BMC Proceedings

Poster presentation

Open Access

Rabies virus has more than one trick up its sleeve to manipulate the host defences

Monique Lafon*[1], Heinz Wiendl[2] and Thiravat Hemachudha[3]

Address: [1]Institut Pasteur, Paris France, [2]University of Würzburg, Germany and [3]Molecular Biology Laboratory for Neurological Diseases, Department of Medicine, Chulalongkorn University Hospital, Bangkok, Thailand

Email: Monique Lafon* - mlafon@pasteur.fr

* Corresponding author

from Infectious diseases of the nervous system: pathogenesis and worldwide impact
Paris, France. 10–13 September 2008

Published: 23 September 2008

BMC Proceedings 2008, **2**(Suppl 1):P35

This abstract is available from: http://www.biomedcentral.com/1753-6561/2/S1/P35

Rabies virus is a pathogen well adapted to the mammalian nervous system where it infects the neurons. It causes rabies- an acute myelo-encephalitis- fatal in most mammalian species, and humans in particular. Rabies virus is transmitted by saliva of an infected animal through bites or scratches, by unfortunate transplantation of organs originated from unsuspected rabid donors and more rarely by aerosols. Rabies virus enters the nervous system via a motor neuron through the neuromuscular junction, or via a sensory nerve through nerve spindles. It then travels from one neuron to the next, along the spinal cord to the brain. Then, rabies virus infection reaches the salivary glands and virus particles are excreted in the saliva. Intriguingly, once the rabies virus has entered the CNS, its progression is interrupted neither by destruction of the infected neuron nor by the immune response, two classical strategies developed by the host to usually battle viral infection. Successful invasion of the nervous system by rabies virus seems to be the result of rabies virus capacity to escape the host mechanisms of defence. We showed that rabies virus neuroinvasiveness results of the selection of multiple factors: not only neuronotropic rabies virus avoids to induce neuron cell death, but also "protective "T cells that migrate into the infected nervous system are exhausted or killed by apoptosis, as a result of the overexpression by the infected neurons of at least three immunosubversive molecules: Fas-L, HLA-G and B7-H1. We also observed that fast killing virus strains limit local inflammation of the infected nervous tissues. Preservation of the integrity of neurons and neuronal network can be understood as a perquisite for the long journey of the virus through the nervous system from the site of entry up to the salivary glands. One would expect that the host 's natural capacity to fight such a well-adapted virus is greatly limited, explaining why in the absence of post-exposure vaccination, rabies is one of the very few human infections with a near 100% mortality rate. Implications of these findings for new rabies treatment will be discussed.