

Protease inhibitor resistance involves multiple stages of the HIV-1 life cycle

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HIV-1 protease inhibitors are very effective antiviral drugs. These drugs target HIV-1 proteases, which are required for viral replication. Despite the success of protease inhibitors for suppressing HIV-1, some patients do not respond to protease inhibitor therapy. For most patients, the lack of response is not due to mutation of the HIV-1 protease.

In this issue of the *Journal of Clinical Investigation*, Robert Silcano and colleagues at Johns Hopkins University identify the effects of protease inhibitors on different stages of viral replication. The authors found that protease inhibitors do not prevent virus release from infected cells, but do prevent viral entry into new cells, and have an effect on the reverse transcription and post-transcription stages of the HIV-1 life cycle.

Additionally, mutations in the viral [envelope protein](#), which is involved in cell entry, were associated with resistance to protease inhibitor treatment. In the accompanying Attending Physician article, John Bartlett of Duke University discusses how these findings may dictate testing for HIV-1 envelope mutations in patients that have not responded to treatment with [protease inhibitors](#).

More information: Multi-step inhibition explains HIV-1 protease inhibitor pharmacodynamics and resistance, *J Clin Invest.* 2013;123(9):3848–3860. [DOI: 10.1172/JCI67399](https://doi.org/10.1172/JCI67399)

Lack of protease inhibitor resistance following treatment failure—too good to be true? *J Clin Invest.* 2013;123(9):3704–3705. [DOI: 10.1172/JCI71784](https://doi.org/10.1172/JCI71784)

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