Taxonomic proposal to the ICTV Executive Committee



This form should be used for all taxonomic proposals. Please complete all those modules that are applicable (and then delete the unwanted sections).

Code(s) assigned:	2008.014,016V	(to be completed by ICTV officers)
Short title: Create adenovirus A in ger (e.g. 6 new species ir Modules attached (please check all that	species Human adenovirus nus Aviadenovirus, family n the genus <i>Zetavirus</i> ; re-cla <b>1</b> apply): 6	as G in genus Mastadenovirus and species Falcon 7 Adenoviridae assification of the family <i>Zetaviridae</i> etc.) $2 \square 3 \square 4 \square 5 \boxtimes 7 \square$

# Author(s) with e-mail address(es) of the proposer:

Balázs Harrach (harrach@vmri.hu) on behalf of the Adenoviridae Study Group

# **ICTV-EC** or Study Group comments and response of the proposer:

# MODULE 5: NEW SPECIES

Code	2008.014V.01		(assigned by ICTV officers)	
To create 1 new species assigned as fol		w species assigned as fo	llows: Fill in all that apply. Ideally, species	
G	enus:	Aviadenovirus	should be placed within a genus, but it is	
Subfat	mily:	Unassigned	acceptable to propose a species that is within a Subfamily or Family but not	
Fai	mily:	Adenoviridae	assigned to an existing genus (in which	
0	rder:	Unassigned	case put "unassigned" in the genus box)	

#### Name(s) of proposed new species:

Falcon adenovirus A

#### Argument to justify the creation of the new species:

If the species are to be assigned to an existing genus, list the criteria for species demarcation and explain how the proposed members meet these criteria.

Falconid adenovirus 1 has been described to occur in at least four different bird species from the family Falconidae. Based on the hexon and DNA polymerase proteins, the virus is sufficiently distant phylogenetically from members of all other adenovirus (AdV) species to merit the establishment of a new species.

# **References:**

- Dean J, Latimer KS, Oaks JL, Schrenzel M, Redig PT, Wunschmann A (2006) Falcon adenovirus infection in breeding Taita falcons (*Falco fasciinucha*). J Vet Diag Invest 18, 282–286
- Oaks JL, Schrenzel M, Rideout B, Sandfort C (2005) Isolation and epidemiology of falcon adenovirus. J Clin Microbiol 43, 3414–3420
- Schrenzel M, Oaks JL, Rotstein D, Maalouf G, Snook E, Sandfort C, Rideout B (2005) Characterization of a new species of adenovirus in falcons. J Clin Microbiol 43, 3402– 3413
- Schrenzel M, Snook E, Gagneux P (2007) Molecular assays for detection of falcon adenovirus. J Vet Diagn Invest 19, 479–485
- Tomaszewski EK, Phalen DN Title (2007) Falcon adenovirus in an American kestrel (*Falco sparverius*). J Avian Med Surgery 21, 135-139
- Van Wettere AJ, Wunschmann A, Latimer KS, Redig PT (2005) Adenovirus infection in taita falcons (*Falco fasciinucha*) and hybrid falcons (*Falco rusticolus* x *Falco peregrinus*) J Avian Med Surgery 19, 280-285

#### Annexes:

Include as much information as necessary to support the proposal. The use of Figures and Tables is strongly recommended.

Closely related AdVs have been isolated from and/or detected in various falcon species, including the Northern aplomado falcon (*Falco femoralis*), kestrel (*F. sparverius*), taita (*F. fasciinucha*) and orange-breasted falcon (*F. deiroleucus*). The first isolate was named

falconid adenovirus 1. The sequence identity between this and the other viruses detected in falcon species is 98.6-99.5%. This virus cluster shows a large phylogenetic distance from other avian AdVs (**Fig. 1**).

GenBank accession numbers of AdVs isolated from various falcon species:

Northern aplomado falcon:	AY683541,	6257 bp,	penton base to hexon (partial)
American kestrel:	DQ460220,	1276 bp,	hexon (partial)
Orange-breasted falcon:	AY683555,	350 bp,	hexon (partial)
Taita falcon:	AY683554,	350 bp,	hexon (partial)

Since adenoviruses are considered to have co-evolved with their hosts, the level of separation of falcon and fowl adenoviruses is probably a consequence of the ancient divergence of these avian lineages.

**Fig. 1.** [Next page] Phylogenetic tree of AdVs based on a distance matrix analysis of hexon amino acid sequences. Protdist (categories matrix), Fitch (global rearrangements) programs of the PHYLIP 3.65 package. Unrooted tree with white sturgeon AdV-1 chosen as outgroup. AdVs are marked by the name of the host and the serotype number (or only by the serotype number in case of human AdVs (HAdVs)). AdVs that belong to the same species are grouped by light-blue ovals. HAdV species are indicated by their abbreviations.



