ANTI-ELTD1 MONOCLONAL ANTIBODY THERAPY
PRINCIPAL INVESTIGATOR

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Glioblastoma Multiforme (GBM) is the most aggressive malignant primary brain tumor in adults with a high recurrence and mortality rate.

GBM is a high-grade glioma that is invasive, highly vascular and resistant to apoptosis.

Less than 5% of all patients surviving more than 5 years post-diagnosis and 16,000 patients die of GBM in the US annually.

ELTD1 (Epidermal growth factor, Latrophilin and seven-transmembrane domain-containing1) is associated with angiogenesis and is highly expressed in vascular endothelium of high-grade GBM.
Anti-ELTD1 antibody (Ab) can be used as GBM therapy

- Current standard of care for GBM includes surgical resection followed by combination of radiation with temozolomide (TMZ)/bevacizumab (humanized VEGF mAb)
- TMZ resistance and bevacizumab side effects such as hemorrhage, blood clots and GI perforation indicate that a therapy targeting several tumorigenesis pathways is needed
FINDINGS

C-Met, a cell receptor, is associated with tumor growth, proliferation and angiogenesis.

Ki-67 is a nuclear protein strongly associated with cellular proliferation, tumor growth and metastasis.

Representative C-met IHC images (20×) of untreated (A), monovalent monoclonal Ab (mmAb) (B), and single chain variable fragment (scFv) (C) anti-ELTD1 treated animals. Quantitative C-met (D)

Ki-67 positivity staining in the tumor region of each group (E). Representative Ki-67 IHC images (20×) of untreated (F), mmAb (G), and scFv (H) anti-ELTD1 treated animals.

Anti-ELTD1 mmAb and scFv reduce tumor angiogenesis and proliferation.
Anti-ELTD1 mmAb and scFv reduce tumor cell migration and increase tumor cell apoptosis
SUMMARY

- Anti-ELTD1 mmAb or scFV therapy is effective in a highly aggressive (G55) orthotopic rodent xenograft model of GBM
  - Reduces tumor volumes and increases animal survival
  - Reduces tumor microvascularity and angiogenesis
  - Reduces tumor cell proliferation and migration
  - Increases tumor cell apoptosis

- Unlike bevacizumab (VEGF mAb), using an antibody against ELTD1 doesn't cause hemorrhage