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PennState Cancer Institute

Infectivity of HPV 16 Variants with Drug Inhibitors

Hannah Smith[1], Janice Milici [2] Craig Meyers [2]

[1] Central Dauphin East Senior High School [2] PennState Hershey, College of Medicine

Introduction: HPV and Cervical Cancer

The two most common forms of the Human papillomavirus (HPV) are known to be the cause of 70% of cervical cancers, which is the third most common cancer among women world wide. It is crucial, therefore, to better understand this virus in order to create treatments that will not only prevent HPV infection among a population, but also partially eliminate cervical cancer.

HPV variants: HPV 16 and HPV 18, the two most common cancer-inducing types of HPV, have evolved over time to give us many variants. These are named after the geographic region from which they originated. This study focuses on HPV 16 variants (**Figure 1**).

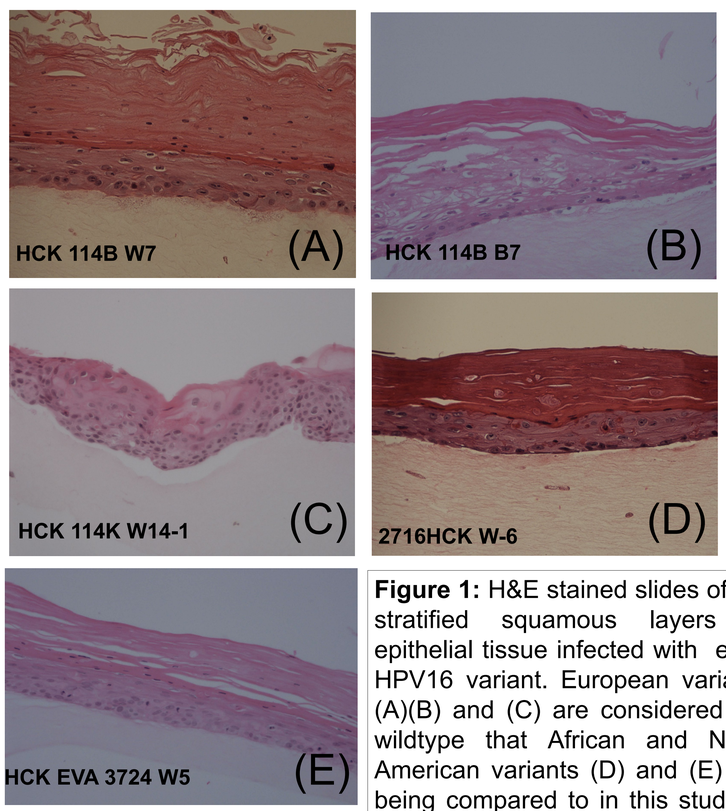


Figure 1: H&E stained slides of the stratified squamous layers of epithelial tissue infected with each HPV16 variant. European variants (A)(B) and (C) are considered the wildtype that African and North American variants (D) and (E) are being compared to in this study of infectivity.

Methods

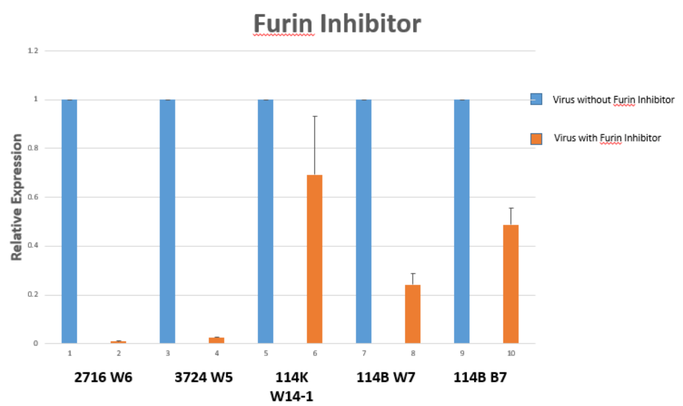
Furin and Heparin Sulfate, were the two drugs that were tested on these HPV 16 variants in order to see how their inhibitory properties may affect infectivity.

HaCaT cells were grown and cultured in a 24-well cell plate with HaCaT media, and were then "infected" with the virus. Each variant was added to two wells: one without the drug of interest, and one with the drug. The cell plate was then incubated at 37ºC for 48 hours.
After infection, the **RNA was harvested** from the cells using an rneasy Mini kit (Qiagen).

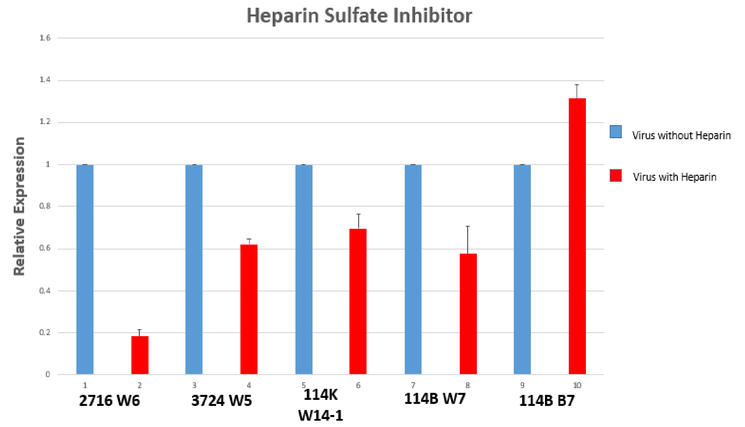
RT-qPCR was used to give us the relative infectivity for each of the HPV variants with and without the presence of one of our three drugs of interest.

Results

(*Furin was added to the virus preps along with media and was incubated in a 37ºC water bath for one hour before being added to HaCat cell plate.)*



Furin Inhibitor: Infectivity was greatly reduced and almost completely diminished for 2716 and 3724 variants with the furin inhibitor drug. The European variants did show a decrease in infectivity as well, but not in as substantial as the African or North American.



Heparin Sulfate Inhibitor: Infectivity was only greatly reduced for the 2716 variant in the presence of Heparin Sulfate inhibitor drug. The other variants showed a small decrease in infectivity, with the exception of 114B7, which actually showed an increase in infectivity with the drug.

Conclusion

This study gave better understanding to the key components involved in the infectivity pathway of several HPV16 variants, especially compared to our wildtype European 114B variant. Both Furin and Heparin Sulfate inhibitors have shown to greatly decrease the relative infection for the 2716 African variant, and the 3724 North American Variant, with little difference seen in the European variants. This shows the us the dependence that these two varients have on Furin and Heparin in order to infect cells. This is consistent with previous studies that have come to a similar conclusion of these drugs' affects on these HPV 16 variants. Overall, future studies will be focused on what this difference in infectivity pathways among variants tells us of the virus' life cycle.

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