# MODULE 5: NEW SPECIES

Code	2008.016V.01		(assigned by ICTV officers)			
To create 1 new species assigned as follows		llows:	Fill in all that apply. Ideally, species			
Ge	nus:	Mastadenovirus		should be placed within a genus, but it is		
Subfan	nily:	Unassigned		acceptable to propose a species that is within a Subfamily or Family but not		
Fan	nily:	Adenoviridae		assigned to an existing genus (in whic		
Or	rder:	Unassigned		case put "unassigned" in the genus box)		

# Name(s) of proposed new species:

Human adenovirus G

# Argument to justify the creation of the new species:

The proposed species *Human adenovirus G* (containing HAdV-52, simian adenovirus 1 (SAdV-1) and probably several further Old World monkey AdVs) shows adequate phylogenetic distances (based on any of the major proteins properly applicable in phylogenetic calculations) to the members of all other known AdV species, including all the other primate AdV species. Six human AdV species have been accepted officially, and thus the presently proposed species should get the next available letter (G). The complete sequences of HAdV-52 and SAdV-1 have been determined. These viruses show a specifically different genome organization from other HAdVs. They can be differentiated even from the closest species, *Human adenovirus F*, the members of which (HAdV-40 and HAdV-41) lack the gene encoding the 12.5 K protein in the E3 region, as well as the RGD motif in the penton base. The genome organization together with the calculated phylogenetic distances justify the creation of a new species.

# **References:**

- de Jong JC, Osterhaus AD (2008) Human adenovirus type 52: a type 41 in disguise? Letter to the editor. J Virol 82, 3809
- Jones MS, Harrach B (2008) Human adenovirus type 52: a type 41 in disguise? Letter to the editor. Authors' reply. J Virol 82, 3809-3810
- Jones MS, Harrach B, Ganac RD, Gozum MMA, dela Cruz WP, Riedel B, Pan C, Delwart EL, Schnurr DP (2007): New adenovirus species found in patient presenting with gastroenteritis. J Virol 81, 5978-5984
- Kovács GM, Harrach B, Zakhartchouk AN, Davison AJ (2005): The complete genome sequence of simian adenovirus 1 an Old World monkey adenovirus with two fiber genes. J Gen Virol 86, 1681-1686

Roy S, Clawson DS, Wilson JM (2005) Methods of generating chimeric adenovirus and uses for such chimeric adenovirus. Patent: PCT WO/2005/001103-A 06-JAN-2005

# Annexes:

A novel HAdV, the 52nd type (hence HAdV-52), has been characterized, and its genome has been sequenced (**Fig. 2**). It merits the establishment of a new AdV species, proposed *Human* 

adenovirus G. Phylogenetically, the closest AdV is SAdV-1, which would be another member of this species (**Fig. 3**). The next closest characterized AdV is SAdV-7, which will most probably be defined as a further member of this species.

GenBank accession	numbers:		
HAdV-52:	DQ923122,	34,250 bp,	complete genome
SAdV-1:	AY771780,	34,450 bp,	complete genome
SAdV-7:	DQ792570,	31,045 bp,	complete genome

In the past, G+C content had been used to help classify HAdV species. The differences between the G+C contents of HAdV-52 (55.1%) and SAdV-1 (55%) and the members of *Human adenovirus F* (HAdV-40 and HAdV-41; 51.2 and 50.8%, respectively) are significant enough to support the proposed new species.

The most variable and therefore most informative component of AdV genomes (including HAdVs) are the E3 and E4 regions, because they show genus- and species-specific differences. The sequences coding for the E3 12.5K protein and the E4 dUTPase-related protein in HAdV-52 are absent from HAdV-40 and HAdV-41 (**Fig. 2**). The absence of these two genes from the members of the species *Human adenovirus F* make them quite different from HAdV-52 and SAdV-1, as well as other primate AdVs. Another striking difference between HAdV-52 and many other AdVs is the absence of the E3 19K protein gene from HAdV-52, whereas it is present in members of the species *Human adenovirus B*, *Human adenovirus C* and *Human adenovirus D*.

AdV entry is known to occur by attachment of the fiber-knob to different receptors on the surface of susceptible cells and subsequent internalization by an interaction between the penton base and cellular  $\alpha_v$  integrins. HAdV-52 and SAdV-1 have the integrin-binding motif on the penton base, but HAdV-40 and HAdV-41 do not. This unique feature of the two members of the species *Human adenovirus F* is further evidence for their distinctness from the members of the proposed new genus.

Multiple genome content differences necessitate the need to establish a species for HAdV-52 and SAdV-1 separate from the six established HAdV species and the species *Simian adenovirus A*. The species distinctions are human constructs that primarily reflect evolutionary differences among viruses. In the case of HAdV-52 and SAdV-1, the phylogenetic distances (which are at least as great as those differentiating the other HAdV species, **Fig. 3**), the different genome organizations (**Fig. 2**) and the different G+C contents support the proposal for a new species.

Attempts to amplify HAdV-52, using a multiplex assay that amplifies the fiber gene of every established HAdV species, have been unsuccessful. Sequence analysis demonstrated that the PCR primers are mismatched. The best forward primer (AdC1) matches 17 of 22 bases in HAdV-52, and the reverse primer (AdC2) matches only 9 of 20 nucleotides. These data are consistent with HAdV-52 being a member of a new species.

Antisera to SAdV-1, which neutralized SAdV-1 quite well, had a weak ability to neutralize HAdV-52 at a dilution of less than or equal to 1:32. In addition, HAdV-52 has been detected by PCR from a human fecal sample in a separate gastroenteritis outbreak. These results demonstrated that HAdV-52 is serologically different from SAdV-1 and is of human origin.



**Fig. 2.** Genome organization of (A) HAdV-52 (proposed *Human adenovirus G*) and (B) HAdV-40 (*Human adenovirus 40*).



Fig. 3. Phylogenetic trees based on three proteins of primate AdVs.