Glioblastoma stem cells (GSCs) are invasive, treatment-resistant brain cancer cells that express downregulated in renal cell carcinoma (DRR), also called FAM107A, a genetic driver of GSC invasion. We developed antibody-antisense oligonucleotide (AON) conjugates to target and reduce DRR/FAM107A expression. Specifically, we used antibodies against antigens expressed on the GSCs, such as CD44 and EphA2, conjugated to chemically modified AONs against DRR/FAM107A, which were designed as chimeras of DNA and 2'-deoxy-2'-fluoro-beta-D-arabinonucleic acid (FANA) for increased nuclease stability and mRNA affinity. We demonstrate that these therapeutic conjugates successfully internalize, accumulate, and reduce DRR/FAM107A expression in patient-derived GSCs. This is the first example of an antibody-antisense strategy against cancer stem cells [1)].

1)
Arnold AE, Malek-Adamian E, Le PU, Meng A, Martínez-Montero S, Petrecca K, Damha MJ, Shoichet MS. Antibody-Antisense Oligonucleotide Conjugate Downregulates a Key Gene in Glioblastoma Stem Cells. Mol Ther Nucleic Acids. 2018 Jun 1;11:518-527. doi: 10.1016/j.omtn.2018.04.004. Epub 2018 Apr 19. PubMed PMID: 29858087.