

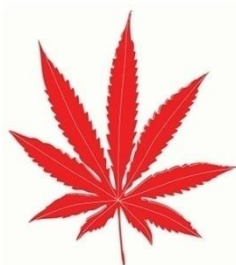


Conference Abstract

5th The Holy Quran & Science Conference and Exhibition – 2018

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Conference Abstract

The therapeutic targeting of tumorigenic EphA2+/EphA3+ brain tumor initiating cells with bi-specific antibody in human glioblastoma

Maleeha Qazi

She studies at McMaster University in Biochemistry with a focus on brain cancer stem cell biology, and plans to defend her thesis in the Spring of 2019. .

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Consent for publication: Author is agreed to submit this abstract for publication in this research journal.

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Speakers Profile

Maleeha Qazi completed her Hon. B.Sc degree from McMaster University, majoring in Biochemistry and Biomedical Sciences Co-op. She completed her Co-op positions at The Hospital for Sick Children and in the Department of Surgery at McMaster University. She then started her graduate studies at McMaster University in Biochemistry with a focus on brain cancer stem cell biology, and plans to defend her thesis in the Spring of 2019. .

Abstract

Surah Al Mumin of the Holy Quran describes the early development of the human fetus in detail that can be verified with modern scientific advances (Chapter 23, Verses 13-15). The study of human embryogenesis has led to a better understanding of congenital disorders, cellular regeneration, and cancer. In this study, we describe the role of Ephrin receptors, a family of cell-surface receptor tyrosine kinases implicated in the regulation of human embryonic development, in the context of human glioblastoma, the most common and aggressive brain tumor.

Introduction: Human glioblastoma (hGBM) carries a dismal prognosis and inevitably relapses despite aggressive therapy. Many of the 14 members of the Eph receptor tyrosine kinase family are expressed in hGBM initiating cells (GICs) and constitute potential molecular targets. We hypothesize that multiple members of the EphR family play a critical role in hGBM recurrence.

Methods: Using a highly specific human EphR antibody panel, we identified differential expression of EphRs in recurrent hGBM (rGBM). We further characterized EphR co-expression using mass cytometry. Using in vitro and in vivo assays, we identified multiple EphRs that mark the GIC population in rGBM. We tested the therapeutic potential of co-targeting multiple EphR using a bispecific antibody (BsAb) and identified the mechanism of action.

Results: Here we show that EphA2 and EphA3 co-expression marks a highly tumorigenic cell population in rGBM with higher in vitro and in vivo self-renewal and proliferation capacity as compared to EphA2+/EphA3-, EphA2-/EphA3+ or EphA2-/EphA3- cells. Knockdown of EphA2 and EphA3 blocks this self-renewal and proliferation capacity. We find that EphA2+/EphA3+ also express multiple GIC markers. We generated a BsAb that co-targets EphA2 and EphA3. In vitro treatment of rGBM with BsAb led to phosphorylation of EphA2 and EphA3, eventually leading to receptor internalization and degradation. The cellular effect of EphA2/A3 blockade was mediated through the down regulation of Akt and MAPK. Intracranial treatment of immune-deficient mice harboring hGBM with BsAb resulted in non-invasive and significantly smaller tumors.

Conclusion: EphA2 and EphA3 co-expression marks a previously unknown GIC population in rGBM. Co-targeting of both EphA2 and EphA3 may serve as a potential therapeutic strategy for rGBM, leading to improved patient survival.

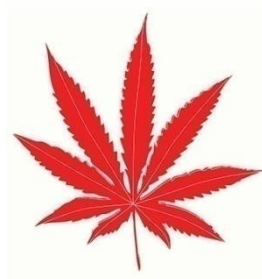
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Competing Interests:

The authors declare no competing interests

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