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LONG ALKYLCHAIN IMINOSUGARS BLOCK THE HCV P7 ION CHANNEL

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The small p7 protein of the hepatitis C virus (HCV) and the closely related bovine viral diarrhea virus (BVDV) can form ion channels in artificial membranes (see

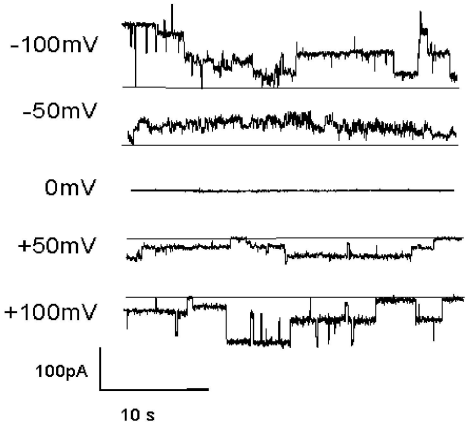

Figure 1. Channel recordings of synthetic HCV p7 inserted into a black lipid membrane (BLM). Channel activity is shown for +/– 50 mV and +/– 100 mV. The closed state is shown as a solid line. Channel openings are deviations from this line. Solutions are the same in the cis and trans chamber: 0.5 M KCl, 5 mM Hepes, 1 mM CaCl2, pH 7.4. HCV p7 is added on the trans side to a final concentration of approximately 50 microM. Scale bars are 10 s and 100 pA.

John S. Axford (ed.), Glycobiology and Medicine, 3-4.

Fig. 1). Ion channel activity can be suppressed by long alkylchain iminosugar derivatives, which have been shown to be antiviral in BVDV infectivity assays. Treatment with these inhibitors does not affect viral RNA replication. However, the infectivity of virions secreted in the presence of the inhibitors is impaired. The physiological role of the p7 ion channel during the viral life cycle is unknown and is being investigated using inhibitory iminosugars as well as a BVDV construct from which p7 has been deleted.

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http://www.springer.com/978-0-387-25514-9

Glycobiology and Medicine
Proceedings of the 7th Jenner Glycobiology and Medicine Symposium.
Axford, J.S. (Ed.)
2005, XI, 153 p., Hardcover
ISBN: 978-0-387-25514-9