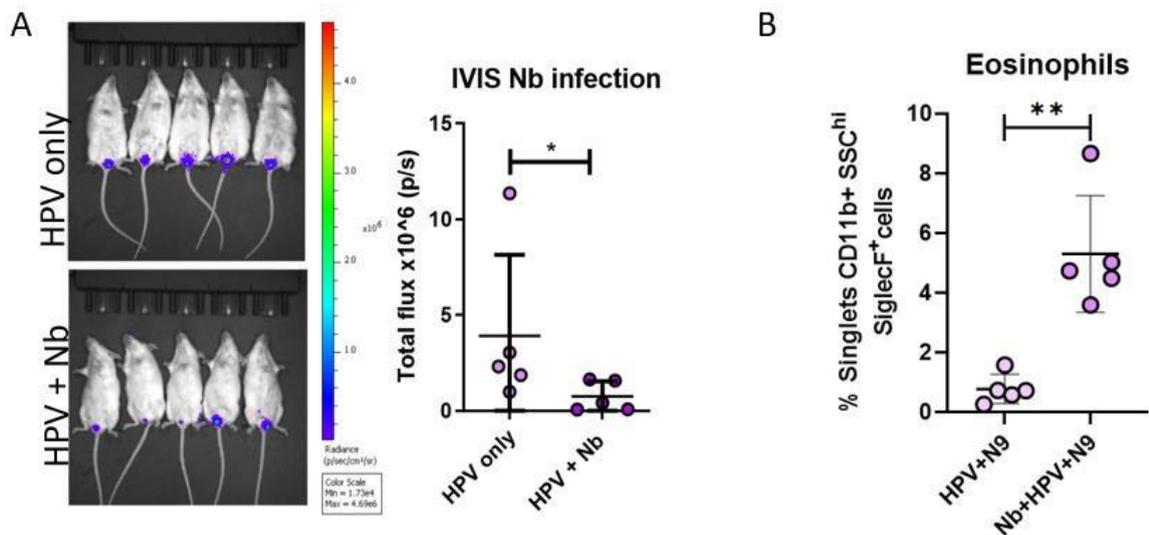


## Regulation of HPV infection following a helminth infection

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**Figure 1: *N. brasiliensis* infection decreases HPV infection in vivo.** A: female BALB/c mice were infected with *N. brasiliensis* L3 larvae. Nine days later, mice were infected intravaginally with HPV-16 pseudovirions containing a firefly luciferase reporter gene. Two days later, mice were imaged on the IVIS after intravaginal administration of luciferin. Infection with *N. brasiliensis* significantly decreased HPV infection, represented by the lower luminescent signal in the co-infected mice. B: the decrease in HPV infection was associated with an increase in eosinophils in the FGT. Nonparametric student's t-tests were performed. \* $p < 0.05$ , \*\* $p < 0.01$ .

**Introduction:** Soil-transmitted helminths (STHs) are parasitic worms common in tropical climates, including South Africa. The immunomodulatory effects of STHs have led researchers to investigate how STHs influence unrelated diseases. Human Papillomavirus (HPV) is one of the most common sexually transmitted viral infections. Persistent infections with oncogenic strains may lead to cervical cancer, a leading cause of cancer-related deaths in women in South Africa. Currently, little is known about the association between co-endemic STH and HPV infections.

**Methodology:** To determine the effect of helminth exposure on HPV risk, we used both *in vitro* and *in vivo* approaches: For *in vitro* analysis, epithelial cell lines were exposed to helminth antigens and infected with HPV-16 pseudovirions containing a Gaussia luciferase reporter gene, where luciferase is excreted extracellularly upon successful infection. For the *in vivo* coinfection model, mice were infected with murine hookworm *Nippostrongylus brasiliensis* and HPV-16 pseudovirions containing a Firefly luciferase reporter gene, where the luciferase remains within the cell following successful infection. Luminescent signal was measured using an illuminometer for *in vitro* experiments and the *In Vivo* Imaging System (IVIS) for *in vivo* experiments. The female genital tract (FGT) of mice was harvested for further immunological analysis.

**Results:** *in vitro* experiments demonstrated that exposure to helminth antigens from *N. brasiliensis* and *H. polygyrus*, decreased HPV infection in epithelial cell lines. This was then supported by *in vivo* analysis, where *N. brasiliensis* antigen exposure or infection significantly decreased HPV infection (Fig 1A). This was associated with a significant increase in eosinophil accumulation in the FGT (Fig 1B), a site that is uncolonized by the helminth.

**Discussion:** STHs elicit systemic immunomodulatory effects and have the ability to alter susceptibility to other pathogens in uncolonized tissue. Here we show that the hookworm *N. brasiliensis* decreases HPV infection in the FGT.

**Keywords:** soil-transmitted helminths, parasites, virology, immunology, mouse model, hookworm, human papillomavirus, pseudovirion