TRPV1-Mediated Stress Tolerance Signaling in Glioblastoma Under Capsaicin Treatment

Zaman, Iqraa (School: George Washington High School)

Glioblastoma is a highly aggressive and treatment-resistant brain tumor with a five-year survival rate of 6.9%, necessitating exploration of novel therapeutic strategies. Transient receptor potential vanilloid-1 (TRPV1) has gained prominence in cancer research due to its altered expression in tumor cells under capsaicin treatment. As TRPV1's role in regulating cellular stress tolerance and survival signaling in glioblastoma remains unclear, this study investigates TRPV1-mediated capsaicin-induced stress responses in glioblastoma. Wild-type (WT) and TRPV1 knockout (TRPV1KO) glioblastoma cells were compared using CCK-8 assays, RNA-seq, and RT-qPCR to evaluate cellular responses to capsaicin treatment. WT cells tolerated capsaicin concentrations up to 175 μM, whereas TRPV1KO cells exhibited reduced viability at 164 μM, indicating TRPV1-dependent cytoprotection. Transcriptomic profiling revealed activation of the MAPK-HSF1-HSP signaling network in WT cells, driving expression of feedback regulators to limit stress-induced damage. Conversely, TRPV1KO cells failed to trigger proper MAPK feedback, resulting in apoptosis. Notably, two long non-coding RNAs, MSTRG.50699 and MSTRG.66879, were identified as potential cis-regulators of DUSP1 and MYC (log2Fold Change=1 and FDR=0.05), respectively. Furthermore, the long non-coding RNA CASC11, co-expressed with MYC, was markedly upregulated in WT cells, forming a CASC11-MYC-miR-182 regulatory axis that enhances cellular survival under capsaicin stress. Collectively, these findings identify TRPV1 as a central coordinator of stress tolerance in glioblastoma through facilitation of the novel TRPV1-dependent CASC11–MYC–miR-182 regulatory axis, highlighting its potential as a target for future capsaicin-based therapies.

Awards Won: