18th International Conference on
Cancer Research
April 04-05, 2022
WEBINAR

Targeting Treg cells with GITR activation alleviates resistance to immunotherapy in murine glioblastomas

Hye-Jung Kim
Massachusetts General Hospital, USA

Glioblastoma (GBM) shows high levels of resistance to currently available treatments including the Standard of Care and immunotherapy, representing the most fatal cancer type. Our study revealed that immune suppression by regulatory T cells (Treg) secondary to therapy with immune checkpoint blocker (anti-PD1) confers this resistance. In the GBM tumor microenvironment, Treg cells with increased suppressive phenotype were found of which frequency and anergic phenotype increase after ICB therapy, potentially contributing to the resistance. Targeting Treg has a dual-barreled effect on enhancing anti-tumor immunity: GBM is highly infiltrated with Treg while CD8 T cells are excluded. In view of Treg's intrinsic reactivity to self-antigens, mobilizing converted Treg as effector T cells can be an effective strategy to a tumor type that expresses a low level of neoantigens including GBM. Our study revealed that GITR (glucocorticoid induced TNFR family related protein) is a desirable therapeutic target based on its increased expression on GBM Tregs as compared to peripheral Tregs. Engagement of GITR with agonistic antibody led to conversion of Treg to Th1- like effector T cells, which is accompanied with downregulation of Helios and IL-10 expression that are associated with Treg suppressive function. Through combining anti-GITR with anti-PD1 therapy, tumor recognition by converted Treg and CD8 T cells could be enhanced via IFNγ induced promotion of MHC class I and II expression by GBM cells, which also resulted in T cell memory formation in the long-term survivors. To obtain clinically relevant information, we established a standard of care regimen consisting of surgery, radiation, and chemotherapy for orthotopic mouse GBM. We found that the anti-GITR +anti-PD1 therapy tailored to the GBM specific TME synergizes with the standard of care, suggesting a translational potential in patients.

Biography

Hye-Jung Kim is affiliated from Massachusetts General Hospital, USA. Her research interest includes Immuno-oncology, Precision Medicine, Tumor Immunology etc.

Received: January 24, 2022; **Accepted**: January 26, 2022; **Published**: April 4, 2022