BMC Proceedings

Poster presentation

Open Access

Borna disease virus phosphoprotein interferes with neuronal function and contributes to neurobehavioral disorders

Christine Prat[1], Sonja Schmid[2], Martin Schwemmle[2] and Daniel Gonzalez-Dunia*[1]

Address: [1]INSERM U563, Toulouse, France and [2]Department of Virology, Institute for Medical Microbiology and Hygiene, University of Freiburg, Germany

Email: Daniel Gonzalez-Dunia* - Daniel.dunia@inserm.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):P56

This abstract is available from: http://www.biomedcentral.com/1753-6561/2/S1/P56

Infection by Borna disease virus (BDV) enables the study of the molecular mechanisms whereby a virus can persist in the central nervous system and lead to altered brain function, in the absence of overt cytolysis and inflammation. This neurotropic virus infects a wide variety of vertebrates and causes behavioral diseases. The basis of BDV-induced behavioral impairment remains largely unknown.

Previously, we have shown that BDV specifically blocks the activity-dependent enhancement of synaptic activity, both by studying the recycling of synaptic vesicles and by using electrophysiological approaches on BDV-infected neuronal networks grown on microelectrode arrays. This suggested defects in long-term potentiation, one key component of learning at the cellular level. Studies of signaling pathways involved in synaptic potentiation revealed that this blockade was due to an interference with PKC-dependent signaling in neurons, likely due to the viral phosphoprotein (P).

Here, we used recombinant BDV with mutated PKC phosphorylation sites on P [1], and showed that this mutation restored the phosphorylation of PKC substrates in neurons after stimulation. Moreover, using primary neuronal cultures grown on micro-electrode arrays (MEA), we provide evidence that the activity-dependent enhancement of synaptic activity was restored when cultures were infected with the P-mutated virus. Therefore, preventing P protein phosphorylation by PKC completely restores normal neuronal activity upon stimulation in infected neurons.

Together, these findings illustrate a novel mechanism whereby a viral protein can cause synaptic dysfunction and contribute to neurobehavioral disorders.

References

1. Schmid S, Mayer D, Schneider U, Schwemmle M: **Functional characterization of the major and minor phosphorylation sites of the P protein of Borna disease virus.** *J Virol* 2007, **81:**5497-5507.