

Do Human Adenoviruses of Species HAdV-B originate from Gorillas?



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Background. Human adenoviruses (HAdVs) of species B (HAdV-B) are important pathogens causing respiratory tract-, eye- and urinary tract infections. AdVs that are closely related to HAdV-B have been previously identified in gorillas and chimpanzees living in the wild and in captivity. In phylogenetic analysis, these human and great ape HAdV-B form a highly mixed cluster which indicates that inter-species transmission events may have occurred in the evolution of HAdV-B viruses. Great ape adenoviruses are shed frequently in the feces, and in a previous pilot study we noted that gorillas predominantly shed HAdV-B.

Aims of the study:

To investigate the genoprevalence of HAdV-B in gorillas, chimpanzees and humans from Africa
To investigate the diversity of gorilla HAdV-B, in comparison to chimpanzee and human HAdV-B

Results. Fecal samples of 280 lowland and mountain gorillas, 133 Western and Eastern chimpanzees and 132 humans from Africa were analysed with generic HAdV-B PCR. 40% of the gorillas were HAdV-B positive, but only 7% and 1.5% of the chimpanzees and humans, respectively. With generic HAdV-E PCR, none of the tested gorillas and humans, but 65% of the chimpanzees were HAdV-E positive. With generic HAdV-D PCR, none of the tested gorilla and chimpanzees, but 43% of the humans were HAdV-D positive (Figure 1). This indicated that only gorillas are broadly infected with and shed HAdV-B. HAdV-D naturally infect only humans and HAdV-E chimpanzees (Figure 1).

The high prevalence of HAdV-B in gorillas was underscored by the fact that the short HAdV-B PCR and the long-distance HAdV-B PCR detected in 25% of the gorilla samples different HAdV-B viruses (Figure 2).

From 13% of the HAdV-B positive samples a five-gene block (pVII, pV, pX, pVI, hexon; 5.6 kb) could be amplified, sequenced and subjected to phylogenetic analysis. In the phylogenetic tree that includes also the corresponding HAdV-B sequences from Genbank, the gorilla HAdV-B reveal a high genetic diversity, in contrast to the human and chimpanzee HAdV-B. The gorilla HAdV-B sequences (i) are located at the basis and at the tips of the tree, (ii) are intermixed with those of chimpanzees and humans and (iii) outscore those of humans and chimpanzees (Figure 3).

