Short Communication

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Journal of Geriatric Research

2022
Vol 6. No. 4

Human born a disease virus infection impacts host proteome andhistone lysine acetylation in human oligodendroglia cells

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Abstract

Borna disease virus (BDV) replicates in the nucleus and establishes persistent infections in mammalian hosts. Most publications implicating BDV in human disease have focused on neuropsychiatric disorders including unipolar depression, bipolar disorder and schizophrenia; however, BDV has also been linked to brain tumors (glioblastoma multiforme). A human BDV strain was used to address the first time, how BDV infection impacts the proteome and histone lysine acetylation (Kac) of human oligodendroglia (OL) cells, thus allowing a better understanding of infection-driven pathophysiology in vitro. Proteome and histone lysine acetylation were profiled through stable isotope labeling for cell culture (SILAC)-based quantitative proteomics. The quantifiable proteome was annotated using bioinformatics. Histone acetylation changes were validated by biochemistry assays. Post BDV infection, 4383 quantifiable differential proteins were identified. Sixteen of the thirty identified Kac sites in core histones presented altered acetylation levels post infection. BDV infection appears to preferentially dysregulate membrane, nuclear, and chromosomal host protein expression while affecting metabolic pathways, immune response, DNA replication, DNA repair, and transcription regulation. BDV infection was found to affect histone acetylation of specific lysine residues. Moreover, BDV infection affected the expression of many transcription factors, several histone acetyltransferases and histone deacetylases. As histone Kac epigenetically regulates gene transcriptional activation, the differential acetylation of specific lysine residues may have impacted the changes in the host proteome profile.

Received: June 08, 2022; **Accepted:** June 18, 2022; **Published:** June 28, 2022

Biography

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