

URLs

Ephrin B2: <http://us.expasy.org/uniprot/Q5JV56>

Hendra virus: <http://www.ncbi.nlm.nih.gov/genomes/framik.cgi?db=genome&gi=13716>

Nipah virus: <http://www.ncbi.nlm.nih.gov/genomes/framik.cgi?db=genome&gi=15627>

VIROLOGY

Henipavirus receptor identified

Ephrin B2, a member of the ephrin receptor tyrosine kinase family, has been identified as the cell-surface receptor for **Hendra virus** and **Nipah virus**.

Hendra virus and Nipah virus are members of the new genus Henipavirus in the *Paramyxoviridae* family. Both viruses have an unusually broad species tropism, encompassing many mammals, including humans, horses, pigs, cats, dogs and fruit bats. It had previously been shown that henipaviruses attach to and enter host cells using their fusion (F) and attachment (G) cell-surface glycoproteins, and the cell-surface receptor for both viruses had been shown to be protease sensitive. Now,

using two different approaches, the identity of this receptor has been revealed.

Negrete *et al.* identified the receptor for Nipah virus by immunoprecipitating permissive and non-permissive cell lines using the ectodomain of the Nipah virus G protein fused to the Fc region of human IgG1 as bait. The immunoprecipitation identified a 48-kDa membrane protein, and subsequent trypsin digestion and mass-spectrometry analysis identified the protein as human ephrin B2. Further cell-based experiments demonstrated that ephrin B2 is required for the formation of endothelial syncytia, a characteristic of Nipah virus infection. Finally, recombinant vesicular stomatitis virus pseudotyped with the Nipah virus F and G proteins was shown to require ephrin B2 for cell entry.

Bonaparte *et al.* used a microarray approach in their work to identify the receptor for both members of the Henipavirus genus. Previous work by this group had identified a human cell line that is non-permissive for henipavirus fusion and infection, and mRNA from this cell line and three permissive cell lines was used in an Affymetrix gene chip analysis to screen for genes that were differentially expressed. Based on prior observations, 21 candidate receptor genes that encode membrane-expressed proteins of the expected size range were identified. Ten candidates were chosen for fur-

ther analysis, and cell-fusion assays identified human ephrin B2 as the receptor for both Hendra virus and Nipah virus, extending the findings of Negrete *et al.* Bonaparte *et al.* went on to use live-virus-infection assays of human and primate cells to confirm that *in vivo*, henipavirus infection occurs through ephrin B2.

The identification of the receptor is a huge breakthrough for researchers working on these emerging viruses, and will hopefully aid efforts to understand their pathogenesis and facilitate the development of effective therapies.

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References and links

ORIGINAL RESEARCH PAPERS Bonaparte, M. L. *et al.* Ephrin-B2 ligand is a functional receptor for Hendra virus and Nipah virus. *Proc. Natl Acad. Sci. USA* 5 July 2005 (doi:10.1073/pnas.0504887102) | Negrete, O. A. *et al.* EphrinB2 is the entry receptor for Nipah virus, an emergent deadly paramyxovirus. *Nature* 6 July 2005 (doi:10.1038/nature03838)

