**Tenofovir Diphosphate Concentration-Response Relationship for HIV Prevention in Vaginal Tissue**

Melanie R. Nicol1, Cindi W. Emerson1,2, Julie A. E. Nelson1,2, Craig Sykes1,2, Heather Asher Prince3, Kristine B. Patterson1, Angela D. M. Kushaba1,2

1. Eshelman School of Pharmacy 2. Center for AIDS Research 3. School of Medicine; University of North Carolina at Chapel Hill, NC, USA

## ABSTRACT

Tenofovir diphosphate (TFV-dp) is a prodrug of tenofovir that is administered via the vagina for preexposure prophylaxis (PrEP) against HIV infection. A concentration-response relationship was established for TFV-dp concentrations from 1, 10, 100, and 1000 fmol/mg for explant tissue using qPCR. Emax was 0.802 for a fold change of 3.67. A mean fold change of 3.64 ± 1.4 was observed for TFV-dp concentrations of 1 fmol/mg, and a mean fold change of 3.59 ± 1.4 was observed for TFV-dp concentrations of 10 fmol/mg.

## RESULTS

### METHODS

- **Fresh vaginal tissues** were obtained from donors undergoing surgical repair for vaginal prolapse. All subjects provided written informed consent. The Ethics Review Board approved the study.
- **Explant** cultures were used to evaluate the effect of TFV-dp concentrations on viral RNA abundance.
- **TCID** was quantified using qPCR and normalized to baseline using a standard curve.
- **Explant** cultures were incubated with TFV-dp for 72 h.

### RESULTS

- **Spliced RNA** fold change from baseline was calculated for each explant. TFV-dp concentrations of 1 fmol/mg resulted in a mean fold change of 3.64 ± 1.4, while TFV-dp concentrations of 10 fmol/mg resulted in a mean fold change of 3.59 ± 1.4.

### CONCLUSIONS

- **PrEP** with TFV-dp concentrations of 1 fmol/mg may be effective in preventing HIV infection.

## REFERENCES


## ACKNOWLEDGMENTS

UNC Lineberger Cancer Center Translational Cancer Program sponsored all ongoing tissue studies in the study. The UNC-Translational Pathology Laboratory performed immunohistochemical and IHC studies. Dr. Yan Fung, UNC Pathologist, assisted with IHC staining.

Dr. Elizabeth Gallie and the UNC Tissue Core were assisted with procurement of vaginal tissues. This work was supported by U19 AI089011 and P01 AI091223 from the National Institute of Allergy and Infectious Diseases (NIAID), T32 GM086530 (Maile), and the American Foundation for Pharmaceutical Education (AFPE) Program Award.