

Distinct Immune Signatures Of Radiation-Induced Meningiomas With NF2-Fusion

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Introduction:

The incidence of radiation-induced meningiomas is on the rise, as oncological evolves and cancer survival improves. Previously, our laboratory demonstrated that RIMs harbor a distinct genomic landscape compared to sporadic tumors. Notably, genomic rearrangement resulting in a NF2-fusion gene with a nonrecurrent reciprocal gene was observed in a subset of RIMs. We aimed to compare the gene expression profiles of NF2-Fusion and NF2-Wild Type (NF2-WT) RIMs.

Methods:

RNA sequencing using Illumina HiSeq was performed on 7 NF2-Fusion and 12 NF2-WT RIMs. Short read sequences obtained from sequencing were mapped to reference human genome(hg19). We performed differential expression analysis using edgeR statistical packages. Pathway analysis was performed using Gene Set Enrichment Analysis (GSEA). Immunohistochemistry was performed to validate findings.

Results:

Principal component analysis revealed that 5/7 of NF2-Fusion RIMs had similar gene expression profiles. Pathway analysis demonstrated that there was upregulation of immune pathways in the NF2-Fusion RIMs compared to sporadic counterparts. Immunohistochemistry staining for immune markers was performed to validate the immune pathway signatures. PD-L1 staining was positive in 0% and 100% of tumoral and inflammatory cells, respectively, in NF2-Fusion tumors. In contrast, 50% of NF2-WT RIMs had PD-L1 expression in tumoral and inflammatory cells. In addition, there was a higher CD lymphocyte infiltration in NF2-WT (42.2 vs 12.4 number of positive cells per HPF).

Discussion:

Preliminary data in our lab demonstrates that NF2-Fusion tumors have a distinct immune microenvironment compared to NF2-WT tumors. Our data suggest that NF2-Fusion RIMs may not be an ideal candidate for anti-PDL1 therapy.