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Inhibition of Akt kinase activity suppresses entry and replication of influenza virus

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The possibility of the pandemic spread of influenza viruses highlights the need for an effective cure for this life-threatening disease. Influenza A virus, belonging to a family of orthomyxoviruses, is a negative-strand RNA virus which encodes 11 viral proteins. A numbers of intracellular signaling pathways in the host cells interact with influenza, the viral proteins, which affect various stages of viral infection and replication. In this study, we investigated how inhibition of Akt kinase activity impacts on influenza virus infection by using “*Akt-in*”, a peptide Akt inhibitor. In PR8 influenza-infected A549 cells, Akt interacted with the NS1 (Non-structural protein1), and hence increased phosphorylation of Akt kinase activity and NS1. Treatment of cells with either “TCL1- or TCL1b-based *Akt-in*” efficiently suppressed Akt kinase activity while decreasing the levels of phosphorylated NS1; this, in turn, inhibited viral replication in a dose- and time-dependent manner. The inhibitory effect on viral replication appears to not be due to inhibition of the production of inflammatory cytokines, including IL-6 and IL-8, in the host cells. Inhibition of Akt kinase activity in the host cells inhibited the efficiency of viral entry, which is associated with decreased levels of phosphorylated glycogen synthase kinase 3, a substrate of Akt. Further, *Akt-in* treatment of the host cells, which inhibited Akt kinase activity, modestly enhanced induction of autophagy. Taken together, inhibition of Akt kinase activity in host cells may have therapeutic advantages for influenza virus infection by inhibiting viral entry and replication.

Biography

Masayuki Noguchi has completed his PhD in the year 1999 from Jikei University of Medicine. He is the Professor in Division of Cancer Biology, Institute for Genetic Medicine, Hokkaido University, Japan. He was the member of American Society of Microbiology in the year 2000 and also Editorial Board Member for *Journal of Bio Chemistry*. He has published more than 70 papers in reputed journals.

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