Scientists develop vaccine against cattle disease

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(Phys.org) —Malignant catarrhal fever (MCF) is a disease that is almost always fatal in cattle. Cows contract MCF after coming into contact with wildebeest carrying a form of herpes virus known as alcelaphine herpesvirus 1 (AlHV-1). In a paper published in the *Proceedings of the National Academy of Sciences*, Benjamin Dewals of the Faculty of Veterinary Medicine at the University of Liège in Belgium and his team report that they have discovered the gene that enables AlHV-1 infection to progress to MCF, and they have developed a vaccine against the

disease.

Every year, 1.3 million wildebeest migrate across eastern Africa. Almost all of them carry the AlHV-1 virus, which has no effect on them. When wildebeest enter grazing areas, young wildebeest spread the virus through their nasal secretions, infecting cattle. Infected cattle develop MCF, which causes immune cell production to spin out of control, leading to death within a few weeks. MCF is devastating to the Masai people of the region, whose lives depend on livestock farming. Wildebeest in zoos can also spread AlHV-1, causing MCF, for which there is no cure, in some endangered ruminant species.

Herpes viruses such as AlHV-1 can replicate in cells that they infect, or they can remain dormant, in a latent state. To determine which method AlHV-1 uses, Dewals and his team infected calves with the virus. All of the calves developed MCF. The researchers then analyzed cellular and viral RNA from the calves' lymph nodes. They discovered that the virus took the form of episomes, ringed structures that indicate latency, and that infected T-cells contained high levels of the gene ORF73, which codes for a protein needed to maintain latency.

Dewals and his colleagues then created a recombinant form of AlHV-1 that lacked ORF73. While this version of the virus was still able to replicate, rabbits infected with it never developed MCF. When the researchers infected these rabbits with normal AlHV-1, the rabbits did not develop the disease, indicating that the knockout virus could be act as a vaccine.

According to the team, the virus' latency creates an evolutionary advantage for both itself and the wildebeest. Because AlHV-1 can persist in wildebeest without causing it any harm, it spreads easily through the entire population, gaining a huge number of hosts. At the same time, the virus kills other species that compete with wildebeest for resources.

Transmission of AlHV-1 is highest during wildebeest calving season. Animals weakened by MCF would attract the attention of predators that would otherwise prey on wildebeest calves.

More information: An essential role for γ-herpesvirus latency-associated nuclear antigen homolog in an acute lymphoproliferative disease of cattle, *PNAS*, Published online before print April 29, 2013, doi: 10.1073/pnas.1216531110

Abstract

Wildebeests carry asymptomatically alcelaphine herpesvirus 1 (AlHV-1), a γ-herpesvirus inducing malignant catarrhal fever (MCF) to several ruminant species (including cattle). This acute and lethal lymphoproliferative disease occurs after a prolonged asymptomatic incubation period after transmission. Our recent findings with the rabbit model indicated that AlHV-1 infection is not productive during MCF. Here, we investigated whether latency establishment could explain this apparent absence of productive infection and sought to determine its role in MCF pathogenesis. First, whole-genome cellular and viral gene expression analyses were performed in lymph nodes of MCF-developing calves. Whereas a severe disruption in cellular genes was observed, only 10% of the entire AlHV-1 genome was expressed, contrasting with the 45% observed during productive infection in vitro. In vivo, the expressed viral genes included the latency-associated nuclear antigen homolog ORF73 but none of the regions known to be essential for productive infection. Next, genomic conformation analyses revealed that AlHV-1 was essentially episomal, further suggesting that MCF might be the consequence of a latent infection rather than abortive lytic infection. This hypothesis was further supported by the high frequencies of infected CD8+ T cells during MCF using immunodetection of ORF73 protein and single-cell RT-PCR approaches. Finally, the role of latency-associated ORF73 was addressed. A lack of ORF73 did not impair initial virus replication in vivo, but it rendered AlHV-1 unable to induce MCF

and persist in vivo and conferred protection against a lethal challenge with a WT virus. Together, these findings suggest that a latent infection is essential for MCF induction.