Within-host influenza dynamics: a small-scale mathematical modeling approach.

Manchanda H, Seidel N, Krumbholz A, Sauerbrei A, Schmidtke M, Guthke R (2014) Within-host influenza dynamics: a small-scale mathematical modeling approach. *Biosystems* 118, 51-59. PubMed

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Projects

Optimization of the influenza neuraminidase inhibitor therapy by use of secondary bacterial infections
Details

Abstract

The emergence of new influenza viruses like the pandemic H1N1 influenza A virus in 2009 (A(H1N1)pdm09) with unpredictable difficulties in vaccine coverage and established antiviral treatment protocols emphasizes the need of new murine models to prove the activity of novel antiviral compounds in vivo. The aim of the present study was to develop a small-scale mathematical model based on easily attainable experimental data to explain differences in influenza kinetics induced by different virus strains in mice. To develop a three-dimensional ordinary differential equation model of influenza dynamics, the following variables were included: (i) viral pathogenicity (P), (ii) antiviral immune defense (D), and (iii) inflammation due to pro-inflammatory response (I). Influenza virus-induced symptoms (clinical score S) in mice provided the basis for calculations of P and I. Both, mono- and biphasic course of mild to severe influenza induced by three clinical A(H1N1)pdm09 strains and one European swine H1N2 virus were comparatively and quantitatively studied by fitting the mathematical model to the experimental data. The model hypothesizes reasons for mild and severe influenza with mono- as well as biphasic course of disease. According to modeling results, the second peak of the biphasic course of infection is caused by inflammation. The parameters (i) maximum primary pathogenicity, (ii) viral infection rate, and (iii) rate of activation of the immune system represent most important parameters that quantitatively characterize the different pattern of virus-specific influenza kinetics.

Identifier

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