KDDF
Korea Drug Development Fund

Asset #27

Ramot At Tel Aviv University

EHDV-TAU, a Novel Oncolytic Virus

Therapeutic Area	Oncology	**Indications**	Bladder/Prostate Cancer, Melanoma
Modality	Oncolytic Virotherapy	**Development Stage**	Target Identification/Validation

Overview

Background

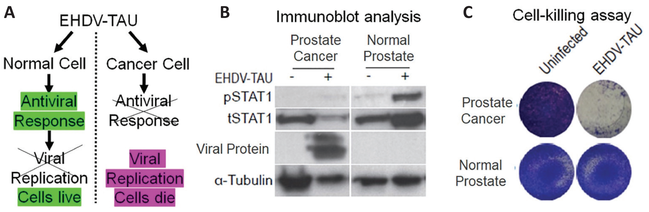
- Directed evolution enabled to develop the oncolytic virus, EHDV-TAU. A clone of the epizootic hemorrhagic disease virus selected on interferon-defective human prostate cells.
- The directed evolution process increased the viral replication by 10E7 (10 million fold) on this subset of human prostate cancer cells. Virus was tested on multiple tumor models. Infection of tumors is inversely correlated to IFN/JAK/STAT signaling.

Technology Advantages

- Veterinary Arbovirus (no pre-existing neutralizing immunity)
- In vitro evolution in interferon-defective human cancer cells
- Kills cancer cells through different processes Replicates to high titers in cancer cells but not normal cells
- Potent stimulator of immunity (e.g., via dsRNA genome or cytolytic cell death)
- Kills subset of immunocompetent cells via Oncolysis By Non-Productive Viral Infection (ONPVI)
- Stimulates secretion of immune-modulatory cytokines/ chemokines

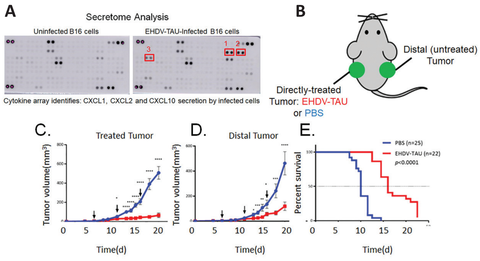
Key Data

EHDV-TAU replicates in, and kills, cancer cells while sparing normal cells



A- Schematic depiction of the experiment. B- Immunoblot analysis of EHDV-TAU infection of prostate cancer (LNCaP) or normal prostate epithelial cells. C- Crystal violet staining of cultures of prostate cancer cells or normal prostate epithelial cells infected or not with EHDV-TAU. Experiments with multiple different cancer cell lines demonstrate the effectiveness of EHDV-TAU against a variety of tumors of different origins, including: Prostate, Melanoma, Bladder, Ovarian, Lung, Breast, Glioblastoma, Astrocytoma, Osteosarcoma

EHDV-TAU inhibits directly-treated and distal tumors and stimulates anti-tumor immunity



(A) Secretome assay. EHDV-TAU stimulates secretion of CXCL1, CXCL2 and CXCL10 in B16F10 melanoma cells. (B) Schematic depiction of in vivo oncolysis experiment. (C-D), Graphs depict the growth of B16F10 tumors directly treated with EHDV-TAU or PBS treated (C), or distal tumors (D). (E) Survival plot of tumor-bearing mice in the double-tumor model receiving EHDV-TAU (n = 23) or PBS (n = 25). Of note, no significant differences in mouse weight were observed between the treatment groups, indicative of lack of EHDV-TAU-induced detrimental health effects.

IP Status & Publication(s)

Intellectual Property

Patent Number	Patent Family
US 11484558 B2 (2022.11.01)	US

Publication(s)

- Dellac at al. (2020) Constitutive low expression of antiviral effectors sensitizes melanoma cells to a novel oncolytic virus. International Journal of Cancer
- Ehrlich at al. (2021) Oncolytic virotherapy: the cancer cell side. Cancers
- Barer at al. (2023) Lipocalin-2 regulates the expression of interferon-stimulated genes and the susceptibility of prostate cancer cells to oncolytic virus infection. European Journal of Cell Biology
- Danziger at al (2016) Combined genetic and epigenetic interferences with interferon signaling expose prostate cancer cells to viral infection. Oncotarget
- Danziger at al (2018) Interleukin-6 and Interferon-α Signaling via JAK1–STAT Differentially Regulate Oncolytic versus Cytoprotective Antiviral States. Frontiers in Immunology