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Gene Silencing in HIV-1 Latency by Polycomb Repressive Group

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Latently infected memory T cells, which are a major obstacle to HIV-1 eradication, are very rare (1 million) in a patient and have a long half-life of over 44 months on average. The molecular linkage between HIV-1 latency and epigenetic control is not fully understood. We investigated HIV-1 latency related with Polycomb group (PcG)-proteins mediated gene silencing in novel HIV-1 latently infected cell lines, NCHA cells. The expression profiles for histone deacetylases (HDACs) and PcG proteins (EED, BMI1, RING2) in NCHA cells were characterized by RT-PCR, ELISA, IP, and western blot. The levels of histone acetylation and methylation at histone H3 Lys⁹ (H3K9) and Lys²⁷ (H3K27) in HIV-1 latently infected cells were analyzed by western blot and chromatin immunoprecipitation-sequencing (ChIP-seq).

Histone H3K9 and H3K27 acetylations in NCHA cells showed no difference in parental and NCHA cells, whereas the levels of di- and tri-methylation at histone H3K9 and H3K27 were dramatically increased in NCHA cells except ACH2 cells. The expression of EED which is a component of polycomb repressive complex 2 (PRC2), and BMI-1 and RING2 which are constituents of PRC1 were upregulated in NCHA cells. In addition, more ubiquitylation at histone H2A was detected in NCHA cells. Also, high enrichment of H3K9me3 in the chromatin states of HIV-1 proviral genome was observed in HIV-latent cells, whereas there was no enrichment of H3K27me3.

Our result demonstrates that tri-methylation of H3K27 and H2A ubiquitylation via polycomb repressive complexes should be involved in HIV-1 latency and contribute to epigenetic gene silencing.

Biography

Dr. Kyung-Chang Kim has completed his Ph.D from Korea University, Korea, in this year. He is the staff scientist of Korea National Institute of Health. He works in a diagnosis of HIV and researches on HIV Latency.