



(22) **Date de dépôt/Filing Date:** 2002/11/12
(41) **Mise à la disp. pub./Open to Public Insp.:** 2003/05/22
(45) **Date de délivrance/Issue Date:** 2017/06/06
(62) **Demande originale/Original Application:** 2 465 868
(30) **Priorités/Priorities:** 2001/11/13 (US60/350,607);
2001/12/17 (US60/341,117); 2002/05/01 (US60/377,066);
2002/06/05 (US60/386,675)

(51) **Cl.Int./Int.Cl.** **C12N 15/35** (2006.01),
A61K 48/00 (2006.01), **C07K 14/015** (2006.01),
C12N 15/864 (2006.01), **C12N 15/87** (2006.01),
C12N 7/01 (2006.01)

(72) **Inventeurs/Inventors:**
GAO, GUANGPING, US;
WILSON, JAMES M., US;
ALVIRA, MAURICIO R., US

(73) **Propriétaire/Owner:**
THE TRUSTEES OF THE UNIVERSITY OF
PENNSYLVANIA, US

(74) **Agent:** GOWLING WLG (CANADA) LLP

(54) **Titre :** METHODE DE DETECTION ET/OU D'IDENTIFICATION DE SEQUENCES DE VIRUS ASSOCIES AUX ADENOVIRUS (AAV) ET D'ISOLATION DE NOUVELLES SEQUENCES AINSI IDENTIFIEES
(54) **Title:** A METHOD OF DETECTING AND/OR IDENTIFYING ADENO-ASSOCIATED VIRUS (AAV) SEQUENCES AND ISOLATING NOVEL SEQUENCES IDENTIFIED THEREBY

(57) **Abrégé/Abstract:**

A method for detecting and isolating AAV sequences in a sample of DNA obtained from tissue or cells is provided. The invention further provides AAV sequences identified by this method, and vectors constructed using these sequences.



ABSTRACT

A method for detecting and isolating AAV sequences in a sample of DNA obtained from tissue or cells is provided. The invention further provides AAV sequences identified by this method, and vectors constructed using these sequences.

A METHOD OF DETECTING AND/OR IDENTIFYING ADENO-ASSOCIATED
VIRUS (AAV) SEQUENCES AND ISOLATING NOVEL SEQUENCES IDENTIFIED
THEREBY

5 BACKGROUND OF THE INVENTION

Adeno-associated virus (AAV), a member of the Parvovirus family, is a small
nonenveloped, icosahedral virus with single-stranded linear DNA genomes of 4.7 kilobases
(kb) to 6 kb. AAV is assigned to the genus, Dependovirus, because the virus was discovered
as a contaminant in purified adenovirus stocks. AAV's life cycle includes a latent phase at
10 which AAV genomes, after infection, are site specifically integrated into host chromosomes
and an infectious phase in which, following either adenovirus or herpes simplex virus
infection, the integrated genomes are subsequently rescued, replicated, and packaged into
infectious viruses. The properties of non-pathogenicity, broad host range of infectivity,
including non-dividing cells, and potential site-specific chromosomal integration make AAV
15 an attractive tool for gene transfer.

Recent studies suggest that AAV vectors may be the preferred vehicle for gene
therapy. To date, there have been 6 different serotypes of AAVs isolated from human or
non-human primates (NHP) and well characterized. Among them, human serotype 2 is the
first AAV that was developed as a gene transfer vector; it has been widely used for efficient
20 gene transfer experiments in different target tissues and animal models. Clinical trials of the
experimental application of AAV2 based vectors to some human disease models are in
progress, and include such diseases as cystic fibrosis and hemophilia B.

What are desirable are AAV-based constructs for gene delivery.

25 SUMMARY OF THE INVENTION

In one aspect, the invention provides a novel method of detecting and identifying
AAV sequences from cellular DNAs of various human and non-human primate (NHP)
tissues using bioinformatics analysis, PCR based gene amplification and cloning technology,
based on the nature of latency and integration of AAVs in the absence of helper virus co-
30 infection.

In another aspect, the invention provides method of isolating novel AAV sequences
detected using the above described method of the invention. The invention further comprises
methods of generating vectors based upon these novel AAV serotypes, for serology and gene

transfer studies solely based on availability of capsid gene sequences and structure of rep/cap gene junctions.

In still another aspect, the invention provides a novel method for performing studies of serology, epidemiology, biodistribution and mode of transmission, using reagents

5 according to the invention, which include generic sets of primers/probes and quantitative real time PCR.

In yet another aspect, the invention provides a method of isolating complete and infectious genomes of novel AAV serotypes from cellular DNA of different origins using RACE and other molecular techniques.

10 In a further aspect, the invention provides a method of rescuing novel serotypes of AAV genomes from human and NHP cell lines using adenovirus helpers of different origins.

In still a further aspect, the invention provides novel AAV serotypes, vectors containing same, and methods of using same.

15 These and other aspects of the invention will be readily apparent from the following detailed description of the invention.

BRIEF DESCRIPTION OF THE DRAWINGS

Figs. 1A through 1AAAR provide an alignment of the nucleic acid sequences encoding at least the cap proteins for the AAV serotypes. The full-length sequences including the ITRs, the rep region, and the capsid region are provided for novel AAV serotype 7 [SEQ ID NO:1], and for previously published AAV1 [SEQ ID NO:6], AAV2 [SEQ ID NO:7]; and AAV3 [SEQ ID NO:8]. Novel AAV serotypes AAV8 [SEQ ID NO:4] and AAV9 [SEQ ID NO:5] are the subject of co-filed applications. The other novel clones of the invention provided in this alignment include: 42-2 [SEQ ID NO:9], 42-8 [SEQ ID NO:27], 42-15 [SEQ ID NO:28], 42-5b [SEQ ID NO: 29], 42-1b [SEQ ID NO:30]; 42-13 [SEQ ID NO: 31], 42-3a [SEQ ID NO: 32], 42-4 [SEQ ID NO:33], 42-5a [SEQ ID NO: 34], 42-10 [SEQ ID NO:35], 42-3b [SEQ ID NO: 36], 42-11 [SEQ ID NO: 37], 42-6b [SEQ ID NO:38], 43-1 [SEQ ID NO: 39], 43-5 [SEQ ID NO: 40], 43-12 [SEQ ID NO:41], 43-20 [SEQ ID NO:42], 43-21 [SEQ ID NO: 43], 43-23 [SEQ ID NO:44], 43-25 [SEQ ID NO: 45], 44.1 [SEQ ID NO:47], 44.5 [SEQ ID NO:47], 223.10 [SEQ ID NO:48], 223.2 [SEQ ID NO:49], 223.4 [SEQ ID NO:50], 223.5 [SEQ ID NO: 51], 223.6 [SEQ ID NO: 52], 223.7 [SEQ ID NO: 53], A3.4 [SEQ ID NO: 54], A3.5 [SEQ ID NO:55], A3.7 [SEQ ID NO: 56], A3.3 [SEQ ID NO:57], 42.12 [SEQ ID NO: 58], 44.2 [SEQ ID NO: 59]. The nucleotide sequences of the signature regions of AAV10 [SEQ ID NO: 117], AAV11 [SEQ ID NO:

118] and AAV12 [SEQ ID NO:119] are provided in this figure. Critical landmarks in the structures of AAV genomes are shown. Gaps are demonstrated by dots. The 3' ITR of AAV1 [SEQ ID NO:6] is shown in the same configuration as in the published sequences. TRS represents terminal resolution site. Notice that AAV7 is the only AAV reported that uses
 5 GTG as the initiation codon for VP3.

Figs. 2A through 2F are an alignment of the amino acid sequences of the proteins of the vp1 capsid proteins of previously published AAV serotypes 1 [SEQ ID NO:64], AAV2 [SEQ ID NO:70], AAV3 [SEQ ID NO: 71], AAV4 [SEQ ID NO:63], AAV5 [SEQ ID NO:114], and AAV6 [SEQ ID NO:65] and novel AAV sequences of the invention,
 10 including: C1 [SEQ ID NO:60], C2 [SEQ ID NO:61], C5 [SEQ ID NO:62], A3-3 [SEQ ID NO:66], A3-7 [SEQ ID NO:67], A3-4 [SEQ ID NO:68], A3-5 [SEQ ID NO: 69], 3.3b [SEQ ID NO: 62], 223.4 [SEQ ID NO: 73], 223-5 [SEQ ID NO:74], 223-10 [SEQ ID NO:75], 223-2 [SEQ ID NO:76], 223-7 [SEQ ID NO: 77], 223-6 [SEQ ID NO: 78], 44-1 [SEQ ID NO: 79], 44-5 [SEQ ID NO:80], 44-2 [SEQ ID NO:81], 42-15 [SEQ ID NO: 84], 42-8 [SEQ ID NO: 85], 42-13 [SEQ ID NO:86], 42-3A [SEQ ID NO:87], 42-4 [SEQ ID NO:88], 42-5A [SEQ ID NO:89], 42-1B [SEQ ID NO:90], 42-5B [SEQ ID NO:91], 43-1 [SEQ ID NO: 92], 43-12 [SEQ ID NO: 93], 43-5 [SEQ ID NO:94], 43-21 [SEQ ID NO:96], 43-25 [SEQ ID NO: 97], 43-20 [SEQ ID NO:99], 24.1 [SEQ ID NO: 101], 42.2 [SEQ ID NO:102], 7.2 [SEQ ID NO: 103], 27.3 [SEQ ID NO: 104], 16.3 [SEQ ID NO: 105], 42.10 [SEQ ID NO: 106],
 15 42-3B [SEQ ID NO: 107], 42-11 [SEQ ID NO: 108], F1 [SEQ ID NO: 109], F5 [SEQ ID NO: 110], F3 [SEQ ID NO:111], 42-6B [SEQ ID NO: 112], 42-12 [SEQ ID NO: 113]. Novel serotypes AAV8 [SEQ ID NO:95] and AAV9 [SEQ ID NO:100] are the subject of co-filed patent applications.

Figs. 3A through 3C provide the amino acid sequences of the AAV7 rep
 25 proteins [SEQ ID NO:3].

DETAILED DESCRIPTION OF THE INVENTION

In the present invention, the inventors have found a method which takes advantage of the ability of adeno-associated virus (AAV) to penetrate the nucleus, and, in the absence of a
 30 helper virus co-infection, to integrate into cellular DNA and establish a latent infection. This method utilizes a polymerase chain reaction (PCR)-based strategy for detection, identification and/or isolation of sequences of AAVs from DNAs from tissues of human and non-human primate origin as well as from other sources. Advantageously, this method is

also suitable for detection, identification and/or isolation of other integrated viral and non-viral sequences, as described below.

The invention further provides nucleic acid sequences identified according to the methods of the invention. One such adeno-associated virus is of a novel serotype, termed
 5 herein serotype 7 (AAV7). Other novel adeno-associated virus serotypes provided herein include AAV10, AAV11, and AAV12. Still other novel AAV serotypes identified according to the methods of the invention are provided in the present specification. See, Figures and Sequence Listing, which is incorporated by reference.

Also provided are fragments of these AAV sequences. Among particularly desirable
 10 AAV fragments are the cap proteins, including the vp1, vp2, vp3, the hypervariable regions, the rep proteins, including rep 78, rep 68, rep 52, and rep 40, and the sequences encoding these proteins. Each of these fragments may be readily utilized in a variety of vector systems and host cells. Such fragments may be used alone, in combination with other AAV
 15 sequences or fragments, or in combination with elements from other AAV or non-AAV viral sequences. In one particularly desirable embodiment, a vector contains the AAV cap and/or rep sequences of the invention.

As described herein, alignments are performed using any of a variety of publicly or commercially available Multiple Sequence Alignment Programs, such as "Clustal W", accessible through Web Servers on the internet. Alternatively, Vector NTI utilities are also
 20 used. There are also a number of algorithms known in the art which can be used to measure nucleotide sequence identity, including those contained in the programs described above. As another example, polynucleotide sequences can be compared using Fasta, a program in GCG Version 6.1. Fasta provides alignments and percent sequence identity of the regions of the best overlap between the query and search sequences. For instance, percent sequence
 25 identity between nucleic acid sequences can be determined using Fasta with its default parameters (a word size of 6 and the NOPAM factor for the scoring matrix) as provided in GCG Version 6.1, herein incorporated by reference. Similar programs are available for amino acid sequences, e.g., the "Clustal X" program. Generally, any of these programs are used at default settings, although one of skill in the art can alter these settings as needed.
 30 Alternatively, one of skill in the art can utilize another algorithm or computer program which provides at least the level of identity or alignment as that provided by the referenced algorithms and programs.

The term "substantial homology" or "substantial similarity," when referring to a nucleic acid, or fragment thereof, indicates that, when optimally aligned with appropriate

nucleotide insertions or deletions with another nucleic acid (or its complementary strand), there is nucleotide sequence identity in at least about 95 to 99% of the aligned sequences. Preferably, the homology is over full-length sequence, or an open reading frame thereof, or another suitable fragment which is at least 15 nucleotides in length. Examples of suitable fragments are described herein.

The term "substantial homology" or "substantial similarity," when referring to amino acids or fragments thereof, indicates that, when optimally aligned with appropriate amino acid insertions or deletions with another amino acid, there is amino acid sequence identity in at least about 95 to 99% of the aligned sequences. Preferably, the homology is over full-length sequence, or a protein thereof, e.g., a cap protein, a rep protein, or a fragment thereof which is at least 8 amino acids, or more desirably, at least 15 amino acids in length. Examples of suitable fragments are described herein.

By the term "highly conserved" is meant at least 80% identity, preferably at least 90% identity, and more preferably, over 97% identity. Identity is readily determined by one of skill in the art by resort to algorithms and computer programs known by those of skill in the art.

The term "percent sequence identity" or "identical" in the context of nucleic acid sequences refers to the residues in the two sequences which are the same when aligned for maximum correspondence. The length of sequence identity comparison may be over the full-length of the genome, the full-length of a gene coding sequence, or a fragment of at least about 500 to 5000 nucleotides, is desired. However, identity among smaller fragments, e.g. of at least about nine nucleotides, usually at least about 20 to 24 nucleotides, at least about 28 to 32 nucleotides, at least about 36 or more nucleotides, may also be desired. Similarly, "percent sequence identity" may be readily determined for amino acid sequences, over the full-length of a protein, or a fragment thereof. Suitably, a fragment is at least about 8 amino acids in length, and may be up to about 700 amino acids. Examples of suitable fragments are described herein.

The AAV sequences and fragments thereof are useful in production of rAAV, and are also useful as antisense delivery vectors, gene therapy vectors, or vaccine vectors. The invention further provides nucleic acid molecules, gene delivery vectors, and host cells which contain the AAV sequences of the invention.

As described herein, the vectors of the invention containing the AAV capsid proteins of the invention are particularly well suited for use in applications in which the neutralizing antibodies diminish the effectiveness of other AAV serotype based vectors, as well as other viral vectors. The rAAV vectors of the invention are particularly advantageous in rAAV readministration and repeat gene therapy.

These and other embodiments and advantages of the invention are described in more detail below. As used throughout this specification and the claims, the terms "comprising" and "including" and their variants are inclusive of other components, elements, integers, steps and the like. Conversely, the term "consisting" and its variants is exclusive of other components, elements, integers, steps and the like.

I. Methods of the Invention

A. Detection of Sequences Via Molecular Cloning

In one aspect, the invention provides a method of detecting and/or identifying target nucleic acid sequences in a sample. This method is particularly well suited for detection of viral sequences which are integrated into the chromosome of a cell, e.g., adeno-associated viruses (AAV) and retroviruses, among others. The specification makes reference to AAV, which is exemplified herein. However, based on this information, one of skill in the art may readily perform the methods of the invention on retroviruses [e.g., feline leukemia virus (FeLV), HTLV I and HTLV II], and lentivirinae [e.g., human immunodeficiency virus (HIV), simian immunodeficiency virus (SIV), feline immunodeficiency virus (FIV), equine infectious anemia virus, and spumavirinae)], among others. Further, the method of the invention may also be used for detection of other viral and non-viral sequences, whether integrated or non-integrated into the genome of the host cell.

As used herein, a sample is any source containing nucleic acids, e.g., tissue, tissue culture, cells, cell culture, and biological fluids including, without limitation, urine and blood. These nucleic acid sequences may be DNA or RNA from plasmids, natural DNA or RNA from any source, including bacteria, yeast, viruses, and higher organisms such as plants or animals. DNA or RNA is extracted from the sample by a variety of techniques known to those of skill in the art, such as those described by Sambrook, Molecular Cloning: A Laboratory Manual (New York: Cold Spring Harbor Laboratory). The origin of the sample and the method by which the nucleic acids are obtained for application of the method of the

invention is not a limitation of the present invention. Optionally, the method of the invention can be performed directly on the source of DNA, or on nucleic acids obtained (e.g., extracted) from a source.

The method of the invention involves subjecting a sample containing DNA to
 5 amplification via polymerase chain reaction (PCR) using a first set of primers specific for a first region of double-stranded nucleic acid sequences, thereby obtaining amplified sequences.

As used herein, each of the "regions" is predetermined based upon the alignment of the nucleic acid sequences of at least two serotypes (e.g., AAV) or strains (e.g.,
 10 lentiviruses), and wherein each of said regions is composed of sequences having a 5' end which is highly conserved, a middle which is preferably, but necessarily, variable, and a 3' end which is highly conserved, each of these being conserved or variable relative to the sequences of the at least two aligned AAV serotypes. Preferably, the 5' and/or 3' end is highly conserved over at least about 9, and more preferably, at least 18 base pairs (bp).
 15 However, one or both of the sequences at the 5' or 3' end may be conserved over more than 18 bp, more than 25 bp, more than 30 bp, or more than 50 bp at the 5' end. With respect to the variable region, there is no requirement for conserved sequences, these sequences may be relatively conserved, or may have less than 90, 80, or 70% identity among the aligned serotypes or strains.

Each of the regions may span about 100 bp to about 10 kilobase pairs in
 20 length. However, it is particularly desirable that one of the regions is a "signature region", i.e., a region which is sufficiently unique to positively identify the amplified sequence as being from the target source. For example, in one embodiment, the first region is about 250 bp in length, and is sufficiently unique among known AAV sequences, that it positively
 25 identifies the amplified region as being of AAV origin. Further, the variable sequences within this region are sufficiently unique that can be used to identify the serotype from which the amplified sequences originate. Once amplified (and thereby detected), the sequences can be identified by performing conventional restriction digestion and comparison to restriction digestion patterns for this region in any of AAV1, AAV2, AAV3, AAV4, AAV5, or AAV6,
 30 or that of AAV7, AAV10, AAV11, AAV12, or any of the other novel serotypes identified by the invention, which is predetermined and provided by the present invention.

Given the guidance provided herein, one of skill in the art can readily identify such regions among other integrated viruses to permit ready detection and identification of these sequences. Thereafter, an optimal set of generic primers located

within the highly conserved ends can be designed and tested for efficient amplification of the selected region from samples. This aspect of the invention is readily adapted to a diagnostic kit for detecting the presence of the target sequence (e.g., AAV) and for identifying the AAV serotype, using standards which include the restriction patterns for the AAV serotypes described herein or isolated using the techniques described herein. For example, quick
 5 identification or molecular serotyping of PCR products can be accomplished by digesting the PCR products and comparing restriction patterns.

Thus, in one embodiment, the "signature region" for AAV spans about bp 2800 to about 3200 of AAV 1 [SEQ ID NO:6], and corresponding base pairs in AAV 2,
 10 AAV3, AAV4, AAV5, and AAV6. More desirably, the region is about 250 bp, located within bp 2886 to about 3143 bp of AAV 1 [SEQ ID NO:6], and corresponding base pairs in AAV 2 [SEQ ID NO:7], AAV3 [SEQ ID NO:8], and other AAV serotypes. See, Fig. 1. To permit rapid detection of AAV in the sample, primers which specifically amplify this signature region are utilized. However, the present invention is not limited to the exact
 15 sequences identified herein for the AAV signature region, as one of skill in the art may readily alter this region to encompass a shorter fragment, or a larger fragment of this signature region.

The PCR primers are generated using techniques known to those of skill in the art. Each of the PCR primer sets is composed of a 5' primer and a 3' primer. See, e.g.,
 20 Sambrook et al, cited herein. The term "primer" refers to an oligonucleotide which acts as a point of initiation of synthesis when placed under conditions in which synthesis of a primer extension product which is complementary to a nucleic acid strand is induced. The primer is preferably single stranded. However, if a double stranded primer is utilized, it is treated to separate its strands before being used to prepare extension products. The primers may be
 25 about 15 to 25 or more nucleotides, and preferably at least 18 nucleotides. However, for certain applications shorter nucleotides, e.g., 7 to 15 nucleotides are utilized.

The primers are selected to be sufficiently complementary to the different strands of each specific sequence to be amplified to hybridize with their respective strands. Therefore, the primer sequence need not reflect the exact sequence of the region being
 30 amplified. For example, a non-complementary nucleotide fragment may be attached to the 5' end of the primer, with the remainder of the primer sequence being completely complementary to the strand. Alternatively, non-complementary bases or longer sequences can be interspersed into the primer, provided that the primer sequence has sufficient

complementarity with the sequence of the strand to be amplified to hybridize therewith and form a template for synthesis of the extension product of the other primer.

The PCR primers for the signature region according to the invention are based upon the highly conserved sequences of two or more aligned sequences (e.g., two or more AAV serotypes). The primers can accommodate less than exact identity among the two or more aligned AAV serotypes at the 5' end or in the middle. However, the sequences at the 3' end of the primers correspond to a region of two or more aligned AAV serotypes in which there is exact identity over at least five, preferably, over at least nine base pairs, and more preferably, over at least 18 base pairs at the 3' end of the primers. Thus, the 3' end of the primers is composed of sequences with 100% identity to the aligned sequences over at least five nucleotides. However, one can optionally utilize one, two, or more degenerate nucleotides at the 3' end of the primer.

For example, the primer set for the signature region of AAV was designed based upon a unique region within the AAV capsid, as follows. The 5' primer was based upon nt 2867-2891 of AAV2 [SEQ ID NO:7], 5'-GGTAATTCCTCCGGAAATTGGCATT3'. See, Fig. 1. The 3' primer was designed based upon nt 3096-3122 of AAV2 [SEQ ID NO:7], 5'-GACTCATCAACAACAACCTGGGGATTTC-3'. However, one of skill in the art may have readily designed the primer set based upon the corresponding regions of AAV 1, AAV3, AAV4, AAV5, AAV6, or based upon the information provided herein, AAV7, AAV10, AAV11, AAV12, or another novel AAV of the invention. In addition, still other primer sets can be readily designed to amplify this signature region, using techniques known to those of skill in the art.

B. Isolation of Target Sequences

As described herein, the present invention provides a first primer set which specifically amplifies the signature region of the target sequence, e.g., an AAV serotype, in order to permit detection of the target. In a situation in which further sequences are desired, e.g., if a novel AAV serotype is identified, the signature region may be extended. Thus, the invention may further utilize one or more additional primer sets.

Suitably, these primer sets are designed to include either the 5' or 3' primer of the first primer set and a second primer unique to the primer set, such that the primer set amplifies a region 5' or 3' to the signature region which anneals to either the 5' end or the 3' end of the signature region. For example, a first primer set is composed of a 5' primer, P1

and a 3' primer P2 to amplify the signature region. In order to extend the signature region on its 3' end, a second primer set is composed of primer P1 and a 3' primer P4, which amplifies the signature region and contiguous sequences downstream of the signature region. In order to extend the signature region on its 5' end, a third primer set is composed of a 5' primer, P5, and primer P2, such that the signature region and contiguous sequences upstream of the signature region are amplified. These extension steps are repeated (or performed at the same time), as needed or desired. Thereafter, the products results from these amplification steps are fused using conventional steps to produce an isolated sequence of the desired length.

The second and third primer sets are designed, as with the primer set for the signature region, to amplify a region having highly conserved sequences among the aligned sequences. Reference herein to the term "second" or "third" primer set is for each of discussion only, and without regard to the order in which these primers are added to the reaction mixture, or used for amplification. The region amplified by the second primer set is selected so that upon amplification it anneals at its 5' end to the 3' end of the signature region. Similarly, the region amplified by the third primer set is selected so that upon amplification it anneals at its 3' end anneals to the 5' end of the signature region. Additional primer sets can be designed such that the regions which they amplify anneal to the either the 5' end or the 3' end of the extension products formed by the second or third primer sets, or by subsequent primer sets.

For example, where AAV is the target sequence, a first set of primers (P1 and P2) are used to amplify the signature region from the sample. In one desirable embodiment, this signature region is located within the AAV capsid. A second set of primers (P1 and P4) is used to extend the 3' end of the signature region to a location in the AAV sequence which is just before the AAV 3' ITR, i.e., providing an extension product containing the entire 3' end of the AAV capsid when using the signature region as an anchor. In one embodiment, the P4 primer corresponds to nt 4435 to 4462 of AAV2 [SEQ ID NO:7], and corresponding sequences in the other AAV serotypes. This results in amplification of a region of about 1.6 kb, which contains the 0.25 kb signature region. A third set of primers (P3 and P2) is used to extend the 5' end of signature region to a location in the AAV sequences which is in the 3' end of the rep genes, i.e., providing an extension product containing the entire 5' end of the AAV capsid when using the signature region as an anchor. In one embodiment, the P3 primer corresponds to nt 1384 to 1409 of AAV2 [SEQ ID NO:7], and corresponding sequences in the other AAV serotypes. This results in amplification of a region of about 1.7

kb, which contains the 0.25 kb signature region. Optionally, a fourth set of primers are used to further extend the extension product containing the entire 5' end of the AAV capsid to also include the rep sequences. In one embodiment, the primer designated P5 corresponds to nt 108 to 133 of AAV2 [SEQ ID NO:7], and corresponding sequences in the other AAV serotypes and is used in conjunction with the P2 primer.

Following completion of the desired number of extension steps, the various extension products are fused, making use of the signature region as an anchor or marker, to construct an intact sequence. In the example provided herein, AAV sequences containing, at a minimum, an intact AAV cap gene are obtained. Larger sequences may be obtained, depending upon the number of extension steps performed.

Suitably, the extension products are assembled into an intact AAV sequence using methods known to those of skill in the art. For example, the extension products may be digested with DraIII, which cleaves at the DraIII site located within the signature region, to provide restriction fragments which are re-ligated to provide products containing (at a minimum) an intact AAV cap gene. However, other suitable techniques for assembling the extension products into an intact sequence may be utilized. See, generally, Sambrook et al, cited herein.

As an alternative to the multiple extension steps described above, another embodiment of the invention provides for direct amplification of a 3.1 kb fragment which allows isolation of full-length cap sequences. To directly amplify a 3.1 kb full-length cap fragment from NHP tissue and blood DNAs, two other highly conserved regions were identified in AAV genomes for use in PCR amplification of large fragments. A primer within a conserved region located in the middle of the rep gene is utilized (AV1ns: 5' GCTGCGTCAACTGGACCAATGAGAAC 3', nt of SEQ ID NO:6) in combination with the 3' primer located in another conserved region downstream of the Cap gene (AV2cas: 5' CGCAGAGACCAAAGTTCAACTGAAACGA 3', SEQ ID NO: 7) for amplification of AAV sequences including the full-length AAV cap. Typically, following amplification, the products are cloned and sequence analysis is performed with an accuracy of $\geq 99.9\%$. Using this method, the inventors have isolated at least 50 capsid clones which have subsequently been characterized. Among them, 37 clones were derived from Rhesus macaque tissues (rh.1 – rh.37), 6 clones from cynomologous macaques (cy.1 – cy.6), 2 clones from Baboons (bb.1 and bb.2) and 5 clones from Chimps (ch.1 – ch.5). These clones are identified

elsewhere in the specification, together with the species of animal from which they were identified and the tissues in that animal these novel sequences have been located.

C. Alternative method for isolating novel AAV

In another aspect, the invention provides an alternative method for isolating novel AAV from a cell. This method involves infecting the cell with a vector which provides helper functions to the AAV; isolating infectious clones containing AAV; sequencing the isolated AAV; and comparing the sequences of the isolated AAV to known AAV serotypes, whereby differences in the sequences of the isolated AAV and known AAV serotypes indicates the presence of a novel AAV.

In one embodiment, the vector providing helper functions provides essential adenovirus functions, including, e.g., E1a, E1b, E2a, E4ORF6. In one embodiment, the helper functions are provided by an adenovirus. The adenovirus may be a wild-type adenovirus, and may be of human or non-human origin, preferably non-human primate (NHP) origin. The DNA sequences of a number of adenovirus types are available from Genbank, including type Ad5 [Genbank Accession No. M73260]. The adenovirus sequences may be obtained from any known adenovirus serotype, such as serotypes 2, 3, 4, 7, 12 and 40, and further including any of the presently identified human types [see, e.g., Horwitz, cited above]. Similarly adenoviruses known to infect non-human animals (e.g., chimpanzees) may also be employed in the vector constructs of this invention. See, e.g., US Patent No. 6,083,716. In addition to wild-type adenoviruses, recombinant viruses or non-viral vectors (e.g., plasmids, episomes, etc.) carrying the necessary helper functions may be utilized. Such recombinant viruses are known in the art and may be prepared according to published techniques. See, e.g., US Patent No. 5,871,982 and US Patent 6,251,677, which describe a hybrid Ad/AAV virus. The selection of the adenovirus type is not anticipated to limit the following invention. A variety of adenovirus strains are available from the American Type Culture Collection, Manassas, Virginia, or available by request from a variety of commercial and institutional sources. Further, the sequences of many such strains are available from a variety of databases including, e.g., PubMed and GenBank.

In another alternative, infectious AAV may be isolated using genome walking technology (Siebert *et al.*, 1995, *Nucleic Acid Research*, 23:1087-1088, Frieznier-Degen *et al.*, 1986, *J. Biol. Chem.* 261:6972-6985, BD Biosciences Clontech, Palo Alto, CA). Genome walking is particularly well suited for identifying and isolating the sequences adjacent to the novel sequences identified according to the method of the invention. For

example, this technique may be useful for isolating inverted terminal repeat (ITRs) of the novel AAV serotype, based upon the novel AAV capsid and/or rep sequences identified using the methods of the invention. This technique is also useful for isolating sequences adjacent to other AAV and non-AAV sequences identified and isolated according to the present invention. See, Examples 3 and 4.

The methods of the invention may be readily used for a variety of epidemiology studies, studies of biodistribution, monitoring of gene therapy via AAV vectors and vector derived from other integrated viruses. Thus, the methods are well suited for use in pre-packaged kits for use by clinicians, researchers, and epidemiologists.

