Lentiviral hepatitis B pseudotype entry requires sodium taurocholate co-transporting polypeptide and additional hepatocyte-specific factors.

Hepatitis B virus (HBV) is one of the world's major unconquered infections, resulting in progressive liver disease, and current treatments rarely cure infection. A limitation to discovering new therapies is our limited knowledge of HBV entry and dissemination pathways that hinders the development of in vitro culture systems. To address this gap in our understanding we optimized the genesis of infectious lentiviral pseudoparticles (HBVpps). The recent discovery that the bile salt transporter sodium taurocholate co-transporting polypeptide (NTCP) acts as a receptor for HBV enabled us to assess the receptor dependency of HBVpp infection. HBVpps preferentially infect hepatoma cells expressing NTCP, whereas other non-liver cells engineered to express NTCP do not support infection, suggesting that additional hepatocyte-specific factors are required for HBVpp internalization. These results highlight the value of the HBVpp system to dissect the pathways of HBV entry and dissemination.