Increased Clinical Relevance of Orthotopic Glioma Models Through Bioluminescence and MR Imaging


Molecular Imaging, Inc., Ann Arbor, MI

Introduction
Glioblastoma multiforme (GBM) is the most common and most aggressive form of malignant primary brain tumors, affecting nearly 35,000 people in the United States. Most preclinical studies in glioma utilize survival as the primary endpoint to study, which provides limited information about disease progression and response to treatment. We have characterized two orthotopic human glioma cell lines, Gli36 and LN827 that have been modified to express luciferase in order to enable in vivo monitoring of disease progression and response to treatment using bioluminescence imaging (BLI). Anatomical magnetic resonance imaging (MRI) was also performed to directly correlate bioluminescence signal with tumor burden.

Methods
Gli36 (luc-dsRed)(resc) and LN827 (pMMP-LucNeo) cells were implanted intracranially (5x10^4 cells in 2µl) into CB.17 SCID mice on Day 0. BLI scans were acquired on Day 6 and 10 to ensure disease progression prior to starting treatment, and then every 5-7 days to track tumor growth. Temozolomide treatment (100mg/kg, PO, QDx5) was used as a positive control to validate sensitivity of these cell lines to an accepted standard of care for glioma.

Results
• Gli36 (luc-dsRed)(resc) and LN827 (luc-dsRed)(resc) exhibited high tumor take-rates.
• Both cell lines were highly sensitive to treatment with temozolomide, resulting in a significant increase in lifespan and significant tumor growth delay as determined by BLI.
• BLI and MRI showed good correlation between BLI signals and anatomical tumor volumes.

Conclusions
• We have successfully characterized two luciferase-enabled glioma cell lines for in vivo imaging of disease progression.
• Bioluminescence imaging provides an efficient, non-invasive means of quantifying disease progression and response to therapy.