



Development of vaccine inducing mucosal immune responses

Outline

A large number of pathogens gain access to the human body via mucosa such as oral, nasal or genital mucosa. Therefore, the best defense against these predominantly mucosal pathogens is mucosal vaccines that are capable of inducing both systemic and mucosal immunity. It has been shown that tissue-specific gene transfer by a viral vector could be achieved naturally and effectively through cell specificity of the virus receptors. Human parainfluenza type 2 virus (hPIV2) is one of the human respiratory pathogens and a member of the genus Rubulavirus of the family Paramyxoviridae in the order Mononegavirales, possessing a single-stranded, nonsegmented and negative-stranded RNA genome. As technology advances of reverse genetics, hPIV2 became to use for potential viral vector candidates for vaccine. In the present study, we assess the capacity of a novel mucosal vaccine using recombinant hPIV2 as a vaccine vehicle to induce Ag-specific mucosal immune responses. The hPIV2 was engineered to express Ag85B of Mycobacteria(hPIV2/Ag85B). Mice inhaled with the hPIV2 /Ag85B showed a substantial reduction in the inflammation induced by Mycobacteria tuberculosis compared with control mice when the immunized mice were challenged with a Mycobacterium tuberculosis. The results of this study have provided evidence for the potential utility of a hPIV2 vector as an approach to development of mucosal vaccine.

Expected Outcome

Vaccine strategies that can stimulate mucosal and systemic immune response are useful, since many pathogenic viruses and bacteria establish their initial infections through mucosal surfaces. The hPIV2 is one of the major human respiratory pathogens without visible pathogenicity. The hPIV2 vector without M or F gene is much safer than original hPIV2 vector in our system, since M or F gene-eliminated hPIV2 can not replicate in vivo. In the present study, we investigated the potential of an hPIV2 as a nasal vaccine vehicle that presents foreign immunogenic proteins and stimulates mucosal immunity without the addition of any kind of adjuvant. These findings provide evidences for the possibility of hPIV2 as a nasal vaccine vector and its continued exploration as a vehicle for eliciting pathogen-specific immunity by nasal administration.

Development of nasal vaccine using hPIV2

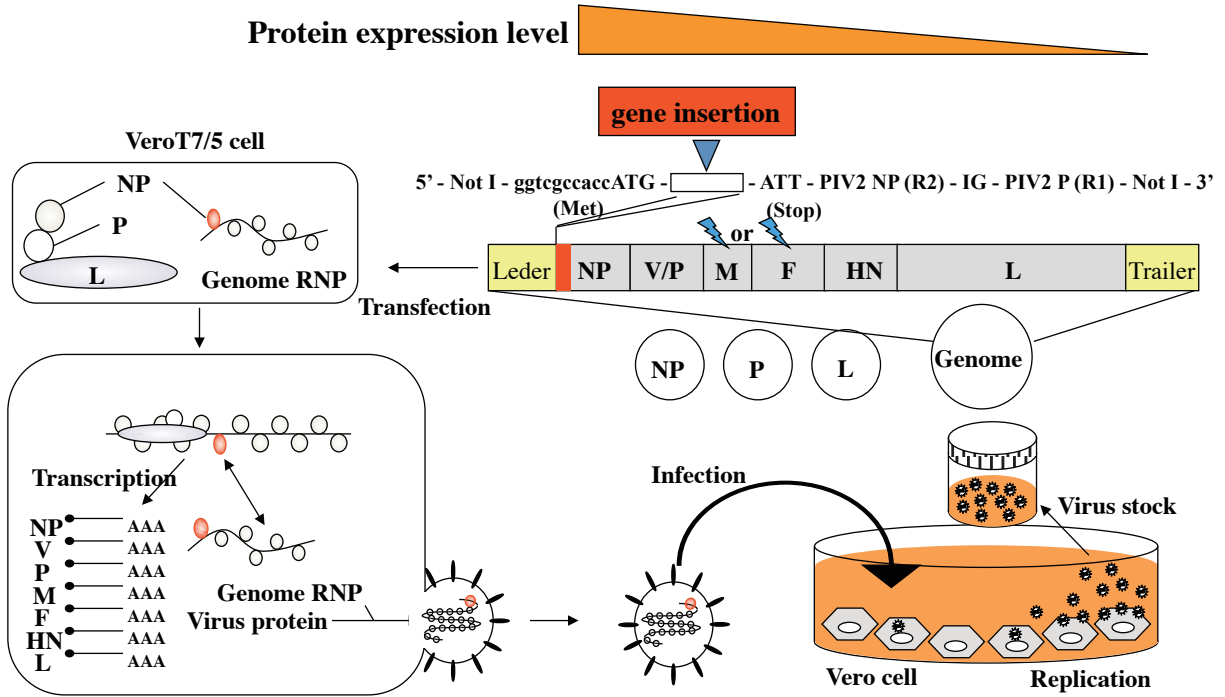
Human parainfluenza type 2 virus (hPIV2)

- Human respiratory virus
- *Rubulavirus* of the family *Paramyxoviridae*
- negative-stranded RNA genome ~ 15.6 kb
- extremely low pathogenicity
- infect with human, macaque and suckling hamster

hPIV2 vector

- developed by technology of reverse genetics
- high-level expression of products by foreign gene
- replication incompetent by elimination of M or F gene

Construction of hPIV2 vaccine



Nasal tuberculosis vaccine using hPIV2

