respiratory syncitial virus (RSV) from the pneumoviruses and mumps virus (MuV) from the rubulaviruses represent significant human pathogens. Whereas vaccination programmes for mumps are widely available, uptake of the triple measles, mumps and rubella (MMR) vaccine has declined owing to misrepresentation in the media concerning autism risk, leading to increased seroprevalence and multiple regional outbreaks among children. RSV remains a major issue for both juvenile health as a leading cause of severe respiratory tract infections with strong links to asthma, and also in the elderly where it is often misdiagnosed as influenza. No vaccine exists for RSV, but passive immunisation with palivizumab (Synagis) is used for high-risk infants.

Deletion of MuV SH has been shown to induce an attenuated phenotype with respect to neurovirulence; however, recent studies suggest that this is likely due to disrupted virus transcription rather than SH deficiency *per se*.[283] SH appears to be dispensable for the growth of MuV[284] or RSV[285] in many cell culture systems, yet has also been shown to antagonise TNFα-mediated apoptosis.[286,287] SH-deleted RSV replicated to 10-fold reduced titres in small animal models[288] and 40-fold lower titres than wild-type in chimpanzees with considerably reduced rhinorrhoea.[289] SH therefore appears to act as a virulence factor, playing a host-specific role in virus growth and pathology. Within infected cells, SH is present both as an unmodified 7.5 kDa species and in carbohydrate-modified forms. All forms of SH oligomerise in cells and both *in vitro* and *in silico* studies support pentameric stoichiometry.[19,20,290] although recent EM studies of recombinant SH in DHPC detergent showed the formation of both pentamers and hexamers, with pore diameters of 1.9 and 2.6 nm, respectively.[18]

SH is predicted to contain a single TM domain and so comprise a class 1 viroporin of 64 amino acids. Although no information regarding viroporin activity has been reported for MuV SH, RSV SH was shown to induce bacterial membrane permeability to small molecules such as hygromycin,[291] and peptides corresponding to both the TM domain and full-length protein form cation-selective channels in bilayers.[19] Interestingly, activity for TM peptides is reduced by low pH,[19] whereas full-length channels are activated when the pK_a is lowered below that of histidine.[20] NMR-derived models of pentameric SH protein reveal the presence of His22 within the predicted channel lumen and also His51 located towards the C-terminus of the protein; the latter is absent from TM peptides.[20] Of these, His51 is the more highly conserved of the two residues, although mutation of either in isolation to alanine retains pH-activated channel activity. Only double His mutants are defective for channel activity, suggesting that the two residues may cooperate in a redundant fashion to effect channel opening. Although inactivation of TM peptides in response to lowered pH would seemingly argue against this hypothesis, it seems that the functionality of these residues as sensors/gates is likely to be context dependent. Computer models of SH hexamers in a DOPA–DOPC bilayer predict a potential Trp15 gate residue to be present in close proximity to His22, although this would lie outside the predicted TM region (His22 to Cys43) defined by hydrogen–deuterium exchange in DMPC bilayers.[18] To date, small-molecule