Quantitative proteomics analysis revealed compromised chicken dendritic cells function at early stage of very virulent infectious Bursal disease virus infection

ABSTRACT

Chicken dendritic cells (DCs) have been demonstrated to be susceptible to infectious bursal disease virus (IBDV), a causative agent of acute and immunosuppressed disease in young chicks known as infectious bursal disease. Further functional characterization of IBDV-infected DCs of chickens is required to provide a better understanding on the influence of the virus on chicken bone marrow-derived dendritic cells (BM-DCs) following very virulent (vv) IBDV infection. Membrane proteins of BM-DCs were extracted and the proteins were further denatured and reduced before performing labeling with isobaric tags for relative and absolute quantitation. The differential expression protein profiles were identified and quantified using liquid chromatography coupled with tandem mass spectrometry, and later validated using flow cytometry and real-time reverse transcriptase PCR. The analysis has identified 134 differentially regulated proteins from a total of 283 proteins (cutoff values of ≤ 0.67, ≥ 1.5, and ProtScore >1.3 at 95% confidence interval), which produced high-yield membrane fractions. The entry of vvIBDV into the plasma membrane of BM-DCs was observed at 3 hr postinfection by the disruption of several important protein molecule functions, namely apoptosis, RNA/DNA/protein synthesis, and transport and cellular organization, without the activation of proteins associated with signaling. At the later stage of infection, vvIBDV induced expression of several proteins, namely CD200 receptor 1-A, integrin alpha-5, HSP-90, cathepsin, lysosomal-associated membrane protein, and Ras-related proteins, which play crucial roles in signaling, apoptosis, stress response, and antigen processing as well as in secretion of danger-associated proteins. These findings collectively indicated that the chicken DCs are expressing various receptors regarded as potential targets for pathogen interaction during viral infection. Therefore, fundamental study of the interaction of DCs and IBDV will provide valuable information in understanding the role of professional antigen-presenting cells in chickens and their molecular interactions during IBDV infection and vaccination.

Keyword: Antigen-presenting cells (APC); Bone marrow–derived dendritic cells (BM-DCs); Infectious bursal disease (IBD); Infectious bursal disease virus (IBDV); Isobaric tag for relative and absolute quantitation (iTRAQ)