Abstract Submitted
for the MAR16 Meeting of
The American Physical Society

The kinetics and location of intra-host HIV evolution to evade cellular immunity are predictable JOHN BARTON, Massachusetts Inst of Tech-MIT, NILU GOONETILLEKE, University of North Carolina, THOMAS BUTLER, Massachusetts Inst of Tech-MIT, BRUCE WALKER, Ragon Institute of MGH, MIT Harvard, ANDREW MCMICHAEL, University of Oxford, ARUP CHAKRABORTY, Massachusetts Inst of Tech-MIT — Human immunodeficiency virus (HIV) evolves within infected persons to escape targeting and clearance by the host immune system, thereby preventing effective immune control of infection. Knowledge of the timing and pathways of escape that result in loss of control of the virus could aid in the design of effective strategies to overcome the challenge of viral diversification and immune escape. We combined methods from statistical physics and evolutionary dynamics to predict the course of *in vivo* viral sequence evolution in response to T cell-mediated immune pressure in a cohort of 17 persons with acute HIV infection. Our predictions agree well with both the location of documented escape mutations and the clinically observed time to escape. We also find that that the mutational pathways to escape depend on the viral sequence background due to epistatic interactions. The ability to predict escape pathways, and the duration over which control is maintained by specific immune responses prior to escape, could be exploited for the rational design of immunotherapeutic strategies that may enable long-term control of HIV infection.

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Date submitted: 05 Nov 2015 Electronic form version 1.4