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Vectorized Antibodies for the Treatment of Solid Tumors

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Vectorized Antibodies for the Treatment of Solid Tumors

Background & Unmet Need

- Antibody therapies have well established therapeutic effects, but are limited by their durability and ability to localize to some solid tumors
- While anti-angiogenic antibody therapies, such as bevacizumab, have been tested against ovarian cancer, transient and low peritoneal drug levels are likely a factor in treatment failure
- Systemic administration of monoclonal antibodies against vascular endothelial growth factor (VEGF) and epidermal growth factor receptor (EGFR) for glioblastoma are limited by the blood-brain barrier and clinical results have been disappointing
- **Unmet Need:** More efficacious and sustained delivery of antibody therapies to solid tumor sites such as ovarian cancer and glioblastoma

Technology Overview

- **The Technology:** AAV vector encoding therapeutic antibodies to treat solid tumors
- The AAV vector, AAVrh.10, can encode therapeutic antibodies for VEGF, EGFR, and CXCL12 for *in situ* production
- Unlike traditional antibody therapy, the vectorized antibody mediates persistent local expression of the encoded antibody
- **PoC Data:** Administration of the vector encoding bevacizumab (AAVrh10.BevMab) via intraperitoneal injection mediates persistent and high levels of the antibody in the peritoneal cavity
- Administration of AAVrh10.BevMab reduced tumor growth, increased mouse survival of ovarian cancer, and is synergistic with chemotherapy
- Delivery of encoded VEGF or EGFR via the AAVrh.10 vector directly into the brain of xenograft mouse models of GBM showed reduction in tumor size and increased survival of mice

Inventors:
Ronald G. Crystal
Arash Rafil Tabrizi
Stephen Kaminsky
Martin Hicks
Viviane Tabar

Patents:
US Patent 10,946,094
US Patent Application Filed

Publications:
Hicks et al. *PLoS One*. 2016.
Hicks et al. *Cancer Gene Ther*. 2015.
Xie et al. *Gynecol Onol*. 2014.

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Cornell Reference:
D-6050, D-6903

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Technology Applications

- AAV-mediated bevacizumab therapy for the suppression of ovarian cancer growth
- Therapeutic antibody treatment for glioblastoma or other CNS cancers

Technology Advantages

- Provides persistent and high levels of antibodies without repeated antibody administration
- Encoded antibodies are generated *in situ* at the site of injection, bypassing the blood-brain barrier

Supporting Data / Figures

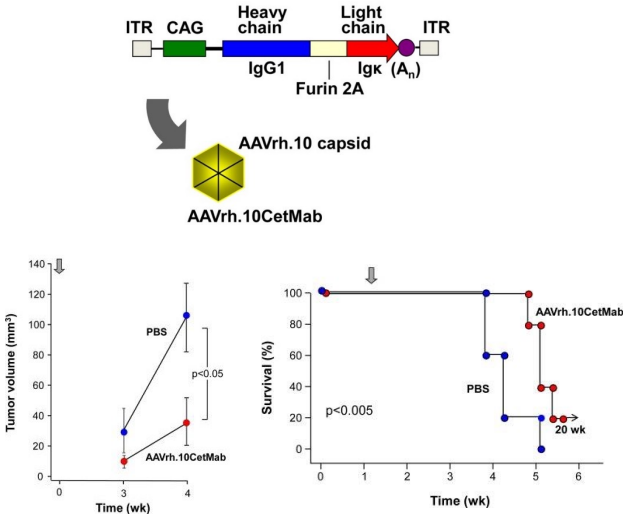

Figure 1: Top: Design of AAVrh.10 vector expressing anti-EGFR (cetuximab) **Bottom:** Treatment of mice with human glioblastoma xenografts 8 days after xenograft implementation shows reduced tumor volume and increased survival.

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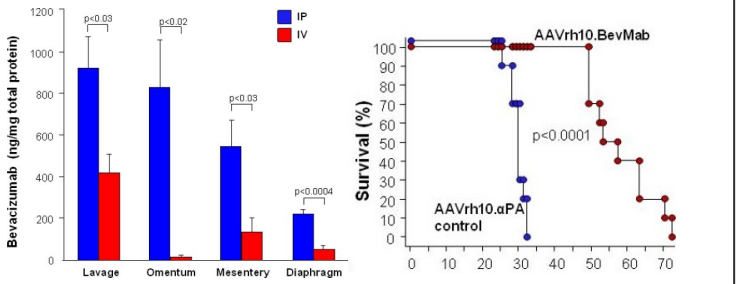

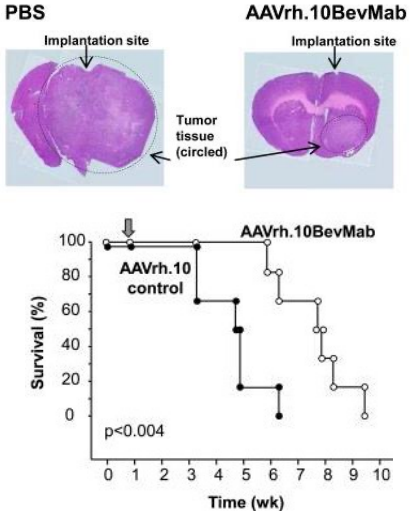

Figure 1: Left: Local expression of bevacizumab in peritoneal cavity is persistent 9 weeks after intraperitoneal administration of AAVrh10.BevMab and increases survival in mice with established ovarian cancer cell line xenografts. **Right:** Treatment with AAVrh.10BevMab vector reduces tumor size in mouse brains implanted with GBM tumor and increases survival of mice with established human glioblastoma xenografts.

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