Novel Use of Phenolic Compounds for Epstein-Barr Virus Lytic Induction

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Epstein-Barr virus is an oncogenic herpesvirus which causes over 150,000 fatalities annually and has no FDA-approved treatment. Latent EBV is characterized by limited gene expression, which allows it to evade immune detection. Artificially inducing lytic replication increases gene expression and allows targeted treatment of EBV seropositive tumors. This research evaluated the efficacy of two natural polyphenolic compounds in terms of I) their ability to inhibit primary EBV infection and II) their effect on latently infected Burkitt's lymphoma cells. In Phase I, EBV was conjugated with FITC, allowing for visualization of infection. Ramos cells were assessed at three time-points: 24, 48, and 72 hours. EBV infection was apparent when assessed via microscopy. Both resveratrol and corilagin upregulated BZLF1 expression and increased viral load. Thus, primary EBV infection was not inhibited. In Phase II, Raji, an EBV+ cell line, was treated with either phenolic compounds or 3mM sodium butyrate. RT-qPCR for lytic genes BZLF1 and BALF5 concluded that resveratrol enhanced the expression of these genes, while corilagin inhibited it. Increased viral load was seen in resveratrol treated groups, due to the upregulation of these lytic genes. Overall, resveratrol and sodium butyrate mediated lytic induction provides a potential future treatment combination to be evaluated in the therapy of EBV seropositive tumors. Additionally, inhibitory effects of corilagin in lytic EBV infections mimic nucleosides, which have been previously shown to inhibit both EBV and cellular proliferation.

Awards Won:

First Award of $5,000

Intel ISEF Best of Category Award of $5,000