A series of novel sialoglycopolypeptides carrying *N*-glycolylneuraminic acid (Neu5Gc)-containing trisaccharides having α(2 → 3)- and α(2 → 6)-linkages in the side chains of γ-polyglutamic acid (γ-PGA) were designed as competitive inhibitors against equine influenza viruses (EIV), which critically recognize the Neu5Gc residue for receptor binding. Using horse red blood cells (HRBC) we successfully evaluated the binding activity of the multivalent Neu5Gc ligands to both equine and canine influenza viruses in the hemagglutination inhibition (HI) assay. Our findings show the multivalent α2,3-linked Neu5Gc-ligands (3a–c and 7) selectively inhibit hemagglutination mediated by both influenza viruses and display a strong inhibitory activity. Our results indicate that the multivalent Neu5Gc-ligands can be used as novel probes to elucidate the mechanism of infection/adhesion of Neu5Gc-binding influenza viruses.

Chemoenzymatic synthesis of novel sialoglycopolypeptides carrying *N*-glycolylneuraminic acid-containing trisaccharides.