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HEPARAN SULFATE IS A SELECTIVE ATTACHMENT FACTOR FOR THE AVIAN CORONAVIRUS IBV BEAUDETTE

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Infectious bronchitis virus (IBV) is a coronavirus infecting domestic fowl. It was originally isolated in the 1930s and continues to cause major problems in the poultry industry. The avian coronavirus infectious bronchitis virus (IBV) strain Beaudette is an embryo-adapted virus that has extended species tropism in cell culture. In order to understand the acquired tropism of the Beaudette strain, this study compared the S protein sequences of several IBV strains. The Beaudette strain was found to contain a putative heparan sulfate (HS)-binding site, indicating that the Beaudette virus may use HS as a selective receptor.

Coronaviruses show strong species and tissue tropism, and a major factor in this specificity is the virus receptor on host cells. The coronavirus receptor is generally considered to be the primary determinant of host range and this has recently been shown in some detail for SARS-CoV. Viruses isolated during the 2002–2003 SARS outbreak, during the much less severe 2003–2004 outbreak, and from palm civets were analyzed. All three S proteins bound to and utilized palm civet ACE2 efficiently, but the latter two S proteins utilized human ACE2 markedly less efficiently, and the lower affinity S proteins could be complemented by incorporating specific mutations.

Like most coronaviruses, clinical isolates of IBV show distinct tropism both *in vivo* and in cell culture. The prototype IBV strain (M41) causes an acute, highly contagious respiratory disease in chickens. The virus can also replicate in the gastrointestinal tract, oviduct and kidney, where it can be highly nephropathogenic with the potential to cause up to 44% mortality; in some cases infection of the

proventriculus leads to 75–100% mortality in young birds. IBV is distributed worldwide, and in the United States several serotypes (e.g., Arkansas and Delaware) are currently circulating in addition to the originally identified Massachusetts type. Most isolates of IBV replicate well in the developing chicken embryo following inoculation of the allantoic cavity and high titers of virus can be isolated from the allantoic fluid. IBV Beaudette is no longer pathogenic for adult birds, but rapidly kills embryos. In terms of host cells, IBV M41 is normally restricted to infection of primary chicken cells; however the Beaudette strain of IBV is known to be able to infect a range of cells in culture. IBV Beaudette therefore represents a significant virus that has extended its host range based on very limited changes in its S protein.

In this study, a bioinformatic analysis of the S protein of IBV M41 and Beaudette, and identified a unique heparin-binding consensus sequence on the Beaudette S protein. Researchers showed that IBV Beaudette infection is specifically inhibited by soluble heparin, and is restricted for infection in heparan sulfate-deficient cells, which indicates that the specific utilization of heparan sulfate as an attachment factor is involved in the extended species tropism of IBV Beaudette, most likely in conjunction with sialic acid moieties as well as an additional specific, but unidentified, receptor protein utilized by all strains of IBV.

In conclusion, to ascertain the requirements of cell surface HS for Beaudette infectivity, researchers assayed for infectivity in the presence of soluble heparin as a competitor, and determined infectivity in mutant cell lines with no HS or glycosaminoglycan expression. The results indicate that HS plays a role as an attachment factor for IBV, working in concert with other factors like sialic acid to mediate virus binding to cells, and may explain in part the extended tropism of IBV Beaudette.

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