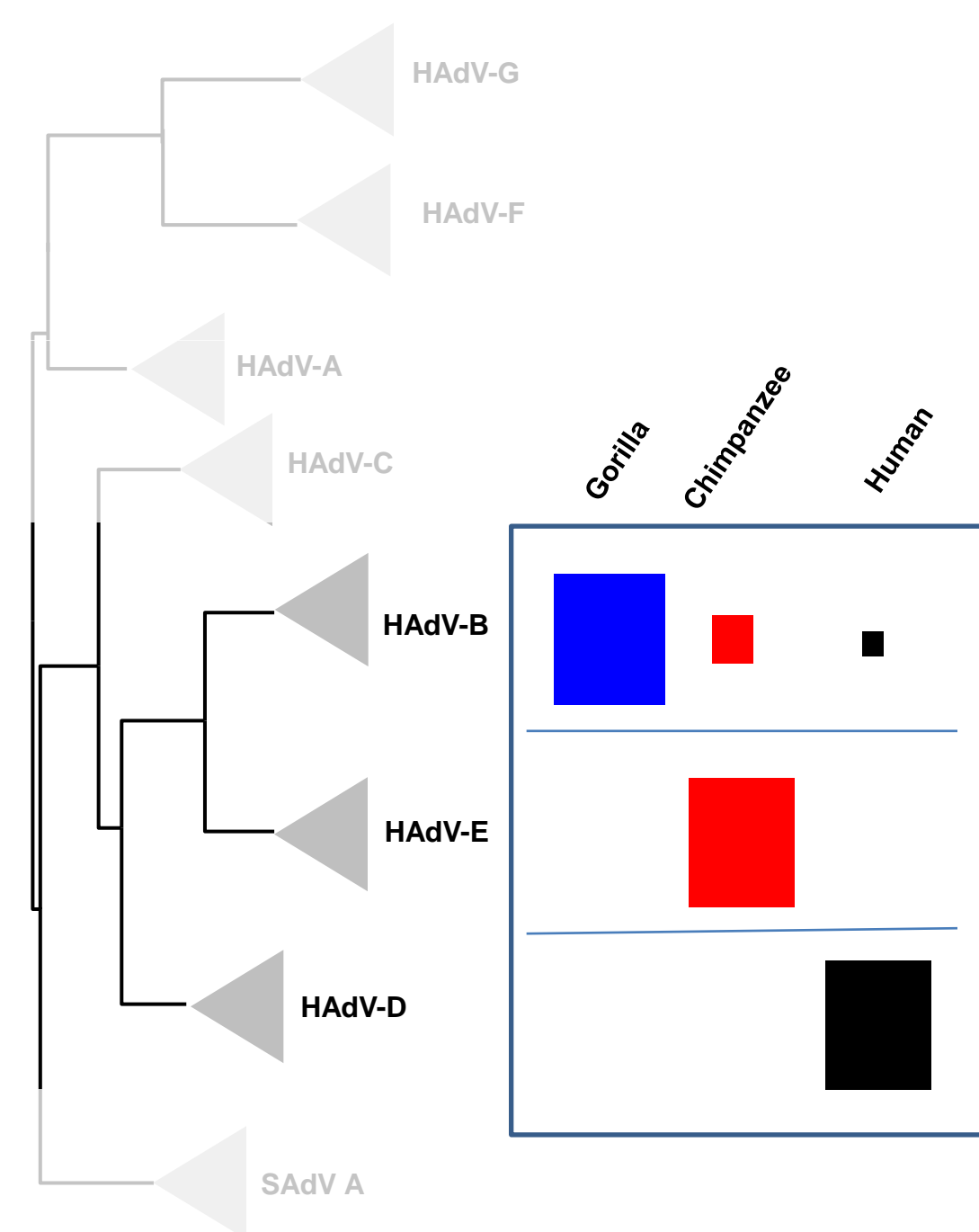


Figure 1. Phylogenetic tree of HAdVs and genoprevalence of HAdV-B, -D, -E in gorillas, chimpanzees and humans.

The tree was designed on the basis of results from 3 specific PCRs (AdV-B,-D,-E). Presented are findings of our samples excluding sequences from GenBank. The PCR results are schematically depicted with closed coloured squares (gorillas: blue; chimpanzees: red; human: black). The size of the squares indicates the respective genoprevalence.

Methods. Fecal samples were collected from African great apes living in their natural habitats (lowland and mountain gorillas, 5 locations), Western and Eastern chimpanzees (6 locations) and bonobos (1 location). Fecal samples of humans were collected in the Democratic Republic of Congo, in the Central African Republic and in Cote d'Ivoire.

Three PCR assays were carried out for generic detection of the hexon gene of primate AdVs of species HAdV-B, -D or -E, respectively.

From AdV-B-positive samples a 5,6 kb block of 5 genes (pVII to hexon) was then amplified by long distance PCR and sequenced. A multiple alignment was generated using all novel AdV-B sequences and corresponding AdV-B sequences available in Genbank.

Phylogenetic analysis was performed using the Maximum-likelihood module of Geneious pro software.

