Book of Abstracts

2008 Health Canada Science Forum

4.08 Synthetic Receptors of the Influenza Hemagglutinin to Differentiate Human and Avian Viruses

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SUMMARY: We have used chemi-enzymatic protocols to synthesize analogues of the avian and human influenza virus receptors. Conjugated forms of the synthetic influenza receptors can be used to distinguish human and avian strains. Soluble forms of the synthetic receptors could inhibit virus binding and have potential therapeutic applications.

OBJECTIVES: To synthesize analogues of the avian and human influenza virus receptors that can be used to differentiate human and avian viruses based on the hemagglutinin specificity.

DESIGN AND METHOD: The influenza virus binds to sialylated glycans on host cells using the hemagglutinin on its surface. The specificity of a strain for a host depends on the specificity of its hemagglutinin. Human strains bind to NeuAca2,6Gal only. Avian strains bind predominantly to NeuAca2,3Gal. We have used an -2,6- and an -2,3-sialyltransferases to synthesize azidoethyl derivatives of NeuAc-2,6-lactose and NeuAc-2,3-lactose, respectively. The azidoethyl tails of the two sialyllactose derivatives were chemically reduced and used to conjugate the compounds to mouse serum albumin. The glycoconjugates were coated to ELISA plates and used to capture human (H1N1, H3N2 and Influenza B) and avian (H5N1) influenza strains.

RESULTS: We have successfully used bacterial sialyltransferases to synthesize preparative amounts (100 mg) of NeuAc-2,6-lactose-azidoethyl and NeuAc-2,3-lactose-azidoethyl. These sialyllactose derivatives were conjugated to mouse serum albumin and coated to ELISA plates. A H3N2 and a B strains bound to the NeuAc-2,6-lactose-conjugate while a H1N1 and a H5N1 strains bound to the NeuAc-2,3-lactose-conjugate.

CONCLUSIONS: This project could have diagnostic and therapeutic applications. NeuAca2,6Gal-1,4-Glc-azide could be used as a diagnostic tool to detect the human influenza virus. It could be used to differentiate human and avian influenza viruses. It could also help identify avian strains that have acquired the ability to bind to NeuAca2,6Gal; which have a higher potential for human-to-human transmission. Soluble forms of the synthetic receptors could inhibit virus binding and have potential therapeutic applications. Since the influenza virion carries a neuraminidase, the synthetic receptors need to be improved by making non-cleavable forms of the NeuAc-2,6-lactose and NeuAc-2,3-lactose. A promising approach is to synthesize S-linked sialyllactosides. This work should provide insightful information pertinent to the development of synthetic receptors useful for the detection of human and avian influenza viruses and related quality control methods for pandemic influenza vaccines.