Title

DDRE-50. INVESTIGATING THE ROLE OF LonP1 IN GLIOBLASTOMA TUMOR PROGRESSION

Journal

Neuro-oncology, 23(Suppl 6)

ISSN

1522-8517

Authors

Douglas, Christopher
Bota, Daniela
Di, Kaijun
et al.

Publication Date

2021-11-01

DDRE-50. INVESTIGATING THE ROLE OF LONP1 IN GLIOBLASTOMA TUMOR PROGRESSION

Christopher Douglas[1], Daniela Bota [2], Kaijun Di[1], Bhaskar Das[3], and Javier Lepe[1]; [1]University of California, Irvine, Irvine, CA, USA, [2]Department of Neurology, University of California, Irvine, Irvine, CA, USA, [3]Long Island University, Bronx, NY, USA

Glioblastoma (GBM), a WHO grade IV brain cancer, exhibits strong treat-ment resistance and a high rate of reoccurrence, which gives it a dismal prognosis, a 5% survival rate in the first 5 years. LonP1, a mitochondrial master regulator, can drive metabolic transformation, cytokine production, EMT, and treatment resistance in various cancer types, but its role in GBM remains unexplored. Our research group has previously shown that LonP1 is overexpressed in human malignant gliomas, particularly glioblastoma, and that this is associated with disease prognosis. Here, we present findings that demonstrate that LonP1 seems to drive enhanced tumor progression, invasiveness, angiogenesis in different high grade glioblastomas based on TCGA-subtype. Furthermore, in collaboration with Professor Bhaskar Das, we have validated a lead compound, BT317, with on-target inhibition of LonP1 protease activity. BT317 has enhanced activity against glioma stem cell lines (GSC) and has demonstrated low toxicity and efficacy in an intra-cranial xenograft model. This preliminary data highlights the potential of using combinatorial, pharmacological LonP1 and proteasome inhibition as a novel strategy for targeting specific subtypes of GBM.