World Academy of Science, Engineering and Technology
International Journal of Biotechnology and Bioengineering
Vol:11, No:05, 2017

Potential Activities of Human Endogenous Retroviral kDNA in Melanoma Pathogenesis and HIV-1 Infection

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Abstract : Human endogenous retroviral elements (HERVs) comprise approximately 8% of the human genome. They are thought to be germline-integrated genetic remnants of retroviral infections. Although HERV sequences are highly defective, some, especially the K type (HERV-K), have been shown to be expressed and may have biological activities in the pathogenesis of cancer, chronic inflammation and autoimmune diseases. We found that HERV-K GAG and ENV proteins were strongly expressed in pleomorphic melanoma cells. We also detected a critical role of HERV-K ENV in mediating intercellular fusion and colony formation of melanoma cells. Interestingly, we found that levels of HERV-K GAG and ENV expression correlated with the activation of ERK and loss of p16INK4A in melanoma cells, and inhibition of MEK or CDK4, especially in combination, reduced HERV-K expression in melanoma cells. We also performed a reverse transcription-polymerase chain reaction (RT-PCR) assay using DNase I digestion to remove “contaminating” HERV-K genomic DNA and examined HERV-K RNA expression in plasma samples from HIV-1 infected individuals. We found a covariation between HERV-K RNA expression and CD4 cell counts in HIV-1 positive samples. Although a causal link between HERV-K activation and melanoma development, and between HERV-K activation, HIV-1 infection and CD4 cell count have yet to be determined, existing data support the further research efforts in HERV-K.

Keywords : CD4 cell, HERV-K, HIV-1, melanoma
Conference Title : ICMBB 2017 : International Conference on Molecular Biotechnology and Bioinformatics
Conference Location : Rome, Italy
Conference Dates : May 04-05, 2017