

Selective pressure acting on influenza virus neuraminidase protein and relation with development of resistance to antiviral drugs

Correia V, Santos LA, Gíria M, Rebelo-de-Andrade H

17th International Bioinformatics Workshop on Virus Evolution and Molecular Epidemiology, 27th – 31st August 2012, Belgrade, Serbia

Abstract:

Neuraminidase (NA) protein of influenza viruses has the particularity of being under antibody and antiviral drug selective pressure, as it is one of the main surface antigens and the target of neuraminidase inhibitors (NAIs).

The aim of this study is to investigate the selective pressure (SP) acting on the NA of seasonal and pandemic influenza viruses. It comprises two objectives: (a) to evaluate the contribution of positive SP for the emergence of NAIs resistant viruses; and (b) to determine the impact of NAIs introduction into clinic and its wide use during pandemic on the SP acting on NA.

For the 1st objective it will be analysed the SP acting on the sites associated with NAIs resistance or reduction in susceptibility. The 2nd objective implies a differential evolutionary pressure analysis according to time, with 3 sub-datasets of NA sequences being considered: (1) before worldwide introduction of NAIs into clinic (1999); (2) before wide use of oseltamivir during A(H1N1)2009 pandemic (2009); and (3) from 2009 to date.

A large dataset of full-length NA coding sequences will be used for each (sub)type/variant, comprising sequences obtained at national level (since 2000/2001) and sequences available at GISAID and NCBI. A(H1N1)seasonal dataset was already created, including a total of 1523 sequences, from which 94 belong to 1st sub-dataset, 1094 to 2nd and 335 to 3rd. All SP analysis will be performed using the expertise acquired with this workshop.

This study may contribute for understanding the role of antiviral drug selective pressure in NAIs resistance, patterns of emergency of resistant viruses and NA evolution.