Modeling the Impact of Inoculum Dose on Within-host Virus Dynamics

Yan Li[1], Andreas Handel[1,2]

***Short Abstract* — The outcome of any infection results from a complicated interplay between the pathogen and the host's immune response (IR). The number of pathogens that start an infection – inoculum dose – often has strong impact on the infection dynamics. For acute virus infections, a higher inoculum dose often results in earlier and higher virus peak. The purpose of our study is to understand and model the impact of inoculum dose on within-host virus dynamics. We found that experimentally observed virus data can be reproduced with mathematical models that contain some form of pathogen-independent IR, models without IR or with only pathogen-dependent IR can't do it.**

***Keywords* — inoculum dose-dependent virus dynamics, virus peak, time required to the virus peak, virus increase rate, pathogen-independent IR, pathogen-dependent IR.**

I. Introduction

THE outcome of any infection results from a complicated interplay between pathogen and the host's immune response (IR) [1]. Viruses, small infectious agents, can infect almost all types of organisms, they replicate inside the living cells of organisms to cause infectious diseases. Usually, the number of viruses that start a virus infection – inoculum dose – often has strong impact on the infection dynamics. For acute virus infections, a higher inoculum dose often results in earlier and higher virus peak levels with faster virus increase rate [2-5].

Mathematical models have been widely used to gain quantitative understandings of within-host virus dynamics of many different virus infections [1,7]. However, until now on the impact of inoculum dose on within-host virus dynamics has not been studied by mathematical models.

The purpose of our study is to understand and model the impact of inoculum dose on within-host virus dynamics. We characterized the within-host virus growth features, including virus peak, time required to the virus peak, virus increase rate, and infectious duration, as a function of inoculum doses from experimentally observed virus titer results [2-5], and found that we can reproduce experimentally observed virus data with mathematical models that contain some form of pathogen-independent IR. Models without IR or with only pathogen-dependent IR can not reproduce experimentally observed virus data.

[1]Institute of Bioinformatics, the University of Georgia, Athens, GA, USA. E-mail: yanli@uga.edu

[2]Department of Epidemiology and Biostatistics, the University of Georgia, Athens, GA, USA. E-mail: ahandel@uga.edu

II. Result and Conclusion

The time series virus titer results from four different acute virus infection experiments [2-5] were fitted very well by the phenomenological empirical equation [6]. The characterized within-host virus growth features with this empirical equation elucidated that the direct inoculum dose-dependent relationship can be seen from virus peak, timer required to the virus peak, and virus increase rate, but no obvious trend can be seen for the infectious duration. As inoculum dose increased, virus peak and virus increase rate increased as well, but time required to the virus peak decreased.

To reproduce such inoculum dose-dependent within-host virus dynamics, mathematical models without IR and with IR have been systematically explored [7]. Mathematical models exploration revealed that models without host IR or with only pathogen-dependent IR can not reproduce the experimentally observed virus data.

However, we can reproduce the inoculum dose-dependent experimentally observed virus data with mathematical models that contain some form of pathogen-independent IR. This indicated that biologically pathogen-independent IR plays an important role on the inoculum dose-dependent within-host virus dynamics, and it should not be neglected by mathematical modeling study.

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