The sites of virus replication in the respiratory tract represent complex microenvironments, in which extracellular proteases are present in large amounts. Some of these proteases (trypsin, tryptase) can play a role both in virus replication (Riteau B. et al. 2006; LeBouder F. et al. 2008) and innate immune responses as they are important mediators of inflammatory processes through the activation of a family of receptors called Protease-Activated Receptors (PARs) (Steinhoff M. et al. 2005; Vergnolle N. et al. 2008).

To date four PARs, activated by different proteases, have been cloned (PAR1-4). After cleavage of the receptor by proteases, the newly released amino-terminal sequence binds and activates internally the receptor.

The role of PAR1 in lung IAV infection has never been documented. However elevated PAR levels of pAR1 have been observed in the airways of IAV-infected mice (Lan RS. et al. 2004), suggesting a role for this receptor in the pathogenesis of viral disease. The specific role for PAR1 activation/inactivation in vivo or in vitro has never been addressed.

SUMMARY OF THE INVENTION:

In one aspect, there is provided the use of ~~The invention relates to~~ a PAR1 antagonist in the manufacture of a medicament for ~~use in~~ the treatment or prevention of an influenza virus type A infection in a subject.

In another aspect, there is provided a pharmaceutical composition comprising (i) at least one PAR-1 antagonist, and (ii) at least one Protease- Activated Receptors -2 (PAR-2) agonist.

In yet another aspect, there is provided the use of the pharmaceutical composition as defined above in the manufacture of a medicament for the treatment or prevention of an influenza virus type A infection in a subject.

Brief description of the drawings

Figure 1 A: PAR1 agonists increase virus replication in epithelial cells. A549 were infected with IAV A/PR/8/34 and treated or not with the PAR1 agonist peptide. After the indicated times post-infection, the infectious virus titers in the culture supernatants were determined by plaque assay.