10

II. Diagnostic Kit

In another aspect, the invention provides a diagnostic kit for detecting the presence of a known or unknown adeno-associated virus (AAV) in a sample. Such a kit may contain a first set of 5' and 3' PCR primers specific for a signature region of the AAV nucleic acid sequence. Alternatively, or additionally, such a kit can contain a first set of 5' and 3' PCR primers specific for the 3.1 kb fragment which includes the full-length AAV capsid nucleic acid sequence identified herein (e.g., the AV1ns and AV2cas primers.) Optionally, a kit of the invention may further contain two or more additional sets of 5' and 3' primers, as described herein, and/or PCR probes. These primers and probes are used according to the present invention amplify signature regions of each AAV serotype, e.g., using quantitative PCR.

The invention further provides a kit useful for identifying an AAV serotype detected according to the method of the invention and/or for distinguishing novel AAV from known AAV. Such a kit may further include one or more restriction enzymes, standards for AAV serotypes providing their "signature restriction enzyme digestions analyses", and/or other means for determining the serotype of the AAV detected.

In addition, kits of the invention may include, instructions, a negative and/or positive control, containers, diluents and buffers for the sample, indicator charts for signature comparisons, disposable gloves, decontamination instructions, applicator sticks or containers, and sample preparator cups, as well as any desired reagents, including media, wash reagents and concentration reagents. Such reagents may be readily selected from among the reagents described herein, and from among conventional concentration reagents. In one desirable embodiment, the wash reagent is an isotonic saline solution which has been

30

buffered to physiologic pH, such as phosphate buffered saline (PBS); the elution reagent is PBS containing 0.4 M NaCl, and the concentration reagents and devices. For example, one of skill in the art will recognize that reagents such as polyethylene glycol (PEG), or NH_4SO_4 may be useful, or that devices such as filter devices. For example, a filter device with a 100 K membrane would concentrate rAAV.

The kits provided by the present invention are useful for performing the methods described herein, and for study of biodistribution, epidemiology, mode of transmission of novel AAV serotypes in human and NHPs.

Thus, the methods and kits of the invention permit detection, identification, and isolation of target viral sequences, particularly integrated viral sequences. The methods and kits are particularly well suited for use in detection, identification and isolation of AAV sequences, which may include novel AAV serotypes.

In one notable example, the method of the invention facilitated analysis of cloned AAV sequences by the inventors, which revealed heterogeneity of proviral sequences between cloned fragments from different animals, all of which were distinct from the known six AAV serotypes, with the majority of the variation localized to hypervariable regions of the capsid protein. Surprising divergence of AAV sequences was noted in clones isolated from single tissue sources, such as lymph node, from an individual rhesus monkey. This heterogeneity is best explained by apparent evolution of AAV sequence within individual animals due, in part, to extensive homologous recombination between a limited number of co-infecting parenteral viruses. These studies suggest sequence evolution of widely disseminated virus during the course of a natural AAV infection that presumably leads to the formation of swarms of quasispecies which differ from one another in the array of capsid hypervariable regions. This is the first example of rapid molecular evolution of a DNA virus in a way that formerly was thought to be restricted to RNA viruses.

Sequences of several novel AAV serotypes identified by the method of the invention and characterization of these serotypes is provided.

III. Novel AAV Serotypes

A. Nucleic Acid Sequences

Nucleic acid sequences of novel AAV serotypes identified by the methods of the invention are provided. See, SEQ ID NO:1, 9 – 59, and 117 – 120, which are incorporated by reference herein. See also, Fig. 1 and the sequence listing.

For novel serotype AAV7, the full-length sequences, including the AAV 5' ITRs, capsid, rep, and AAV 3' ITRs are provided in SEQ ID NO:1.

For other novel AAV serotypes of the invention, the approximately 3.1 kb fragment isolated according to the method of the invention is provided. This fragment
5 contains sequences encoding full-length capsid protein and all or part of the sequences encoding the rep protein. These sequences include the clones identified below.

For still other novel AAV serotypes, the signature region encoding the capsid protein is provided. For example, the AAV10 nucleic acid sequences of the invention include those illustrated in Fig. 1 [See, SEQ ID NO:117, which spans 255 bases]. The
10 AAV11 nucleic acid sequences of the invention include the DNA sequences illustrated in Fig. 1 [See, SEQ ID NO:118 which spans 258 bases]. The AAV12 nucleic acid sequences of the invention include the DNA sequences illustrated in Fig. 1 [See, SEQ ID NO:119, which consists of 255 bases]. Using the methodology described above, further AAV10, AAV11 and AAV12 sequences can be readily identified and used for a variety of purposes, including
15 those described for AAV7 and the other novel serotypes herein.

Figure 1 provides the non-human primate (NHP) AAV nucleic acid sequences of the invention in an alignment with the previously published AAV serotypes, AAV 1 [SEQ ID NO:6], AAV2 [SEQ ID NO:7], and AAV3 [SEQ ID NO:8]. These novel NHP sequences include those provided in the following Table I, which are identified by
20 clone number:

Table 1

AAV Cap Sequence	Clone Number	Source		
		Species	Tissue	SEQ ID NO (DNA)
Rh.1	Clone 9 (AAV9)	Rhesus	Heart	5
Rh.2	Clone 43.1	Rhesus	MLN	39
Rh.3	Clone 43.5	Rhesus	MLN	40
Rh.4	Clone 43.12	Rhesus	MLN	41
Rh.5	Clone 43.20	Rhesus	MLN	42
Rh.6	Clone 43.21	Rhesus	MLN	43
Rh.7	Clone 43.23	Rhesus	MLN	44

Table 1 (cont'd)

Rh.8	Clone 43.25	Rhesus	MLN	45
Rh.9	Clone 44.1	Rhesus	Liver	46
Rh.10	Clone 44.2	Rhesus	Liver	59
Rh.11	Clone 44.5	Rhesus	Liver	47
Rh.12	Clone 42.1B	Rhesus	MLN	30
Rh.13	42.2	Rhesus	MLN	9
Rh.14	Clone 42.3A	Rhesus	MLN	32
Rh.15	Clone 42.3B	Rhesus	MLN	36
Rh.16	Clone 42.4	Rhesus	MLN	33
Rh.17	Clone 42.5A	Rhesus	MLN	34
Rh.18	Clone 42.5B	Rhesus	MLN	29
Rh.19	Clone 42.6B	Rhesus	MLN	38
Rh.20	Clone 42.8	Rhesus	MLN	27
Rh.21	Clone 42.10	Rhesus	MLN	35
Rh.22	Clone 42.11	Rhesus	MLN	37
Rh.23	Clone 42.12	Rhesus	MLN	58
Rh.24	Clone 42.13	Rhesus	MLN	31
Rh.25	Clone 42.15	Rhesus	MLN	28
Rh.26	Clone 223.2	Rhesus	Liver	49
Rh.27	Clone 223.4	Rhesus	Liver	50
Rh.28	Clone 223.5	Rhesus	Liver	51
Rh.29	Clone 223.6	Rhesus	Liver	52
Rh.30	Clone 223.7	Rhesus	Liver	53
Rh.31	Clone 223.10	Rhesus	Liver	48
Rh.32	Clone C1	Rhesus	Spleen, Duo, Kid & Liver	19
Rh.33	Clone C3	Rhesus		20
Rh.34	Clone C5	Rhesus		21
Rh.35	Clone F1	Rhesus	Liver	22
Rh.36	Clone F3	Rhesus		23
Rh.37	Clone F5	Rhesus		24
Cy.1	Clone 1.3	Cyno	Blood	14
Cy.2	Clone 13.3B	Cyno	Blood	15
Cy.3	Clone 24.1	Cyno	Blood	16
Cy.4	Clone 27.3	Cyno	Blood	17
Cy.5	Clone 7.2	Cyno	Blood	18
Cy.6	Clone 16.3	Cyno	Blood	10

Table 1 (cont'd)				
bb.1	Clone 29.3	Baboon	Blood	11
bb.2	Clone 29.5	Baboon	Blood	13
Ch.1	Clone A3.3	Chimp	Blood	57
Ch.2	Clone A3.4	Chimp	Blood	54
Ch.3	Clone A3.5	Chimp	Blood	55
Ch.4	Clone A3.7	Chimp	Blood	56

A novel NHP clone was made by splicing capsids fragments of two chimp adenoviruses into an AAV2 rep construct. This new clone, A3.1, is also termed Ch.5 [SEQ ID NO:20]. Additionally, the present invention includes two human AAV sequences, termed
5 H6 [SEQ ID NO:25] and H2 [SEQ ID NO:26].

The AAV nucleic acid sequences of the invention further encompass the strand which is complementary to the strands provided in the sequences provided in Fig. 1 and the Sequence Listing [SEQ ID NO:1, 9 – 59, 117 – 120], nucleic acid sequences, as well as the RNA and cDNA sequences corresponding to the sequences provided in Fig. 1 and the
10 Sequence Listing [SEQ ID NO:1, 9 – 59, 117-120], and their complementary strands. Also included in the nucleic acid sequences of the invention are natural variants and engineered modifications of the sequences of Fig1 and the Sequence Listing [SEQ ID NO:1, 9 – 59, 117-120], and their complementary strands. Such modifications include, for example, labels which are known in the art, methylation, and substitution of one or more of the naturally
15 occurring nucleotides with a degenerate nucleotide.

Further included in this invention are nucleic acid sequences which are greater than 85%, preferably at least about 90%, more preferably at least about 95%, and most preferably at least about 98 to 99% identical or homologous to the sequences of the invention, including Fig. 1 and the Sequence Listing [SEQ ID NO:1, 9 – 59, 117-120].
20 These terms are as defined herein.

Also included within the invention are fragments of the novel AAV sequences identified by the method described herein. Suitable fragments are at least 15 nucleotides in length, and encompass functional fragments, i.e., fragments which are of biological interest. In one embodiment, these fragments are fragments of the novel
25 sequences of Fig. 1 and the Sequence Listing [SEQ ID NO:1, 9 – 59, 117-120], their complementary strands, cDNA and RNA complementary thereto.

Examples of suitable fragments are provided with respect to the location of these fragments on AAV1, AAV2, or AAV7. However, using the alignment provided herein (obtained using the Clustal W program at default settings), or similar techniques for

generating an alignment with other novel serotypes of the invention, one of skill in the art can readily identify the precise nucleotide start and stop codons for desired fragments.

Examples of suitable fragments include the sequences encoding the three variable proteins (vp) of the AAV capsid which are alternative splice variants: vp1 [e.g., nt 2222 to 4435 of AAV7, SEQ ID NO: 1]; vp2 [e.g., nt 2633 to 4435 of AAV7, SEQ ID NO: 1]; and vp3 [e.g., nt 2831 to 4435 of AAV7, SEQ ID NO: 1]. It is notable that AAV7 has an unusual GTG start codon. With the exception of a few house-keeping genes, such a start codon has not previously been reported in DNA viruses. The start codons for vp1, vp2 and vp3 for other AAV serotypes have been believed to be such that they permit the cellular mechanism of the host cell in which they reside to produce vp1, vp2 and vp3 in a ratio of 10%:10%:80%, respectively, in order to permit efficient assembly of the virion. However, the AAV7 virion has been found to assemble efficiently even with this rare GTG start codon. Thus, the inventors anticipate this it is desirable to alter the start codon of the vp3 of other AAV serotypes to contain this rare GTG start codon, in order to improve packaging efficiency, to alter the virion structure and/or to alter location of epitopes (e.g., neutralizing antibody epitopes) of other AAV serotypes. The start codons may be altered using conventional techniques including, e.g., site directed mutagenesis. Thus, the present invention encompasses altered AAV virions of any selected serotype, composed of a vp 3, and/or optionally, vp 1 and/or vp2 having start codons altered to GTG.

Other suitable fragments of AAV, include a fragment containing the start codon for the AAV capsid protein [e.g., nt 468 to 3090 of AAV7, SEQ ID NO: 1, nt 725 to 3090 of AAV7, SEQ ID NO: 1, and corresponding regions of the other AAV serotypes]. Still other fragments of AAV7 and the other novel AAV serotypes identified using the methods described herein include those encoding the rep proteins, including *rep* 78 [e.g., initiation codon 334 of Fig 1 for AAV7], *rep* 68 [initiation codon nt 334 of Fig. 1 for AAV7], *rep* 52 [initiation codon 1006 of Fig. 1 for AAV7], and *rep* 40 [initiation codon 1006 of Fig. 1 for AAV7] Other fragments of interest may include the AAV 5' inverted terminal repeats ITRs, [nt 1 to 107 of Fig. 1 for AAV7]; the AAV 3' ITRs [nt 4704 to 4721 of Fig. 1 for AAV7], P19 sequences, AAV P40 sequences, the rep binding site, and the terminal resolute site (TRS). Still other suitable fragments will be readily apparent to those of skill in the art. The corresponding regions in the other novel serotypes of the invention can be readily determined by reference to Figure 1, or by utilizing conventional alignment techniques with the sequences provided herein.

In addition to including the nucleic acid sequences provided in the figures and Sequence Listing, the present invention includes nucleic acid molecules and sequences which are designed to express the amino acid sequences, proteins and peptides of the AAV serotypes of the invention. Thus, the invention includes nucleic acid sequences which

5 encode the following novel AAV amino acid sequences: C1 [SEQ ID NO:60], C2 [SEQ ID NO:61], C5 [SEQ ID NO:62], A3-3 [SEQ ID NO:66], A3-7 [SEQ ID NO:67], A3-4 [SEQ ID NO:68], A3-5 [SEQ ID NO: 69], 3.3b [SEQ ID NO: 62], 223.4 [SEQ ID NO: 73], 223-5 [SEQ ID NO:74], 223-10 [SEQ ID NO:75], 223-2 [SEQ ID NO:76], 223-7 [SEQ ID NO: 77], 223-6 [SEQ ID NO: 78], 44-1 [SEQ ID NO: 79], 44-5 [SEQ ID NO:80], 44-2 [SEQ ID NO:81], 42-15 [SEQ ID NO: 84], 42-8 [SEQ ID NO: 85], 42-13 [SEQ ID NO:86], 42-3A [SEQ ID NO:87], 42-4 [SEQ ID NO:88], 42-5A [SEQ ID NO:89], 42-1B [SEQ ID NO:90], 42-5B [SEQ ID NO:91], 43-1 [SEQ ID NO: 92], 43-12 [SEQ ID NO: 93], 43-5 [SEQ ID NO:94], 43-21 [SEQ ID NO:96], 43-25 [SEQ ID NO: 97], 43-20 [SEQ ID NO:99], 24.1 [SEQ ID NO: 101], 42.2 [SEQ ID NO:102], 7.2 [SEQ ID NO: 103], 27.3 [SEQ ID NO: 104],

10 16.3 [SEQ ID NO: 105], 42.10 [SEQ ID NO: 106], 42-3B [SEQ ID NO: 107], 42-11 [SEQ ID NO: 108], F1 [SEQ ID NO: 109], F5 [SEQ ID NO: 110], F3 [SEQ ID NO:111], 42-6B [SEQ ID NO: 112], and/or 42-12 [SEQ ID NO: 113], and artificial AAV serotypes generated using these sequences and/or unique fragments thereof.

As used herein, artificial AAV serotypes include, without limitation, AAV

20 with a non-naturally occurring capsid protein. Such an artificial capsid may be generated by any suitable technique, using a novel AAV sequence of the invention (e.g., a fragment of a vp1 capsid protein) in combination with heterologous sequences which may be obtained from another AAV serotype (known or novel), non-contiguous portions of the same AAV serotype, from a non-AAV viral source, or from a non-viral source. An artificial AAV

25 serotype may be, without limitation, a chimeric AAV capsid, a recombinant AAV capsid, or a "humanized" AAV capsid.

B. AAV Amino Acid Sequences, Proteins and Peptides

The invention provides proteins and fragments thereof which are encoded by the nucleic acid sequences of the novel AAV serotypes identified herein, including, e.g.,

30 AAV7 [nt 825 to 3049 of AAV7, SEQ ID NO: 1] the other novel serotypes provided herein. Thus, the capsid proteins of the novel serotypes of the invention, including: H6 [SEQ ID NO: 25], H2 [SEQ ID NO: 26], 42-2 [SEQ ID NO:9], 42-8 [SEQ ID NO:27], 42-15 [SEQ ID NO:28], 42-5b [SEQ ID NO: 29], 42-1b [SEQ ID NO:30]; 42-13 [SEQ ID NO: 31], 42-3a

[SEQ ID NO: 32], 42-4 [SEQ ID NO:33], 42-5a [SEQ ID NO: 34], 42-10 [SEQ ID NO:35], 42-3b [SEQ ID NO: 36], 42-11 [SEQ ID NO: 37], 42-6b [SEQ ID NO:38], 43-1 [SEQ ID NO: 39], 43-5 [SEQ ID NO: 40], 43-12 [SEQ ID NO:41], 43-20 [SEQ ID NO:42], 43-21 [SEQ ID NO: 43], 43-23 [SEQ ID NO:44], 43-25 [SEQ ID NO: 45], 44.1 [SEQ ID NO:47], 44.5 [SEQ ID NO:47], 223.10 [SEQ ID NO:48], 223.2 [SEQ ID NO:49], 223.4 [SEQ ID NO:50], 223.5 [SEQ ID NO: 51], 223.6 [SEQ ID NO: 52], 223.7 [SEQ ID NO: 53], A3.4 [SEQ ID NO: 54], A3.5 [SEQ ID NO:55], A3.7 [SEQ ID NO: 56], A3.3 [SEQ ID NO:57], 42.12 [SEQ ID NO: 58], and 44.2 [SEQ ID NO: 59], can be readily generated using conventional techniques from the open reading frames provided for the above-listed clones.

The invention further encompasses AAV serotypes generated using sequences of the novel AAV serotypes of the invention, which are generated using synthetic, recombinant or other techniques known to those of skill in the art. The invention is not limited to novel AAV amino acid sequences, peptides and proteins expressed from the novel AAV nucleic acid sequences of the invention and encompasses amino acid sequences, peptides and proteins generated by other methods known in the art, including, e.g., by chemical synthesis, by other synthetic techniques, or by other methods. For example, the sequences of any of C1 [SEQ ID NO:60], C2 [SEQ ID NO:61], C5 [SEQ ID NO:62], A3-3 [SEQ ID NO:66], A3-7 [SEQ ID NO:67], A3-4 [SEQ ID NO:68], A3-5 [SEQ ID NO: 69], 3.3b [SEQ ID NO: 62], 223.4 [SEQ ID NO: 73], 223-5 [SEQ ID NO:74], 223-10 [SEQ ID NO:75], 223-2 [SEQ ID NO:76], 223-7 [SEQ ID NO: 77], 223-6 [SEQ ID NO: 78], 44-1 [SEQ ID NO: 79], 44-5 [SEQ ID NO:80], 44-2 [SEQ ID NO:81], 42-15 [SEQ ID NO: 84], 42-8 [SEQ ID NO: 85], 42-13 [SEQ ID NO:86], 42-3A [SEQ ID NO:87], 42-4 [SEQ ID NO:88], 42-5A [SEQ ID NO:89], 42-1B [SEQ ID NO:90], 42-5B [SEQ ID NO:91], 43-1 [SEQ ID NO: 92], 43-12 [SEQ ID NO: 93], 43-5 [SEQ ID NO:94], 43-21 [SEQ ID NO:96], 43-25 [SEQ ID NO: 97], 43-20 [SEQ ID NO:99], 24.1 [SEQ ID NO: 101], 42.2 [SEQ ID NO:102], 7.2 [SEQ ID NO: 103], 27.3 [SEQ ID NO: 104], 16.3 [SEQ ID NO: 105], 42.10 [SEQ ID NO: 106], 42-3B [SEQ ID NO: 107], 42-11 [SEQ ID NO: 108], F1 [SEQ ID NO: 109], F5 [SEQ ID NO: 110], F3 [SEQ ID NO:111], 42-6B [SEQ ID NO: 112], and/or 42-12 [SEQ ID NO: 113] by be readily generated using a variety of techniques.

Suitable production techniques are well known to those of skill in the art. See, e.g., Sambrook et al, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Press (Cold Spring Harbor, NY). Alternatively, peptides can also be synthesized by the well known solid phase peptide synthesis methods (Merrifield, *J. Am. Chem. Soc.*, 85:2149

(1962); Stewart and Young, Solid Phase Peptide Synthesis (Freeman, San Francisco, 1969) pp. 27-62). These and other suitable production methods are within the knowledge of those of skill in the art and are not a limitation of the present invention.

Particularly desirable proteins include the AAV capsid proteins, which are
 5 encoded by the nucleotide sequences identified above. The sequences of many of the capsid proteins of the invention are provided in an alignment in Fig. 2 and/or in the Sequence Listing, SEQ ID NO: 2 and 60 to 115, which is incorporated by reference herein. The AAV capsid is composed of three proteins, vp1, vp2 and vp3, which are alternative splice variants. The full-length sequence provided in these figures is that of vp1. Based on the numbering of
 10 the AAV7 capsid [SEQ ID NO:2], the sequences of vp2 span amino acid 138 - 737 of AAV7 and the sequences of vp3 span amino acids 204 - 737 of AAV7. With this information, one of skill in the art can readily determine the location of the vp2 and vp3 proteins for the other novel serotypes of the invention.

Other desirable proteins and fragments of the capsid protein include the
 15 constant and variable regions, located between hypervariable regions (HPV) and the sequences of the HPV regions themselves. An algorithm developed to determine areas of sequence divergence in AAV2 has yielded 12 hypervariable regions (HVR) of which 5 overlap or are part of the four previously described variable regions. [Chiorini *et al*, *J. Virol*, 73:1309-19 (1999); Rutledge *et al*, *J. Virol.*, 72:309-319] Using this algorithm and/or the
 20 alignment techniques described herein, the HVR of the novel AAV serotypes are determined.

For example, with respect to the number of the AAV2 vp1 [SEQ ID NO:70], the HVR are located as follows: HVR1, aa 146-152; HVR2, aa 182-186; HVR3, aa 262-264; HVR4, aa 381-383; HVR5, aa 450-474; HVR6, aa 490-495; HVR7, aa 500-504; HVR8, aa 514-522; HVR9, aa 534-555; HVR10, aa 581-594; HVR11, aa 658-667; and HVR12, aa 705-719.
 25 Utilizing an alignment prepared in accordance with conventional methods and the novel sequences provided herein [See, e.g., Figure 2], one can readily determine the location of the HVR in the novel AAV serotypes of the invention. For example, utilizing Figure 2, one can readily determine that for AAV7 [SEQ ID NO:2], HVR1 is located at aa 146 – 152; HVR2 is located at 182-187; HVR3 is located at aa 263-266, HVR4 is located at aa 383-385, HVR5 is
 30 located at aa 451-475; HVR6 is located at aa 491-496 of AAV7; HVR7 is located at aa 501-505; HVR8 is located at aa 513-521; HVR9 is located at 533-554; HVR10 is located at aa 583-596; HVR11 is located at aa 660-669; HVR12 is located at aa 707-721. Using the

information provided herein, the HVRs for the other novel serotypes of the invention can be readily determined.

In addition, within the capsid, amino acid cassettes of identity have been identified. These cassettes are of particular interest, as they are useful in constructing artificial serotypes, e.g., by replacing a HVR1 cassette of a selected serotype with an HVR1 cassette of another serotype. Certain of these cassettes of identity are noted in Fig. 2. See, Fig. 2, providing the Clustal X alignment, which has a ruler is displayed below the sequences, starting at 1 for the first residue position. The line above the ruler is used to mark strongly conserved positions. Three characters (*, :, .) are used. "*" indicates positions which have a single, fully conserved residue. ":" indicates that a "strong" group is fully conserved "." Indicates that a "weaker" group is fully conserved. These are all the positively scoring groups that occur in the Gonnet Pam250 matrix. The strong groups are defined as a strong score >0.5 and the weak groups are defined as weak score <0.5.

Additionally, examples of other suitable fragments of AAV capsids include, with respect to the numbering of AAV2 [SEQ ID NO:70], aa 24 – 42, aa 25 – 28; aa 81 – 85; aa133-165; aa 134 – 165; aa 137-143; aa 154-156; aa 194-208; aa 261-274; aa 262-274; aa 171-173; aa 413-417; aa 449-478; aa 494-525; aa 534-571; aa 581-601; aa 660-671; aa 709-723. Still other desirable fragments include, for example, in AAV7, amino acids 1 to 184 of SEQ ID NO:2, amino acids 199 to 259; amino acids 274 to 446; amino acids 603 to 659; amino acids 670 to 706; amino acids 724 to 736; aa 185 to 198; aa 260 to 273; aa447 to 477; aa495 to 602; aa660 to 669; and aa707 to 723. Still other desirable regions, based on the numbering of AAV7 [SEQ ID NO:2], are selected from among the group consisting of aa 185 to 198; aa 260 to 273; aa447 to 477; aa495 to 602; aa660 to 669; and aa707 to 723. Using the alignment provided herein performed using the Clustal X program at default settings, or using other commercially or publicly available alignment programs at default settings, one of skill in the art can readily determine corresponding fragments of the novel AAV capsids of the invention.

Other desirable proteins are the AAV rep proteins [aa 1 to 623 of SEQ ID NO:3 for AAV7] and functional fragments thereof, including, e.g., aa 1 to 171, aa 172 to 372, aa 373 to 444, aa 445 to 623 of SEQ ID NO:3, among others. Suitably, such fragments are at least 8 amino acids in length. See, Fig. 3. Comparable regions can be identified in the proteins of the other novel AAV of the invention, using the techniques described herein and those which are known in the art. In addition, fragments of other desired lengths may be

readily utilized. Such fragments may be produced recombinantly or by other suitable means, e.g., chemical synthesis.

The sequences, proteins, and fragments of the invention may be produced by any suitable means, including recombinant production, chemical synthesis, or other synthetic means. Such production methods are within the knowledge of those of skill in the art and are not a limitation of the present invention.

IV. Production of rAAV with novel AAV capsids

The invention encompasses novel, wild-type AAV serotypes identified by the invention, the sequences of which wild-type AAV serotypes are free of DNA and/or cellular material with these viruses are associated in nature. In another aspect, the present invention provides molecules which utilize the novel AAV sequences of the invention, including fragments thereof, for production of molecules useful in delivery of a heterologous gene or other nucleic acid sequences to a target cell.

The molecules of the invention which contain sequences of a novel AAV serotype of the invention include any genetic element (vector) which may be delivered to a host cell, e.g., naked DNA, a plasmid, phage, transposon, cosmid, episome, a protein in a non-viral delivery vehicle (e.g., a lipid-based carrier), virus, etc. which transfer the sequences carried thereon. The selected vector may be delivered by any suitable method, including transfection, electroporation, liposome delivery, membrane fusion techniques, high velocity DNA-coated pellets, viral infection and protoplast fusion. The methods used to construct any embodiment of this invention are known to those with skill in nucleic acid manipulation and include genetic engineering, recombinant engineering, and synthetic techniques. See, e.g., Sambrook et al, Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Press, Cold Spring Harbor, NY.

In one embodiment, the vectors of the invention contain sequences encoding a novel AAV capsid of the invention (e.g., AAV7 capsid, AAV 44-2 (rh.10), an AAV10 capsid, an AAV11 capsid, an AAV12 capsid), or a fragment of one or more of these AAV capsids. Alternatively, the vectors may contain the capsid protein, or a fragment thereof, itself.

Optionally, vectors of the invention may contain sequences encoding AAV rep proteins. Such *rep* sequences may be from the same AAV serotype which is providing the cap sequences. Alternatively, the present invention provides vectors in which the *rep* sequences are from an AAV serotype which differs from that which is providing the *cap*

sequences. In one embodiment, the *rep* and *cap* sequences are expressed from separate sources (e.g., separate vectors, or a host cell and a vector). In another embodiment, these *rep* sequences are expressed from the same source as the *cap* sequences. In this embodiment, the *rep* sequences may be fused in frame to *cap* sequences of a different AAV serotype to form a
 5 chimeric AAV vector. Optionally, the vectors of the invention further contain a minigene comprising a selected transgene which is flanked by AAV 5' ITR and AAV 3' ITR.

Thus, in one embodiment, the vectors described herein contain nucleic acid sequences encoding an intact AAV capsid which may be from a single AAV serotype (e.g., AAV7 or another novel AAV). Alternatively, these vectors contain sequences encoding
 10 artificial capsids which contain one or more fragments of the AAV7 (or another novel AAV) capsid fused to heterologous AAV or non-AAV capsid proteins (or fragments thereof). These artificial capsid proteins are selected from non-contiguous portions of the AAV7 (or another novel AAV) capsid or from capsids of other AAV serotypes. For example, it may be desirable to modify the coding regions of one or more of the AAV vp1, e.g., in one or more
 15 of the hypervariable regions (i.e., HPV1-12), or vp2, and/or vp3. In another example, it may be desirable to alter the start codon of the vp3 protein to GTG. These modifications may be to increase expression, yield, and/or to improve purification in the selected expression systems, or for another desired purpose (e.g., to change tropism or alter neutralizing antibody epitopes).

20 The vectors described herein, e.g., a plasmid, are useful for a variety of purposes, but are particularly well suited for use in production of a rAAV containing a capsid comprising AAV sequences or a fragment thereof. These vectors, including rAAV, their elements, construction, and uses are described in detail herein.

In one aspect, the invention provides a method of generating a recombinant adeno-associated virus (AAV) having an AAV serotype 7 (or another novel AAV) capsid, or a
 25 portion thereof. Such a method involves culturing a host cell which contains a nucleic acid sequence encoding an adeno-associated virus (AAV) serotype 7 (or another novel AAV) capsid protein, or fragment thereof, as defined herein; a functional *rep* gene; a minigene composed of, at a minimum, AAV inverted terminal repeats (ITRs) and a transgene; and
 30 sufficient helper functions to permit packaging of the minigene into the AAV7 (or another novel AAV) capsid protein.

The components required to be cultured in the host cell to package an AAV minigene in an AAV capsid may be provided to the host cell in *trans*. Alternatively, any one or more

of the required components (e.g., minigene, *rep* sequences, *cap* sequences, and/or helper functions) may be provided by a stable host cell which has been engineered to contain one or more of the required components using methods known to those of skill in the art. Most suitably, such a stable host cell will contain the required component(s) under the control of an inducible promoter. However, the required component(s) may be under the control of a constitutive promoter. Examples of suitable inducible and constitutive promoters are provided herein, in the discussion of regulatory elements suitable for use with the transgene. In still another alternative, a selected stable host cell may contain selected component(s) under the control of a constitutive promoter and other selected component(s) under the control of one or more inducible promoters. For example, a stable host cell may be generated which is derived from 293 cells (which contain E1 helper functions under the control of a constitutive promoter), but which contains the *rep* and/or *cap* proteins under the control of inducible promoters. Still other stable host cells may be generated by one of skill in the art.

