The role of TRAIL in the immune responses to influenza viruas infection.

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TNF-related -apoptosis-inducing ligand (TRAIL) preferentially induce apoptosis of various tumor cells, but not normal cells. However, it was revealed that various cytokines and virus infection differentially regulate TRAIL and TRAIL-receptors (TRAIL-Rs) expression. It was demonstrated that virus infection changes the pattern of human TRAIL-Rs expression on normal cells, that were resistant to TRAIL-mediated apoptosis, and makes them susceptible to TRAIL-mediated apoptosis. Since the previous studies about function of TRAIL has been performed mainly *in vitro*, its physiological role in immune response to virus infection remains unknown.

In the present study, we investigated the expression of TRAIL in the lung of influenza virus-infected mice and the function of TRAIL in immune response to influenza virus infection. Influenza virus infection increased TRAIL mRNA expression in the lung. TRAIL protein expression was induced on NK cells existing in the lung 4 days after infection. Furthermore, 7 days after infection, TRAIL protein expression was detected not only on NK cells but also on CD4 and CD8 T cells. The abundance of TRAIL expressed on a NK cell and the number of TRAIL-expressing NK cells were increased on day 7 compared to day4. However, NK cells and T cells existing in the lung of uninfected mice did not express a detectable level of TRAIL on their surface. DR5, which is a mouse TRAIL-R, was constitutively expressed at mRNA level in the lung of uninfected mice, and its expression level was not affected by virus infection. Administration of anti-TRAIL monoclonal antibody, which block TRAIL without killing of TRAIL-expressing cells, to mice during influenza virus infection, significantly delayed virus clearance in the lung. These results suggest that TRAIL plays an important role in immune response to virus infection.