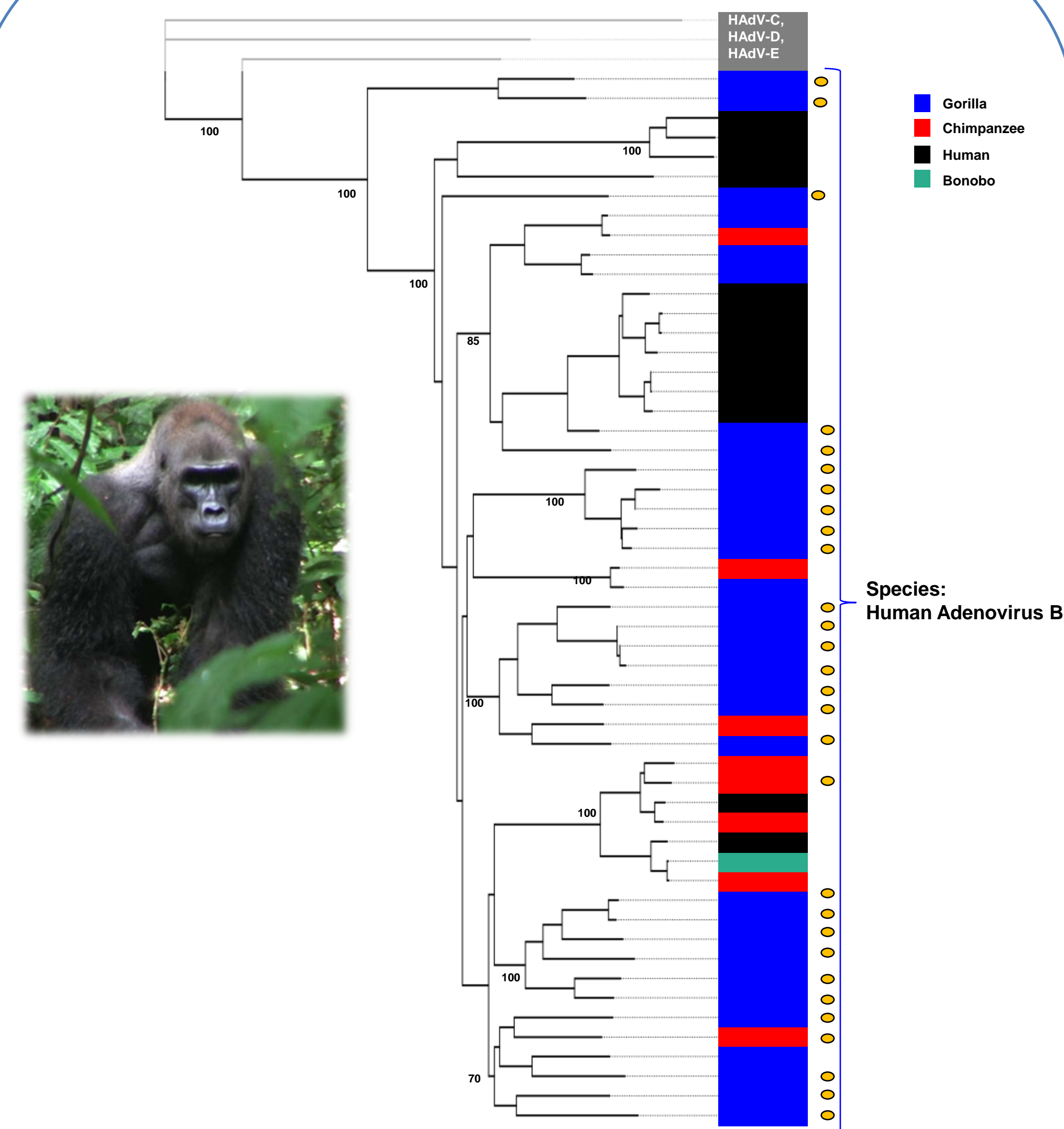


Figure 3. Phylogenetic analysis of HAdV-B. The tree was constructed on the basis of a multiple alignment of 5 genes (pVII, pV, pX, pVI, hexon; 5.6 kb). Included were all HAdV-B sequences from this study and the corresponding sequences from GenBank. Sequences from gorillas, chimpanzees, bonobo and humans are marked in blue, red, green and black, respectively. Sequences from this study are marked with orange symbols.

Discussion. This is the first comprehensive study on HAdV-B in wild great apes. Within the HAdV-B species, the mixed phylogenetic clusters of gorilla, chimpanzee, bonobo and human HAdVs indicate that host switches were a component of the evolution of human and non-human primate HAdV-B. From the high genoprevalence of HAdV-B in gorillas it is hypothesized that the ancestors of HAdV-B originally were gorilla viruses that have been transmitted during HAdV-B evolution from gorillas to chimpanzees and humans.

Taken together, our data underscore the concept of AdVs having the potential to cross the borders between closely related host species, in particular those between nonhuman primates (NHPs) and humans.

Presently, transmission of such viruses is most likely to occur at places with close physical contact between NHPs and humans, such as zoos and other animal facilities or during hunting and preparation of bush meat.

