Washington University in St. Louis
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ZBTB46, A NOVEL TARGET FOR CANCER THERAPY

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T-020458 — Zbtb46, a novel target for cancer therapy

Technology Description

Solid neoplasms are difficult to treat using immune checkpoint inhibitors in part because of the immunosuppressive nature of the tumor microenvironment. Researchers at Washington University School of Medicine, led by Dr. Kyunghee Choi, have found a novel transcriptional regulator of both tumor endothelial function and immunity. This gene, called Zbtb46, is actively downregulated in a variety of solid tumors, and its expression inversely correlates with disease outcomes. Enforced expression of Zbtb46 reversed the immune suppression, myeloid skewing, and vascular dysregulation seen in animal xenograft models. As a standalone product or in combination with ICI or anti-VEGF agents, Zbtb46 overexpression shows promise as a new type of immune-gene therapy.

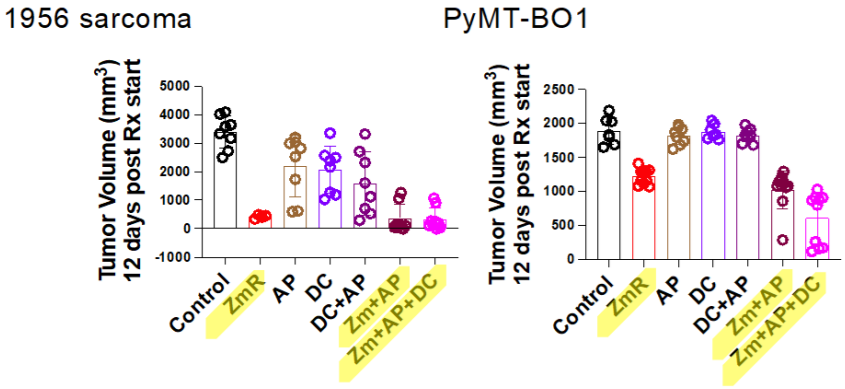

Figure – Single agent or combination efficacy of Zbtb46 overexpression (ZmR) in two types of murine xenograft solid tumor models. Highlighted groups involve the use of Zbtb46 agent, and tumor volume is measured after 12 days post-therapy start. Other agents used are anti-PD1 antibody (AP) and anti-VEGFR2 antibody(DC). Zbtb46 was delivered via intraperitoneal injection of mRNA-containing nanoparticles.

Stage of Research

Formulations validated in animal models include plasmid-based and mRNA-based delivery.

Preliminary toxicity studies show long term dosing of Zbtb46 is well-tolerated.

Applications

Treatment of solid malignancies

Key Advantages

Potential to use as a single therapeutic or in combination with existing immunotherapy or anti-

angiogenesis agent.

Zbtb46 overexpression has enhanced the functions of immune effector cells such as cytotoxic T cells and dendritic cells in animal models.

Patents: US provisional application filed.

Related Web Links: BioRxiv pre-print available here.