



INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI  
SHORT ABSTRACT OF THESIS



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Thesis Title: Characterization of Anatid herpesvirus 1 (vaccine strain) and understanding the role of viperin and cholesterol in its infection

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**SHORT ABSTRACT**

Anatid herpesvirus 1 (AnHV-1) is the causative agent of duck viral enteritis (DVE) of the Anatidae family. The disease is a highly contagious disease characterized by high mortality rates, decreased egg production thus can cause significant economic losses and posing major to traditional agriculture across the globe. The etiological agent of the disease AnHV-1 is a member of the family *Herpesviridae*, genus *Mardivirus*, and subfamily *Alphaherpesvirinae*.

The disease is controlled by vaccination to the flock with chick embryo adapted attenuated vaccine in developed countries. We propagated and characterized the vaccine strain of AnHV-1 in continuous cell lines Vero, DF-1, QT-35, and MDCK. Compared to chick embryo adapted live vaccine virus, heterologous cell culture system will provide a system devoid of other avian infectious agents and it can be used for propagation and cultivation of AnHV-1 vaccine strain for developing cell culture-based vaccines on a mass scale. A hallmark of a viral infection is a profound reaction by infected cells. Cytokines are released mainly secreted by immune cells in response to infection and help synchronize immune system response and, their concentration varies during infection and function as immunomodulatory. We systemically explored the expression profile of cytokines in different organs and peripheral blood mononuclear cells (PBMC). Our results showed that AnHV-1 could replicate in several tissues and the expression of several cytokines were up-regulated especially in the brain and spleen of infected ducks and well in PBMC. Modulation of innate immune-related genes upon infection with vaccine strain will provide information regarding the protective efficacy of vaccination. Interferon (IFN) response is the first line of defence against viral infection, which activate the induction of a broad array of antiviral proteins. Virus inhibitory protein, endoplasmic reticulum-associated, IFN-inducible (Viperin) is an IFN-induced protein that obstructs the replication of a variety of viruses by diverse mechanisms. We modeled the structure of chicken viperin protein and showed IFN-induced antiviral protein viperin inhibits AnHV-1 and localizes to lipid droplets in DF-1 cells. It has also been found that the concentration of cholesterol was reduced in viperin overexpressed cells. In addition, a recombinant virus expressing viperin was constructed and recovered using the Newcastle disease virus vector to interrogate its function in viral infection and another therapeutic potential.

Cholesterol is an essential component of the cell membrane and involves in the life cycle of several viruses. During the infection, the immune response also targets the lipid pathway as an approach for virus elimination. The inhibitory function of viperin is related to reduce cholesterol on the membrane of DF-1 cells. We examined the role of cholesterol for both the target cell membrane and the viral envelope. We observed that cholesterol depletion from the cellular membrane results in the inhibition of AnHV-1 infection. The inhibitory effect was moderately restored by exogenous replenishment of cholesterol. Furthermore, the inhibition of endogenous cholesterol synthesis by a statin drug also inhibited the infectivity of AnHV-1. Presumably, the removal of cholesterol from the AnHV-1 envelope might be disrupting the viral envelope resulting in its diminished infectivity. Our finding highlights the engagement of cholesterol in AnHV-1 infectivity and the cellular cholesterol level could be exploited as a potential antiviral against viral infections