



HAL
open science

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

Fabrice Michel, Sylvia Eiler, Florence Granger, Jean-François Mouscadet, Marina Gottikh, Alexis Nazabal, Stéphane Emiliani, Richard Benarous, Dino Moras, Patrick Schultz, et al.

► **To cite this version:**

Fabrice Michel, Sylvia Eiler, Florence Granger, Jean-François Mouscadet, Marina Gottikh, et al.. Structural basis for HIV-1 DNA integration in the human genome. *Frontiers of Retrovirology: Complex retroviruses, retroelements and their hosts*, Sep 2009, Montpellier, France. pp.P79, 10.1186/1742-4690-6-S2-P79 . inserm-00663599

HAL Id: inserm-00663599

<https://inserm.hal.science/inserm-00663599v1>

Submitted on 27 Jan 2012

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Poster presentation

Open Access

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

Fabrice Michel¹, Sylvia Eiler¹, Florence Granger¹, Jean-François Mouscadet², Marina Gottikh³, Alexis Nazabal⁴, Stéphane Emiliani⁵, Richard Benarous⁶, Dino Moras¹, Patrick Schultz¹ and Marc Ruff*¹

Address: ¹IGBMC, UDS, U596 Inserm, UMR7104 CNRS, 67404 Illkirch; France, ²Laboratoire de Biotechnologie et Pharmacologie Génétique Appliquée, CNRS, UMR8113, ENS-Cachan, 94235 Cachan, France, ³Belozersky Institute of Physico-Chemical Biology, Moscow State University, 119992 Moscow, Russia, ⁴CovalX, Technoparkstrasse, 1, CH-8005, Zürich, Switzerland, ⁵Institut Cochin, Université Paris Descartes, CNRS (UMR8104), Inserm, U567, Paris, France and ⁶CellVir SAS, Evry, France; Hybrigenics SA, Paris, France

* Corresponding author

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

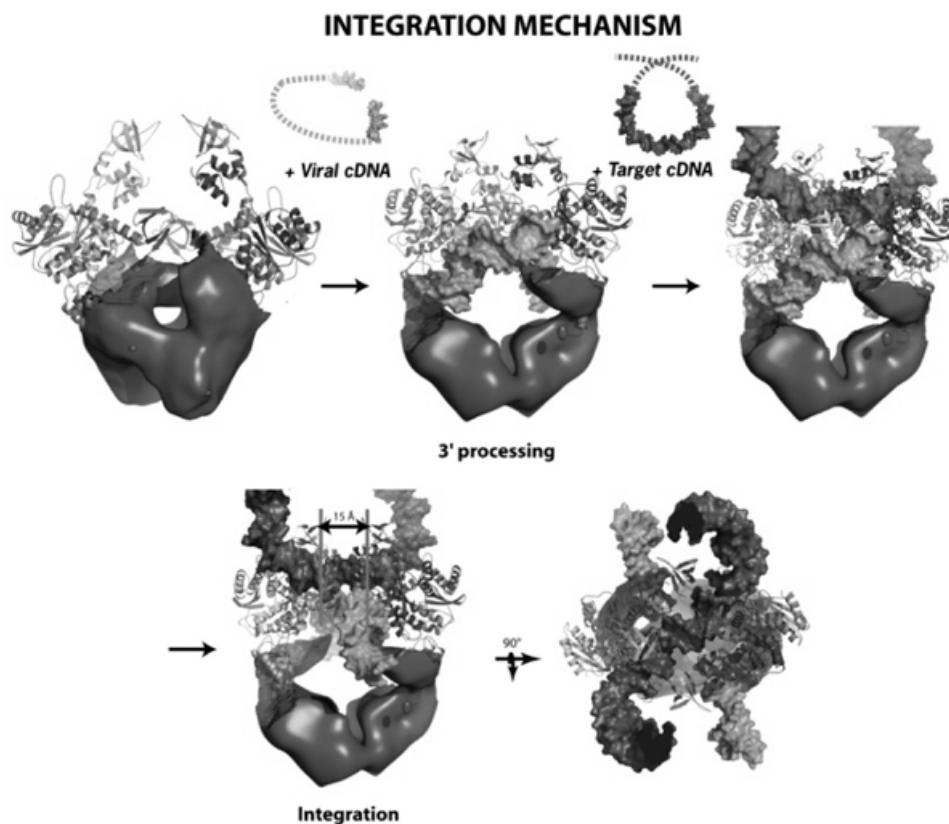
Published: 24 September 2009

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>

© 2009 Michel et al; licensee BioMed Central Ltd.

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 unambiguously 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 the integration 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.

Publish with **BioMed Central** and every scientist can read your work free of charge

"BioMed Central will be the most significant development for disseminating the results of biomedical research in our lifetime."

Sir Paul Nurse, Cancer Research UK

Your research papers will be:

- available free of charge to the entire biomedical community
- peer reviewed and published immediately upon acceptance
- cited in PubMed and archived on PubMed Central
- yours — you keep the copyright

Submit your manuscript here:
http://www.biomedcentral.com/info/publishing_adv.asp

