Hamilton Institute

Combining Pharmacology and Mutational Dynamics to Understand and Combat Drug Resistance in HIV

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Abstract:
The cure for HIV remains to be found, even after 25 years of research. The use of highly active antiretroviral therapy (HAART) has led to a dramatic decline in morbidity associated with the infection. However, the virus develops drug resistance, thereby eliminating treatment options and putting the patient in risk of death. Up to now, the mechanisms of resistance development are poorly understood.
A population of species (like HIV) can respond to a novel threat (drug treatment) by generating offspring with an adapted phenotype (drug resistance).
During the first month of HAART, the concentration of virus in the blood is reduced by at least five orders of magnitude. This reduction of viral abundance is, however, not paralleled by a reduction in the probability to develop resistance.
Stable, ongoing replication of HIV in compartments, which are not reflected by clinical measurements (HIV concentration in the blood), might explain this inconsistency. The reasons for insufficient drug penetration, and consequently -inhibition, can be elucidated by studying the pharmacology of antiviral drugs.
While the two aspects, pharmacology and viral dynamics are often studied separately, we aim at combining them. To this end, we developed mathematical modeling approaches that enable to simultaneously consider the pharmacology of drugs, their distinct mechanism of action, viral dynamics and the ability of the virus to adapt to the pharmacological challenge. The mathematical models are constructed in a way that allows the use of various *in vitro* and *in vivo* data for parameterization. Consequently, the models can be used to study reasons for resistance emergence.

Venue: Seminar Room, Hamilton Institute, Rye Hall, NUI Maynooth

Time: 2.00 - 3.00pm (followed by tea/coffee)

Travel directions are available at www.hamilton.ie

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