Saquinavir Increases Phosphorylated Eukaryotic Elongation Factor 2 (peEF2) at the Anal Transition Zone in Transgenic Mice

G. Bartelt DO '26[1], L.C. Gunder MS[2], S. Haggerty[3], E. Yao BS[2], T.H. Moyer BS[2], H. Johnson MD[2], K. Smith BS[4], N. Sherer PhD[4], E.H. Carchman MD[2,4]

[1]*Des Moines University School of Osteopathic Medicine*
[2]*University of Wisconsin - Madison Department of Surgery*
[3]*Undergraduate at the University of Wisconsin - Madison*
[4]*McArdle Laboratory for Cancer Research*

Background: A hallmark of cancer development is eukaryotic elongation factor 2 (eEF2) overexpression. Saquinavir (SQV) has shown to prevent tumorigenesis in an HPV mouse model of anal disease. Our goal was to assess peEF2 expression, as a marker of eEF2 inactivation, in mice with or without topical SQV treatment. We hypothesized that SQV treatment would increase peEF2 expression.

Methods: *K14E6/E7* mice with high-grade anal dysplasia that express HPV16 E6/E7 oncoproteins in their epithelium were randomized into treatment groups: no treatment (N = 23), topical 7,12-Dimethylbenz(a)anthracene (DMBA) only (N = 22), topical SQV (2.5%) only (N = 16), and topical SQV with DMBA (N = 10). DMBA use ensured progression of high-grade anal dysplasia to cancer within 20 weeks. At 20 weeks anuses were harvested and Immunofluorescent staining for peEF2 was performed. Tissues were imaged for peEF2 localization at the anal transition (ATZ). Fisher's exact tests (due to sample size) were performed to analyze peEF2 localization.

Results: 11 of 16 samples in the SQV only group showed localized peEF2 staining at the ATZ; a significant increase compared to control where 6 of 23 samples showed localized staining ($p=0.01$). 9 of 10 samples in the SQV+DMBA group showed localized staining at the ATZ; a significant increase compared to DMBA only where 11 of 22 samples showed localized staining ($p=0.049$).

Conclusion: Saquinavir increased staining of peEF2 along squamous epithelium at the ATZ, indicating eEF2 inactivation. Further investigation is required to evaluate if this is required for cancer prevention with SQV.