Poliovirus dissemination and host functions

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【Outline of survey】

Poliovirus (PV), the causative agent of poliomyelitis, is known to be a neurotropic RNA virus. Humans are only natural host. However, the virus can be experimentally transferred to monkeys. In humans, PV ingestion occurs by oral infection. After multiplication in the alimentary tract, PV moves into theblood, and then invades the central nervous system (CNS) through the blood brain barrier (BBB). Poliomyelitis occurs as a result of destruction of motor neurons by lytic replication of the virus in the anterior horn of the spinal cord. Retrograde axonal transport system from the skeletal muscle is also involved in PV dissemination. In this study, we clarify functions of host factors involved in PV replication in the alimentary tract and the CNS and PV dissemination through the BBB and axons, and try to understand the basis on PV infection phenomena. To put it concretely, we will analyze relationship between viral replication and IFN system in the alimentary tract and mechanisms for BBB permeation, retrograde axonal transport and initiation of viral replication after the transport. To perform the above studies at molecular level, primary cultured neurons, neuroblastoma cells, capillary endothelial cells, and the transgenic mice susceptible to poliovirus will be used.

【Expected results】

This studies on PV must be a good model studies on dissemination pathways of neurotropic viruses, because BBB permeation and axonal transport are common pathways to many neurotropic viruses. In addition, analysis of viral infection phenomena, which is an unique approach with a virus as a probe, must lead us to important discoveries in a field of biology, which are difficult to find by studies using only hosts, as so far recognized.

【References by the principal researcher】

• Blockade of poliovirus-induced cytopathic effect in neural cells by monoclonal Antibody against poliovirus or human poliovirus receptor. A. Yanagiya, Q. Jia , S. Ohka, et al. J. Virol. 79:1523-1532, 2005.

【Term of project】 FY2006－2010

【Budget allocation】31,800,000 yen

【Homepage address】 http://microbiology.m.u-tokyo.ac.jp/