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Preface

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Preface

Three events in the last 20 years stand out as shaping our current understanding of the dynamics of virus infections. First, the emergence of the human immunodeficiency virus (HIV) epidemic gave impetus to the study of persistent viruses, which were previously thought to cause only rare and unimportant diseases. There is still an urgent need to answer basic questions on the dynamics of HIV infection: Can the virus be eradicated from latent reservoirs? Must an effective HIV vaccine, whether therapeutic or preventive, give persistent antigenic stimulation? Is HIV-1-mediated toxicity or the immune response more important in depleting the $CD4^+$ T cells?

Second, the invention of the polymerase chain reaction has simplified not only the detection and quantification of viruses, but also the detection of viral sequence variation, allowing formal tests of immune escape and evolution. The third event was the development of synthetic tetramers of HLA class I molecules as ligands to identify and quantify peptide-specific $CD8^+$ T lymphocytes. This technique has dramatically increased the speed and precision of experiments on antiviral T-cell responses, and has made it possible to quantify antigen-specific cells without the danger of unwanted selection *in vitro*. Because of the special importance of $CD8^+$ T cells in the immune response to viruses, the use of these class I tetramers has had a remarkable impact on the field within four years: see, for example, the article by Doherty *et al*. (this issue). Of course, these events have been accompanied by fundamental advances in immunology, particularly, in this regard, the elucidation of T-cell recognition of antigen at the molecular level.

So, why is it important to understand virus dynamics? The answer is because it is increasingly clear that the dynamics of virus replication and the immune response directly determine the clinical outcome of the infection. In many persistent virus infections, the rate of progression and the risk of disease are strongly correlated with the virus load at equilibrium, or quasi-equilibrium in the case of HIV-1. In transient virus infections, the relative kinetics of virus replication and the immune response determine the amount of tissue damage and inflammation that are caused; this can make the difference between life and death of the host.

However, HIV is not the only persistent virus. In the last 20 years many new viruses have been discovered, and it has become obvious that many viruses persist for the lifetime of the host. New viruses will continue to emerge, and as always in biology each will have its own lessons to teach us.

Mathematics has an essential and growing importance in this emerging field of virus dynamics, not because of inherent dynamical complexity in the individual processes of virus replication and the immune response, but rather because there are many such processes, all of which are highly interdependent. This is why intuition can be an unreliable guide to understanding these dynamics. No experiment will ever (*pace* Karl Popper) prove the truth of a mathematical model, but a model can formally prove the inadequacy of a given set of assumptions.

The papers in this issue reflect the range of current interests in the field of virus dynamics, from molecular immunology to mathematics. We anticipate with excitement the general rules that will emerge in the field in the next few years.

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