**Materials & Methods**

Human papillomaviruses (HPVs) are epitheliotropic DNA viruses and are the causative agents of a number of benign and malignant diseases including skin warts, genital warts, and cancers. Nitric oxide (NO) is a gas produced by L-arginine metabolism in the presence of the enzyme nitric oxide synthase (NOS). The NO molecule has anti-viral properties, but the lack of pharmaceutical formulations for NO prevents its widespread use as an anti-viral drug. Recombinant NO-releasing compounds have recently been developed in our laboratory by Novan Therapeutics. These compounds are macromolecules that can be applied as a topical treatment allowing for easy administration and delivery of NO at site of infection.

The papillomas were measured weekly in three axes (length, width, height) and the geometric mean diameter was calculated. The mean ± SEM for each treatment group is plotted.

**Results**

The complete cessation of wart growth at sites inoculated with E8 mutant CRPV DNA following topical NO treatment in an animal model. NO release rate and concentration influence anti-viral efficacy. Lower concentrations and release rates showed limited efficacy. Treatment with both fast and slow NO-releasing formulations could inhibit papilloma growth, however the faster NO release rate improved treatment efficacy, suggesting that NO release rate affects efficacy. Inhibition of E8 papilloma growth at the end of treatment with SB216 (1.5% NO) (93% inhibition) and SB206 (1.5% NO) (88% inhibition) was statistically significant (p<0.05).

**Conclusions**

The results of this study demonstrated in vivo inhibition of papilloma growth in a well-characterized (CRPV) animal model. Treatment with fast and slow NO-releasing formulations could inhibit papilloma growth, however the faster NO release rate improved treatment efficacy, suggesting that NO release rate affects efficacy. Inhibition of E8 papilloma growth at the end of treatment with SB216 (1.5% NO) (93% inhibition) and SB206 (1.5% NO) (88% inhibition) was statistically significant (p<0.05). Treatment with fast and slow NO-releasing formulations could inhibit papilloma growth, however the faster NO release rate improved treatment efficacy, suggesting that NO release rate affects efficacy. Inhibition of E8 papilloma growth at the end of treatment with SB216 (1.5% NO) (93% inhibition) and SB206 (1.5% NO) (88% inhibition) was statistically significant (p<0.05).