The minigene, *rep* sequences, *cap* sequences, and helper functions required for producing the rAAV of the invention may be delivered to the packaging host cell in the form of any genetic element which transfer the sequences carried thereon. The selected genetic element may be delivered by any suitable method, including those described herein. The methods used to construct any embodiment of this invention are known to those with skill in nucleic acid manipulation and include genetic engineering, recombinant engineering, and synthetic techniques. See, e.g., Sambrook et al, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Press, Cold Spring Harbor, NY. Similarly, methods of generating rAAV virions are well known and the selection of a suitable method is not a limitation on the present invention. See, e.g., K. Fisher et al, *J. Virol.*, 70:520-532 (1993) and US Patent 5,478,745.

A. The Minigene

The minigene is composed of, at a minimum, a transgene and its regulatory sequences, and 5' and 3' AAV inverted terminal repeats (ITRs). It is this minigene which is packaged into a capsid protein and delivered to a selected host cell.

1. The transgene

The transgene is a nucleic acid sequence, heterologous to the vector sequences flanking the transgene, which encodes a polypeptide, protein, or other product, of interest. The nucleic acid coding sequence is operatively linked to regulatory

components in a manner which permits transgene transcription, translation, and/or expression in a host cell.

The composition of the transgene sequence will depend upon the use to which the resulting vector will be put. For example, one type of transgene sequence includes a reporter sequence, which upon expression produces a detectable signal. Such reporter sequences include, without limitation, DNA sequences encoding β -lactamase, β -galactosidase (LacZ), alkaline phosphatase, thymidine kinase, green fluorescent protein (GFP), chloramphenicol acetyltransferase (CAT), luciferase, membrane bound proteins including, for example, CD2, CD4, CD8, the influenza hemagglutinin protein, and others well known in the art, to which high affinity antibodies directed thereto exist or can be produced by conventional means, and fusion proteins comprising a membrane bound protein appropriately fused to an antigen tag domain from, among others, hemagglutinin or Myc.

These coding sequences, when associated with regulatory elements which drive their expression, provide signals detectable by conventional means, including enzymatic, radiographic, colorimetric, fluorescence or other spectrographic assays, fluorescent activating cell sorting assays and immunological assays, including enzyme linked immunosorbent assay (ELISA), radioimmunoassay (RIA) and immunohistochemistry. For example, where the marker sequence is the LacZ gene, the presence of the vector carrying the signal is detected by assays for beta-galactosidase activity. Where the transgene is green fluorescent protein or luciferase, the vector carrying the signal may be measured visually by color or light production in a luminometer.

However, desirably, the transgene is a non-marker sequence encoding a product which is useful in biology and medicine, such as proteins, peptides, RNA, enzymes, or catalytic RNAs. Desirable RNA molecules include tRNA, dsRNA, ribosomal RNA, catalytic RNAs, and antisense RNAs. One example of a useful RNA sequence is a sequence which extinguishes expression of a targeted nucleic acid sequence in the treated animal.

The transgene may be used to correct or ameliorate gene deficiencies, which may include deficiencies in which normal genes are expressed at less than normal levels or deficiencies in which the functional gene product is not expressed. A preferred type of transgene sequence encodes a therapeutic protein or polypeptide which is expressed in a host cell. The invention further includes using multiple transgenes, e.g., to correct or ameliorate a gene defect caused by a multi-subunit protein. In certain situations, a

different transgene may be used to encode each subunit of a protein, or to encode different peptides or proteins. This is desirable when the size of the DNA encoding the protein subunit is large, e.g., for an immunoglobulin, the platelet-derived growth factor, or a dystrophin protein. In order for the cell to produce the multi-subunit protein, a cell is
 5 infected with the recombinant virus containing each of the different subunits. Alternatively, different subunits of a protein may be encoded by the same transgene. In this case, a single transgene includes the DNA encoding each of the subunits, with the DNA for each subunit separated by an internal ribozyme entry site (IRES). This is desirable when the size of the DNA encoding each of the subunits is small, e.g., the total size of the DNA encoding the
 10 subunits and the IRES is less than five kilobases. As an alternative to an IRES, the DNA may be separated by sequences encoding a 2A peptide, which self-cleaves in a post-translational event. See, e.g., M.L. Donnelly, *et al*, *J. Gen. Virol.*, 78(Pt 1):13-21 (Jan 1997); Furler, S., *et al*, *Gene Ther.*, 8(11):864-873 (June 2001); Klump H., *et al.*, *Gene Ther.*, 8(10):811-817 (May 2001). This 2A peptide is significantly smaller than an IRES, making it well suited for
 15 use when space is a limiting factor. However, the selected transgene may encode any biologically active product or other product, e.g., a product desirable for study.

Suitable transgenes may be readily selected by one of skill in the art. The selection of the transgene is not considered to be a limitation of this invention.

2. Regulatory Elements

20 In addition to the major elements identified above for the minigene, the vector also includes conventional control elements necessary which are operably linked to the transgene in a manner which permits its transcription, translation and/or expression in a cell transfected with the plasmid vector or infected with the virus produced by the invention. As used herein, "operably linked" sequences include both
 25 expression control sequences that are contiguous with the gene of interest and expression control sequences that act in *trans* or at a distance to control the gene of interest.

Expression control sequences include appropriate transcription initiation, termination, promoter and enhancer sequences; efficient RNA processing signals such as splicing and polyadenylation (polyA) signals; sequences that
 30 stabilize cytoplasmic mRNA; sequences that enhance translation efficiency (i.e., Kozak consensus sequence); sequences that enhance protein stability; and when desired, sequences that enhance secretion of the encoded product. A great number of expression control

sequences, including promoters which are native, constitutive, inducible and/or tissue-specific, are known in the art and may be utilized.

Examples of constitutive promoters include, without limitation, the retroviral Rous sarcoma virus (RSV) LTR promoter (optionally with the RSV enhancer), the cytomegalovirus (CMV) promoter (optionally with the CMV enhancer) [see, 5 e.g., Boshart *et al*, *Cell*, 41:521-530 (1985)], the SV40 promoter, the dihydrofolate reductase promoter, the β -actin promoter, the phosphoglycerol kinase (PGK) promoter, and the EF1 α promoter [Invitrogen].

Inducible promoters allow regulation of gene expression and can be regulated by exogenously supplied compounds, environmental factors such as 10 temperature, or the presence of a specific physiological state, e.g., acute phase, a particular differentiation state of the cell, or in replicating cells only. Inducible promoters and inducible systems are available from a variety of commercial sources, including, without limitation, Invitrogen, Clontech and Ariad. Many other systems have 15 been described and can be readily selected by one of skill in the art. Examples of inducible promoters regulated by exogenously supplied promoters include the zinc-inducible sheep metallothioneine (MT) promoter, the dexamethasone (Dex)-inducible mouse mammary tumor virus (MMTV) promoter, the T7 polymerase promoter system [WO 98/10088]; the ecdysone insect promoter [No *et al*, *Proc. Natl. Acad. Sci. USA*, 93:3346-3351 (1996)], the 20 tetracycline-repressible system [Gossen *et al*, *Proc. Natl. Acad. Sci. USA*, 89:5547-5551 (1992)], the tetracycline-inducible system [Gossen *et al*, *Science*, 268:1766-1769 (1995), see also Harvey *et al*, *Curr. Opin. Chem. Biol.*, 2:512-518 (1998)], the RU486-inducible system [Wang *et al*, *Nat. Biotech.*, 15:239-243 (1997) and Wang *et al*, *Gene Ther.*, 4:432-441 (1997)] and the rapamycin-inducible system [Magari *et al*, *J. Clin. Invest.*, 100:2865-2872 25 (1997)]. Still other types of inducible promoters which may be useful in this context are those which are regulated by a specific physiological state, e.g., temperature, acute phase, a particular differentiation state of the cell, or in replicating cells only.

In another embodiment, the native promoter for the transgene will be used. The native promoter may be preferred when it is desired that expression of the 30 transgene should mimic the native expression. The native promoter may be used when expression of the transgene must be regulated temporally or developmentally, or in a tissue-specific manner, or in response to specific transcriptional stimuli. In a further embodiment,

other native expression control elements, such as enhancer elements, polyadenylation sites or Kozak consensus sequences may also be used to mimic the native expression.

Another embodiment of the transgene includes a transgene operably linked to a tissue-specific promoter. For instance, if expression in skeletal muscle is desired, a promoter active in muscle should be used. These include the promoters from genes encoding skeletal β -actin, myosin light chain 2A, dystrophin, muscle creatine kinase, as well as synthetic muscle promoters with activities higher than naturally-occurring promoters (see Li *et al.*, *Nat. Biotech.*, 17:241-245 (1999)). Examples of promoters that are tissue-specific are known for liver (albumin, Miyatake *et al.*, *J. Virol.*, 71:5124-32 (1997); hepatitis B virus core promoter, Sandig *et al.*, *Gene Ther.*, 3:1002-9 (1996); alpha-fetoprotein (AFP), Arbuthnot *et al.*, *Hum. Gene Ther.*, 7:1503-14 (1996)), bone osteocalcin (Stein *et al.*, *Mol. Biol. Rep.*, 24:185-96 (1997)); bone sialoprotein (Chen *et al.*, *J. Bone Miner. Res.*, 11:654-64 (1996)), lymphocytes (CD2, Hansal *et al.*, *J. Immunol.*, 161:1063-8 (1998); immunoglobulin heavy chain; T cell receptor α chain), neuronal such as neuron-specific enolase (NSE) promoter (Andersen *et al.*, *Cell. Mol. Neurobiol.*, 13:503-15 (1993)), neurofilament light-chain gene (Piccioli *et al.*, *Proc. Natl. Acad. Sci. USA*, 88:5611-5 (1991)), and the neuron-specific vgf gene (Piccioli *et al.*, *Neuron*, 15:373-84 (1995)), among others.

Optionally, plasmids carrying therapeutically useful transgenes may also include selectable markers or reporter genes may include sequences encoding geneticin, hygromycin or purimycin resistance, among others. Such selectable reporters or marker genes (preferably located outside the viral genome to be rescued by the method of the invention) can be used to signal the presence of the plasmids in bacterial cells, such as ampicillin resistance. Other components of the plasmid may include an origin of replication. Selection of these and other promoters and vector elements are conventional and many such sequences are available [see, e.g., Sambrook *et al.*, and references cited therein].

The combination of the transgene, promoter/enhancer, and 5' and 3' ITRs is referred to as a "minigene" for ease of reference herein. Provided with the teachings of this invention, the design of such a minigene can be made by resort to conventional techniques.

3. Delivery of the Minigene to a Packaging Host Cell

The minigene can be carried on any suitable vector, e.g., a plasmid, which is delivered to a host cell. The plasmids useful in this invention may be

engineered such that they are suitable for replication and, optionally, integration in prokaryotic cells, mammalian cells, or both. These plasmids (or other vectors carrying the 5' AAV ITR-heterologous molecule-3'TTR) contain sequences permitting replication of the minigene in eukaryotes and/or prokaryotes and selection markers for these systems.

5 Selectable markers or reporter genes may include sequences encoding geneticin, hygromycin or purimycin resistance, among others. The plasmids may also contain certain selectable reporters or marker genes that can be used to signal the presence of the vector in bacterial cells, such as ampicillin resistance. Other components of the plasmid may include an origin of replication and an amplicon, such as the amplicon system employing the Epstein Barr
10 virus nuclear antigen. This amplicon system, or other similar amplicon components permit high copy episomal replication in the cells. Preferably, the molecule carrying the minigene is transfected into the cell, where it may exist transiently. Alternatively, the minigene (carrying the 5' AAV ITR-heterologous molecule-3' ITR) may be stably integrated into the genome of the host cell, either chromosomally or as an episome. In certain embodiments,
15 the minigene may be present in multiple copies, optionally in head-to-head, head-to-tail, or tail-to-tail concatamers. Suitable transfection techniques are known and may readily be utilized to deliver the minigene to the host cell.

Generally, when delivering the vector comprising the minigene by transfection, the vector is delivered in an amount from about 5 μ g to about 100 μ g DNA, and
20 preferably about 10 to about 50 μ g DNA to about 1×10^4 cells to about 1×10^{13} cells, and preferably about 10^5 cells. However, the relative amounts of vector DNA to host cells may be adjusted, taking into consideration such factors as the selected vector, the delivery method and the host cells selected.

B. *Rep* and *Cap* Sequences

25 In addition to the minigene, the host cell contains the sequences which drive expression of the novel AAV capsid protein (e.g., AAV7 or other novel AAV capsid or an artificial capsid protein comprising a fragment of one or more of these capsids) in the host cell and rep sequences of the same serotype as the serotype of the AAV ITRs found in the minigene. The AAV *cap* and *rep* sequences may be independently obtained
30 from an AAV source as described above and may be introduced into the host cell in any manner known to one in the art as described above. Additionally, when pseudotyping a novel AAV capsid of the invention, the sequences encoding each of the essential rep proteins may be supplied by the same AAV serotype, or the sequences encoding the rep proteins may

be supplied by different AAV serotypes (e.g., AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, or one of the novel serotypes identified herein). For example, the *rep*78/68 sequences may be from AAV2, whereas the *rep*52/40 sequences may from AAV1.

In one embodiment, the host cell stably contains the capsid protein under the control of a suitable promoter, such as those described above. Most desirably, in this embodiment, the capsid protein is expressed under the control of an inducible promoter. In another embodiment, the capsid protein is supplied to the host cell in *trans*. When delivered to the host cell in *trans*, the capsid protein may be delivered via a plasmid which contains the sequences necessary to direct expression of the selected capsid protein in the host cell. Most desirably, when delivered to the host cell in *trans*, the plasmid carrying the capsid protein also carries other sequences required for packaging the rAAV, e.g., the *rep* sequences.

In another embodiment, the host cell stably contains the *rep* sequences under the control of a suitable promoter, such as those described above. Most desirably, in this embodiment, the essential *rep* proteins are expressed under the control of an inducible promoter. In another embodiment, the *rep* proteins are supplied to the host cell in *trans*. When delivered to the host cell in *trans*, the *rep* proteins may be delivered via a plasmid which contains the sequences necessary to direct expression of the selected *rep* proteins in the host cell. Most desirably, when delivered to the host cell in *trans*, the plasmid carrying the capsid protein also carries other sequences required for packaging the rAAV, e.g., the *rep* and *cap* sequences.

Thus, in one embodiment, the *rep* and *cap* sequences may be transfected into the host cell on a single nucleic acid molecule and exist stably in the cell as an episome. In another embodiment, the *rep* and *cap* sequences are stably integrated into the genome of the cell. Another embodiment has the *rep* and *cap* sequences transiently expressed in the host cell. For example, a useful nucleic acid molecule for such transfection comprises, from 5' to 3', a promoter, an optional spacer interposed between the promoter and the start site of the *rep* gene sequence, an AAV *rep* gene sequence, and an AAV *cap* gene sequence.

Optionally, the *rep* and/or *cap* sequences may be supplied on a vector that contains other DNA sequences that are to be introduced into the host cells. For instance, the vector may contain the rAAV construct comprising the minigene. The vector may

comprise one or more of the genes encoding the helper functions, e.g., the adenoviral proteins E1, E2a, and E4ORF6, and the gene for VAI RNA.

Preferably, the promoter used in this construct may be any of the constitutive, inducible or native promoters known to one of skill in the art or as discussed
 5 above. In one embodiment, an AAV P5 promoter sequence is employed. The selection of the AAV to provide any of these sequences does not limit the invention.

In another preferred embodiment, the promoter for *rep* is an inducible promoter, as are discussed above in connection with the transgene regulatory elements. One preferred promoter for *rep* expression is the T7 promoter. The vector comprising the *rep*
 10 gene regulated by the T7 promoter and the *cap* gene, is transfected or transformed into a cell which either constitutively or inducibly expresses the T7 polymerase. See WO 98/10088, published March 12, 1998.

The spacer is an optional element in the design of the vector. The spacer is a DNA sequence interposed between the promoter and the *rep* gene ATG start site.
 15 The spacer may have any desired design; that is, it may be a random sequence of nucleotides, or alternatively, it may encode a gene product, such as a marker gene. The spacer may contain genes which typically incorporate start/stop and polyA sites. The spacer may be a non-coding DNA sequence from a prokaryote or eukaryote, a repetitive non-coding sequence, a coding sequence without transcriptional controls or a coding sequence with
 20 transcriptional controls. Two exemplary sources of spacer sequences are the λ phage ladder sequences or yeast ladder sequences, which are available commercially, e.g., from Gibco or Invitrogen, among others. The spacer may be of any size sufficient to reduce expression of the *rep78* and *rep68* gene products, leaving the *rep52*, *rep40* and *cap* gene products expressed at normal levels. The length of the spacer may therefore range from about 10 bp
 25 to about 10.0 kbp, preferably in the range of about 100 bp to about 8.0 kbp. To reduce the possibility of recombination, the spacer is preferably less than 2 kbp in length; however, the invention is not so limited.

Although the molecule(s) providing *rep* and *cap* may exist in the host cell transiently (i.e., through transfection), it is preferred that one or both of the *rep* and *cap*
 30 proteins and the promoter(s) controlling their expression be stably expressed in the host cell, e.g., as an episome or by integration into the chromosome of the host cell. The methods employed for constructing embodiments of this invention are conventional genetic engineering or recombinant engineering techniques such as those described in the references

above. While this specification provides illustrative examples of specific constructs, using the information provided herein, one of skill in the art may select and design other suitable constructs, using a choice of spacers, P5 promoters, and other elements, including at least one translational start and stop signal, and the optional addition of polyadenylation sites.

5 In another embodiment of this invention, the rep or cap protein may be provided stably by a host cell.

C. The Helper Functions

The packaging host cell also requires helper functions in order to package the rAAV of the invention. Optionally, these functions may be supplied by a herpesvirus. Most desirably, the necessary helper functions are each provided from a human or non-human primate adenovirus source, such as those described above and/or are available from a variety of sources, including the American Type Culture Collection (ATCC), Manassas, VA (US). In one currently preferred embodiment, the host cell is provided with and/or contains an E1a gene product, an E1b gene product, an E2a gene product, and/or an E4 ORF6 gene product. The host cell may contain other adenoviral genes such as VAI RNA, but these genes are not required. In a preferred embodiment, no other adenovirus genes or gene functions are present in the host cell.

By "adenoviral DNA which expresses the E1a gene product", it is meant any adenovirus sequence encoding E1a or any functional E1a portion. Adenoviral DNA which expresses the E2a gene product and adenoviral DNA which expresses the E4 ORF6 gene products are defined similarly. Also included are any alleles or other modifications of the adenoviral gene or functional portion thereof. Such modifications may be deliberately introduced by resort to conventional genetic engineering or mutagenic techniques to enhance the adenoviral function in some manner, as well as naturally occurring allelic variants thereof. Such modifications and methods for manipulating DNA to achieve these adenovirus gene functions are known to those of skill in the art.

The adenovirus E1a, E1b, E2a, and/or E4ORF6 gene products, as well as any other desired helper functions, can be provided using any means that allows their expression in a cell. Each of the sequences encoding these products may be on a separate vector, or one or more genes may be on the same vector. The vector may be any vector known in the art or disclosed above, including plasmids, cosmids and viruses. Introduction into the host cell of the vector may be achieved by any means known in the art or as disclosed above, including transfection, infection, electroporation, liposome delivery,

membrane fusion techniques, high velocity DNA-coated pellets, viral infection and protoplast fusion, among others. One or more of the adenoviral genes may be stably integrated into the genome of the host cell, stably expressed as episomes, or expressed transiently. The gene products may all be expressed transiently, on an episome or stably integrated, or some of the gene products may be expressed stably while others are expressed transiently. Furthermore, the promoters for each of the adenoviral genes may be selected independently from a constitutive promoter, an inducible promoter or a native adenoviral promoter. The promoters may be regulated by a specific physiological state of the organism or cell (i.e., by the differentiation state or in replicating or quiescent cells) or by exogenously-added factors, for example.

D. Host Cells And Packaging Cell Lines

The host cell itself may be selected from any biological organism, including prokaryotic (e.g., bacterial) cells, and eukaryotic cells, including, insect cells, yeast cells and mammalian cells. Particularly desirable host cells are selected from among any mammalian species, including, without limitation, cells such as A549, WEHI, 3T3, 10T1/2, BHK, MDCK, COS 1, COS 7, BSC 1, BSC 40, BMT 10, VERO, WI38, HeLa, 293 cells (which express functional adenoviral E1), Saos, C2C12, L cells, HT1080, HepG2 and primary fibroblast, hepatocyte and myoblast cells derived from mammals including human, monkey, mouse, rat, rabbit, and hamster. The selection of the mammalian species providing the cells is not a limitation of this invention; nor is the type of mammalian cell, i.e., fibroblast, hepatocyte, tumor cell, etc. The most desirable cells do not carry any adenovirus gene other than E1, E2a and/or E4 ORF6; nor do they contain any other virus gene which could result in homologous recombination of a contaminating virus during the production of rAAV; and it is capable of infection or transfection of DNA and expression of the transfected DNA. In a preferred embodiment, the host cell is one that has *rep* and *cap* stably transfected in the cell.

One host cell useful in the present invention is a host cell stably transformed with the sequences encoding *rep* and *cap*, and which is transfected with the adenovirus E1, E2a, and E4ORF6 DNA and a construct carrying the minigene as described above. Stable *rep* and/or *cap* expressing cell lines, such as B-50 (PCT/US98/19463), or those described in U.S. Patent No. 5,658,785, may also be similarly employed. Another desirable host cell contains the minimum adenoviral DNA which is sufficient to express E4 ORF6. Yet other cell lines can be constructed using the novel AAV *rep* and/or novel AAV *cap* sequences of the invention.

The preparation of a host cell according to this invention involves techniques such as assembly of selected DNA sequences. This assembly may be accomplished utilizing conventional techniques. Such techniques include cDNA and genomic cloning, which are well known and are described in Sambrook et al., cited above, use of overlapping oligonucleotide sequences of the adenovirus and AAV genomes, combined with polymerase chain reaction, synthetic methods, and any other suitable methods which provide the desired nucleotide sequence.

Introduction of the molecules (as plasmids or viruses) into the host cell may also be accomplished using techniques known to the skilled artisan and as discussed throughout the specification. In preferred embodiment, standard transfection techniques are used, e.g., CaPO₄ transfection or electroporation, and/or infection by hybrid adenovirus/AAV vectors into cell lines such as the human embryonic kidney cell line HEK 293 (a human kidney cell line containing functional adenovirus E1 genes which provides *trans*-acting E1 proteins).

These novel AAV-based vectors which are generated by one of skill in the art are beneficial for gene delivery to selected host cells and gene therapy patients since no neutralization antibodies to AAV7 have been found in the human population. Further, early studies show no neutralizing antibodies in cyno monkey and chimpanzee populations, and less than 15% cross-reactivity of AAV 7 in rhesus monkeys, the species from which the serotype was isolated. One of skill in the art may readily prepare other rAAV viral vectors containing the AAV7 capsid proteins provided herein using a variety of techniques known to those of skill in the art. One may similarly prepare still other rAAV viral vectors containing AAV7 sequence and AAV capsids of another serotype. Similar advantages are conferred by the vectors based on the other novel AAV of the invention.

Thus, one of skill in the art will readily understand that the AAV7 sequences of the invention can be readily adapted for use in these and other viral vector systems for *in vitro*, *ex vivo* or *in vivo* gene delivery. Similarly, one of skill in the art can readily select other fragments of the novel AAV genome of the invention for use in a variety of rAAV and non-rAAV vector systems. Such vectors systems may include, e.g., lentiviruses, retroviruses, poxviruses, vaccinia viruses, and adenoviral systems, among others. Selection of these vector systems is not a limitation of the present invention.

Thus, the invention further provides vectors generated using the nucleic acid and amino acid sequences of the novel AAV of the invention. Such vectors are

useful for a variety of purposes, including for delivery of therapeutic molecules and for use in vaccine regimens. Particularly desirable for delivery of therapeutic molecules are recombinant AAV containing capsids of the novel AAV of the invention. These, or other vector constructs containing novel AAV sequences of the invention may be used in vaccine
5 regimens, e.g., for co-delivery of a cytokine, or for delivery of the immunogen itself.

V. Recombinant Viruses And Uses Thereof

Using the techniques described herein, one of skill in the art may generate a rAAV having a capsid of a novel serotype of the invention, or a novel capsid containing one or
10 more novel fragments of an AAV serotype identified by the method of the invention. In one embodiment, a full-length capsid from a single serotype, e.g., AAV7 [SEQ ID NO: 2] can be utilized. In another embodiment, a full-length capsid may be generated which contains one or more fragments of a novel serotype of the invention fused in frame with sequences from another selected AAV serotype. For example, a rAAV may contain one or more of the novel
15 hypervariable region sequences of an AAV serotype of the invention. Alternatively, the unique AAV serotypes of the invention may be used in constructs containing other viral or non-viral sequences.

It will be readily apparent to one of skill in the art one embodiment, that certain serotypes of the invention will be particularly well suited for certain uses. For example,
20 vectors based on AAV7 capsids of the invention are particularly well suited for use in muscle; whereas vectors based on rh.10 (44-2) capsids of the invention are particularly well suited for use in lung. Uses of such vectors are not so limited and one of skill in the art may utilize these vectors for delivery to other cell types, tissues or organs. Further, vectors based upon other capsids of the invention may be used for delivery to these or other cells, tissues or
25 organs.

A. Delivery of Transgene

In another aspect, the present invention provides a method for delivery of a transgene to a host which involves transfecting or infecting a selected host cell with a vector generated with the sequences of the AAV of the invention. Methods for delivery are well
30 known to those of skill in the art and are not a limitation of the present invention.

In one desirable embodiment, the invention provides a method for AAV-mediated delivery of a transgene to a host. This method involves transfecting or infecting a

selected host cell with a recombinant viral vector containing a selected transgene under the control of sequences which direct expression thereof and AAV capsid proteins.

Optionally, a sample from the host may be first assayed for the presence of antibodies to a selected AAV serotype. A variety of assay formats for detecting neutralizing antibodies are well known to those of skill in the art. The selection of such an assay is not a limitation of the present invention. See, e.g., Fisher et al, *Nature Med.*, 3(3):306-312 (March 1997) and W. C. Manning et al, *Human Gene Therapy*, 9:477-485 (March 1, 1998). The results of this assay may be used to determine which AAV vector containing capsid proteins of a particular serotype are preferred for delivery, e.g., by the absence of neutralizing antibodies specific for that capsid serotype.

In one aspect of this method, the delivery of vector with a selected AAV capsid proteins may precede or follow delivery of a gene via a vector with a different serotype AAV capsid protein. Similarly, the delivery of vector with other novel AAV capsid proteins of the invention may precede or follow delivery of a gene via a vector with a different serotype AAV capsid protein. Thus, gene delivery via rAAV vectors may be used for repeat gene delivery to a selected host cell. Desirably, subsequently administered rAAV vectors carry the same transgene as the first rAAV vector, but the subsequently administered vectors contain capsid proteins of serotypes which differ from the first vector. For example, if a first vector has AAV7 capsid proteins [SEQ ID NO:2], subsequently administered vectors may have capsid proteins selected from among the other serotypes, including AAV1, AAV2, AAV3A, AAV3B, AAV4, AAV6, AAV10, AAV11, and AAV12, or any of the other novel AAV capsids identified herein including, without limitation: A3.1, H2, H6, C1, C2, C5, A3-3, A3-7, A3-4, A3-5, 3.3b, 223.4, 223-5, 223-10, 223-2, 223-7, 223-6, 44-1, 44-5, 44-2, 42-15, 42-8, 42-13, 42-3A, 42-4, 42-5A, 42-1B, 42-5B, 43-1, 43-12, 43-5, 43-21, 43-25, 43-20, 24.1, 42.2, 7.2, 27.3, 16.3, 42.10, 42-3B, 42-11, F1, F5, F3, 42-6B, and/or 42-12.

The above-described recombinant vectors may be delivered to host cells according to published methods. The rAAV, preferably suspended in a physiologically compatible carrier, may be administered to a human or non-human mammalian patient. Suitable carriers may be readily selected by one of skill in the art in view of the indication for which the transfer virus is directed. For example, one suitable carrier includes saline, which may be formulated with a variety of buffering solutions (e.g., phosphate buffered saline). Other exemplary carriers include sterile saline, lactose, sucrose, calcium phosphate,

gelatin, dextran, agar, pectin, peanut oil, sesame oil, and water. The selection of the carrier is not a limitation of the present invention.

Optionally, the compositions of the invention may contain, in addition to the rAAV and carrier(s), other conventional pharmaceutical ingredients, such as preservatives, or chemical stabilizers. Suitable exemplary preservatives include chlorobutanol, potassium sorbate, sorbic acid, sulfur dioxide, propyl gallate, the parabens, ethyl vanillin, glycerin, phenol, and parachlorophenol. Suitable chemical stabilizers include gelatin and albumin.

The viral vectors are administered in sufficient amounts to transfect the cells and to provide sufficient levels of gene transfer and expression to provide a therapeutic benefit without undue adverse effects, or with medically acceptable physiological effects, which can be determined by those skilled in the medical arts. Conventional and pharmaceutically acceptable routes of administration include, but are not limited to, direct delivery to the selected organ (e.g., intraportal delivery to the liver), oral, inhalation (including intranasal and intratracheal delivery), intraocular, intravenous, intramuscular, subcutaneous, intradermal, and other parental routes of administration. Routes of administration may be combined, if desired.

Dosages of the viral vector will depend primarily on factors such as the condition being treated, the age, weight and health of the patient, and may thus vary among patients. For example, a therapeutically effective human dosage of the viral vector is generally in the range of from about 1 ml to about 100 ml of solution containing concentrations of from about 1×10^9 to 1×10^{16} genomes virus vector. A preferred human dosage may be about 1×10^{13} to 1×10^{16} AAV genomes. The dosage will be adjusted to balance the therapeutic benefit against any side effects and such dosages may vary depending upon the therapeutic application for which the recombinant vector is employed. The levels of expression of the transgene can be monitored to determine the frequency of dosage resulting in viral vectors, preferably AAV vectors containing the minigene. Optionally, dosage regimens similar to those described for therapeutic purposes may be utilized for immunization using the compositions of the invention.

Examples of therapeutic products and immunogenic products for delivery by the AAV-containing vectors of the invention are provided below. These vectors may be used for a variety of therapeutic or vaccinal regimens, as described herein. Additionally, these vectors may be delivered in combination with one or more other vectors or active ingredients in a desired therapeutic and/or vaccinal regimen.

