MECHANISMS UNDERLYING HUMAN MESENCHYMAL STROMAL CELL (MSC) RECRUITMENT AND MIGRATION TO HUMAN GLIOMA

LATA MENON, PHD

Glioblastoma (GBM) is an aggressive and rapidly fatal brain tumor for which no effective therapy exists. A fundamental reason for the failure of many potential therapies is the infiltrative manner in which GBM cells migrate into the normal brain away from the main tumor, resulting in recurrence. Our previous BSF funded studies have shown that Mesenchymal Stromal Cells (MSC) exhibit an intrinsic homing property enabling them to migrate towards glioma tumors. Therefore, MSC expressing therapeutic genes deliver/secrete the therapeutic proteins at tumor vicinity and ultimately inhibit tumor growth. This approach allows the use of modified MSC as cell based drug delivery system for the treatment of GBM.

The current study evaluated mechanisms that facilitated or influenced the migration of MSC towards GBM. Two approaches were used: (1) We analyzed the glioma environment to identify distinct tumor specific signals and (2) To identify the response factors which result in MSC homing to glioma cells. During the past year, several studies were performed to address the proposed Aims. Initially studies were done in cultured glioma cells to confirm MSC migration. In order to more closely recapitulate, the glioma tumor properties we used primary glioma stem cell lines - obtained from Dr Keith Ligon, Department of Pathology, BWH. We then identified the factors secreted in both glioma and MSC cells *in vitro*. Our results indicate that a wide range of glioma secreted factors are involved in the MSC migration, several signaling molecules including factors involved in chemotaxis, inflammatory responses, angiogenesis were identified.

Unravelling the mechanisms that allow MSC to migrate towards the infiltrate tumor cells will allow the development of new therapeutic strategies to enhance the recruitment, and targeting of MSC for the treatment of malignant gliomas. Our promising data suggests that modifying MSC, will enhance the migration towards gliomas, thereby allow the secretion of therapeutic proteins at tumor site. Increased understanding of the pathways involved in stimulating tumor-specific MSC migration will potentially result in increased efficacy of this novel therapeutic approach.

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