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Human immunodeficiency virus impairs reverse cholesterol transport from macrophages

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We demonstrate that HIV-1, via Nef, impairs ATP-binding cassette transporter A1 (ABCA1)-dependent cholesterol efflux from human macrophages. At least two mechanisms were involved: first, HIV infection and transfection with Nef induced post-transcriptional down-regulation of ABCA1; and second, Nef caused redistribution of ABCA1 to the plasma membrane and inhibited internalization of apolipoprotein A-I. Binding of Nef to ABCA1 was required for down-regulation and redistribution of ABCA1. Stimulation of cholesterol efflux from macrophages reduced infectivity of produced virions, and this effect correlated with a decreased amount of virion-associated cholesterol. Therefore, impairment of cholesterol efflux is essential to viral replication as it ensures proper cholesterol content in nascent HIV particles. This impairment may be a contributing factor to atherosclerosis in HIV patients.