B. Therapeutic Transgenes

Useful therapeutic products encoded by the transgene include hormones and growth and differentiation factors including, without limitation, insulin, glucagon, growth hormone (GH), parathyroid hormone (PTH), growth hormone releasing factor (GRF),
 5 follicle stimulating hormone (FSH), luteinizing hormone (LH), human chorionic gonadotropin (hCG), vascular endothelial growth factor (VEGF), angiopoietins, angiostatin, granulocyte colony stimulating factor (GCSF), erythropoietin (EPO), connective tissue growth factor (CTGF), basic fibroblast growth factor (bFGF), acidic fibroblast growth factor (aFGF), epidermal growth factor (EGF), transforming growth factor α (TGF α), platelet-
 10 derived growth factor (PDGF), insulin growth factors I and II (IGF-I and IGF-II), any one of the transforming growth factor β superfamily, including TGF β , activins, inhibins, or any of the bone morphogenic proteins (BMP) BMPs 1-15, any one of the heregluin/neuregulin/ARIA/neu differentiation factor (NDF) family of growth factors, nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF), neurotrophins NT-3 and
 15 NT-4/5, ciliary neurotrophic factor (CNTF), glial cell line derived neurotrophic factor (GDNF), neurturin, agrin, any one of the family of semaphorins/collapsins, netrin-1 and netrin-2, hepatocyte growth factor (HGF), ephrins, noggin, sonic hedgehog and tyrosine hydroxylase.

Other useful transgene products include proteins that regulate the immune
 20 system including, without limitation, cytokines and lymphokines such as thrombopoietin (TPO), interleukins (IL) IL-1 through IL-25 (including, IL-2, IL-4, IL-12, and IL-18), monocyte chemoattractant protein, leukemia inhibitory factor, granulocyte-macrophage colony stimulating factor, Fas ligand, tumor necrosis factors α and β , interferons α , β , and γ , stem cell factor, flk-2/flt3 ligand. Gene products produced by the immune system are also
 25 useful in the invention. These include, without limitations, immunoglobulins IgG, IgM, IgA, IgD and IgE, chimeric immunoglobulins, humanized antibodies, single chain antibodies, T cell receptors, chimeric T cell receptors, single chain T cell receptors, class I and class II MHC molecules, as well as engineered immunoglobulins and MHC molecules. Useful gene products also include complement regulatory proteins such as complement regulatory
 30 proteins, membrane cofactor protein (MCP), decay accelerating factor (DAF), CR1, CF2 and CD59.

Still other useful gene products include any one of the receptors for the hormones, growth factors, cytokines, lymphokines, regulatory proteins and immune system

proteins. The invention encompasses receptors for cholesterol regulation, including the low density lipoprotein (LDL) receptor, high density lipoprotein (HDL) receptor, the very low density lipoprotein (VLDL) receptor, and the scavenger receptor. The invention also encompasses gene products such as members of the steroid hormone receptor superfamily including glucocorticoid receptors and estrogen receptors, Vitamin D receptors and other nuclear receptors. In addition, useful gene products include transcription factors such as *jun*, *fos*, *max*, *mad*, serum response factor (SRF), AP-1, AP2, *myb*, MyoD and myogenin, ETS-box containing proteins, TFE3, E2F, ATF1, ATF2, ATF3, ATF4, ZF5, NFAT, CREB, HNF-4, C/EBP, SP1, CCAAT-box binding proteins, interferon regulation factor (IRF-1), Wilms tumor protein, ETS-binding protein, STAT, GATA-box binding proteins, e.g., GATA-3, and the forkhead family of winged helix proteins.

Other useful gene products include, carbamoyl synthetase I, ornithine transcarbamylase, arginosuccinate synthetase, arginosuccinate lyase, arginase, fumarylacetate hydrolase, phenylalanine hydroxylase, alpha-1 antitrypsin, glucose-6-phosphatase, porphobilinogen deaminase, factor VIII, factor IX, cystathione beta-synthase, branched chain ketoacid decarboxylase, albumin, isovaleryl-coA dehydrogenase, propionyl CoA carboxylase, methyl malonyl CoA mutase, glutaryl CoA dehydrogenase, insulin, beta-glucosidase, pyruvate carboxylase, hepatic phosphorylase, phosphorylase kinase, glycine decarboxylase, H-protein, T-protein, a cystic fibrosis transmembrane regulator (CFTR) sequence, and a dystrophin cDNA sequence. Still other useful gene products include enzymes such as may be useful in enzyme replacement therapy, which is useful in a variety of conditions resulting from deficient activity of enzyme. For example, enzymes that contain mannose-6-phosphate may be utilized in therapies for lysosomal storage diseases (e.g., a suitable gene includes that encoding β -glucuronidase (GUSB)).

Other useful gene products include non-naturally occurring polypeptides, such as chimeric or hybrid polypeptides having a non-naturally occurring amino acid sequence containing insertions, deletions or amino acid substitutions. For example, single-chain engineered immunoglobulins could be useful in certain immunocompromised patients. Other types of non-naturally occurring gene sequences include antisense molecules and catalytic nucleic acids, such as ribozymes, which could be used to reduce overexpression of a target.

Reduction and/or modulation of expression of a gene is particularly desirable for treatment of hyperproliferative conditions characterized by hyperproliferating cells, as

are cancers and psoriasis. Target polypeptides include those polypeptides which are produced exclusively or at higher levels in hyperproliferative cells as compared to normal cells. Target antigens include polypeptides encoded by oncogenes such as myb, myc, fyn, and the translocation gene bcr/abl, ras, src, P53, neu, trk and EGRF. In addition to oncogene products as target antigens, target polypeptides for anti-cancer treatments and protective regimens include variable regions of antibodies made by B cell lymphomas and variable regions of T cell receptors of T cell lymphomas which, in some embodiments, are also used as target antigens for autoimmune disease. Other tumor-associated polypeptides can be used as target polypeptides such as polypeptides which are found at higher levels in tumor cells including the polypeptide recognized by monoclonal antibody 17-1A and folate binding polypeptides.

Other suitable therapeutic polypeptides and proteins include those which may be useful for treating individuals suffering from autoimmune diseases and disorders by conferring a broad based protective immune response against targets that are associated with autoimmunity including cell receptors and cells which produce "self"-directed antibodies. T cell mediated autoimmune diseases include Rheumatoid arthritis (RA), multiple sclerosis (MS), Sjögren's syndrome, sarcoidosis, insulin dependent diabetes mellitus (IDDM), autoimmune thyroiditis, reactive arthritis, ankylosing spondylitis, scleroderma, polymyositis, dermatomyositis, psoriasis, vasculitis, Wegener's granulomatosis, Crohn's disease and ulcerative colitis. Each of these diseases is characterized by T cell receptors (TCRs) that bind to endogenous antigens and initiate the inflammatory cascade associated with autoimmune diseases.

C. Immunogenic Transgenes

Alternatively, or in addition, the vectors of the invention may contain AAV sequences of the invention and a transgene encoding a peptide, polypeptide or protein which induces an immune response to a selected immunogen. For example, immunogens may be selected from a variety of viral families. Example of desirable viral families against which an immune response would be desirable include, the picornavirus family, which includes the genera rhinoviruses, which are responsible for about 50% of cases of the common cold; the genera enteroviruses, which include polioviruses, coxsackieviruses, echoviruses, and human enteroviruses such as hepatitis A virus; and the genera aphthoviruses, which are responsible for foot and mouth diseases, primarily in non-human animals. Within the picornavirus family of viruses, target antigens include the VP1, VP2, VP3, VP4, and VPG. Another viral

family includes the calcivirus family, which encompasses the Norwalk group of viruses, which are an important causative agent of epidemic gastroenteritis. Still another viral family desirable for use in targeting antigens for inducing immune responses in humans and non-human animals is the togavirus family, which includes the genera alphavirus, which include

5 Sindbis viruses, Ross River virus, and Venezuelan, Eastern & Western Equine encephalitis, and rubivirus, including Rubella virus. The flaviviridae family includes dengue, yellow fever, Japanese encephalitis, St. Louis encephalitis and tick borne encephalitis viruses. Other target antigens may be generated from the Hepatitis C or the coronavirus family, which includes a number of non-human viruses such as infectious bronchitis virus (poultry),

10 porcine transmissible gastroenteric virus (pig), porcine hemagglutinating encephalomyelitis virus (pig), feline infectious peritonitis virus (cats), feline enteric coronavirus (cat), canine coronavirus (dog), and human respiratory coronaviruses, which may cause the common cold and/or non-A, B or C hepatitis. Within the coronavirus family, target antigens include the

15 E1 (also called M or matrix protein), E2 (also called S or Spike protein), E3 (also called HE or hemagglutinin-esterase) glycoprotein (not present in all coronaviruses), or N (nucleocapsid). Still other antigens may be targeted against the rhabdovirus family, which includes the genera vesiculovirus (e.g., Vesicular Stomatitis Virus), and the general lyssavirus (e.g., rabies). Within the rhabdovirus family, suitable antigens may be derived from the G protein or the N protein. The family filoviridae, which includes hemorrhagic fever viruses such as

20 Marburg and Ebola virus may be a suitable source of antigens. The paramyxovirus family includes parainfluenza Virus Type 1, parainfluenza Virus Type 3, bovine parainfluenza Virus Type 3, rubulavirus (mumps virus, parainfluenza Virus Type 2, parainfluenza virus Type 4, Newcastle disease virus (chickens), rinderpest, morbillivirus, which includes measles and canine distemper, and pneumovirus, which includes respiratory syncytial virus.

25 The influenza virus is classified within the family orthomyxovirus and is a suitable source of antigen (e.g., the HA protein, the N1 protein). The bunyavirus family includes the genera bunyavirus (California encephalitis, La Crosse), phlebovirus (Rift Valley Fever), hantavirus (pneumonia is a hemorrhagic fever virus), nairovirus (Nairobi sheep disease) and various unassigned bunyaviruses. The arenavirus family provides a source of antigens against LCM

30 and Lassa fever virus. The reovirus family includes the genera reovirus, rotavirus (which causes acute gastroenteritis in children), orbiviruses, and cultivirus (Colorado Tick fever, Lebombo (humans), equine encephalosis, blue tongue).

The retrovirus family includes the sub-family oncorivirinal which encompasses such human and veterinary diseases as feline leukemia virus, HTLV I and HTLV II, lentivirinal (which includes human immunodeficiency virus (HIV), simian immunodeficiency virus (SIV), feline immunodeficiency virus (FIV), equine infectious anemia virus, and spumavirinal). Between the HIV and SIV, many suitable antigens have been described and can readily be selected. Examples of suitable HIV and SIV antigens include, without limitation the gag, pol, Vif, Vpx, VPR, Env, Tat and Rev proteins, as well as various fragments thereof. In addition, a variety of modifications to these antigens have been described. Suitable antigens for this purpose are known to those of skill in the art. For example, one may select a sequence encoding the gag, pol, Vif, and Vpr, Env, Tat and Rev, amongst other proteins. See, e.g., the modified gag protein which is described in US Patent 5,972,596. See, also, the HIV and SIV proteins described in D.H. Barouch et al, J. Virol., 75(5):2462-2467 (March 2001), and R.R. Amara, et al, Science, 292:69-74 (6 April 2001). These proteins or subunits thereof may be delivered alone, or in combination via separate vectors or from a single vector.

The papovavirus family includes the sub-family polyomaviruses (BKU and JCU viruses) and the sub-family papillomavirus (associated with cancers or malignant progression of papilloma). The adenovirus family includes viruses (EX, AD7, ARD, O.B.) which cause respiratory disease and/or enteritis. The parvovirus family feline parvovirus (feline enteritis), feline panleucopeniavirus, canine parvovirus, and porcine parvovirus. The herpesvirus family includes the sub-family alpha herpesvirinae, which encompasses the genera simplexvirus (HSV I, HSV II), varicellovirus (pseudorabies, varicella zoster) and the sub-family beta herpesvirinae, which includes the genera cytomegalovirus (HCMV, muromegalovirus) and the sub-family gamma herpesvirinae, which includes the genera lymphocryptovirus, EBV (Burkitts lymphoma), infectious rhinotracheitis, Marek's disease virus, and rhadinovirus. The poxvirus family includes the sub-family chordopoxvirinae, which encompasses the genera orthopoxvirus (Variola (Smallpox) and Vaccinia (Cowpox)), parapoxvirus, avipoxvirus, capripoxvirus, leporipoxvirus, suipoxvirus, and the sub-family entomopoxvirinae. The hepadnavirus family includes the Hepatitis B virus. One unclassified virus which may be suitable source of antigens is the Hepatitis delta virus. Still other viral sources may include avian infectious bursal disease virus and porcine respiratory and reproductive syndrome virus. The alphavirus family includes equine arteritis virus and various Encephalitis viruses.

The present invention may also encompass immunogens which are useful to immunize a human or non-human animal against other pathogens including bacteria, fungi, parasitic microorganisms or multicellular parasites which infect human and non-human vertebrates, or from a cancer cell or tumor cell. Examples of bacterial pathogens include

5 pathogenic gram-positive cocci include pneumococci; staphylococci; and streptococci. Pathogenic gram-negative cocci include meningococcus; gonococcus. Pathogenic enteric gram-negative bacilli include enterobacteriaceae; pseudomonas, acinetobacteria and eikenella; melioidosis; salmonella; shigella; haemophilus; moraxella; *H. ducreyi* (which causes chancroid); brucella; *Francisella tularensis* (which causes tularemia); yersinia

10 (pasteurella); streptobacillus moniliformis and spirillum; Gram-positive bacilli include listeria monocytogenes; erysipelothrix rhusiopathiae; *Corynebacterium diphtheria* (diphtheria); cholera; *B. anthracis* (anthrax); donovanosis (granuloma inguinale); and bartonellosis. Diseases caused by pathogenic anaerobic bacteria include tetanus; botulism; other clostridia; tuberculosis; leprosy; and other mycobacteria. Pathogenic spirochetal

15 diseases include syphilis; treponematoses: yaws, pinta and endemic syphilis; and leptospirosis. Other infections caused by higher pathogen bacteria and pathogenic fungi include actinomycosis; nocardiosis; cryptococcosis, blastomycosis, histoplasmosis and coccidioidomycosis; candidiasis, aspergillosis, and mucormycosis; sporotrichosis; paracoccidioidomycosis, petriellidiosis, torulopsosis, mycetoma and chromomycosis; and

20 dermatophytosis. Rickettsial infections include Typhus fever, Rocky Mountain spotted fever, Q fever, and Rickettsialpox. Examples of mycoplasma and chlamydial infections include: mycoplasma pneumoniae; lymphogranuloma venereum; psittacosis; and perinatal chlamydial infections. Pathogenic eukaryotes encompass pathogenic protozoans and helminths and infections produced thereby include: amebiasis; malaria; leishmaniasis;

25 trypanosomiasis; toxoplasmosis; *Pneumocystis carinii*; *Trichans*; *Toxoplasma gondii*; babesiosis; giardiasis; trichinosis; filariasis; schistosomiasis; nematodes; trematodes or flukes; and cestode (tapeworm) infections.

Many of these organisms and/or toxins produced thereby have been identified by the Centers for Disease Control [(CDC), Department of Health and Human

30 Services, USA], as agents which have potential for use in biological attacks. For example, some of these biological agents, include, *Bacillus anthracis* (anthrax), *Clostridium botulinum* and its toxin (botulism), *Yersinia pestis* (plague), variola major (smallpox), *Francisella tularensis* (tularemia), and viral hemorrhagic fever, all of which are currently classified as

Category A agents; *Coxiella burnetti* (Q fever); *Brucella* species (brucellosis), *Burkholderia mallei* (glanders), *Ricinus communis* and its toxin (ricin toxin), *Clostridium perfringens* and its toxin (epsilon toxin), *Staphylococcus* species and their toxins (enterotoxin B), all of which are currently classified as Category B agents; and Nipah virus and hantaviruses, which are
 5 currently classified as Category C agents. In addition, other organisms, which are so classified or differently classified, may be identified and/or used for such a purpose in the future. It will be readily understood that the viral vectors and other constructs described herein are useful to deliver antigens from these organisms, viruses, their toxins or other by-products, which will prevent and/or treat infection or other adverse reactions with these
 10 biological agents.

Administration of the vectors of the invention to deliver immunogens against the variable region of the T cells elicit an immune response including CTLs to eliminate those T cells. In rheumatoid arthritis (RA), several specific variable regions of T cell receptors (TCRs) which are involved in the disease have been characterized. These TCRs
 15 include V-3, V-14, V-17 and V α -17. Thus, delivery of a nucleic acid sequence that encodes at least one of these polypeptides will elicit an immune response that will target T cells involved in RA. In multiple sclerosis (MS), several specific variable regions of TCRs which are involved in the disease have been characterized. These TCRs include V-7 and V α -10. Thus, delivery of a nucleic acid sequence that encodes at least one of these polypeptides will
 20 elicit an immune response that will target T cells involved in MS. In scleroderma, several specific variable regions of TCRs which are involved in the disease have been characterized. These TCRs include V-6, V-8, V-14 and V α -16, V α -3C, V α -7, V α -14, V α -15, V α -16, V α -28 and V α -12. Thus, delivery of a nucleic acid molecule that encodes at least one of these polypeptides will elicit an immune response that will target T cells involved in
 25 scleroderma.

Optionally, vectors containing AAV sequences of the invention may be delivered using a prime-boost regimen. A variety of such regimens have been described in the art and may be readily selected. See, e.g., WO 00/11140, published March 2, 2000.

30 Such prime-boost regimens typically involve the administration of a DNA (e.g., plasmid) based vector to prime the immune system to second, booster, administration with a traditional antigen, such as a protein or a recombinant virus carrying the sequences encoding such an antigen. In one embodiment, the invention provides a method of priming

and boosting an immune response to a selected antigen by delivering a plasmid DNA vector carrying said antigen, followed by boosting, e.g., with a vector containing AAV sequences of the invention.

In one embodiment, the prime-boost regimen involves the expression of multiproteins from the prime and/or the boost vehicle. See, e.g., R.R. Amara, Science, 292:69-74 (6 April 2001) which describes a multiprotein regimen for expression of protein subunits useful for generating an immune response against HIV and SIV. For example, a DNA prime may deliver the Gag, Pol, Vif, VPX and Vpr and Env, Tat, and Rev from a single transcript. Alternatively, the SIV Gag, Pol and HIV-1 Env is delivered.

However, the prime-boost regimens are not limited to immunization for HIV or to delivery of these antigens. For example, priming may involve delivering with a first chimp vector of the invention followed by boosting with a second chimp vector, or with a composition containing the antigen itself in protein form. In one or example, the prime-boost regimen can provide a protective immune response to the virus, bacteria or other organism from which the antigen is derived. In another desired embodiment, the prime-boost regimen provides a therapeutic effect that can be measured using convention assays for detection of the presence of the condition for which therapy is being administered.

The priming vaccine may be administered at various sites in the body in a dose dependent manner, which depends on the antigen to which the desired immune response is being targeted. The invention is not limited to the amount or situs of injection(s) or to the pharmaceutical carrier. Rather, the priming step encompasses treatment regimens which include a single dose or dosage which is administered hourly, daily, weekly or monthly, or yearly. As an example, the mammals may receive one or two priming injection containing between about 10 μ g to about 50 μ g of plasmid in carrier. A desirable priming amount or dosage of the priming DNA vaccine composition ranges between about 1 μ g to about 10,000 μ g of the DNA vaccine. Dosages may vary from about 1 μ g to 1000 μ g DNA per kg of subject body weight. The amount or site of injection is desirably selected based upon the identity and condition of the mammal being vaccinated.

The dosage unit of the DNA vaccine suitable for delivery of the antigen to the mammal is described herein. The DNA vaccine is prepared for administration by being suspended or dissolved in a pharmaceutically or physiologically acceptable carrier such as isotonic saline, isotonic salts solution or other formulations which will be apparent to those skilled in such administration. The appropriate carrier will be evident to those skilled in the

art and will depend in large part upon the route of administration. The compositions of the invention may be administered to a mammal according to the routes described above, in a sustained release formulation using a biodegradable biocompatible polymer, or by on-site delivery using micelles, gels and liposomes.

5 Optionally, the priming step of this invention also includes administering with the priming DNA vaccine composition, a suitable amount of an adjuvant, such as are defined herein.

 Preferably, a boosting composition is administered about 2 to about 27 weeks after administering the priming DNA vaccine to the mammalian subject. The administration
10 of the boosting composition is accomplished using an effective amount of a boosting vaccine composition containing or capable of delivering the same antigen as administered by the priming DNA vaccine. The boosting composition may be composed of a recombinant viral vector derived from the same viral source or from another source. Alternatively, the “boosting composition” can be a composition containing the same antigen as encoded in the
15 priming DNA vaccine, but in the form of a protein or peptide, which composition induces an immune response in the host. In another embodiment, the boosting vaccine composition includes a composition containing a DNA sequence encoding the antigen under the control of a regulatory sequence directing its expression in a mammalian cell, e.g., vectors such as well-known bacterial or viral vectors. The primary requirements of the boosting vaccine
20 composition are that the antigen of the vaccine composition is the same antigen, or a cross-reactive antigen, as that encoded by the DNA vaccine.

 Suitably, the vectors of the invention are also well suited for use in regimens which use non-AAV vectors as well as proteins, peptides, and/or other biologically useful therapeutic or immunogenic compounds. These regimens are particularly well suited to gene
25 delivery for therapeutic poses and for immunization, including inducing protective immunity. Such uses will be readily apparent to one of skill in the art.

 Further, a vector of the invention provides an efficient gene transfer vehicle which can deliver a selected transgene to a selected host cell *in vivo* or *ex vivo* even where the organism has neutralizing antibodies to one or more AAV serotypes. In one
30 embodiment, the vector (e.g., an rAAV) and the cells are mixed *ex vivo*; the infected cells are cultured using conventional methodologies; and the transduced cells are re-infused into the patient. Further, the vectors of the invention may also be used for production of a desired gene product *in vitro*. For *in vitro* production, a desired product (e.g., a protein) may be

obtained from a desired culture following transfection of host cells with a rAAV containing the molecule encoding the desired product and culturing the cell culture under conditions which permit expression. The expressed product may then be purified and isolated, as desired. Suitable techniques for transfection, cell culturing, purification, and isolation are
 5 known to those of skill in the art.

The following examples illustrate several aspects and embodiments of the invention.

EXAMPLES

10

Example 1: PCR amplification, cloning and characterization of novel AAV sequences.

Tissues from nonhuman primates were screened for AAV sequences using a PCR method based on oligonucleotides to highly conserved regions of known AAVs. A stretch of AAV sequence spanning 2886 to 3143 bp of AAV1 [SEQ ID NO:6] was selected
 15 as a PCR amplicon in which a hypervariable region of the capsid protein (Cap) that is unique to each known AAV serotype, which is termed herein a "signature region," is flanked by conserved sequences. In later analysis, this signature region was shown to be located between conserved residues spanning hypervariable region 3.

An initial survey of peripheral blood of a number of nonhuman primate
 20 species revealed detectable AAV in a subset of animals from species such as rhesus macaques, cynomologous macaques, chimpanzees and baboons. However, there were no AAV sequences detected in some other species tested, including Japanese macaques, pig-tailed macaques and squirrel monkeys. A more extensive analysis of vector distribution was conducted in tissues of rhesus monkeys of the University of Pennsylvania and Tulane
 25 colonies recovered at necropsy. This revealed AAV sequence throughout a wide array of tissues.

A. *Amplification of an AAV signature region*

DNA sequences of AAV1-6 and AAVs isolated from Goose and Duck were aligned to each other using "Clustal W" at default settings. The alignment for
 30 AAV1-6, and including the information for the novel AAV7, is provided in Fig. 1. Sequence similarities among AAVs were compared.

In the line of study, a 257 bp region spanning 2886 bp to 3143 bp of AAV 1 [SEQ ID NO: 6], and the corresponding region in the genomes of AAV 2-6 genomes [See, Fig. 1], was identified by the inventors. This region is located with the AAV capsid gene and has highly conserved sequences among at both 5' and 3' ends and is relatively variable sequence in the middle. In addition, this region contains a DraIII restriction enzyme site (CACCACGTC, SEQ ID NO:15) . The inventors have found that this region serves as specific signature for each known type of AAV DNA. In other words, following PCR reactions, digestion with endonucleases that are specific to each known serotypes and gel electrophoresis analysis, this regions can be used to definitively identify amplified DNA as being from serotype 1, 2, 3, 4, 5, 6, or another serotype.

The primers were designed, validated and PCR conditions optimized with AAV1, 2 and 5 DNA controls. The primers were based upon the sequences of AAV2: 5' primer, 1S: bp 2867-2891 of AAV2 (SEQ ID NO:7) and 3' primer, 18as, bp 3095-3121 of AAV2 (SEQ ID NO:7).

Cellular DNAs from different tissues including blood, brain, liver, lung, testis, etc. of different rhesus monkeys were studied utilizing the strategy described above. The results revealed that DNAs from different tissues of these monkeys gave rise to strong PCR amplifications. Further restriction analyses of PCR products indicated that they were amplified from AAV sequences different from any published AAV sequences.

PCR products (about 255 bp in size) from DNAs of a variety of monkey tissues have been cloned and sequenced. Bioinformatics study of these novel AAV sequences indicated that they are novel AAV sequences of capsid gene and distinct from each other. Fig. 1 includes in the alignment the novel AAV signature regions for AAV10-12 [SEQ ID NO:117, 118 and 119, respectively]. Multiple sequence alignment analysis was performed using the Clustal W (1.81) program. The percentage of sequence identity between the signature regions of AAV 1-7 and AAV 10-12 genomes is provided below.

Table 1. Sequences for Analysis

Sequence #	AAV Serotype	Size (bp)
1	AAV1	258
2	AAV2	255
3	AAV3	255
4	AAV4	246
5	AAV5	258
6	AAV6	258
7	AAV7	258
10	AAV10	255
11	AAV11	258
12	AAV12	255

Table 3. Pairwise Alignment (Percentage of Identity)

	AAV2	AAV3	AAV4	AAV5	AAV6	AAV7	AAV10	AAV11	AAV12
AAV1	90	90	81	76	97	91	93	94	93
AAV2		93	79	78	90	90	93	93	92
AAV3			80	76	90	92	92	92	92
AAV4				76	81	84	82	81	79
AAV5					75	78	79	79	76
AAV6						91	92	94	94
AAV7							94	92	92
AAV10								95	93
AAV11									94

Over 300 clones containing novel AAV serotype sequences that span the selected 257 bp region were isolated and sequenced. Bioinformatics analysis of these 300+ clones suggests that this 257 bp region is critical in serving as a good land marker or signature sequence for quick isolation and identification of novel AAV serotype.

B. Use of the signature region for PCR amplification.

The 257 bp signature region was used as a PCR anchor to extend PCR amplifications to 5' of the genome to cover the junction region of rep and cap genes (1398 bp – 3143 bp, SEQ ID NO:6) and 3' of the genome to obtain the entire cap gene sequence (2866 bp – 4600 bp, SEQ ID NO:6). PCR amplifications were carried out using the standard conditions, including denaturing at 95°C for 0.5-1 min, annealing at 60-65°C for 0.5-1 min and extension at 72° C for 1 min per kb with a total number of amplification cycles ranging from 28 to 42.

Using the aligned sequences as described in "A", two other relative conserved regions were identified in the sequence located in 3' end of rep genes and 5' to the

257 bp region and in the sequence down stream of the 257 bp fragment but before the AAV' 3 ITR. Two sets of new primers were designed and PCR conditions optimized for recovery of entire capsid and a part of rep sequences of novel AAV serotypes. More specifically, for the 5' amplification, the 5' primer, AV1Ns, was GCTGCGTCAACTGGACCAATGAGAAC
 5 [nt 1398-1423 of AAV1, SEQ ID NO:6] and the 3' primer was 18as, identified above. For the 3' amplification, the 5' primer was 1s, identified above, and the 3' primer was AV2Las, TCGTTTCAGTTGAACTTTGGTCTCTGCG [nt 4435-4462 of AAV2, SEQ ID NO:7].

In these PCR amplifications, the 257 bp region was used as a PCR anchor and land marker to generate overlapping fragments to construct a complete capsid
 10 gene by fusion at the DraIII site in the signature region following amplification of the 5' and 3' extension fragments obtained as described herein. More particularly, to generate the intact AAV7 cap gene, the three amplification products (a) the sequences of the signature region; (b) the sequences of the 5' extension; and (c) the sequences of the 3' extension were cloned into a pCR4-Topo [Invitrogen] plasmid backbone according to manufacturer's instructions.
 15 Thereafter, the plasmids were digested with DraIII and recombined to form an intact cap gene.

In this line of work, about 80 % of capsid sequences of AAV7 and AAV 8 were isolated and analyzed. Another novel serotype, AAV9, was also discovered from Monkey #2.

20 Using the PCR conditions described above, the remaining portion of the rep gene sequence for AAV7 is isolated and cloned using the primers that amplify 108 bp to 1461 bp of AAV genome (calculated based on the numbering of AAV2, SEQ ID NO:7). This clone is sequenced for construction of a complete AAV7 genome without ITRs.

C. Direct Amplification of 3.1 kb Cap fragment

25 To directly amplify a 3.1 kb full-length Cap fragment from NHP tissue and blood DNAs, two other highly conserved regions were identified in AAV genomes for use in PCR amplification of large fragments. A primer within a conserved region located in the middle of the rep gene was selected (AV1ns: 5' GCTGCGTCAACTGGACCAATGAGAAC 3', nt 1398-1423 of SEQ ID NO:6) in
 30 combination with the 3' primer located in another conserved region downstream of the Cap gene (AV2cas: 5' CGCAGAGACCAAAGTTCAACTGAAACGA 3', SEQ ID NO:7) for amplification of full-length cap fragments. The PCR products were Topo-cloned according to manufacturer's directions (Invitrogen) and sequence analysis was performed by

Qiagen Genomics (Qiagen Genomics, Seattle, WA) with an accuracy of $\geq 99.9\%$. A total of 50 capsid clones were isolated and characterized. Among them, 37 clones were derived from Rhesus macaque tissues (rh.1 – rh.37), 6 clones from cynomolgous macaques (cy.1 – cy.6), 2 clones from Baboons (bb.1 and bb.2) and 5 clones from Chimps (ch.1 – ch.5).

