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Determinants of the early hepatitis C viral decline after treatment initiation

The standard model of HCV infection and treatment (Neumann et al., 1998, Science 282(5386):103-107) has played an important role in the analysis of HCV RNA decay after the initiation of interferon (IFN)-based therapy. Using this model and assuming that IFN rapidly reduces the average rate of virion production, it has been possible to estimate the antiviral effectiveness of therapy, as well as to estimate the rate of HCV clearance rate. However it will be shown that this model cannot predict the early viral decline observed with some new direct-acting antiviral (DAA) agents if one uses the HCV clearance rate estimated during IFN-based therapy, which hints that the determinants of HCV decline under treatment may not be fully understood.

Indeed one limitation of the standard model is that the intracellular viral replication, which is directly targeted by DAA agents, is not taken into account. In order to provide a more comprehensive understanding of the determinants of the early viral decline after treatment initiation, a new multi-scale model that considers both intra- and extra-cellular level of infection will be introduced. Simulation studies will show that in the framework of this model, the analysis of HCV RNA decay allows to one to dissect the antiviral effectiveness in blocking different stages of viral replication. Based on data from several clinical trials, HCV kinetics under different classes of DAAs will be compared and the implications of this new approach for the estimation of the HCV clearance rate will be discussed.