To Study the Role of DC-SIGN and Autophage on H5N1 Infection of Immature Dendritic Cells

Jason Huang[1*], Chien-Chih Lee[2], Ching-Yu Huang[2]

[1.] Department of Biotechnology and Laboratory Science in Medicine, AIDS Prevention and Research Center, National Yang-Ming University, [2.] Department of Biotechnology and Laboratory Science in Medicine, National Yang-Ming University

Background/Objective

DC-SIGN (Dendritic cell specific ICAM-3 grabbing non-integrin) is a C-type lectin on dendritic cells. Many studies showed that DC-SIGN could be a receptor for various viruses. It also interacts with N-glycan on hemagglutinin (HA) on IAV. In our previous study, we have found that H5N1 showed better infectivity in DC-SIGN expressing cell. In addition, H5N1 induced considerable cytokines production and caused more severe CPE in DC-SIGN expressing cells. Previous studies suggested that the high fatality rate of H5N1 could be caused by mass apoptosis of lung epithelial cell while others suggested cell death by autophage. Therefore, we wonder whether autophage inhibitor can block virus replication or cytokine/chemokine induction in iDCs and whether DC-SIGN signaling on immature DCs(iDCs) participates in H5N1-induced autophage.

Method

Immature dendritic cells were prepared from peripheral blood mononuclear cells for infection. We used DC-SIGN blocking antibody, DC-SIGN downstream Raf-1 inhibitor, or 3-MA for cell pretreatment before H5N1 infection. The virus infectivity, autophage induction, cytokine production and activation markers were compared.

Result

Our data showed that H5N1 induced autophage in iDCs can be reduced with 3MA pretreatment. Although H5N1virus production was not affected in A549 cells by 3MA treatment at different time points, 3MA-treated iDCs showed less virus release at 24 hr. 3MA was demonstrated to lower IP10, RANTES, TNF-alpha, MCP-1, and IL-6 production in iDCs infected by H5N1 but only insignificant decrease in RANTES and MCP-1 in A549 cells. Besides, we also found 3MA pretreatment of iDCs can dampen CD80/86 activation by H5N1 in iDCs. Finally, autophage induction by H5N1 in iDCs was not reduced by DC-SIGN monoclonal antibody or downstream Raf-1 inhibitor.

Conclusion

Our results suggest autophage in H5N1 infected iDC may participate cytokine/chemokine induction and virus production. DC-SIGN signaling is not involved in autophage induction in iDCs by H5N1 infection.