5 To rule out the possibility that sequence diversity within the novel AAV family was not an artifact of the PCR, such as PCR-mediated gene splicing by overlap extension between different partial DNA templates with homologous sequences, or the result of recombination process in bacteria, a series of experiments were performed under identical conditions for VP1 amplification using total cellular DNAs. First, intact AAV7 and AAV8
10 plasmids were mixed at an equal molar ratio followed by serial dilutions. The serially diluted mixtures were used as templates for PCR amplification of 3.1 kb VP1 fragments using universal primers and identical PCR conditions to that were used for DNA amplifications to see whether any hybrid PCR products were generated. The mixture was transformed into bacteria and isolated transformants to look for hybrid clones possibly derived from
15 recombination process in bacterial cells. In a different experiment, we restricted AAV7 and AAV8 plasmids with Msp I, Ava I and HaeI, all of which cut both genomes multiple times at different positions, mixed the digestions in different combinations and used them for PCR amplification of VP1 fragments under the same conditions to test whether any PCR products could be generated through overlap sequence extension of partial AAV sequences. In another
20 experiment, a mixture of gel purified 5' 1.5 kb AAV7 VP1 fragment and 3' 1.7 kb AAV8 VP1 fragment with overlap in the signature region was serially diluted and used for PCR amplification in the presence and absence of 200 ng cellular DNA extracted from a monkey cell line that was free of AAV sequences by TaqMan analysis. None of these experiments demonstrated efficient PCR-mediated overlap sequence production under the conditions of
25 the genomic DNA Cap amplification (data not shown). As a further confirmation, 3 pairs of primers were designed, which were located at different HVRs, and were sequence specific to the variants of clone 42s from Rhesus macaque F953, in different combinations to amplify shorter fragments from mesenteric lymph node (MLN) DNA from F953 from which clone 42s were isolated. All sequence variations identified in full-length Cap clones were found in
30 these short fragments (data not shown).

Example 2: Adeno-Associated Viruses Undergo Substantial Evolution in Primates During Natural Infections

Sequence analysis of selected AAV isolates revealed divergence throughout the genome that is most concentrated in hypervariable regions of the capsid proteins.

5 Epidemiologic data indicate that all known serotypes are endemic to primates, although isolation of clinical isolates has been restricted to AAV2 and AAV3 from anal and throat swabs of human infants and AAV5 from a human condylomatous wart. No known clinical sequelae have been associated with AAV infection.

10 In an attempt to better understand the biology of AAV, nonhuman primates were used as models to characterize the sequelae of natural infections. Tissues from nonhuman primates were screened for AAV sequences using the PCR method of the invention based on oligonucleotides to highly conserved regions of known AAVs (see Example 1). A stretch of AAV sequence spanning 2886 to 3143 bp of AAV1 [SEQ ID NO:6] was selected as a PCR amplicon in which conserved sequences are flanked by a hypervariable region that is unique
15 to each known AAV serotype, termed herein a "signature region."

An initial survey of peripheral blood of a number of nonhuman primate species including rhesus monkeys, cynomolgous monkeys, chimpanzees, and baboons revealed detectable AAV in a subset of animals from all species. A more extensive analysis of vector distribution was conducted in tissues of rhesus monkeys of the University of Pennsylvania
20 and Tulane colonies recovered at necropsy. This revealed AAV sequence throughout a wide array of tissues.

The amplified signature sequences were subcloned into plasmids and individual transformants were subjected to sequence analysis. This revealed substantial variation in nucleotide sequence of clones derived from different animals. Variation in the signature
25 sequence was also noted in clones obtained within individual animals. Tissues harvested from two animals in which unique signature sequences were identified (i.e., colon from 98E044 and heart from 98E056) were further characterized by expanding the sequence amplified by PCR using oligonucleotides to highly conserved sequences. In this way, complete proviral structures were reconstructed for viral genomes from both tissues as
30 described herein. These proviruses differ from the other known AAVs with the greatest sequence divergence noted in regions of the Cap gene.

Additional experiments were performed to confirm that AAV sequences resident to the nonhuman primate tissue represented proviral genomes of infectious virus that is capable

of being rescued and form virions. Genomic DNA from liver tissue of animal 98E056, from which AAV8 signature sequence was detected, was digested with an endonuclease that does not have a site within the AAV sequence and transfected into 293 cells with a plasmid containing an E1 deleted genome of human adenovirus serotype 5 as a source of helper functions. The resulting lysate was passaged on 293 cells once and the lysate was recovered and analyzed for the presence of AAV Cap proteins using a broadly reacting polyclonal antibody to Cap proteins and for the presence and abundance of DNA sequences from the PCR amplified AAV provirus from which AAV8 was derived. Transfection of endonuclease restricted heart DNA and the adenovirus helper plasmid yielded high quantities of AAV8 virus as demonstrated by the detection of Cap proteins by Western blot analysis and the presence of 10^4 AAV8 vector genomes per 293 cell. Lysates were generated from a large-scale preparation and the AAV was purified by cesium sedimentation. The purified preparation demonstrated 26 nm icosohedral structures that look identical to those of AAV serotype 2. Transfection with the adenovirus helper alone did not yield AAV proteins or genomes, ruling out contamination as a source of the rescued AAV.

To further characterize the inter and intra animal variation of AAV signature sequence, selected tissues were subjected to extended PCR to amplify entire Cap open reading frames.

The resulting fragments were cloned into bacterial plasmids and individual transformants were isolated and fully sequenced. This analysis involved mesenteric lymph nodes from three rhesus monkeys (Tulane/V223 – 6 clones; Tulane/T612 – 7 clones; Tulane/F953 – 14 clones), liver from two rhesus monkeys (Tulane/V251 – 3 clones; Penn/00E033 – 3 clones), spleen from one rhesus monkey (Penn/97E043 – 3 clones), heart from one rhesus monkey (IHGT/98E046- 1 clone) and peripheral blood from one chimpanzee (New Iberia/X133 – 5 clones), six cynomologous macaques (Charles River/A1378, A3099, A3388, A3442, A2821, A3242 – 6 clones total) and one Baboon (SFRB/8644 – 2 clones). Of the 50 clones that were sequenced from 15 different animals, 30 were considered non-redundant based on the finding of at least 7 amino acid differences from one another. The non-redundant VP1 clones are numbered sequentially as they were isolated, with a prefix indicating the species of non-human primate from which they were derived. The structural relationships between these 30 non-redundant clones and the previously described 8 AAV serotypes were determined using the SplitsTree program [Huson, D. H. SplitsTree: analyzing and visualizing evolutionary data. *Bioinformatics* 14,

68-73 (1998)] with implementation of the method of split decomposition. The analysis depicts homoplasy between a set of sequences in a tree-like network rather than a bifurcating tree. The advantage is to enable detection of groupings that are the result of convergence and to exhibit phylogenetic relationships even when they are distorted by parallel events.

5 Extensive phylogenetic research will be required in order to elucidate the AAV evolution, whereas the intention here only is to group the different clones as to their sequence similarity.

To confirm that the novel VP1 sequences were derived from infectious viral genomes, cellular DNA from tissues with high abundance of viral DNA was restricted with
10 an endonuclease that should not cleave within AAV and transfected into 293 cells, followed by infection with adenovirus. This resulted in rescue and amplification of AAV genomes from DNA of tissues from two different animals (data not shown).

VP1 sequences of the novel AAVs were further characterized with respect to the nature and location of amino acid sequence variation. All 30 VP1 clones that were shown to
15 differ from one another by greater than 1% amino acid sequence were aligned and scored for variation at each residue. An algorithm developed to determine areas of sequence divergence yielded 12 hypervariable regions (HVR) of which 5 overlap or are part of the 4 previously described variable regions [Kotin, cited above; Rutledge, cited above]. The three-fold-proximal peaks contain most of the variability (HVR5-10). Interestingly the loops
20 located at the 2 and 5 fold axis show intense variation as well. The HVRs 1 and 2 occur in the N-terminal portion of the capsid protein that is not resolved in the X-ray structure suggesting that the N-terminus of the VP1 protein is exposed on the surface of the virion.

Real-time PCR was used to quantify AAV sequences from tissues of 21 rhesus monkeys using primers and probes to highly conserved regions of Rep (one set) and Cap
25 (two sets) of known AAVs. Each data point represents analysis from tissue DNA from an individual animal. This confirmed the wide distribution of AAV sequences, although the quantitative distribution differed between individual animals. The source of animals and previous history or treatments did not appear to influence distribution of AAV sequences in rhesus macaques. The three different sets of primers and probes used to quantify AAV
30 yielded consistent results. The highest levels of AAV were found consistently in mesenteric lymph nodes at an average of 0.01 copies per diploid genome for 13 animals that were positive. Liver and spleen also contained high abundance of virus DNA. There were examples of very high AAV, such as in heart of rhesus macaque 98E056, spleen of rhesus

macaque 97E043 and liver of rhesus macaque RQ4407, which demonstrated 1.5, 3 and 20 copies of AAV sequence per diploid genome respectively. Relatively low levels of virus DNA were noted in peripheral blood mononuclear cells, suggesting the data in tissue are not due to resident blood components (data not shown). It should be noted that this method
 5 would not necessarily capture all AAVs resident to the nonhuman primates since detection requires high homology to both the oligonucleotides and the real time PCR probe. Tissues from animals with high abundance AAV DNA was further analyzed for the molecular state of the DNA, by DNA hybridization techniques, and its cellular distribution, by *in situ* hybridization.

10 The kind of sequence variation revealed in AAV proviral fragments isolated from different animals and within tissues of the same animals is reminiscent of the evolution that occurs for many RNA viruses during pandemics or even within the infection of an individual. In some situations the notion of a wild-type virus has been replaced by the existence of swarms of quasispecies that evolve as a result of rapid replication and mutations
 15 in the presence of selective pressure. One example is infection by HIV, which evolves in response to immunologic and pharmacologic pressure. Several mechanisms contribute to the high rate of mutations in RNA viruses, including low fidelity and lack of proof reading capacity of reverse transcriptase and non-homologous and homologous recombination.

Evidence for the formation of quasispecies of AAV was illustrated in this study by
 20 the systematic sequencing of multiple cloned proviral fragments. In fact, identical sequences could not be found within any extended clones isolated between or within animals. An important mechanism for this evolution of sequence appears to be a high rate of homologous recombination between a more limited number of parenteral viruses. The net result is extensive swapping of hypervariable regions of the Cap protein leading to an array of
 25 chimeras that could have different tropisms and serologic specificities (i.e., the ability to escape immunologic responses especially as it relates to neutralizing antibodies).

Mechanisms by which homologous recombination could occur are unclear. One possibility is that + and - strands of different single stranded AAV genomes anneal during replication as has been described during high multiplicity of infections with AAV recombinants. It is
 30 unclear if other mechanisms contribute to sequence evolution in AAV infections. The overall rate of mutation that occurs during AAV replication appears to be relatively low and the data do not suggest high frequencies of replication errors. However, substantial rearrangements of the AAV genome have been described during lytic infection leading to the

formation of defective interfering particles. Irrespective of the mechanisms that lead to sequence divergence, with few exceptions, *vp1* structures of the quasispecies remained intact without frameshifts or nonsense mutations suggesting that competitive selection of viruses with the most favorable profile of fitness contribute to the population dynamics.

5 These studies have implications in several areas of biology and medicine. The concept of rapid virus evolution, formerly thought to be a property restricted to RNA viruses, should be considered in DNA viruses, which classically have been characterized by serologic assays. It will be important in terms of parvoviruses to develop a new method for describing virus isolates that captures the complexity of its structure and biology, such as with HIV,
10 which are categorized as general families of similar structure and function called Clades. An alternative strategy is to continue to categorize isolates with respect to serologic specificity and develop criteria for describing variants within serologic groups.

Example 3: Vectorology of recombinant AAV genomes equipped with AAV2 ITRs
15 using chimeric plasmids containing AAV2 rep and novel AAV cap genes for serological and gene transfer studies in different animal models.

Chimeric packaging constructs are generated by fusing AAV2 rep with cap sequences of novel AAV serotypes. These chimeric packaging constructs are used, initially, for pseudotyping recombinant AAV genomes carrying AAV2 ITRs by triple transfection in
20 293 cell using Ad5 helper plasmid. These pseudotyped vectors are used to evaluate performance in transduction-based serological studies and evaluate gene transfer efficiency of novel AAV serotypes in different animal models including NHP and rodents, before intact and infectious viruses of these novel serotypes are isolated.

A. *pAAV2GFP*

25 The AAV2 plasmid which contains the AAV2 ITRs and green fluorescent protein expressed under the control of a constitutive promoter. This plasmid contains the following elements: the AAV2 ITRs, a CMV promoter, and the GFP coding sequences.

B. *Cloning of trans plasmid*

To construct the chimeric trans-plasmid for production of recombinant
30 pseudotyped AAV7 vectors, p5E18 plasmid (Xiao *et al.*, 1999, *J. Virol* 73:3994-4003) was partially digested with Xho I to linearize the plasmid at the Xho I site at the position of 3169 bp only. The Xho I cut ends were then filled in and ligated back. This modified p5E18 plasmid was restricted with Xba I and Xho I in a complete digestion to remove the AAV2

cap gene sequence and replaced with a 2267 bp Spe I/Xho I fragment containing the AAV7 cap gene which was isolated from pCRAAV7 6-5+15-4 plasmid.

The resulting plasmid contains the AAV2 rep sequences for Rep78/68 under the control of the AAV2 P5 promoter, and the AAV2 rep sequences for Rep52/40 under the control of the AAV2 P19 promoter. The AAV7 capsid sequences are under the control of the AAV2 P40 promoter, which is located within the Rep sequences. This plasmid further contains a spacer 5' of the rep ORF.

C. *Production of Pseudotyped rAAV*

The rAAV particles (AAV2 vector in AAV7 capsid) are generated using an adenovirus-free method. Briefly, the cis plasmid (pAAV2.1 lacZ plasmid containing AAV2 ITRs), and the trans plasmid pCRAAV7 6-5+15-4 (containing the AAV2 rep and AAV7 cap) and a helper plasmid, respectively, were simultaneously co-transfected into 293 cells in a ratio of 1:1:2 by calcium phosphate precipitation.

For the construction of the pAd helper plasmids, pBG10 plasmid was purchased from Microbix (Canada). A RsrII fragment containing L2 and L3 was deleted from pBHG10, resulting in the first helper plasmid, pAdΔF13. Plasmid AdΔ F1 was constructed by cloning Asp700/SalI fragment with a PmeI/SgfI deletion, isolating from pBHG10, into Bluescript. MLP, L2, L2 and L3 were deleted in the pAdΔF1. Further deletions of a 2.3 kb NruI fragment and, subsequently, a 0.5 kb RsrII/NruI fragment generated helper plasmids pAdΔF5 and pAdΔF6, respectively. The helper plasmid, termed pΔF6, provides the essential helper functions of E2a and E4 ORF6 not provided by the E1-expressing helper cell, but is deleted of adenoviral capsid proteins and functional E1 regions).

Typically, 50 μg of DNA (cis:trans:helper) was transfected onto a 150 mm tissue culture dish. The 293 cells were harvested 72 hours post-transfection, sonicated and treated with 0.5% sodium deoxycholate (37°C for 10 min.) Cell lysates were then subjected to two rounds of a CsCl gradient. Peak fractions containing rAAV vector are collected, pooled and dialyzed against PBS.

Example 4: Creation of infectious clones carrying intact novel AAV serotypes for study of basic virology in human and NHP derived cell lines and evaluation of pathogenesis of novel AAV serotypes in NHP and other animal models.

To achieve this goal, the genome walker system is employed to obtain 5' and 3' terminal sequences (ITRs) and complete construction of clones containing intact novel AAV serotype genomes.

Briefly, utilizing a commercially available Universal Genome Walker Kit [Clontech], genomic DNAs from monkey tissues or cell lines that are identified as positive for the presence of AAV7 sequence are digested with Dra I, EcoR V, Pvu II and Stu I endonucleases and ligated to Genome Walker Adaptor to generate 4 individual Genome Walker Libraries (GWLs). Using DNAs from GWLs as templates, AAV7 and adjacent genomic sequences will be PCR-amplified by the adaptor primer 1 (AP1, provided in the kit) and an AAV7 specific primer 1, followed by a nested PCR using the adaptor primer 2 (AP2) and another AAV7 specific primer 2, both of which are internal to the first set of primers. The major PCR products from the nested PCR are cloned and characterized by sequencing analysis.

In this experiment, the primers covering the 257 bp or other signature fragment of a generic AAV genome are used for PCR amplification of cellular DNAs extracted from Human and NHP derived cell lines to identify and characterize latent AAV sequences. The identified latent AAV genomes are rescued from the positive cell lines using adenovirus helpers of different species and strains.

To isolate infectious AAV clones from NHP derived cell lines, a desired cell line is obtained from ATCC and screened by PCR to identify the 257 bp amplicon, i.e., signature region of the invention. The 257 bp PCR product is cloned and serotyped by sequencing analysis. For these cell lines containing the AAV7 sequence, the cells are infected with SV-15, a simian adenovirus purchased from ATCC, human Ad5 or transfected with plasmid construct housing the human Ad genes that are responsible for AAV helper functions. At 48 hour post infection or transfection, the cells are harvested and Hirt DNA is prepared for cloning of AAV7 genome following Xiao et al., 1999, J. Virol, 73:3994-4003.

30

Example 5 - Production of AAV Vectors

A pseudotyping strategy similar to that of Example 3 for AAV1/7 was employed to produce AAV2 vectors packaged with AAV1, AAV5 and AAV8 capsid proteins. Briefly,

recombinant AAV genomes equipped with AAV2 ITRs were packaged by triple transfection of 293 cells with cis-plasmid, adenovirus helper plasmid and a chimeric packaging construct where the AAV2 rep gene is fused with cap genes of novel AAV serotypes. To create the chimeric packaging constructs, the Xho I site of p5E18 plasmid at 3169 bp was ablated and the modified plasmid was restricted with Xba I and Xho I in a complete digestion to remove the AAV2 cap gene and replace it with a 2267 bp Spe I/Xho I fragment containing the AAV8 cap gene [Xiao, W., et al., (1999) *J Virol* 73, 3994-4003]. A similar cloning strategy was used for creation of chimeric packaging plasmids of AAV2/1 and AAV2/5. All recombinant vectors were purified by the standard CsCl₂ sedimentation method except for AAV2/2, which was purified by single step heparin chromatography.

Genome copy (GC) titers of AAV vectors were determined by TaqMan analysis using probes and primers targeting SV40 poly A region as described previously [Gao, G., et al., (2000) *Hum Gene Ther* 11, 2079-91].

Vectors were constructed for each serotype for a number of *in vitro* and *in vivo* studies. Eight different transgene cassettes were incorporated into the vectors and recombinant virions were produced for each serotype. The recovery of virus, based on genome copies, is summarized in Table 4 below. The yields of vector were high for each serotype with no consistent differences between serotypes. Data presented in the table are average genome copy yields with standard deviation x 10¹³ of multiple production lots of 50 plate (150 mm) transfections.

Table 4. Production of Recombinant Vectors

	AAV2/1	AAV2/2	AAV2/5	AAV2/7	AAV2/8
CMV LacZ	7.30 ± 4.33 (n=9)	4.49 ± 2.89 (n=6)	5.19 ± 5.19 (n=8)	3.42 (n=1)	0.87 (n=1)
CMV EGFP	6.43 ± 2.42 (n=2)	3.39 ± 2.42 (n=2)	5.55 ± 6.49 (n=4)	2.98 ± 2.66 (n=2)	3.74 ± 3.88 (n=2)
TBG LacZ	4.18 (n=1)	0.23 (n=1)	0.704 ± 0.43 (n=2)	2.16 (n=1)	0.532 (n=1)
Alb A1AT	4.67 ± 0.75 (n=2)	4.77 (n=1)	4.09 (n=1)	5.04 (n=1)	2.02 (n=1)
CB A1AT	0.567 (n=1)	0.438 (n=1)	2.82 (n=1)	2.78 (n=1)	0.816 ± 0.679 (n=2)

Table 4 (cont'd).

	AAV2/1	AAV2/2	AAV2/5	AAV2/7	AAV2/8
TBG rhCG	8.51 ± 6.65 (n=6)	3.47 ± 2.09 (n=5)	5.26 ± 3.85 (n=4)	6.52 ± 3.08 (n=4)	1.83 ± 0.98 (n=5)
TBG cFIX	1.24 ± 1.29 (n=3)	0.63 ± 0.394 (n=6)	3.74 ± 2.48 (n=7)	4.05 (n=1)	15.8 ± 15.0 (n=5)

5 Example 6 - Serologic Analysis of Pseudotyped Vectors

C57BL/6 mice were injected with vectors of different serotypes of AAVCBA1AT vectors intramuscularly (5×10^{11} GC) and serum samples were collected 34 days later. To test neutralizing and cross-neutralizing activity of sera to each serotype of AAV, sera was analyzed in a transduction based neutralizing antibody assay [Gao, G. P., et al., (1996) *J Virol* 70, 8934-43]. More specifically, the presence of neutralizing antibodies was determined by assessing the ability of serum to inhibit transduction of 84-31 cells by reporter viruses (AAVCMVEGFP) of different serotypes. Specifically, the reporter virus AAVCMVEGFP of each serotype [at multiplicity of infection (MOI) that led to a transduction of 90% of indicator cells] was pre-incubated with heat-inactivated serum from animals that received different serotypes of AAV or from naïve mice. After 1-hour incubation at 37° C, viruses were added to 84-31 cells in 96 well plates for 48 or 72- hour, depending on the virus serotype. Expression of GFP was measured by FluoroImagin (Molecular Dynamics) and quantified by Image Quant Software. Neutralizing antibody titers were reported as the highest serum dilution that inhibited transduction to less than 50%.

The availability of GFP expressing vectors simplified the development of an assay for neutralizing antibodies that was based on inhibition of transduction in a permissive cell line (i.e., 293 cells stably expressing E4 from Ad5). Sera to selected AAV serotypes were generated by intramuscular injection of the recombinant viruses. Neutralization of AAV transduction by 1:20 and 1:80 dilutions of the antisera was evaluated (See Table 5 below). Antisera to AAV1, AAV2, AAV5 and AAV8 neutralized transduction of the serotype to which the antiserum was generated (AAV5 and AAV8 to a lesser extent than AAV1 and AAV2) but not to the other serotype (i.e., there was no evidence of cross neutralization suggesting that AAV 8 is a truly unique serotype).

Table 5. Serological Analysis of New AAV Serotypes.

Sera:	Immunization Vector	% Infection on 84-31 cells with AAVCMVEGFP virus:									
		AAV2/1		AAV2/2		AAV2/5		AAV2/7		AAV2/8	
		Serum dilution:		Serum dilution:		Serum dilution:		Serum dilution:		Serum dilution:	
		1/20	1/80	1/20	1/80	1/20	1/80	1/20	1/80	1/20	1/80
5	Group 1	0	0	100	100	100	100	100	100	100	100
	Group 2	100	100	0	0	100	100	100	100	100	100
	Group 3	100	100	100	100	16.5	16.5	100	100	100	100
	Group 4	100	100	100	100	100	100	61.5	100	100	100
	Group 5	100	100	100	100	100	100	100	100	26.3	60

10 Human sera from 52 normal subjects were screened for neutralization against selected serotypes. No serum sample was found to neutralize AAV2/7 and AAV2/8 while AAV2/2 and AAV2/1 vectors were neutralized in 20% and 10% of sera, respectively. A fraction of human pooled IgG representing a collection of 60,000 individual samples did not neutralize AAV2/7 and AAV2/8, whereas AAV2/2 and AAV2/1 vectors were neutralized at
15 titers of serum equal to 1/1280 and 1/640, respectively.

Example 7 - *In vivo* Evaluation of Different Serotypes of AAV Vectors

In this study, 7 recombinant AAV genomes, AAV2CBhA1AT, AAV2AlbA1AT, AAV2CMVrhCG, AAV2TBGrhCG, AAV2TBGcFIX, AAV2CMVLacZ and
20 AAV2TBGLacZ were packaged with capsid proteins of different serotypes. In all 7 constructs, minigene cassettes were flanked with AAV2 ITRs. cDNAs of human α -antitrypsin (A1AT) [Xiao, W., et al., (1999) *J Virol* 73, 3994-4003] β -subunit of rhesus monkey choriogonadotropic hormone (CG) [Zoltick, P. W. & Wilson, J. M. (2000) *Mol Ther* 2, 657-9] canine factor IX [Wang, L., et al., (1997) *Proc Natl Acad Sci U S A* 94, 11563-6]
25 and bacterial β -galactosidase (i.e., Lac Z) genes were used as reporter genes. For liver-directed gene transfer, either mouse albumin gene promoter (Alb) [Xiao, W. (1999), cited above] or human thyroid hormone binding globulin gene promoter (TBG) [Wang (1997), cited above] was used to drive liver specific expression of reporter genes. In muscle-directed gene transfer experiments, either cytomegalovirus early promoter (CMV) or chicken β -actin
30 promoter with CMV enhancer (CB) was employed to direct expression of reporters.

For muscle-directed gene transfer, vectors were injected into the right tibialis anterior of 4-6 week old NCR nude or C57BL/6 mice (Taconic, Germantown, NY). In liver-directed gene transfer studies, vectors were infused intraportally into 7-9 week old NCR nude or C57BL/6 mice (Taconic, Germantown, NY). Serum samples were collected intraorbitally at

different time points after vector administration. Muscle and liver tissues were harvested at different time points for cryosectioning and Xgal histochemical staining from animals that received the lacZ vectors. For the re-administration experiment, C56BL/6 mice initially received AAV2/1, 2/2, 2/5, 2/7 and 2/8CBA1AT vectors intramuscularly and followed for A1AT gene expression for 7 weeks. Animals were then treated with AAV2/8TBGcFIX intraportally and studied for cFIX gene expression.

ELISA based assays were performed to quantify serum levels of hA1AT, rhCG and cFIX proteins as described previously [Gao, G. P., et al., (1996) *J Virol* 70, 8934-43; Zoltick, P. W. & Wilson, J. M. (2000) *Mol Ther* 2, 657-9; Wang, L., et al., *Proc Natl Acad Sci U S A* 94, 11563-6]. The experiments were completed when animals were sacrificed for harvest of muscle and liver tissues for DNA extraction and quantitative analysis of genome copies of vectors present in target tissues by TaqMan using the same set of primers and probe as in titration of vector preparations [Zhang, Y., et al., (2001) *Mol Ther* 3, 697-707].

The performance of vectors base on the new serotypes were evaluated in murine models of muscle and liver-directed gene transfer and compared to vectors based on the known serotypes AAV1, AAV2 and AAV5. Vectors expressing secreted proteins (alpha-antitrypsin (A1AT) and chorionic gonadotropin (CG)) were used to quantitate relative transduction efficiencies between different serotypes through ELISA analysis of sera. The cellular distribution of transduction within the target organ was evaluated using lacZ expressing vectors and X-gal histochemistry .

The performance of AAV vectors in skeletal muscle was analyzed following direct injection into the tibialis anterior muscles. Vectors contained the same AAV2 based genome with the immediate early gene of CMV or a CMV enhanced β -actin promoter driving expression of the transgene. Previous studies indicated that immune competent C57BL/6 mice elicit limited humoral responses to the human A1AT protein when expressed from AAV vectors [Xiao, W., et al., (1999) *J Virol* 73, 3994-4003].

In each strain, AAV2/1 vector produced the highest levels of A1AT and AAV2/2 vector the lowest, with AAV2/7 and AAV2/8 vectors showing intermediate levels of expression. Peak levels of CG at 28 days following injection of nu/nu NCR mice showed the highest levels from AAV2/7 and the lowest from AAV2/2 with AAV2/8 and AAV2/1 in between. Injection of AAV2/1 and AAV2/7 lacZ vectors yielded gene expression at the injection sites in all muscle fibers with substantially fewer lacZ positive fibers observed with AAV2/2 and AAV 2/8 vectors. These data indicate that the efficiency of transduction with

AAV2/7 vectors in skeletal muscle is similar to that obtained with AAV2/1, which is the most efficient in skeletal muscle of the previously described serotypes [Xiao, W. (1999), cited above; Chao, H., et al., (2001) *Mol Ther* 4, 217-22; Chao, H., et al., (2000) *Mol Ther* 2, 619-23].

5 Similar murine models were used to evaluate liver-directed gene transfer. Identical doses of vector based on genome copies were infused into the portal veins of mice that were analyzed subsequently for expression of the transgene. Each vector contained an AAV2 based genome using previously described liver-specific promoters (i.e., albumin or thyroid hormone binding globulin) to drive expression of the transgene. More particularly, CMVCG
10 and TBGCG minigene cassettes were used for muscle and liver-directed gene transfer, respectively. Levels of rhCG were defined as relative units (RUs x 10³). The data were from assaying serum samples collected at day 28, post vector administration (4 animals per group). As shown in Table 3, the impact of capsid proteins on the efficiency of transduction of A1AT vectors in nu/nu and C57BL/6 mice and CG vectors in C57BL/6 mice was
15 consistent (See Table 6).

Table 6. Expression of β -unit of Rhesus Monkey Chorionic Gonadotropin (rhCG)

<u>Vector</u>	<u>Muscle</u>	<u>Liver</u>
AAV2/1	4.5 $\pm$ 2.1	1.6 $\pm$ 1.0
20 AAV2	0.5 $\pm$ 0.1	0.7 $\pm$ 0.3
AAV2/5	ND*	4.8 $\pm$ 0.8
AAV2/7	14.2 $\pm$ 2.4	8.2 $\pm$ 4.3
AAV2/8	4.0 $\pm$ 0.7	76.0 $\pm$ 22.8

* Not determined in this experiment.

25

In all cases, AAV2/8 vectors yielded the highest levels of transgene expression that ranged from 16 to 110 greater than what was obtained with AAV2/2 vectors; expression from AAV2/5 and AAV2/7 vectors was intermediate with AAV2/7 higher than AAV2/5. Analysis of X-Gal stained liver sections of animals that received the corresponding lacZ
30 vectors showed a correlation between the number of transduced cells and overall levels of transgene expression. DNAs extracted from livers of C57BL/6 mice who received the A1AT vectors were analyzed for abundance of vector DNA using real time PCR technology.

The amount of vector DNA found in liver 56 days after injection correlated with the levels of transgene expression (See Table 7). For this experiment, a set of probe and primers targeting the SV40 polyA region of the vector genome was used for TaqMan PCR. Values shown are means of three individual animals with standard deviations. The animals were sacrificed at day 56 to harvest liver tissues for DNA extraction. These studies indicate that AAV8 is the most efficient vector for liver-directed gene transfer due to increased numbers of transduced hepatocytes.

Table 7 - Real Time PCR Analysis for Abundance of AAV Vectors in nu/nu Mouse Liver Following Injection of 1×10^{11} Genome Copies of Vector.

