, the role of IL13Ra2 in glioma is not fully understood.
This study confirms that high levels of IL13Ra2 expression are associated with highly aggressive tumors and shorter survival. Further investigations on target therapy with this model are currently in progress.

References

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