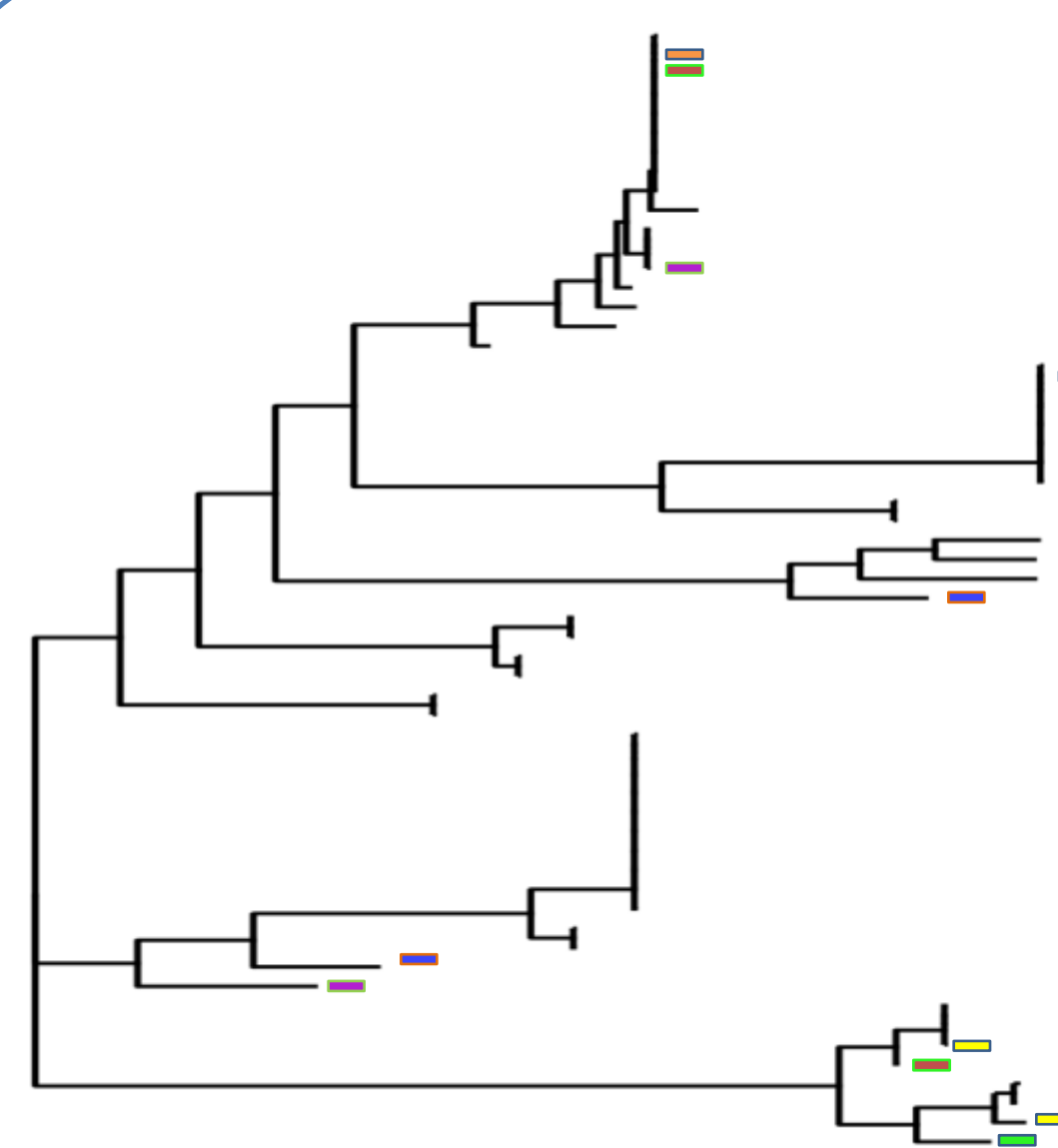


Figure 2. Multiple infection of gorillas with HAdV-B viruses. Fecal samples were HAdV-B-positive in both hexon PCR and in LD PCR. In the phylogenetic tree those sequence pairs are highlighted by coloured rectangles which are each positioned in different clades of the tree and therefore originate from different HAdV-B viruses.

Summary. In the first comprehensive study on HAdV-B in wild great apes a high prevalence and high genetic diversity of HAdV-B was detected in wild gorillas. In wild chimpanzees and in humans the prevalence was low. In phylogenetic analysis, HAdV-B of gorillas, chimpanzees and humans are intermixing. It is hypothesized that the ancestors of HAdV-B originally were gorilla viruses that have been transmitted during HAdV-B evolution from gorillas to chimpanzees and humans.

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