AAV vectors/Dose	Genome Copies per Cell
AAV2/1A1bA1AT	0.6 ± 0.36
AAV2A1bA1AT	0.003 ± 0.001
AAV2/5A1bA1AT	0.83 ± 0.64
AAV2/7A1bA1AT	2.2 ± 1.7
AAV2/8A1bA1AT	18 ± 11

The serologic data described above suggest that AAV2/8 vector should not be neutralized *in vivo* following immunization with the other serotypes. C57BL/6 mice received intraportal injections of AAV2/8 vector expressing canine factor IX (10^{11} genome copies) 56 days after they received intramuscular injections of A1AT vectors of different serotypes. High levels of factor IX expression were obtained 14 days following infusion of AAV2/8 into naïve animals (17 ± 2 $\mu\text{g/ml}$, $n=4$) which were not significantly different that what was observed in animals immunized with AAV2/1 (31 ± 23 $\mu\text{g/ml}$, $n=4$), AAV2/2 (16 $\mu\text{g/ml}$, $n=2$), and AAV2/7 (12 $\mu\text{g/ml}$, $n=2$). This contrasts to what was observed in AAV2/8 immunized animals that were infused with the AAV2/8 factor IX vector in which no detectable factor IX was observed (< 0.1 $\mu\text{g/ml}$, $n=4$).

Oligonucleotides to conserved regions of the cap gene did amplify sequences from rhesus monkeys that represented unique AAVs. Identical cap signature sequences were found in multiple tissues from rhesus monkeys derived from at least two different colonies. Full-length rep and cap open reading frames were isolated and sequenced from single

sources. Only the cap open reading frames of the novel AAVs were necessary to evaluate their potential as vectors because vectors with the AAV7 or AAV8 capsids were generated using the ITRs and rep from AAV2. This also simplified the comparison of different vectors since the actual vector genome is identical between different vector serotypes. In fact, the
 5 yields of recombinant vectors generated using this approach did not differ between serotypes.

Vectors based on AAV7 and AAV8 appear to be immunologically distinct (i.e., they are not neutralized by antibodies generated against other serotypes). Furthermore, sera from humans do not neutralize transduction by AAV7 and AAV8 vectors, which is a substantial
 10 advantage over the human derived AAVs currently under development for which a significant proportion of the human population has pre-existing immunity that is neutralizing [Chirmule, N., et al., (1999) *Gene Ther* 6, 1574-83].

The tropism of each new vector is favorable for *in vivo* applications. AAV2/7 vectors appear to transduce skeletal muscle as efficiently as AAV2/1, which is the
 15 serotype that confers the highest level of transduction in skeletal muscle of the primate AAVs tested to date [Xiao, W., cited above; Chou (2001), cited above, and Chou (2000), cited above]. Importantly, AAV2/8 provides a substantial advantage over the other serotypes in terms of efficiency of gene transfer to liver that until now has been relatively disappointing in terms of the numbers of hepatocytes stably transduced. AAV2/8
 20 consistently achieved a 10 to 100-fold improvement in gene transfer efficiency as compared to the other vectors. The basis for the improved efficiency of AAV2/8 is unclear, although it presumably is due to uptake via a different receptor that is more active on the basolateral surface of hepatocytes. This improved efficiency will be quite useful in the development of liver-directed gene transfer where the number of transduced cells is critical, such as in urea
 25 cycle disorders and familial hypercholesterolemia.

Thus, the present invention provides a novel approach for isolating new AAVs based on PCR retrieval of genomic sequences. The amplified sequences were easily incorporated into vectors and tested in animals. The lack of pre-existing immunity to AAV7 and the favorable tropism of the vectors for muscle indicates that AAV7 is suitable for use as a
 30 vector in human gene therapy and other *in vivo* applications. Similarly, the lack of pre-existing immunity to the AAV serotypes of the invention, and their tropisms, renders them useful in delivery of therapeutic molecules and other useful molecules.

Example 9 – Tissue Tropism Studies

In the design of a high throughput functional screening scheme for novel AAV constructs, a non-tissue specific and highly active promoter, CB promoter (CMV enhanced chicken β actin promoter) was selected to drive an easily detectable and quantifiable reporter gene, human α anti-trypsin gene. Thus only one vector for each new AAV clone needs to be made for gene transfer studies targeting 3 different tissues, liver, lung and muscle to screen for tissue tropism of a particular AAV construct. The following table summarizes data generated from 4 novel AAV vectors in the tissue tropism studies (AAVCBA1AT), from which a novel AAV capsid clone, 44.2, was found to be a very potent gene transfer vehicle in all 3 tissues with a big lead in the lung tissue particularly. Table 8 reports data obtained (in $\mu\text{g A1AT/mL serum}$) at day 14 of the study.

Table 8

Vector	Target Tissue		
	Lung	Liver	Muscle
AAV2/1	ND	ND	45 $\pm$ 11
AAV2/5	0.6 $\pm$ 0.2	ND	ND
AAV2/8	ND	84 $\pm$ 30	ND
AAV2/rh.2 (43.1)	14 $\pm$ 7	25 $\pm$ 7.4	35 $\pm$ 14
AAV2/rh.10 (44.2)	23 $\pm$ 6	53 $\pm$ 19	46 $\pm$ 11
AAV2/rh.13 (42.2)	3.5 $\pm$ 2	2 $\pm$ 0.8	3.5 $\pm$ 1.7
AAV2/rh.21 (42.10)	3.1 $\pm$ 2	2 $\pm$ 1.4	4.3 $\pm$ 2

A couple of other experiments were then performed to confirm the superior tropism of AAV 44.2 in lung tissue. First, AAV vector carried CC10hA1AT minigene for lung specific expression were pseudotyped with capsids of novel AAVs were given to Immune deficient animals (NCR nude) in equal volume (50 μl each of the original preps without dilution) via intratracheal injections as provided in the following table. In Table 9, 50 μl of each original prep per mouse, NCR Nude, detection limit $\geq 0.033 \mu\text{g/mL}$, Day 28

Table 9

Vector	Total GC in 50 μ l vector	μ g of A1AT/ml with 50 μ l vector	μ g of A1AT/ml with 1×10^{11} vector	Relative Gene transfer as compared to rh.10 (clone 44.2)
2/1	3×10^{12}	2.6 ± 0.5	0.09 ± 0.02	2.2
2/2	5.5×10^{11}	< 0.03	< 0.005	< 0.1
2/5	3.6×10^{12}	0.65 ± 0.16	0.02 ± 0.004	0.5
2/7	4.2×10^{12}	1 ± 0.53	0.02 ± 0.01	0.5
2/8	7.5×10^{11}	0.9 ± 0.7	0.12 ± 0.09	2.9
2/ch.5 (A.3.1)	9×10^{12}	1 ± 0.7	0.01 ± 0.008	0.24
2/rh.8 (43.25)	4.6×10^{12}	26 ± 21	0.56 ± 0.46	13.7
2/rh.10 (44.2)	2.8×10^{12}	115 ± 38	4.1 ± 1.4	100
2/rh.13 (42.2)	6×10^{12}	7.3 ± 0.8	0.12 ± 0.01	2.9
2/rh.21 (42.10)	2.4×10^{12}	9 ± 0.9	0.38 ± 0.04	9.3
2/rh.22 (42.11)	2.6×10^{12}	6 ± 0.4	0.23 ± 0.02	5.6
2/rh.24 (42.13)	1.1×10^{11}	0.4 ± 0.3	0.4 ± 0.3	1

The vectors were also administered to immune competent animals (C57BL/6) in equal
5 genome copies (1×10^{11} GC) as shown in the Table 10. (1×10^{11} GC per animal, C57BL/6, day
14, detection limit $\geq 0.033 \mu\text{g/ml}$)

Table 10

AAV Vector	μ g of A1AT/ml with 1×10^{11} vector	Relative Gene transfer as compared to rh.10 (clone 44.2)
2/1	0.076 ± 0.031	2.6
2/2	0.1 ± 0.09	3.4
2/5	0.084 ± 0.033	2.9
2/7	0.33 ± 0.01	11
2/8	1.92 ± 1.3	2.9
2/ch.5 (A.3.1)	0.048 ± 0.004	1.6
2/rh.8 (43.25)	1.7 ± 0.7	58
2/rh.10 (44.2)	2.93 ± 1.7	100
2/rh.13 (42.2)	0.45 ± 0.15	15
2/rh.21 (42.10)	0.86 ± 0.32	29
2/rh.22 (42.11)	0.38 ± 0.18	13
2/rh.24 (42.13)	0.3 ± 0.19	10

10 The data from both experiments confirmed the superb tropism of clone 44.2 in lung-
directed gene transfer.

Interestingly, performance of clone 44.2 in liver and muscle directed gene transfer was also outstanding, close to that of the best liver transducer, AAV8 and the best muscle transducer AAV1, suggesting that this novel AAV has some intriguing biological significance.

To study serological properties of those novel AAVs, pseudotyped AAVGFP vectors were created for immunization of rabbits and in vitro transduction of 84-31 cells in the presence and absence of antisera against different capsids. The data are summarized below:

Table 11a. Cross-NAB assay in 8431 cells and adenovirus (Adv) coinfection
Infection in 8431 cells (coinfected with Adv) with:

Serum from rabbit immunized with:	10 ⁹ GC	10 ⁹ GC	10 ⁹ GC	10 ¹⁰ GC
	<i>rh.13</i>	<i>rh.21</i>	<i>rh.22</i>	<i>rh.24</i>
AAV2/42.2	AAV2/42.2	AAV2/42.10	AAV2/42.11	AAV2/42.13
AAV2/1	1/20	1/20	1/20	No NAB
AAV2/2	1/640	1/1280	1/5120	No NAB
AAV2/5	No NAB	1/40	1/160	No NAB
AAV2/7	1/81920	1/81920	1/40960	1/640
AAV2/8	1/640	1/640	1/320	1/5120
Ch.5 AAV2/A3	1/20	1/160	1/640	1/640
<i>rh.8</i> AAV2/43.25	1/20	1/20	1/20	1/320
<i>rh.10</i> AAV2/44.2	No NAB	No NAB	No NAB	1/5120
<i>rh.13</i> AAV2/42.2	1/5120	1/5120	1/5120	No NAB
<i>rh.21</i> AAV2/42.10	1/5120	1/10240	1/5120	1/20
<i>rh.22</i> AAV2/42.11	1/20480	1/20480	1/40960	No NAB
<i>rh.24</i> AAV2/42.13	No NAB	1/20	1/20	1/5120

Table 11b. Cross-NAB assay in 8431 cells and Adv coinfection

Infection in 8431 cells (coinfected with Adv) with:

Serum from rabbit immunized with:	10 ⁹ GC	10 ¹⁰ GC	10 ¹⁰ GC	10 ⁹ GC	10 ⁹ GC
	<i>rh.12</i>	<i>ch.5</i>	<i>rh.8</i>	<i>rh.10</i>	<i>rh.20</i>
	AAV2/42.1B	AAV2/A3	AAV2/43.25	AAV2/44.2	AAV2/42.8.2
AAV2/1	No NAB	1/20480	No NAB	1/80	ND
AAV2/2	1/20	No NAB	No NAB	No NAB	ND
AAV2/5	No NAB	1/320	No NAB	No NAB	ND
AAV2/7	1/2560	1/640	1/160	1/81920	ND
AAV2/8	1/10240	1/2560	1/2560	1/81920	ND
<i>ch.5</i> AAV2/A3	1/1280	1/10240	ND	1/5120	1/320
<i>rh.8</i> AAV2/43.25	1/1280	ND	1/20400	1/5120	1/2560
<i>rh.10</i> AAV2/44.2	1/5120	ND	ND	1/5120	1/5120
<i>rh.13</i> AAV2/42.2	1/20	ND	ND	No NAB	1/320
<i>rh.21</i> AAV2/42.10	1/20	ND	ND	1/40	1/80
<i>rh.22</i> AAV2/42.11	No NAB	ND	ND	ND	No NAB
<i>rh.24</i> AAV2/42.13	1/5120	ND	ND	ND	1/2560

Table 12

Titer of rabbit sera			Titer after Boosting
Vector		Titer d21	
<i>ch.5</i>	AAV2/A3	1/10,240	1/40,960
<i>rh.8</i>	AAV2/43.25	1/20,400	1/163,840
<i>rh.10</i>	AAV2/44.2	1/10,240	1/527,680
<i>rh.13</i>	AAV2/42.2	1/5,120	1/20,960
<i>rh.21</i>	AAV2/42.10	1/20,400	1/81,920
<i>rh.22</i>	AAV2/42.11	1/40,960	ND
<i>rh.24</i>	AAV2/42.13	1/5,120	ND

5

Table 13 a. Infection in 8431 cells (coinfected with Adv) with GFP

	10 ⁹ GC/well	10 ⁹ GC/well	10 ⁹ GC/well	10 ⁹ GC/well	10 ⁹ GC/well	10 ⁹ GC/well
						<i>ch.5</i>
	AAV2/1	AAV2/2	AAV2/5	AAV2/7	AAV2/8	AAV2/A3
# GFU/field	128	>200	95	56	13	1
	83	>200	65	54	11	1

Table 13b. Infection in 8431 cells (coinfecting with Adv) with GFP

	10 ⁹ GC/well	10 ⁹ GC/well	10 ⁹ GC/well	10 ⁹ GC/well	10 ⁹ GC/well	10 ⁹ GC/well	10 ⁹ GC/well
	<i>rh.8</i>	<i>rh.10</i>	<i>rh.13</i>	<i>rh.21</i>	<i>rh.22</i>	<i>rh.24</i>	<i>rh.12</i>
	AAV2/43.25	AAV2/44.2	AAV2/42.2	AAV2/42.10	AAV2/42.11	AAV2/42.13	AAV2/42.1B
# GFU/field	3	13	54	62	10	3	18
	2	12	71	60	14	2	20
			48	47	16	3	12

5 Example 10 – Mouse Model of Familial Hypercholesterolemia

The following experiment demonstrates that the AAV2/7 construct of the invention delivers the LDL receptor and express LDL receptor in an amount sufficient to reduce the levels of plasma cholesterol and triglycerides in animal models of familial hypercholesterolemia.

10 A. Vector Construction

AAV vectors packaged with AAV7 or AAV8 capsid proteins were constructed using a pseudotyping strategy [Hildinger M, *et al.*, *J. Virol* 2001; 75:6199-6203]. Recombinant AAV genomes with AAV2 inverted terminal repeats (ITR) were packaged by triple transfection of 293 cells with the *cis*-plasmid, the adenovirus helper plasmid and a
 15 chimeric packaging construct, a fusion of the capsids of the novel AAV serotypes with the rep gene of AAV2. The chimeric packaging plasmid was constructed as previously described [Hildinger et al, cited above]. The recombinant vectors were purified by the standard CsCl₂ sedimentation method. To determine the yield TaqMan (Applied Biosystems) analysis was performed using probes and primers targeting the SV40 poly(A) region of the vectors [Gao
 20 GP, *et al.*, *Hum Gene Ther.* 2000 Oct 10;11(15):2079-91]. The resulting vectors express the transgene under the control of the human thyroid hormone binding globulin gene promoter (TBG).

B. Animals

LDL receptor deficient mice on the C57BL/6 background were purchased
 25 from the Jackson Laboratory (Bar Harbor, ME, USA) and maintained as a breeding colony. Mice were given unrestricted access to water and obtained a high fat Western Diet (high % cholesterol) starting three weeks prior vector injection. At day -7 as well at day 0, blood was obtained via retroorbital bleeds and the lipid profile evaluated. The mice were randomly divided into seven groups. The vector was injected via an intraportal injection as previously

described ([Chen SJ *et al.*, *Mol Therapy* 2000; 2(3), 256-261]. Briefly, the mice were anaesthetized with ketamine and xylazine. A laparotomy was performed and the portal vein exposed. Using a 30g needle the appropriate dose of vector diluted in 100ul PBS was directly injected into the portal vein. Pressure was applied to the injection site to ensure a stop of the bleeding. The skin wound was closed and draped and the mice carefully monitored for the following day. Weekly bleeds were performed starting at day 14 after liver directed gene transfer to measure blood lipids. Two animals of each group were sacrificed at the time points week 6 and week 12 after vector injection to examine atherosclerotic plaque size as well as receptor expression. The remaining mice were sacrificed at week 20 for plaque measurement and determination of transgene expression.

Table 14

	<i>Vector</i>	<i>dose</i>	<i>n</i>
Group 1	AAV2/7-TBG-hLDLr	1×10^{12} gc	12
Group 2	AAV2/7-TBG-hLDLr	3×10^{11} gc	12
Group 3	AAV2/7-TBG-hLDLr	1×10^{11} gc	12
Group 4	AAV2/8-TBG-hLDLr	1×10^{12} gc	12
Group 5	AAV2/8-TBG-hLDLr	3×10^{11} gc	12
Group 6	AAV2/8-TBG-hLDLr	1×10^{11} gc	12
Group 7	AAV2/7-TBG- LacZ	1×10^{11} gc	16

C. *Serum lipoprotein and liver function analysis*

Blood samples were obtained from the retroorbital plexus after a 6 hour fasting period. The serum was separated from the plasma by centrifugation. The amount of plasma lipoproteins and liver transaminases in the serum were detected using an automatized clinical chemistry analyzer (ACE, Schiapparelli Biosystems, Alpha Wassermann)

D. *Detection of transgene expression*

LDL receptor expression was evaluated by immuno-fluorescence staining and Western blotting. For Western Blot frozen liver tissue was homogenized with lysis buffer (20 mM Tris, pH7.4, 130mM NaCl, 1% Triton^{*} X 100, proteinase inhibitor (complete, EDTA-free, Roche, Mannheim, Germany). Protein concentration was determined using the Micro BCA Protein Assay Reagent Kit (Pierce, Rockford, IL). 40 µg of protein was resolved on 4- 15% Tris-HCl Ready Gels (Biorad, Hercules, CA) and transferred to a nitrocellulose

*TM

membrane (Invitrogen,). To generate Anti-hLDL receptor antibodies a rabbit was injected intravenously with an AdhLDLr prep (1×10^{13} GC). Four weeks later the rabbit serum was obtained and used for Western Blot. A 1:100 dilution of the serum was used as a primary antibody followed by a HRP-conjugated anti-rabbit IgG and ECL chemiluminescent detection (ECL Western Blot Detection Kit, Amersham, Arlington Heights, IL).

E. *Immunocytochemistry*

For determination of LDL receptor expression in frozen liver sections immunohistochemistry analyses were performed. 10um cryostat sections were either fixed in acetone for 5 minutes, or unfixed. Blocking was obtained *via a* 1 hour incubation period with 10% of goat serum. Sections were then incubated for one hour with the primary antibody at room temperature. A rabbit polyclonal antibody anti-human LDL (Biomedical Technologies Inc., Stoughton, MA) was used diluted accordingly to the instructions of the manufacturer. The sections were washed with PBS, and incubated with 1:100 diluted fluorescein goat anti-rabbit IgG (Sigma, St Louis, MO). Specimens were finally examined under fluorescence microscope Nikon Microphot-FXA. In all cases, each incubation was followed by extensive washing with PBS. Negative controls consisted of preincubation with PBS, omission of the primary antibody, and substitution of the primary antibody by an isotype-matched non-immune control antibody. The three types of controls mentioned above were performed for each experiment on the same day.

F. *Gene transfer efficiency*

Liver tissue was obtained after sacrificing the mice at the designated time points. The tissue was shock frozen in liquid nitrogen and stored at -80°C until further processing. DNA was extracted from the liver tissue using a QIAamp DNA Mini Kit (QIAGEN GmbH, Germany) according to the manufacturers protocol. Genome copies of AAV vectors in the liver tissue were evaluated using Taqman analysis using probes and primers against the SV40 poly(A) tail as described above.

G. *Atherosclerotic plaque measurement*

For the quantification of the atherosclerotic plaques in the mouse aorta the mice were anaesthetized (10% ketamine and xylazine, ip), the chest opened and the arterial system perfused with ice-cold phosphate buffered saline through the left ventricle. The aorta was then carefully harvested, slit down along the ventral midline from the aortic arch down to the femoral arteries and fixed in formalin. The lipid-rich atherosclerotic plaques were stained with Sudan IV (Sigma, Germany) and the aorta pinned out flat on a

black wax surface. The image was captured with a Sony DXC-960 MD color video camera. The area of the plaque as well as of the complete aortic surface was determined using Phase 3 Imaging Systems (Media Cybernetics).

H. *Clearance of I¹²⁵ LDL*

5 Two animals per experimental group were tested. A bolus of I¹²⁵ – labeled LDL (generously provided by Dan Rader, U Penn) was infused slowly through the tail vein over a period of 30 sec (1,000,000 counts of [I¹²⁵]-LDL diluted in 100μl sterile PBS/ animal). At time points 3min, 30 min, 1.5hr, 3hr, 6hr after injection a blood sample was obtained *via* the retro-orbital plexus. The plasma was separated off from the whole
10 blood and 10μl plasma counted in the gamma counter. Finally the fractional catabolic rate was calculated from the lipoprotein clearance data.

I. *Evaluation of Liver Lipid accumulation*

Oil Red Staining of frozen liver sections was performed to determine lipid accumulation. The frozen liver sections were briefly rinsed in distilled water followed
15 by a 2 minute incubation in absolute propylene glycol. The sections were then stained in oil red solution (0.5% in propylene glycol) for 16 hours followed by counterstaining with Mayer's hematoxylin solution for 30 seconds and mounting in warmed glycerin jelly solution.

For quantification of the liver cholesterol and triglyceride content liver
20 sections were homogenized and incubated in chloroform/methanol (2:1) overnight. After adding of 0.05% H₂SO₄ and centrifugation for 10 minutes, the lower layer of each sample was collected, divided in two aliquots and dried under nitrogen. For the cholesterol measurement the dried lipids of the first aliquot were dissolved in 1% Triton X-100* in chloroform. Once dissolved, the solution was dried under nitrogen. After dissolving the
25 lipids in ddH₂O and incubation for 30 minutes at 37°C the total cholesterol concentration was measured using a Total Cholesterol Kit (Wako Diagnostics). For the second aliquot the dried lipids were dissolved in alcoholic KOH and incubated at 60°C for 30 minutes. Then 1M MgCl₂ was added, followed by incubation on ice for 10 minutes and centrifugation at 14,000 rpm for 30 minutes. The supernatant was finally evaluated for triglycerides (Wako
30 Diagnostics).

All of the vectors pseudotyped in an AAV2/8 or AAV2/7 capsid lowered total cholesterol, LDL and triglycerides as compared to the control. These test vectors also corrected phenotype of hypercholesterolemia in a dose-dependent manner. A reduction in

* trade-mark

plaque area for the AAV2/8 and AAV2/7 mice was observed in treated mice at the first test (2 months), and the effect was observed to persist over the length of the experiment (6 months).

5 Example 10 – Functional Factor IX Expression and Correction of Hemophilia

A. Knock-Out Mice

Functional canine factor IX (FIX) expression was assessed in hemophilia B mice. Vectors with capsids of AAV1, AAV2, AAV5, AAV7 or AAV8 were constructed to deliver AAV2 5' ITR – liver-specific promoter [LSP] - canine FIX – woodchuck hepatitis
10 post-regulatory element (WPRE) - AAV2 3' ITR. The vectors were constructed as described in Wang et al, 2000, *Molecular Therapy* 2: 154-158), using the appropriate capsids.

Knock-out mice were generated as described in Wang et al, 1997. *Proc. Natl. Acad. Sci. USA* 94: 11563-11566. This model closely mimic the phenotypes of hemophilia
15 B in human.

Vectors of different serotypes (AAV1, AAV2, AAV5, AAV7 and AAV8) were delivered as a single intraportal injection into the liver of adult hemophiliac C57Bl/6 mice in a dose of 1×10^{11} GC/mouse for the five different serotypes and one group received an AAV8 vector at a lower dose, 1×10^{10} GC/mouse. Control group was injected with 1×10^{11}
20 GC of AAV2/8 TBG LacZ3. Each group contains 5-10 male and female mice. Mice were bled bi-weekly after vector administration.

1. ELISA

The canine FIX concentration in the mouse plasma was determined by an ELISA assay specific for canine factor IX, performed essentially as described by
25 Axelrod et al, 1990, *Proc. Natl. Acad. Sci. USA*, 87:5173-5177 with modifications. Sheep anti-canine factor IX (Enzyme Research Laboratories) was used as primary antibody and rabbit anti-canine factor IX ((Enzyme Research Laboratories) was used as secondary antibody. Beginning at two weeks following injection, increased plasma levels of cFIX were detected for all test vectors. The increased levels were sustained at therapeutic levels throughout the
30 length of the experiment, i.e., to 12 weeks. Therapeutic levels are considered to be 5% of normal levels, i.e., at about 250 ng/mL.

The highest levels of expression were observed for the AAV2/8 (at 10^{11}) and AAV2/7 constructs, with sustained superphysiology levels cFIX levels (ten-fold higher than the normal level). Expression levels for AAV2/8 (10^{11}) were approximately 10 fold higher

than those observed for AAV2/2 and AAV2/8 (10^{10}). The lowest expression levels, although still above the therapeutic range, were observed for AAV2/5.

2. *In Vitro Activated Partial Thromboplastin time (aPTT) Assay*

Functional factor IX activity in plasma of the FIX knock-out mice was determined by an *in vitro* activated partial thromboplastin time (aPTT) assay—Mouse blood samples were collected from the retro-orbital plexus into 1/10 volume of citrate buffer. The aPTT assay was performed as described by Wang et al, 1997, *Proc. Natl. Acad. Sci. USA* 94: 11563-11566.

Clotting times by aPTT on plasma samples of all vector injected mice were within the normal range (approximately 60 sec) when measured at two weeks post-injection, and sustained clotting times in the normal or shorter than normal range throughout the study period (12 weeks).

Lowest sustained clotting times were observed in the animals receiving AAV2/8 (10^{11}) and AAV2/7. By week 12, AAV2/2 also induced clotting times similar to those for AAV2/8 and AAV2/7. However, this lowered clotting time was not observed for AAV2/2 until week 12, whereas lowered clotting times (in the 25 – 40 sec range) were observed for AAV2/8 and AAV2/7 beginning at week two.

Immuno-histochemistry staining on the liver tissues harvested from some of the treated mice is currently being performed. About 70-80% of hepatocytes are stained positive for canine FIX in the mouse injected with AAV2/8.cFIX vector.

B. *Hemophilia B Dogs*

Dogs that have a point mutation in the catalytic domain of the F.IX gene, which, based on modeling studies, appears to render the protein unstable, suffer from hemophilia B [Evans et al, 1989, *Proc. Natl. Acad. Sci. USA*, 86:10095-10099]. A colony of such dogs has been maintained for more than two decades at the University of North Carolina, Chapel Hill. The homeostatic parameters of these dogs are well described and include the absence of plasma F.IX antigen, whole blood clotting times in excess of 60 minutes, whereas normal dogs are 6-8 minutes, and prolonged activated partial thromboplastin time of 50-80 seconds, whereas normal dogs are 13-28 seconds. These dogs experience recurrent spontaneous hemorrhages. Typically, significant bleeding episodes are successfully managed by the single intravenous infusion of 10 ml/kg of normal canine plasma; occasionally, repeat infusions are required to control bleeding.

Four dogs are injected intraportally with AAV.cFIX according to the schedule below. A first dog receives a single injection with AAV2/2.cFIX at a dose of 3.7×10^{11} genome copies (GC)/kg. A second dog receives a first injection of AAV2/2.cFIX (2.8×10^{11} GC/kg), followed by a second injection with AAV2/7.cFIX (2.3×10^{13} GC/kg) at day 1180. A third dog receives a single injection with AAV2/2.cFIX at a dose of 4.6×10^{12} GC/kg. The fourth dog receives an injection with AAV2/2.cFIX (2.8×10^{12} GC/kg) and an injection at day 995 with AAV2/7.cFIX (5×10^{12} GC/kg).

The abdomen of hemophilia dogs are aseptically and surgically opened under general anesthesia and a single infusion of vector is administered into the portal vein. The animals are protected from hemorrhage in the peri-operative period by intravenous administration of normal canine plasma. The dog is sedated, intubated to induce general anesthesia, and the abdomen shaved and prepped. After the abdomen is opened, the spleen is moved into the operative field. The splenic vein is located and a suture is loosely placed proximal to a small distal incision in the vein. A needle is rapidly inserted into the vein, then the suture loosened and a 5 F cannula is threaded to an intravenous location near the portal vein threaded to an intravenous location near the portal vein bifurcation. After hemostasis is secured and the catheter balloon inflated, approximately 5.0 ml of vector diluted in PBS is infused into the portal vein over a 5 minute interval. The vector infusion is followed by a 5.0 ml infusion of saline. The balloon is then deflated, the cannula removed and venous hemostasis is secured. The spleen is then replaced, bleeding vessels are cauterized and the operative wound is closed. The animal is extubated having tolerated the surgical procedure well. Blood samples are analyzed as described. [Wang et al, 2000, *Molecular Therapy* 2: 154-158]

Results showing correction or partial correction are anticipated for AAV2/7.

25

What is claimed is:

1. A recombinant adeno-associated virus (AAV) having an AAV capsid which comprises an AAV vp1 capsid protein, an AAV vp2 capsid protein and an AAV vp3 capsid protein, wherein the AAV vp1 capsid protein has the sequence of AAVrh.10, which is amino acids 1 to 738 of SEQ ID NO:81 or a sequence having at least 95% identity to SEQ ID NO: 81, said capsid having packaged therein a minigene having AAV inverted terminal repeats (ITRs) and a heterologous gene operably linked to regulatory sequences which direct its expression in a host cell.
2. The recombinant AAV according to claim 1, wherein the vp3 capsid protein has the sequence of amino acids 204 to 738 of SEQ ID NO: 81 or a sequence at least 95% identical thereto.
3. The recombinant AAV according to claim 1 or 2, wherein the vp2 capsid protein has the sequence of amino acids 138 to 738 of SEQ ID NO: 81 or a sequence at least 95% identical thereto.
4. The recombinant AAV according to claim 1, wherein the vp1 capsid protein has a sequence having at least 99% identity with amino acids 1 to 738 of SEQ ID NO: 81.
5. The recombinant AAV according to claim 1, wherein the vp1 capsid has the sequence of amino acids 1 to 738 of SEQ ID NO: 81.
6. The recombinant AAV according to any one of claims 1 to 5, wherein the ITRs are from AAV2.
7. An isolated AAVrh.10 capsid protein selected from the group consisting of:
 - vp1 capsid protein, amino acids (aa) 1 to 738 of SEQ ID NO: 81;
 - vp2 capsid protein, aa 138 to 738 of SEQ ID NO: 81; and

vp3 capsid protein, aa 204 to 738 of SEQ ID NO: 81.

