Retrovirology

Poster presentation

Proteasome-associated PAAF1 links nucleosome assembly to transcriptional elongation

Mirai Nakamura*[1], Daniel Latreille[2], Irina Lassot[1], Monsef Benkirane[2] and Rosemary Kiernan*[1]

Address: [1]Laboratoires de Régulation des Gènes, Institut de Génétique Humaine, CNRS UPR1142, Montpellier, France and [2]Virologie Moléculaire, Institut de Génétique Humaine, CNRS UPR1142, Montpellier, France

* Corresponding authors

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Increasing evidence suggests that the ubiqutin/proteasome system is directly involved in the regulation of transcription. The human proteasome-associated protein, PAAF1 regulates proteasome assemble and is required for recruitment of 19S-like complex to the HIV-1 promoter by Tat that stimulates transcriptional elongation (Lassot *et al.*, 2007).

Here, we show that PAAF1 is required to couple transcriptional elongation to nucleosome reassembly. Ablation of PAAF1 using siRNA in HeLa cells containing a stably integrated HIV-1 promoter increases HIV-1 transcription. However, the transcripts are largely defective and not result in protein synthesis. ChIP analysis revealed a paucity of core histones as well as an aberrant accumulation of RNA polymerase II particularly at the promoter-proximal region of the LTR in PAAF1 knock-down cells.

We also found that the protein level of the histone chaperone, hSpt6, is decreased post-transcriptionally in PAAF1 knockdown cells. Knockdown of Spt6, like that of PAAF1, showed histone depletion and increased HIV-1 transcription. Furthermore, the phenotype of PAAF1 knock-down could be rescued by over-expression of hSpt6 or inhibition of proteasome activity. PAAF1, as well as hSpt6 and RNA polymerase II, localizes to sites of HIV-1 transcription. Together, these findings suggest that PAAF1 is required for transcriptional elongation through chromatin via regulation of hSpt6