

Control of Retroviral DNA Integration by Cellular Factors

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We have investigated the mechanisms by which HIV targets DNA integration in the human genome. Previous genome-wide studies of HIV DNA integration revealed that transcription units are favored targets. Avian sarcoma-leukosis virus (ASLV) and murine leukemia virus (MLV), in contrast, showed different favored integration targets. MLV favors sequences encoding transcription start sites, while ASLV targets sites sprinkled around the genome in a near-random fashion. Analysis of the effects of gene activity by transcriptional profiling

revealed that HIV integration is particularly favored in active transcription units. Thus each of the three retroviruses analyzed showed unique target site preferences, suggesting that each type of integration complex makes virus-specific interactions with chromatin that guide site selection. We report the identification of a human cell transcription factor that, when mutant, results in reduced HIV DNA integration in transcription units. Genes responsive to this factor could be identified by transcriptional profiling, and these genes could be shown to be preferential targets for HIV DNA integration. Further progress in this area will be discussed.