8. A recombinant adeno-associated virus (AAV) having an AAV capsid which comprises an AAV vp1 capsid protein, an AAV vp2 capsid protein and an AAV vp3 capsid protein, wherein the vp3 capsid protein has the aa sequence of 204 to 738 of SEQ ID NO: 81 or a sequence having at least 95% identity thereto; and a minigene having AAV inverted terminal repeats (ITRs) and a heterologous gene operably linked to regulatory sequences which direct its expression in a host cell.

9. The recombinant AAV according to claim 8, wherein the vp3 capsid has the sequence of amino acids 204 to 738 of SEQ ID NO: 81.

10. A nucleic acid molecule encoding a protein according to claim 7.

11. A nucleic acid molecule encoding a fragment of an adeno-associated virus rh.10 capsid protein, said fragment selected from the group consisting of:

vp1, nt 845 to 3061 of SEQ ID NO: 59;

vp2, nt 1256 to 3061 of SEQ ID NO: 59; and

vp 3, nt 1454 to 3061 of SEQ ID NO: 59.

12. The molecule according to any one of claims 10 to 11, wherein said molecule is a plasmid.

13. The molecule according to any one of claims 10 to 12, wherein said molecule further comprises an AAV *rep* gene.

14. A method of generating a recombinant adeno-associated virus (AAV) having an AAV serotype rh.10 capsid comprising the steps of culturing a host cell containing: (a) a molecule according to any one of claims 10 to 13 which encodes an adeno-associated virus capsid; (b) a functional *rep* gene; (c) a minigene comprising AAV

inverted terminal repeats (ITRs) and a transgene; and (d) sufficient helper functions to permit packaging of the minigene into the AAV capsid protein.

15. A host cell transfected with the AAV according to any one of claims 1 to 6 or 8 to 9, or the molecule according to any one of claims 10 to 13.

16. A composition comprising the AAV according to any one of claims 1 to 6 or 8 to 9 and a physiologically compatible carrier.

17. A composition comprising the molecule according to any one of claims 10 to 13 and a physiologically compatible carrier.

18. The composition of claim 16, wherein the heterologous gene encodes a Factor VIII.

19. The composition of claim 16, wherein the heterologous gene encodes a Factor IX.

20. The composition of claim 16, wherein the heterologous gene encodes alpha-1 antitrypsin (A1AT).

21. The composition of claim 16, wherein the heterologous gene encodes VEGF or GUSB.

22. The composition of claim 16, wherein the heterologous gene encodes an immunoglobulin.

23. The composition of claim 16, wherein the heterologous gene encodes erythropoietin.

24. The composition of claim 16, wherein the heterologous gene encodes a T cell receptor, a chimeric T cell receptor, a single chain T cell receptor, a class I or class II MHC molecule, or an engineered MHC molecule.

25. A recombinant adeno-associated virus (AAV) comprising an AAVrh.10 capsid comprising vp1, vp2 and vp3 proteins, the vp1 having a sequence of amino acids 1 to 738 of SEQ ID NO:81 or a sequence at least 95% identical to SEQ ID NO: 81, said AAV having packaged in the capsid a nucleic acid molecule comprising at least one AAV inverted terminal repeat (ITR) and a non-AAV nucleic acid sequence encoding a gene product operably linked to sequences which direct expression of the product in a host cell.

26. The AAV according to claim 25, wherein the amino acid sequence is at least 99% identical to amino acids 1 to 738 of SEQ ID NO: 81.

27. The AAV according to claim 25, wherein the AAV ITR is from AAV2.

28. A recombinant adeno-associated virus (AAV) comprising an AAVrh.10 capsid comprising vp1, vp2 and vp3 proteins, the vp3 having the amino acid sequence of 204 to 738 of SEQ ID NO: 81 or a sequence at least 95% identical to amino acids 204 to 738 of SEQ ID NO: 81, said AAV having packaged in the capsid a nucleic acid molecule comprising at least one AAV inverted terminal repeat (ITR) and a non-AAV nucleic acid sequence encoding a gene product operably linked to sequences which direct expression of the product in a host cell.

29. A method of generating a recombinant adeno-associated virus (AAV) comprising an AAV rh.10 capsid comprising the steps of culturing a host cell containing: (a) a molecule encoding the AAVrh.10 vp1 capsid protein having a sequence of amino acids 1 to 738 of SEQ ID NO: 81, or a sequence which is at least 95% identical to SEQ ID NO: 81; (b) a functional rep gene; (c) a nucleic acid molecule comprising at least one AAV inverted terminal repeat (ITR) and a non-AAV nucleic acid sequence encoding a

gene product operably linked to sequences which direct expression of the product in a host cell;

and (d) sufficient helper functions to permit packaging of the minigene into the AAV capsid protein.

30. The AAV according to claim 25 or 28, wherein the non-AAV nucleic acid sequence encodes a protein selected from VEGF or GUSB.

31. The AAV according to claim 25 or 28, wherein the non-AAV nucleic acid sequence encodes alpha-1 antitrypsin (A1AT).

32. The AAV according to claim 25, wherein the non-AAV nucleic acid sequence encodes a Factor VIII.

33. The AAV according to claim 25, wherein the non-AAV nucleic acid sequence encodes a Factor IX.

34. The AAV according to claim 25, wherein the non-AAV nucleic acid sequence encodes erythropoietin.

35. A recombinant adeno-associated virus (AAV) comprising an AAV capsid comprising at least AAVrh.10 vp3 having the amino acid sequence of 204 to 738 of SEQ ID NO: 81 or a sequence at least 95% identical to amino acids 204 to 738 of SEQ ID NO: 81 said AAV having packaged in the capsid a nucleic acid molecule comprising at least one AAV inverted terminal repeat (ITR) and a non-AAV nucleic acid sequence encoding a Factor VIII operably linked to sequences which direct expression thereof in a host cell.

36. A recombinant adeno-associated virus (AAV) comprising an AAV capsid comprising at least AAVrh.10 vp3 having the amino acid sequence of 204 to 738 of SEQ ID NO: 81 or an AAV vp3 protein having a sequence at least 95% identical to amino acids 204 to 738 of SEQ ID NO: 81, said AAV having packaged in the capsid a nucleic

acid molecule comprising at least one AAV inverted terminal repeat (ITR) and a non-AAV nucleic acid sequence encoding a Factor IX operably linked to sequences which direct expression thereof in a host cell.

37. The AAV according to claim 28, wherein the vp1 protein has an amino acid sequence of amino acids 1 to 738 of SEQ ID NO:81.

38. The AAV according to claim 28, wherein the vp2 protein has an amino acid sequence of amino acids 138 to 738 of SEQ ID NO:81.

39. The recombinant AAV according to claim 28, wherein the vp1 protein has an amino acid sequence at least 97% identical to amino acids 1 to 738 of SEQ ID NO: 81.

40. The recombinant AAV according to claim 28, wherein the vp3 protein has an amino acid sequence at least 97% identical to amino acids 204 to 738 of SEQ ID NO: 81.

41. The recombinant AAV according to claim 28, wherein the vp3 protein has an amino acid sequence at least 99% identical to amino acids 204 to 738 of SEQ ID NO: 81.

42. A recombinant adeno-associated virus (AAV) comprising an AAVrh.10 capsid comprising vp1, vp2 and vp3 proteins, said vp2 having the amino acid sequence of 138 to 738 of SEQ ID NO: 81 or an AAV vp2 protein having a sequence at least 95% identical to amino acids 138 to 738 of SEQ ID NO: 81, said AAV having packaged in the capsid a nucleic acid molecule comprising at least one AAV inverted terminal repeat (ITR) and a non-AAV nucleic acid sequence encoding a gene product operably linked to sequences which direct expression thereof in a host cell.

43. A recombinant adeno-associated virus (AAV) comprising an AAV capsid comprising at least AAVrh.10 vp3 having the amino acid sequence of 204 to 738 of SEQ

ID NO: 81 or an AAV vp3 protein having a sequence at least 95% identical to amino acids 204 to 738 of SEQ ID NO: 81, said AAV having packaged in the capsid a nucleic acid molecule comprising at least one AAV inverted terminal repeat (ITR) and a non-AAV nucleic acid sequence which encodes erythropoietin operably linked to sequences which direct expression thereof in a host cell.

44. The recombinant AAV according to claim 1 or 25, wherein the capsid protein has the sequence of SEQ ID NO: 84.

45. The recombinant AAV according to claim 1 or 25, wherein the capsid protein has the sequence of SEQ ID NO: 85.

46. The recombinant AAV according to claim 1 or 25, wherein the capsid protein has the sequence of SEQ ID NO: 86.

47. The recombinant AAV according to claim 1 or 25, wherein the capsid protein has the sequence of SEQ ID NO: 87.

48. The recombinant AAV according to claim 1 or 25, wherein the capsid protein has the sequence of SEQ ID NO: 88.

49. The recombinant AAV according to claim 1 or 25, wherein the capsid protein has the sequence of SEQ ID NO: 89.

50. The recombinant AAV according to claim 1 or 25, wherein the capsid protein has the sequence of SEQ ID NO: 90.

51. The recombinant AAV according to claim 1 or 25, wherein the capsid protein has the sequence of SEQ ID NO: 91.

52. The recombinant AAV according to claim 1 or 25, wherein the capsid protein has the sequence of SEQ ID NO: 92.

53. A use of the recombinant AAV according to claim 1 or 25 for treating a lysosomal storage disease, wherein said heterologous gene defined in claim 1 or said non-AAV nucleic acid sequence defined in claim 25 encodes a gene product effective for treating said lysosomal storage disease.

54. A use of the recombinant AAV according to claim 1 or 25 for the manufacture of a medicament for treating a lysosomal storage disease, wherein said heterologous gene defined in claim 1 or said non-AAV nucleic acid sequence defined in claim 25 encodes a gene product effective for treating said lysosomal storage disease.

55. The use of claim 53 or 54, wherein said gene product is an enzyme that contains mannose-6-phosphate.

56. The use of claim 53 or 54, wherein said gene product is β -glucuronidase (GUSB).

57. A recombinant adeno-associated virus (AAV) comprising an AAV capsid comprising at least AAVrh.10 vp3 having the amino acid sequence of 204 to 738 of SEQ ID NO: 81 or an AAV vp3 protein having a sequence at least 95% identical to amino acids 204 to 738 of SEQ ID NO: 81, said AAV having packaged in the capsid a nucleic acid molecule comprising at least one AAV inverted terminal repeat (ITR) and a non-AAV nucleic acid sequence which encodes an immunoglobulin operably linked to sequences which direct expression thereof in a host cell.

58. The recombinant AAV according to claim 57, wherein said immunoglobulin is selected from immunoglobulins IgG, IgM, IgA, IgD, or IgE, chimeric immunoglobulins, human antibodies, humanized antibodies, single chain antibodies, or engineered immunoglobulins.

59. A composition comprising a physiologically compatible carrier and a recombinant adeno-associated viral (AAV) vector having an AAV capsid which comprises AAV vp1 capsid proteins, AAV vp2 capsid proteins and AAV vp3 capsid proteins, wherein a AAV vp1 capsid protein has the sequence of amino acids 1 to 738 of SEQ ID NO:81 or a sequence having at least 95% identity to SEQ ID NO: 81, said capsid having packaged therein a minigene having AAV inverted terminal repeats (ITRs) and a heterologous gene operably linked to regulatory sequences which direct its expression in a host cell.

60. The composition according to claim 59, wherein said heterologous gene encodes a Factor VIII.

61. The composition according to claim 59, wherein said heterologous gene encodes a Factor IX.

62. The composition according to claim 59, wherein said heterologous gene encodes alpha-1 antitrypsin (A1AT).

63. The composition according to claim 59, wherein said heterologous gene encodes VEGF or GUSB.

64. The composition according to claim 59, wherein said heterologous gene encodes an immunoglobulin.

65. The composition according to claim 64, wherein said immunoglobulin is selected from immunoglobulins IgG, IgM, IgA, IgD, or IgE, chimeric immunoglobulins, human antibodies, humanized antibodies, single chain antibodies, or engineered immunoglobulins.

66. The composition according to claim 59, wherein said heterologous gene encodes a T cell receptor, a chimeric T cell receptor, a single chain T cell receptor, a class I or class II MHC molecule, or an engineered MHC molecule.

67. The composition according to claim 59, wherein said heterologous gene encodes erythropoietin.

68. A composition comprising a physiologically compatible carrier and a recombinant adeno-associated viral (AAV) vector having an AAV capsid which comprises AAV vp1 capsid proteins, AAV vp2 capsid proteins and AAV vp3 capsid proteins, wherein a AAV vp3 capsid protein has the sequence of amino acids 204 to 738 of SEQ ID NO:81 or a sequence having at least 95% identity to amino acids 204 to 738 of SEQ ID NO: 81, said capsid having packaged therein a minigene having AAV inverted terminal repeats (ITRs) and a heterologous gene operably linked to regulatory sequences which direct its expression in a host cell.

69. The composition according to claim 68, wherein said heterologous gene encodes a Factor VIII.

70. The composition according to claim 68, wherein said heterologous gene encodes a Factor IX.

71. The composition according to claim 68, wherein said heterologous gene encodes a Factor VIII.

72. The composition according to claim 68, wherein said heterologous gene encodes alpha-1 antitrypsin (A1AT).

73. The composition according to claim 68, wherein said heterologous gene encodes VEGF or GUSB.

74. The composition according to claim 68, wherein said heterologous gene encodes an immunoglobulin.

75. The composition according to claim 68, wherein said immunoglobulin is selected from immunoglobulins IgG, IgM, IgA, IgD, or IgE, chimeric immunoglobulins, human antibodies, humanized antibodies, single chain antibodies, or engineered immunoglobulins.

76. The composition according to claim 68, wherein said heterologous gene encodes a T cell receptor, a chimeric T cell receptor, a single chain T cell receptor, a class I or class II MHC molecule, or an engineered MHC molecule.

77. The composition according to claim 68, wherein said heterologous gene encodes erythropoietin.

FIG. 1A

	1				50
42_2					
42_8					
42_15					
42_5b					
42_1b					
42_13					
42_3a					
42_4					
42_5a					
42_10					
42_3b					
42_11					
42_6b					
43_1					
43_5					
43_12					
43_20					
43_21					
43_23					
43_25					
44_1					
44_5					
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4					
A3_5					
A3_7					
A3_3					
42_12					
AAV1	TTGCCCACTC	CCTCTCTGCG	CGCTCGCTCG	CTCGGTGGGG	CCTGCGGACC
AAV2	TTGGCCACTC	CCTCTCTGCG	CGCTCGCTCG	CTCACTGAGG	CCGGGCGACC
AAV3	TTGGCCACTC	CCTCTATGCG	CACTCGCTCG	CTCGGTGGGG	CCTGGCGACC
AAV8					
AAV9					
AAV7	TTGGCCACTC	CCTCTATGCG	CGCTCGCTCG	CTCGGTGGGG	CCTGCGGACC
44_2					

Fig. 1B

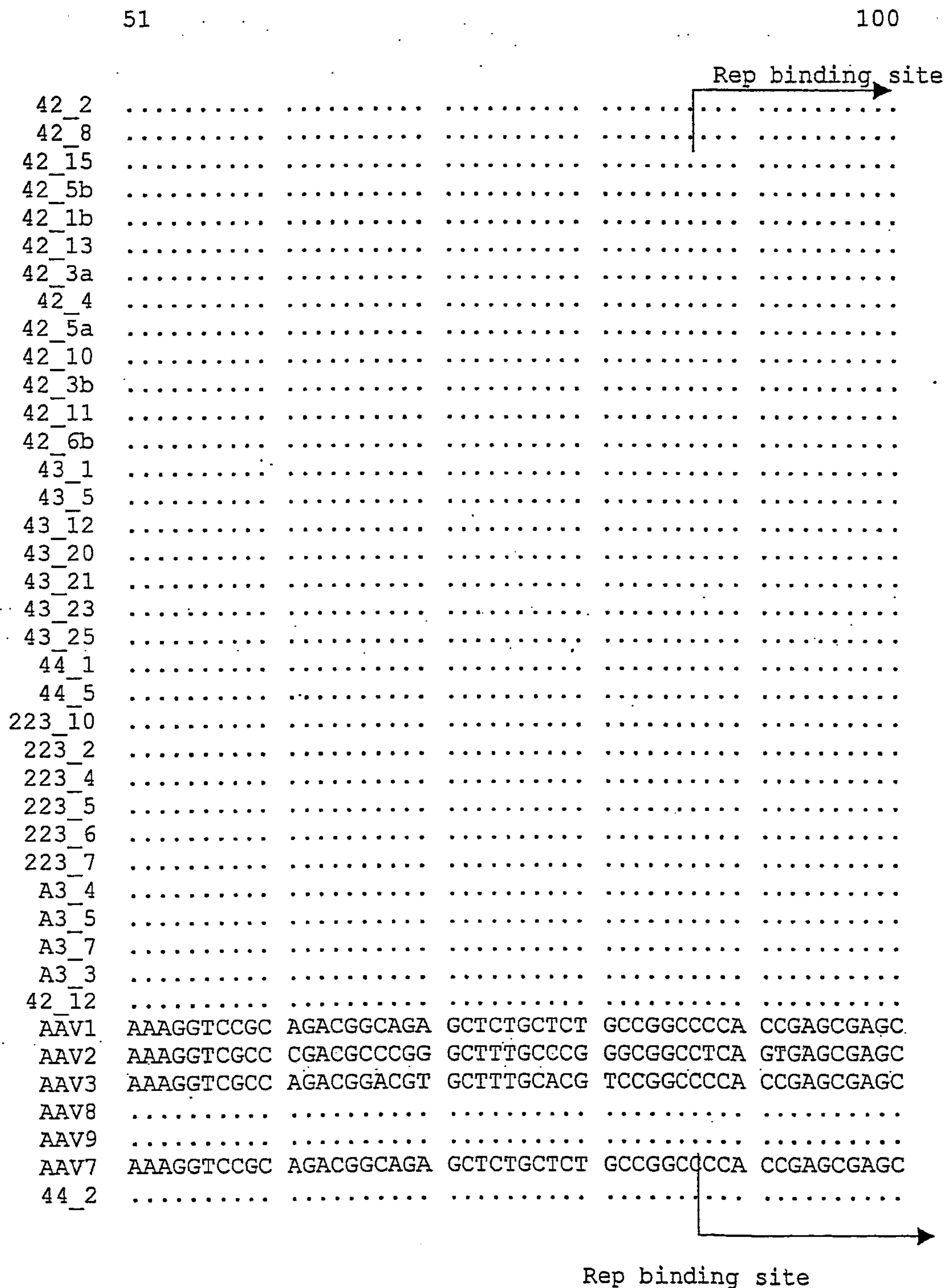


Fig. 1C

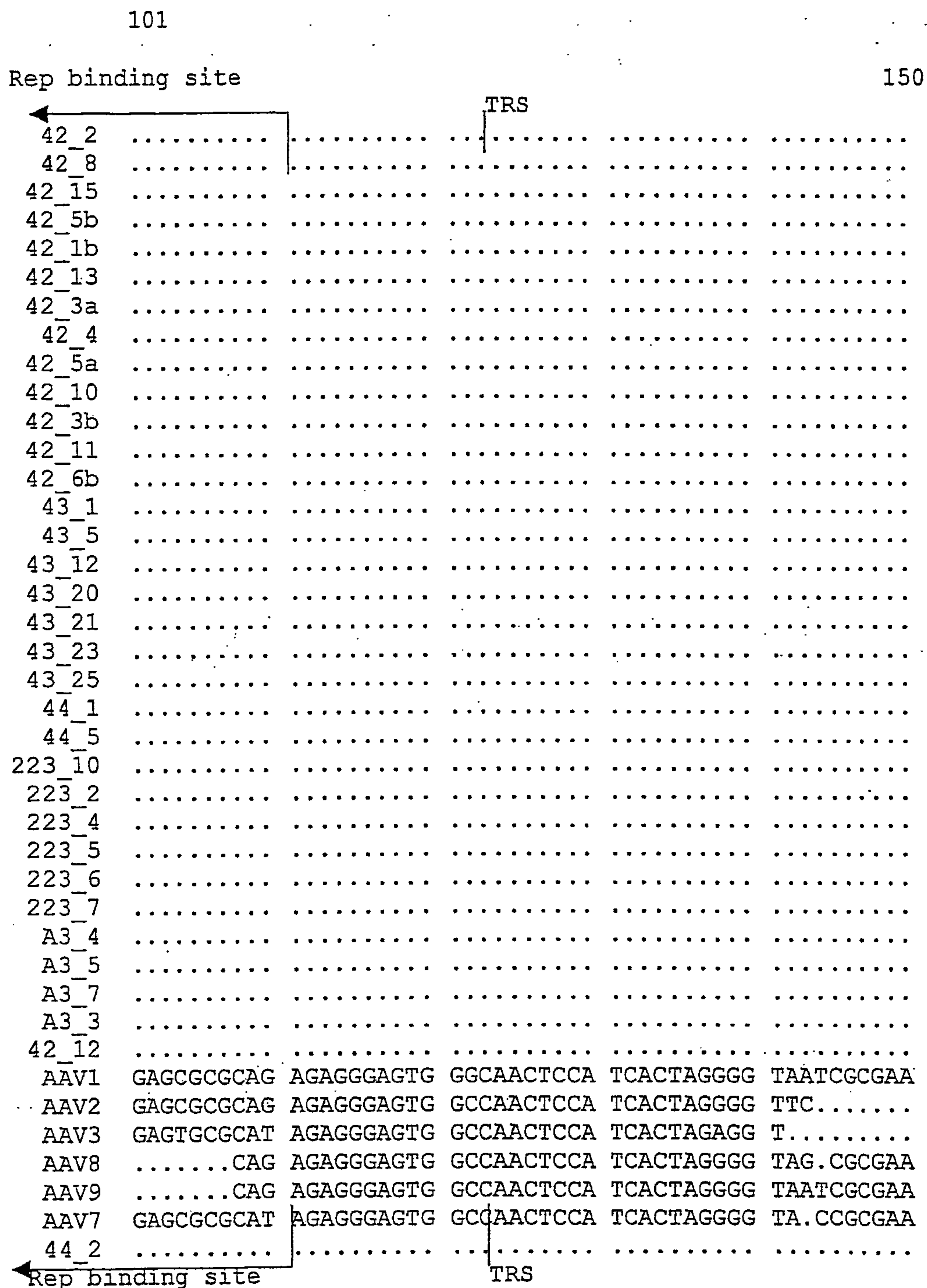


Fig. 1D

	151				200
42_2					
42_8					
42_15					
42_5b					
42_1b					
42_13					
42_3a					
42_4					
42_5a					
42_10					
42_3b					
42_11					
42_6b					
43_1					
43_5					
43_12					
43_20					
43_21					
43_23					
43_25					
44_1					
44_5					
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4					
A3_5					
A3_7					
A3_3					
42_12					
AAV1	GCGCCTCCCA	CGCTGCCGCG	TCAGCGCTGA	CGTAAATTAC	GTCATAGGGG
AAV2	CTG	GAGGGGTGGA	GTCGTGACGT	GAATTACGTC	ATAGGGTTAG
AAV3	ATG	GCAGTGACGT	AACGCGAAGC	GCGCGAAGCG	AGACCACGCC
AAV8	GCGCCTCCCA	CGCTGCCGCG	TCAGCGCTGA	CGTAAATTAC	GTCATAGGGG
AAV9	GCGCCTCCCA	CGCTGCCGCG	TCAGCGCTGA	CGTAGATTAC	GTCATAGGGG
AAV7	GCGCCTCCCA	CGCTGCCGCG	TCAGCGCTGA	CGTAAATCAC	GTCATAGGGG
44_2					

