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Abstract (oral session)

The human bocavirus: genomic head-to-tail intermediates challenge the parvovirus replication model

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The human bocavirus was initially discovered in 2005 as the second pathogenic member of the parvovirus family, next to the human parvovirus B19. HBoV has since been shown to be extremely common worldwide and – to cause a systemic infection in children and adults often resulting in respiratory or gastrointestinal disease. Parvoviruses are assumed to replicate via their genomic terminal hairpin-like structures in a so-called rolling-hairpin model, resulting in head-to-head or tail-to-tail intermediates. Surprisingly, in case of HBoV-1, we identified head-to-tail intermediates in clinical samples that are not compatible with the rolling hairpin model but are a typical feature of the classical rolling circle replication. A further study by Kapoor and co-workers (2011) confirmed our observation and extended the conclusion as those head-to-tail structures may originate from episomal genomes that persist in the infected host cell. In concert with a clinical case recently described by our group, the hypothesis of episomal persistence following rolling circle replication seems a likely explanation. In the described case a child suffering from an autoimmune disease unable to produce an antibody response was infected with HHV6 and coinfected by HBoV. The HBoV shedding was discontinued after cidofovir therapy that successfully suppressed HHV6 titres to levels below the detection limit. The simultaneous disappearance of HBoV and HHV6 may be interpreted as a dependency of HBoV DNA replication on the presence of a herpesviral replication machinery, that in turn is able to initiate rolling circle replication in cis and in trans. Moreover the underlying autoimmune disease gives raise to the hypothesis that the HBoV infection was limited directly or indirectly by the cidofovir treatment rather than by a reconstituted immune response previously shut down by the HHV6 infection. Moreover it appears that HBoV contributes to chronic lung diseases as we observed an association of HBoV with lung fibrosis in several cases, as identified by the Luminex RVP assay. Thereby it remains unclear to which extent the clinical course was aggravated by HBoV or caused by HBoV persistence in turn inducing chronic inflammation resulting in fibrosis. Thereby, one patient suffered from a co-infection with CMV, another herpesvirus potentially acting as a helpervirus and thus supporting the hypothesis that HBoV may alternatively replicate in a rolling circle mechamism supported by helper viruses.