Cellular pathways altered following West Nile virus infection in mouse model using in-gel and off-gel quantitative proteomic analysis.

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Abstract

West Nile Virus (WNV) is responsible, yearly, for thousands of cases of morbidity and mortality in birds, horses and humans. Although human WNV infections are generally asymptomatic, among persons with clinical illness, five percent could develop neurologic symptoms which may be life-threatening and can lead until death. Actually, the lack of effective antiviral treatment and the absence of WNV-licensed vaccine for use in humans are limiting factors to combat WNV infections. To protect population and to abate neurological fatal cases attributed to this vector-borne disease, a better understanding of WNV pathogenesis and neurological injury is therefore necessary. In this aim, based on animal model infected with WNV, an examination of the host CNS protein profile modifications prior and after apparition of clinical signs was performed using comprehensive complementary proteomic approaches including 2D-DIGE and iTRAQ labeling. The first results indicated that a profound host proteome modification could be observed following WNV infection. The bioinformatics analysis (Ingenuity Pathway Analysis) of these results revealed that several major functions were altered during the course of WNV-infection in the mice brain, such as post-translational modifications and protein folding including molecules involved in stress response and ubiquitination pathways, but also an alteration of proteins associated to neurogenesis, clathrin-mediated endocytosis and virus entry. Collectively, these molecular changes could present antagonist roles, some contributing to the neuroinvasion and others participating in the resistance of viral infection. Networks and pathways associated to deregulated proteins are discussed to characterize the pathophysiologic processes of neuroinvasive WNV infection. This study can provide useful clues for antiviral research and the possible further identification of early biomarkers for diagnosis as well as prevention of severe neurological cases of infection caused by WNV.

Topic selection: microbial/infectious disease/microbiome.