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Involvement of Tat Gene in Transcription of HIV Genes

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DESCRIPTION

Tat is a crucial gene that influences HIV replication, HIV departure from latency, and the development of AIDS by boosting the transcription of all HIV genes. The Tat gene regularly mutates *in vivo* and generates variations with different activities, which helps to create drug-resistant clones and heterogeneity in the HIV virus. In order to better comprehend AIDS pathogenesis and therapy, it will be helpful to determine the transcriptional activities of Tat variants. The missense mutation map of all single amino acid Tat variations was recently reported by our team. A portion of the double missense variants in these studies showed intragenic epistasis. However, conducting tests to ascertain the impact of the variations for all double mutant alleles would be too time and money consuming. So, we suggest a GigaAssay/deep learning combination strategy. We tested a deep learning approach using previously published GigaAssay experiments to forecast how transcription activity is impacted by Tat variants with single missense substitutions as a first step to determining activity landscapes for complicated variants. When comparing the expected and experimental actions, our method obtained a 0.94 Pearson correlation coefficient. For a better grasp of the genetic regulation of HIV genome transcription, this hybrid method can be extended to more complicated Tat alleles.

Acquired Immunodeficiency Syndrome (AIDS), which is brought on by the Human Immunodeficiency Virus (HIV), is characterised by a gradual immune system breakdown. With 1,189,700 infected individuals, 18,489 yearly fatalities, and medical costs surpassing $ 50 billion annually, it continues to be a significant health issue in the United States. HIV's replicated RNA genome lacks proofreading and has a high mutation rate of 1 in 10^4 bp, with each 9 kB genome of a virion containing about 10 novel variations. Additionally, a single person with a current HIV virus is thought to produce 10^{11} virions every day. High mutation rates and effective virion production result in a community of viral genomes that is extremely genetically varied and heterogeneous, which is crucial for key pathogenic processes like Antiretroviral Treatment (ARV) resistance, latency, and strain evolution. Variant virions with drug-resistant variants may live and spread after selective pressure from ARV treatment, limiting therapeutic effectiveness. In order to comprehend the pathogenesis of AIDS and how to cure it, it is crucial to understand how HIV develops both within an individual and in global populations.

Premature ageing has been linked to HIV-1 infection in the period of combined antiretroviral treatment. Astrocyte senescence has been hypothesised as a possible factor in HIV-1-induced brain ageing and neurocognitive deficits among other characteristics of HIV-1 related neurocognitive diseases. Recently, it has also been suggested that lncRNAs play crucial parts in the beginning of cellular senescence. Here, we looked into the function of lncRNA TUG1 in the HIV-1 Tat-mediated start of astrocyte senescence using Human Primary Astrocytes (HPAs). We discovered that HPAs subjected to HIV-1 Tat significantly upregulated the expression of the lncRNA TUG1, along with increased expression of p16 and p21, respectively.

As the rates of prescribed and illicit opiate use including the use of street drugs laced with fentanyl and associated overdoses rise, Opioid Use Disorder (OUD) is becoming a more serious issue not only in the United States but around the globe. In addition to worsening the aetiology of neuro HIV and HIV-associated neurocognitive disorders, opioid abuse can raise the chance of contracting bloodborne illnesses like HIV-1. The overlapping conditions of OUD, HIV, and mood illnesses can make therapy more challenging and result in lower drug adherence.

It's significant to note that major depressive disorder is also considered to be influenced by the neuropathogenic processes

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thought to underlie HAND and opioid-induced neuro HIV exacerbation (such as neuroinflammation and synaptodendritic injury). The prevalence of self-reported depressive symptoms is believed to be around 40% in HIV-positive people (PWH), and clinical investigations have shown that MDD rates in PWH are two times greater than those in HIV-negative controls. Neuropsychiatric diseases are a significant health issue for PWH.

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CONFLICT OF INTEREST

There are no conflicts of interest.