

Invited talk:

Repeated low-dose challenge with Simian Immunodeficiency Virus: what can we learn about the role of exposure history and variation in susceptibility?

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To assess the efficacy of HIV vaccine candidates or preventive treatment preclinically, many research groups have started to challenge monkeys repeatedly with low virus doses. These data provide a unique opportunity to assess the importance of exposure history for the acquisition of the infection. I used simple stochastic models to analyze previously published infection experiments involving repeated low-dose challenges. In the mathematical models I allow for differences in the probability of infection across challenges, or across animals. I find no evidence for an immunizing effect of non-infecting challenges in any of the datasets I analyze. There is also no detectable variation in the susceptibilities to the challenges across animals. These results validate the repeated low-dose challenge approach to testing HIV vaccines preclinically: without immunization by non-infecting challenges the repeated low-dose challenge approach will yield the increase in statistical power that has previously been hypothesized. Beyond the preclinical testing of HIV vaccines, these findings corroborate a central assumption in mathematical models forecasting the epidemiological spread of HIV, namely that the exposure history of susceptibles can be neglected. In particular, the lack of evidence for an immunizing effect of exposure casts doubt on the predominant explanation for the resistance of highly exposed, but persistently seronegative individuals, according to which resistance is the result of frequent exposure to HIV.