Retrovirology

BioMed Central

Poster presentation



# Structural basis for HIV-1 DNA integration in the human genome

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*from* Frontiers of Retrovirology: Complex retroviruses, retroelements and their hosts
Montpellier, France. 21-23 September 2009

Published: 24 September 2009

*Retrovirology* 2009, **6**(Suppl 2):P79 doi:10.1186/1742-4690-6-S2-P79

This abstract is available from: http://www.retrovirology.com/content/6/S2/P79



Integration of the human immunodeficiency virus type 1 (HIV-1) cDNA into the human genome is catalyzed by the viral integrase protein that requires the lens epithelium-derived growth factor (LEDGF), a cellular transcriptional coactivator. In the presence of LEDGF, integrase forms a stable complex *in vitro* and importantly becomes soluble by contrast with integrase alone which aggregates and precipitates. Using cryo-electron microscopy (EM) and single-particle reconstruction, we obtained three-dimensional structures of the wild type full length integrase-LEDGF complex with and without DNA [1]. The stoichiometry of the complex was found to be $(integrase)_4$-$(LEDGF)_2$ by mass spectrometry analysis and existing atomic structures were unambiguous positioned in the EM map. *In vitro* functional assays reveal that LEDGF increases integrase activity likely in maintaining a stable and functional integrase structure. DNA-Protein cross-linking experiments show specific interaction between viral DNA and the C-terminal domain of integrase. Upon DNA binding, IN undergoes large conformational changes. Cryo-EM structure underlines the path of viral and target DNA and a model for DNA integration in human DNA is proposed (see fig. 1, overleaf).

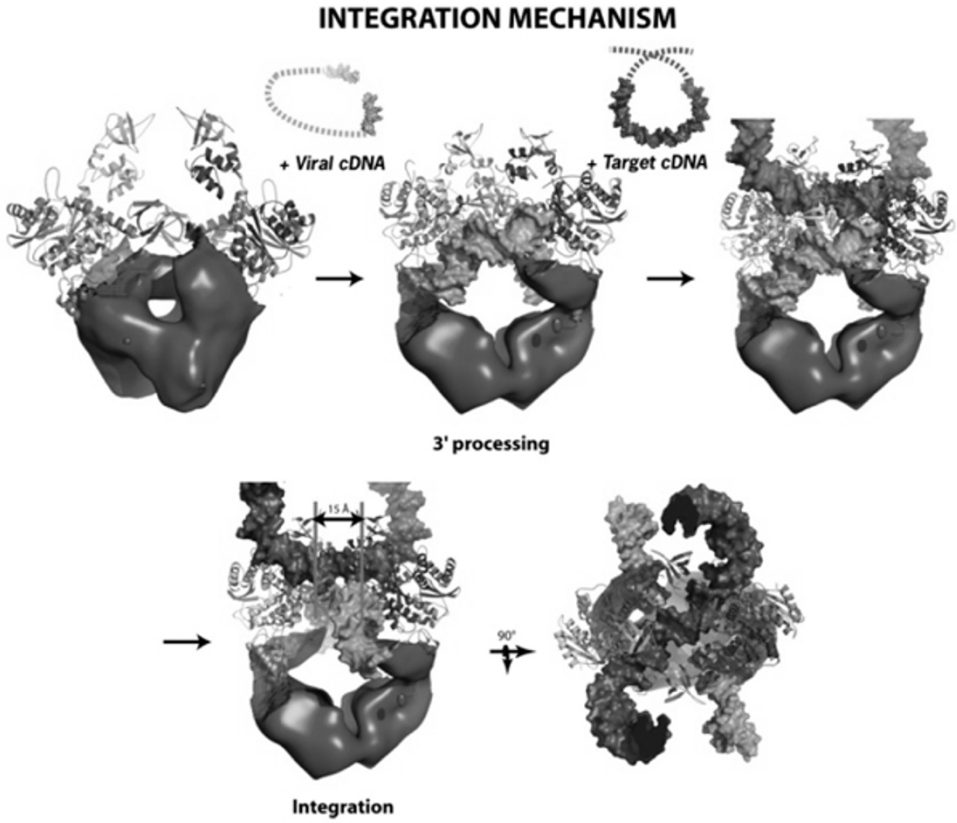


**Figure 1**
**Proposed mechanism for thei ntegration of viral cDNA into the host genome**: The LEDGF envelope is represented in blue; the integrase tetramer is shown as atomic structures. The viral DNA is in orange and the target DNA in red. On target DNA binding, there is a conformational change of the integrase proteins to position the viral DNA for the integration within 5 bases pairs in the target DNA.

## References

1. Michel F, Crucifix C, Granger F, Eiler S, Mouscadet JF, Korolev S, Agapkina J, Ziganshin R, Gottikh M, Nazabal A, Emiliani S, Benarous R, Moras D, Schultz P, Ruff M: **Structural basis for HIV-1 DNA integration in the human genome, role of the LEDGF/P75 cofactor.** *EMBO J* 2009, **28:**980-991.