

Hepatitis D virus (HDV), discovered 40 years ago, is a unique virus requiring hepatitis B virus (HBV) for replication. HDV, with a 1.7 kb circular single-stranded RNA genome, uses HBV surface proteins for its envelope. Its replication involves the delta antigen (HDAg), which interacts with cellular RNA polymerase. HDAg exists in two forms (small and large) with differing functions: S-HDAg promotes replication, while L-HDAg may inhibit S-HDAg and is crucial for assembly. HDV's origin is unknown, but its RNA shares properties with plant viroids and cellular ribozymes. The discovery of a cellular protein, DIPA, with sequence similarity to HDAg suggests a possible cellular origin for HDV, potentially through the capture of a DIPA gene.