The Anti-Tumor Activity of Silvestrol on the Epstein-Barr Virus

Mangtak Andy Kwok
Pharmaceutical Sciences, The Ohio State University

Advisor: Dr. Robert Baiocchi, Department of Internal Medicine Comprehensive Cancer Center, The Ohio State University

The Epstein-Barr virus (EBV) is one of the most common viruses in humans, infecting more than 90% of people worldwide. While most people infected with EBV gain adaptive immunity, immunocompromised patients that are exposed to EBV can end up developing Hodgkin's lymphoma, non-Hodgkin's lymphoma, Burkitt's lymphoma, post-transplant lymphoproliferative disease (EBV-LPD), and nasopharyngeal and gastric carcinoma. Many vaccines and chemo-immunotherapeutic approaches directed against EBV have been studied and developed in clinical trials. None have been successful because they most often lead to either immune suppression, EBV reactivation, or increased risk of lethal infection. The purpose of this study is to identify a vaccine that can deliver direct anti-tumor activity while preserving host-immune surveillance. Silvestrol, a unique agent that is attributed to the inhibition of translation initiation, was tested to see how it interferes with the normal recruitment of mRNA to the elF4F initiation complex, an important step to the synthesis of pro-survival and pro-growth of proteins. Current progress in the research shows that Silvestrol's efficacy is dependent on the presence of CD8+ T cells while interferon responsive factors proteins are lost with Silvestrol treatment. Silvestrol's ability to deplete lymphoblastoid cell lines, possess unique anti-tumor activity, and preserve the host anti-tumor immune function gives it a unique niche in terms of chemotherapeutic medication. This study helps change the future landscape of treatments for patients with EBV-positive malignancies through immune-sparing drugs.