A Quantitative Genetic Interaction Map of HIV Infection

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We have developed a platform for quantitative genetic interaction mapping using viral infectivity as a functional readout and constructed a viral host-dependency epistasis map (vE-MAP) of 356 human genes linked to HIV function, comprising >63,000 pairwise genetic perturbations. The vE-MAP provides an expansive view of the genetic dependencies underlying HIV infection and can be used to identify drug targets and study viral mutations. We found that the RNA deadenylase complex, CNOT, is a central player in the vE-MAP and show that knockout of CNOT1, 10, and 11 suppressed HIV infection in primary T cells by upregulating innate immunity pathways. This phenotype was rescued by deletion of IRF7, a transcription factor regulating interferon-stimulated genes, revealing a previously unrecognized host signaling pathway involved in HIV infection. The vE-MAP represents a generic platform that can be used to study the global effects of how different pathogens hijack and rewire the host during infection.
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