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Oral presentation

Transcription factor binding aites in the pol gene intragenic regulatory region of HIV-1 are important for virus infectivity

Stéphane de Walque, Caroline Vanhulle, Nathalie Vandenhoudt, Benoît Van Driessche, Arsène Burny and Carine Van Lint*

Address: Laboratory of Molecular Virology, University of Brussels, 6041 Gosselies, Belgium

Email: Carine Van Lint* - cvlint@ulb.ac.be

* Corresponding author

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We have previously identified in the pol gene of HIV-1 a new positive transcriptional regulatory element associated with a nuclease-hypersensitive site (HS7) and containing recognition sites for nuclear proteins [1]. We have next further physically characterized each binding site and have shown that the transcription factors Oct-1, Oct-2, PU.1, Sp1 and Sp3 interact in vitro with the pol region. Chromatin immunoprecipitation assays using HIV-infected cell lines demonstrated that Sp1, Sp3, Oct1 and PU.1 are recruited to the HS7 region in vivo. For each site, we have identified mutations abolishing factor binding to their cognate DNA sequences without altering the underlying amino acid sequence of the integrase. By transient transfection assays, we have demonstrated the involvement of the pol binding sites in the transcriptional enhancing activity of the intragenic region. Our functional results with multimerized wild-type and mutated pol binding sites separately have demonstrated that the PU.1, Sp1, Sp3 and Oct-1 transcription factors regulate the transcriptional activity of a heterologous promoter through their respective HS7 binding sites. Finally, we have investigated the physiological role of the HS7 binding sites in HIV-1 replication and have shown that these sites are important for viral infectivity [2]. Current studies are examining the role of AP-1 binding sites located upstream of the HS7 region in the enhancer activity and in the viral replication cycle.

References

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