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Human Parvovirus Expresses a Long Noncoding RNA that is Essential to Virus Replication

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Human Bocavirus 1 (HBoV1), is an autonomously replicating parvovirus. It causes acute respiratory tract infections in young children and has a selective tropism for the apical surface of well-differentiated human airway epithelium (HAE). HBoV1 expressed 4 viral non-structural proteins and 3 vial structural proteins during infection. Here, we identified an additional HBoV1 gene, a viral long noncoding RNA (lncRNA) of 140 nucleotide, named as bocavirus-transcribed small RNA (BocaSR). It is transcribed from an intragenic RNA polymerase III (Pol III) within the 3' noncoding region (nt 5,199-5,338) of the viral genome. BocaSR is essential to viral DNA replication in HEK293 cells as well as virus replication in well-differentiated HAE cultured at an air-liquid interface. Mechanistically, BocaSR regulates the expression of viral non-structural proteins NS1, NS2, NS3, and NP1, but not NS4, and plays a direct role in viral DNA replication through association with the replicating viral genome in the nucleus. Although BocaSR shares a similarity of ~50% in sequence with adenovirus VAI RNA, but functionally differs from it in that its regulation of viral protein expression is independent of RNA-activated protein kinase (PKR). In summary, our study reveals a novel Pol III-driven viral lncRNA that coordinates the expression of viral proteins and regulates viral DNA replication within the nucleus.