Chapter 7
Summary and future prospects

Summary

Rotavirus, the foremost cause of acute infectious diarrhea in pediatric population is a serious public health problem all over the world. Considering the magnitude and associated economic burden of rotavirus infections, different approaches have been continuously attempted to develop a safe and effective intervention to accomplish reduction in the mortality, severity of disease and associated hospitalization. To date two new generation rotavirus vaccines RotaTeq and Rotarix have been licensed in the global market. However, to overcome the issues related to a low level efficacy of rotavirus vaccines in developing countries of Asia and Africa, alternate and adjunct strategies such as oral immunotherapy and antivirals are required to be explored for management of rotavirus infection.

The present study describes the preparation as well as evaluation of specific egg yolk derived immunoglobulins, anti-HRV IgYs against prototype strains of HRV serotypes (KU/G1P[8]; S2/G2P[4]; YO/G3P[8]; ST-3/G4P[6] and F-45/G9P[8]) that cause 90% of the infections in human. Immunization of SPF hens with each of the HRV serotypes yielded high titered anti-HRV IgYs with evidence of multiserotypic neutralizing activity in cell culture based neutralization assay. The anti-HRV-3 IgY was able to neutralize all of the five serotypes used in the study indicating the presence of a wider range of heterotypic neutralizing antibodies. A mouse model of gastroenteritis was developed during the study to evaluate the efficacy of anti-HRV-3 IgY as oral immunotherapy. Oral inoculation of HRV serotype 3, strain YO in 4/5 day old BALB/c mice typically induced the disease with manifestation of diarrhea and dehydration, characteristic pathological lesions and accumulation of rotaviral RNA and antigen in the intestine over a period of 5 days. The ileum was demonstrated to be the most susceptible and supportive part of small intestine for perpetuation of rotavirus infection in mice. The post rotavirus exposure administration of anti-HRV-3 IgY in mice of the present study did have a negative influence on virus replication and associated histopathology in intestine, thereby reducing the severity and duration of diarrhea in the animals. On the other hand, pre exposure treatment
with anti-HRV-3IgY presented an ideal situation, wherein IgY imparted immediate protection from development of rotavirus gastroenteritis in the mice. Thus, the findings of the present study ascertain the potential implication of anti-HRV IgY as oral immunotherapy against rotavirus infection to reduce disease burden in humans.

**Future prospects**

1. The anti-HRV IgY preparations can be explored as oral immunotherapy/immunosupplement in human to reduce the rotavirus disease burden. However, implementation of this approach would require development of a formulation containing anti-HRV IgYs and its clinical trial in different settings of the rotavirus endemic region.

2. The study could serve as a model to develop IgY based antiviral strategies against other enteric viruses of public health importance.

3. The mouse model developed and characterized in the study could be useful to study the mechanisms of rotavirus pathophysiology, innate and cellular immune responses and evaluation of attenuation of candidate vaccines of G3 origin and antivirals.

4. Use of anti-HRV IgYs can be explored in the diagnostic assay for rotavirus detection.