Fig. 1E

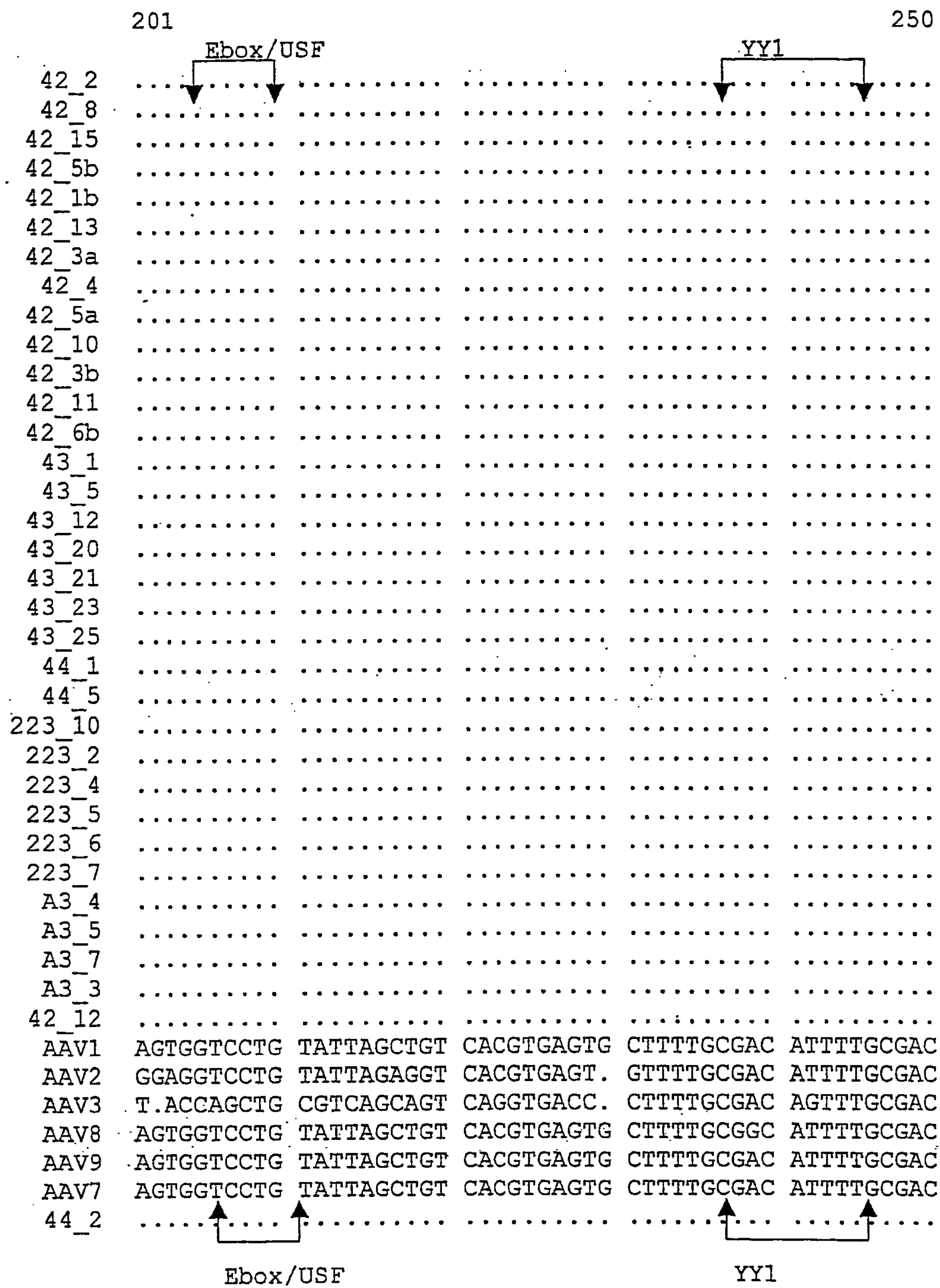


Fig. 1F

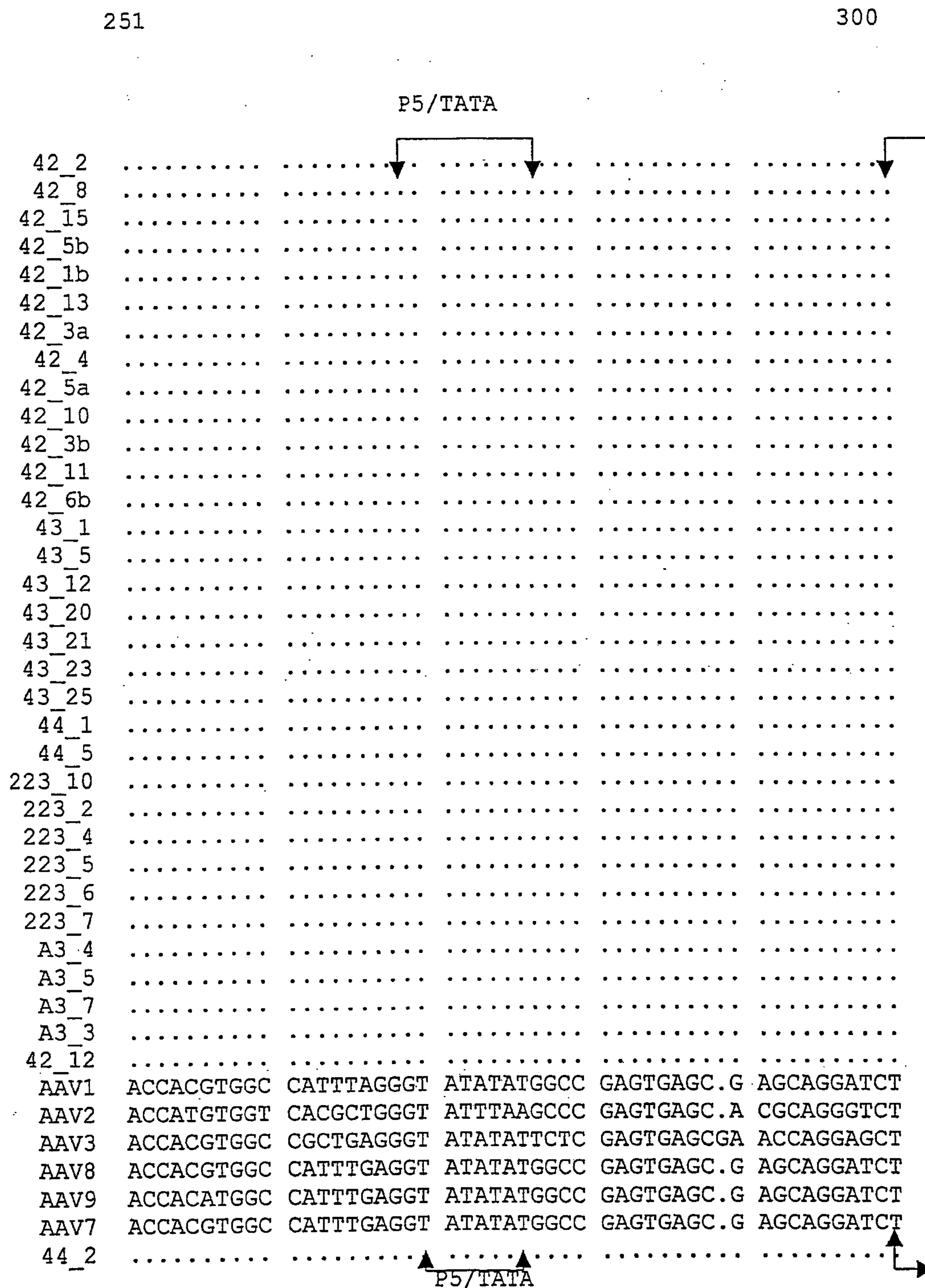


Fig. 1G

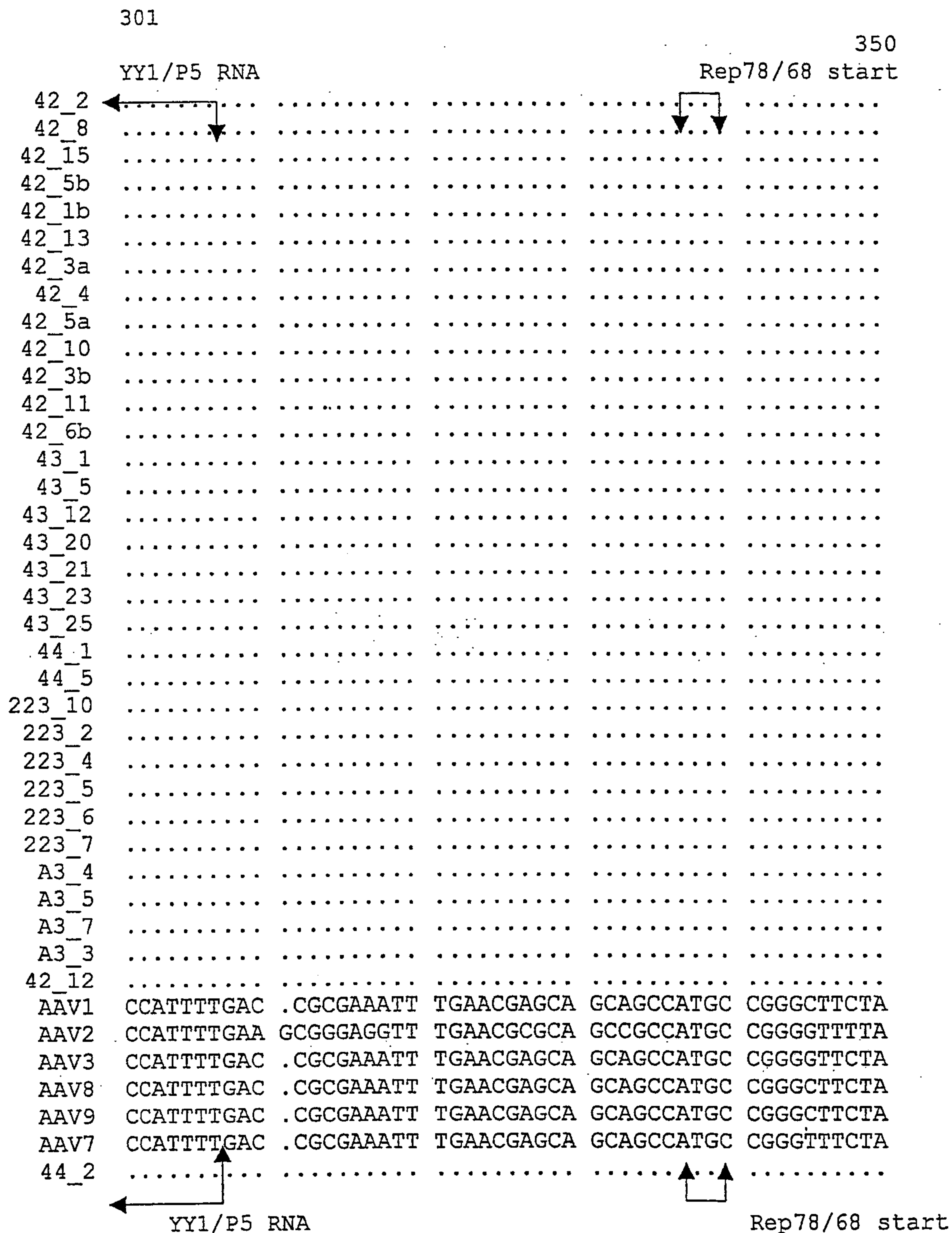


Fig. 1H

	351				400
42_2					
42_8					
42_15					
42_5b					
42_1b					
42_13					
42_3a					
42_4					
42_5a					
42_10					
42_3b					
42_11					
42_6b					
43_1					
43_5					
43_12					
43_20					
43_21					
43_23					
43_25					
44_1					
44_5					
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4					
A3_5					
A3_7					
A3_3					
42_12					
AAV1	CGAGATCGTG	ATCAAGGTGC	CGAGCGACCT	GGACGAGCAC	CTGCCGGGCA
AAV2	CGAGATTGTG	ATTAAGGTCC	CCAGCGACCT	TGACGGGCAT	CTGCCGGGCA
AAV3	CGAGATTGTC	CTGAAGGTCC	CGAGTGACCT	GGACGAGCGC	CTGCCGGGCA
AAV8	CGAGATCGTG	ATCAAGGTGC	CGAGCGACCT	GGACGAGCAC	CTGCCGGGCA
AAV9	CGAGATTGTG	ATCAAGGTGC	CGAGCGACCT	GGACGAGCAC	CTGCCGGGCA
AAV7	CGAGATCGTG	ATCAAGGTGC	CGAGCGACCT	GGACGAGCAC	CTGCCGGGCA
44_2					

Fig. 1I

	401				450
42_2					
42_8					
42_15					
42_5b					
42_1b					
42_13					
42_3a					
42_4					
42_5a					
42_10					
42_3b					
42_11					
42_6b					
43_1					
43_5					
43_12					
43_20					
43_21					
43_23					
43_25					
44_1					
44_5					
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4					
A3_5					
A3_7					
A3_3					
42_12					
AAV1	TTTCTGACTC	GTTTGTGAGC	TGGGTGGCCG	AGAAGGAATG	GGAGCTGCCC
AAV2	TTTCTGACAG	CTTTGTGAAC	TGGGTGGCCG	AGAAGGAATG	GGAGTTGCCG
AAV3	TTTCTAACTC	GTTTGTTAAC	TGGGTGGCCG	AGAAGGAATG	GGACGTGCCG
AAV8	TTTCTGACTC	GTTTGTGAAC	TGGGTGGCCG	AGAAGGAATG	GGAGCTGCCC
AAV9	TTTCTGACTC	TTTGTGAAC	TGGGTGGCCG	AGAAGGAATG	GGAGCTGCCC
AAV7	TTTCTGACTC	GTTTGTGAAC	TGGGTGGCCG	AGAAGGAATG	GGAGCTGCCC
44_2					

Fig. 1J

	451				500
42_2					
42_8					
42_15					
42_5b					
42_1b					
42_13					
42_3a					
42_4					
42_5a					
42_10					
42_3b					
42_11					
42_6b					
43_1					
43_5					
43_12					
43_20					
43_21					
43_23					
43_25					
44_1					
44_5					
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4					
A3_5					
A3_7					
A3_3					
42_12					
AAV1	CCGGATTCTG	ACATGGATCT	GAATCTGATT	GAGCAGGCAC	CCCTGACCGT
AAV2	CCAGATTCTG	ACATGGATCT	GAATCTGATT	GAGCAGGCAC	CCCTGACCGT
AAV3	CCGGATTCTG	ACATGGATCC	GAATCTGATT	GAGCAGGCAC	CCCTGACCGT
AAV8	CCGGATTCTG	ACATGGATCG	GAATCTGATC	GAGCAGGCAC	CCCTGACCGT
AAV9	CCGGATTCTG	ACATGGATCG	GAATCTGATC	GAGCAGGCAC	CCCTGACCGT
AAV7	CCGGATTCTG	ACATGGATCT	GAATCTGATC	GAGCAGGCAC	CCCTGACCGT
44_2					

Fig. 1K

	501				550
42_2					
42_8					
42_15					
42_5b					
42_1b					
42_13					
42_3a					
42_4					
42_5a					
42_10					
42_3b					
42_11					
42_6b					
43_1					
43_5					
43_12					
43_20					
43_21					
43_23					
43_25					
44_1					
44_5					
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4					
A3_5					
A3_7					
A3_3					
42_12					
AAV1	GGCCGAGAAG	CTGCAGCGCG	ACTTCCTGGT	CCAATGGCGC	CGCGTGAGTA
AAV2	GGCCGAGAAG	CTGCAGCGCG	ACTTTCTGAC	GGAATGGCGC	CGTGTGAGTA
AAV3	GGCCGAAAAG	CTTCAGCGCG	AGTTCCTGGT	GGAGTGGCGC	CGCGTGAGTA
AAV8	GGCCGAGAAG	CTGCAGCGCG	ACTTCCTGGT	CCAATGGCGC	CGCGTGAGTA
AAV9	GGCCGAGAAG	CTGTAGCGCG	ACTTCCTGGT	CCAATGGCGC	CGCGTGAGTA
AAV7	GGCCGAGAAG	CTGCAGCGCG	ACTTCCTGGT	CCAATGGCGC	CGCGTGAGTA
44_2					

Fig. 1L

	551				600
42_2					
42_8					
42_15					
42_5b					
42_1b					
42_13					
42_3a					
42_4					
42_5a					
42_10					
42_3b					
42_11					
42_6b					
43_1					
43_5					
43_12					
43_20					
43_21					
43_23					
43_25					
44_1					
44_5					
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4					
A3_5					
A3_7					
A3_3					
42_12					
AAV1	AGGCCCCGGA	GGCCCTCTTC	TTTGTTCAGT	TCGAGAAGGG	CGAGTCCTAC
AAV2	AGGCCCCGGA	GGCCCTTTTC	TTTGTGCAAT	TTGAGAAGGG	AGAGAGCTAC
AAV3	AGGCCCCGGA	GGCCCTCTTT	TTTGTCCAGT	TCGAAAAGGG	GGAGACCTAC
AAV8	AGGCCCCGGA	GGCCCTCTTC	TTTGTTCAGT	TCGAGAAGGG	CGAGAGCTAC
AAV9	AGGCCCCGGA	GGCCCTCTTC	TTTGTTCAGT	TCGAGAAGGG	CGAGAGCTAC
AAV7	AGGCCCCGGA	GGCCCTGTTC	TTTGTTCAGT	TCGAGAAGGG	CGAGAGCTAC
44_2					

Fig. 1M

	601				650
42_2					
42_8					
42_15					
42_5b					
42_1b					
42_13					
42_3a					
42_4					
42_5a					
42_10					
42_3b					
42_11					
42_6b					
43_1					
43_5					
43_12					
43_20					
43_21					
43_23					
43_25					
44_1					
44_5					
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4					
A3_5					
A3_7					
A3_3					
42_12					
AAV1	TTCCACCTCC	ATATTCTGGT	GGAGACCACG	GGGGTCAAAT	CCATGGTGCT
AAV2	TTCCACATGC	ACGTGCTCGT	GGAAACCACC	GGGGTGAAAT	CCATGGTTTT
AAV3	TTCCACCTGC	ACGTGCTGAT	TGAGACCATC	GGGGTCAAAT	CCATGGTGGT
AAV8	TTTCACCTGC	ACGTTCTGGT	CGAGACCACG	GGGGTCAAGT	CCATGGTGCT
AAV9	TTTCACCTGC	ACGTTCTGGT	CGAGACCACG	GGGGTCAAGT	CCATGGTGCT
AAV7	TTCCACCTTC	ACGTTCTGGT	GGAGACCACG	GGGGTCAAGT	CCATGGTGCT
44_2					

Fig. 1N

	651				700
42_2					
42_8					
42_15					
42_5b					
42_1b					
42_13					
42_3a					
42_4					
42_5a					
42_10					
42_3b					
42_11					
42_6b					
43_1					
43_5					
43_12					
43_20					
43_21					
43_23					
43_25					
44_1					
44_5					
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4					
A3_5					
A3_7					
A3_3					
42_12					
AAV1	GGGCCGCTTC	CTGAGTCAGA	TTAGGGACAA	GCT.GGTGCA	GACCATCTAC
AAV2	GGGACGTTTC	CTGAGTCAGA	TTCGCGAAAA	ACT..GATTC	AGAGAATTTA
AAV3	CGGCCGCTAC	GTGAGCCAGA	TTAAAGAGAA	GCT..GGTGA	CCCGCATCTA
AAV8	AGGCCGCTTC	CTGAGTCAGA	TTCGGGAAAA	GCTTGGTCCA	GACCATCTAC
AAV9	AGGCCGCTTC	CTGAGTCAGA	TTCGGGAGAA	GCT.GGTCCA	GACCATCTAC
AAV7	AGGCCGCTTC	CTGAGTCAGA	TTCGGGAGAA	GCT....G..	GTCCAGACCA
44_2					

Fig. 10

	701				750
42_2					
42_8					
42_15					
42_5b					
42_1b					
42_13					
42_3a					
42_4					
42_5a					
42_10					
42_3b					
42_11					
42_6b					
43_1					
43_5					
43_12					
43_20					
43_21					
43_23					
43_25					
44_1					
44_5					
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4					
A3_5					
A3_7					
A3_3					
42_12					
AAV1	C.GCGGGATC	GAGCCG.ACC	CTGCCCAACT	GGTTCGCGGT	GACCAA.GAC
AAV2	CCGCGGGATC	GAGCCG.ACT	TTGCCAAACT	GGTTCGCGGT	CACAAA...G
AAV3	CCGCGGGGTC	GAGCCG.CAG	CTTCCGAACT	GGTTCGCGGT	GACCAA...A
AAV8	CCGCGGGGTC	GAGCCCCACC	TTGCCCAACT	GGTTCGCGGT	GACCAAAGAC
AAV9	C.GCGGGATC	GAGCCG.ACC	CTGCCCAACT	GGTTCGCGGT	GACCAA.GAC
AAV7	TCTACCGCGG	GGTCGAGCCC	ACGCTGCCCA	ACTGGTTCGC	GGTGACCAAG
44_2					

Fig. 1P

	751				800
42_2					
42_8					
42_15					
42_5b					
42_1b					
42_13					
42_3a					
42_4					
42_5a					
42_10					
42_3b					
42_11					
42_6b					
43_1					
43_5					
43_12					
43_20					
43_21					
43_23					
43_25					
44_1					
44_5					
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4					
A3_5					
A3_7					
A3_3					
42_12					
AAV1	GCG.TAATGG	CGCCGGAGGG	GGG.AACAAG	GTGGTGGACG	AGTGCTACAT
AAV2	ACCAGAAATG	GCGCCGGAGG	CGGGAACAAG	GTGGTGGATG	AGTGCTACAT
AAV3	ACGCGAAATG	GCGCCGGGGG	CGGGAACAAG	GTGGTGGACG	ACTGCTACAT
AAV8	GCGGTAATGG	CGCCGGCGGG	GGGGAACAAG	GTGGTGGACG	AGTGCTACAT
AAV9	GCG.TAATGG	CGCCGGCGGG	GGG.AACAAG	GTGGTGGACG	AGTGCTACAT
AAV7	ACGCGTAATG	GCGCCGGCGG	GGGGAACAAG	GTGGTGGACG	AGTGCTACAT
44_2					

Fig. 1Q

	801				850
42_2					
42_8					
42_15					
42_5b					
42_1b					
42_13					
42_3a					
42_4					
42_5a					
42_10					
42_3b					
42_11					
42_6b					
43_1					
43_5					
43_12					
43_20					
43_21					
43_23					
43_25					
44_1					
44_5					
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4					
A3_5					
A3_7					
A3_3					
42_12					
AAV1	CCCCAACTAC	CTCCTGCCCA	AGACTCAGCC	CGAGCTGCAG	TGGGCGTGGA
AAV2	CCCCAATTAC	TTGCTCCCCA	AAACCCAGCC	TGAGCTCCAG	TGGGCGTGGA
AAV3	CCCCAACTAC	CTGCTCCCCA	AGACCCAGCC	CGAGCTCCAG	TGGGCGTGGA
AAV8	CCCCAACTAC	CTCCTGCCCA	AGACTCAGCC	CGAGCTGCAG	TGGGCGTGGA
AAV9	CCCCAACTAC	CTCCTGCCCA	AGACTCAGCC	CGAGCTGCAG	TGGGCGTGGA
AAV7	CCCCAACTAC	CTCCTGCCCA	AGACCCAGCC	CGAGCTGCAG	TGGGCGTGGA
44_2					

Fig. 1R

851

900

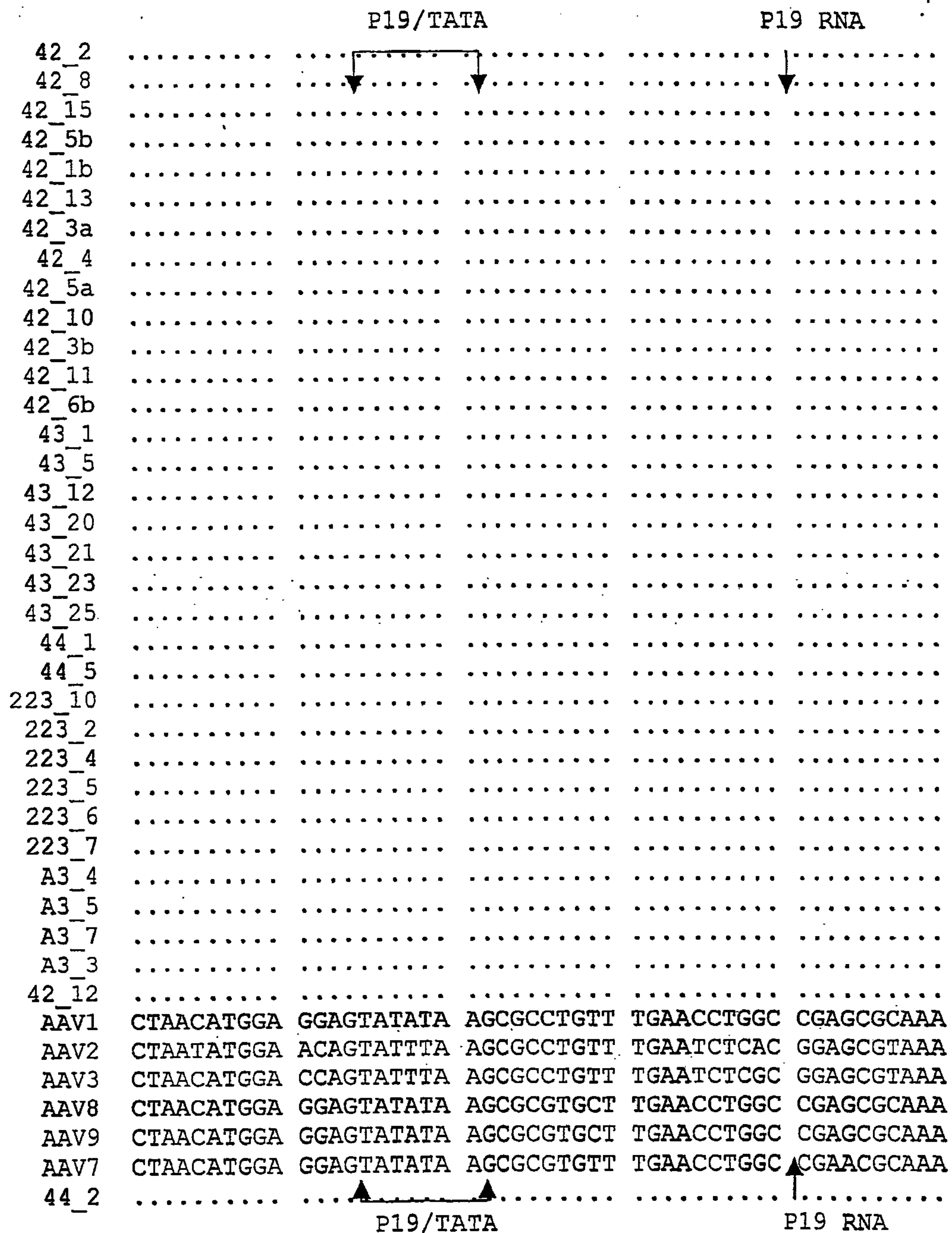


Fig. 1S

	901				950
42_2					
42_8					
42_15					
42_5b					
42_1b					
42_13					
42_3a					
42_4					
42_5a					
42_10					
42_3b					
42_11					
42_6b					
43_1					
43_5					
43_12					
43_20					
43_21					
43_23					
43_25					
44_1					
44_5					
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4					
A3_5					
A3_7					
A3_3					
42_12					
AAV1	CGGCTCGTGG	CGCAGCACCT	GACCCACGTC	AGCCAGACCC	AGGAGCAGAA
AAV2	CGGTTGGTGG	CGCAGCATCT	GACGCACGTG	TCGCAGACGC	AGGAGCAGAA
AAV3	CGGCTGGTGG	CGCAGCATCT	GACGCACGTG	TCGCAGACGC	AGGAGCAGAA
AAV8	CGGCTCGTGG	CGCAGCACCT	GACCCACGTC	AGCCAGACGC	AGGAGCAGAA
AAV9	CGGCTCGTGG	CGCAGCACCT	GACCCACGTC	AGCCAGACGC	AGGAGCAGAA
AAV7	CGGCTCGTGG	CGCAGCACCT	GACCCACGTC	AGCCAGACGC	AGGAGCAGAA
44_2					

Fig. 1T

	951				1000
42_2					
42_8					
42_15					
42_5b					
42_1b					
42_13					
42_3a					
42_4					
42_5a					
42_10					
42_3b					
42_11					
42_6b					
43_1					
43_5					
43_12					
43_20					
43_21					
43_23					
43_25					
44_1					
44_5					
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4					
A3_5					
A3_7					
A3_3					
42_12					
AAV1	CAAGGAGAAT	CTGAACCCCA	ATTCTGACGC	GCCTGTCATC	CGGTCAAAAA
AAV2	CAAAGAGAAT	CAGAATCCCA	ATTCTGATGC	GCCGGTGATC	AGATCAAAAA
AAV3	CAAAGAGAAT	CAGAACCCCA	ATTCTGACGC	GCCGGTCATC	AGGTCAAAAA
AAV8	CAAGGAGAAT	CTGAACCCCA	ATTCTGACGC	GCCCGTGATC	AGGTCAAAAA
AAV9	CAAGGAGAAT	CTGAACCCCA	ATTCTGACGC	GCCCGTGATC	AGGTCAAAAA
AAV7	CAAGGAGAAT	CTGAACCCCA	ATTCTGACGC	GCCCGTGATC	AGGTCAAAAA
44_2					

Fig. 1U

	1001				1050
		Rep52/40	start codon		
42_2			↓ ↓		
42_8					
42_15					
42_5b					
42_1b					
42_13					
42_3a					
42_4					
42_5a					
42_10					
42_3b					
42_11					
42_6b					
43_1					
43_5					
43_12					
43_20					
43_21					
43_23					
43_25					
44_1					
44_5					
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4					
A3_5					
A3_7					
A3_3					
42_12					
AAV1	CCTCCGCGCG	CTACATGGAG	CTGGTCGGGT	GGCTGGTGGA	CCGGGGCATC
AAV2	CTTCAGCCAG	GTACATGGAG	CTGGTCGGGT	GGCTCGTGGA	CAAGGGGATT
AAV3	CCTCAGCCAG	GTACATGGAG	CTGGTCGGGT	GGCTGGTGGA	CCGCGGGATC
AAV8	CCTCCGCGCG	CTATATGGAG	CTGGTCGGGT	GGCTGGTGGA	CCGGGGCATC
AAV9	CCTCCGCGCG	CTACATGGAG	CTGGTCGGGT	GGCTGGTGGA	CCGGGGCATC
AAV7	CCTCCGCGCG	CTACATGGAG	CTGGTCGGGT	GGCTGGTGGA	CCGGGGCATC
44_2			↑ ↑		
		Rep 52/40	start		

Fig. 1V

	1051				1100
42_2					
42_8					
42_15					
42_5b					
42_1b					
42_13					
42_3a					
42_4					
42_5a					
42_10					
42_3b					
42_11					
42_6b					
43_1					
43_5					
43_12					
43_20					
43_21					
43_23					
43_25					
44_1					
44_5					
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4					
A3_5					
A3_7					
A3_3					
42_12					
AAV1	ACCTCCGAGA	AGCAGTGGAT	CCAGGAGGAC	CAGGCCTCGT	ACATCTCCTT
AAV2	ACCTCGGAGA	AGCAGTGGAT	CCAGGAGGAC	CAGGCCTCAT	ACATCTCCTT
AAV3	ACGTCAGAAA	AGCAATGGAT	TCAGGAGGAC	CAGGCCTCGT	ACATCTCCTT
AAV8	ACCTCCGAGA	AGCAGTGGAT	CCAGGAGGAC	CAGGCCTCGT	ACATCTCCTT
AAV9	ACCTCCGAGA	AGCAGTGGAT	CCAGGAGGAC	CAGGCCTCGT	ACATCTCCTT
AAV7	ACCTCCGAGA	AGCAGTGGAT	CCAGGAGGAC	CAGGCCTCGT	ACATCTCCTT
44_2					

Fig. 1W

	1101				1150
42_2					
42_8					
42_15					
42_5b					
42_1b					
42_13					
42_3a					
42_4					
42_5a					
42_10					
42_3b					
42_11					
42_6b					
43_1					
43_5					
43_12					
43_20					
43_21					
43_23					
43_25					
44_1					
44_5					
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4					
A3_5					
A3_7					
A3_3					
42_12					
AAV1	CAACGCCGCT	TCCAACCTCGC	GGTCCCAGAT	CAAGGCCGCT	CTGGACAATG
AAV2	CAATGCGGCC	TCCAACCTCGC	GGTCCCAGAT	CAAGGCTGCC	TTGGACAATG
AAV3	CAACGCCGCC	TCCAACCTCGC	GGTCCCAGAT	CAAGGCCGCG	CTGGACAATG
AAV8	CAACGCCGCC	TCCAACCTCGC	GGTCCCAGAT	CAAGGCCGCG	CTGGACAATG
AAV9	CAACGCCGCC	TCCAACCTCGC	GGTCCCAGAT	CAAGGCCGCG	CTGGACAATG
AAV7	CAACGCCGCC	TCCAACCTCGC	GGTCCCAGAT	CAAGGCCGCG	CTGGACAATG
44_2					

Fig. 1X

	1151				1200
42_2					
42_8					
42_15					
42_5b					
42_1b					
42_13					
42_3a					
42_4					
42_5a					
42_10					
42_3b					
42_11					
42_6b					
43_1					
43_5					
43_12					
43_20					
43_21					
43_23					
43_25					
44_1					
44_5					
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4					
A3_5					
A3_7					
A3_3					
42_12					
AAV1	CCGGCAAGAT	CATGGCGCTG	ACCAAATCCG	CGCCCGACTA	CCTGGTAGGC
AAV2	CGGGAAAGAT	TATGAGCCTG	ACTAAAACCG	CCCCCGACTA	CCTGGTGGGC
AAV3	CCTCCAAGAT	CATGAGCCTG	ACAAAGACGG	CTCCGGACTA	CCTGGTGGGC
AAV8	CCGGCAAGAT	CATGGCGCTG	ACCAAATCCG	CGCCCGACTA	CCTGGTGGGG
AAV9	CCGGCAAGAT	CATGGCGCTG	ACCAAATCCG	CGCCCGACTA	CCTGGTAGGC
AAV7	CCGGCAAGAT	CATGGCGCTG	ACCAAATCCG	CGCCCGACTA	CCTGGTGGGG
44_2					

Fig. 1Y

	1201				1250
42_2					
42_8					
42_15					
42_5b					
42_1b					
42_13					
42_3a					
42_4					
42_5a					
42_10					
42_3b					
42_11					
42_6b			GA	ATTCGCCCTT	TCTACGGCTG
43_1					
43_5					
43_12					
43_20					
43_21					
43_23					
43_25					
44_1					
44_5					
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4					
A3_5					
A3_7					
A3_3					
42_12					
AAV1	CCCGCTCCGC	CCGCGGACAT	TAAAACCAAC	CGCATCTACC	GCATCCTGGA
AAV2	CAGCAGCCCG	TGGAGGACAT	TTCCAGCAAT	CGGATTTATA	AAATTTTGGA
AAV3	AGCAACCCGC	CGGAGGACAT	TACCAAAAAT	CGGATCTACC	AAATCCTGGA
AAV8	CCCTCGCTGC	CCGCGGACAT	TACCCAGAAC	CGCATCTACC	GCATCCTCGC
AAV9	CCTTCACTTC	CGGTGGACAT	TACGCAGAAC	CGCATCTACC	GCATCCTGCA
AAV7	CCCTCGCTGC	CCGCGGACAT	TAAAACCAAC	CGCATCTACC	GCATCCTGGA
44_2					

Fig. 12

	1251				1300
42_2					
42_8					
42_15					
42_5b					
42_1b					
42_13					
42_3a					
42_4					
42_5a					
42_10					
42_3b					
42_11					
42_6b	CGTCAACTGG	ACCAATGAGA	ACTTTCCTT	CAACGATTGC	GTCGACAAGA
43_1					
43_5					
43_12					
43_20					
43_21					
43_23					
43_25					
44_1					
44_5					
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4					
A3_5					
A3_7					
A3_3					
42_12					
AAV1	GCTGAACGGC	TACGAACCTG	CCTACGCCGG	CTCCGTCTTT	CTCGGCTGGG
AAV2	ACTAAACGGG	TACGATCCCC	AATATGCGGC	TTCCGTCTTT	CTGGGATGGG
AAV3	GCTGAACGGG	TACGATCCGC	AGTACGCGGC	CTCCGTCTTC	CTGGGCTGGG
AAV8	TCTCAACGGC	TACGACCCTG	CCTACGCCGG	CTCCGTCTTT	CTCGGCTGGG
AAV9	GCTCAACGGC	TACGACCCTG	CCTACGCCGG	CTCCGTCTTT	CTCGGCTGGG
AAV7	GCTGAACGGG	TACGATCCTG	CCTACGCCGG	CTCCGTCTTT	CTCGGCTGGG
44_2					

Fig. 1AA

	1301				1350
42_2					
42_8					
42_15					
42_5b					
42_1b					
42_13					
42_3a					
42_4					
42_5a					
42_10					
42_3b					
42_11					
42_6b	TGGTGATCTG	GTGGGAGGAG	GGCAAGATGA	CGGCCAAGGT	CGTGGAGTCC
43_1					
43_5					
43_12					
43_20					
43_21					
43_23					
43_25					
44_1					
44_5					
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4					
A3_5					
A3_7					
A3_3					
42_12					
AAV1	CCCAGAAAAG	GTTTCGGGAAG	CGCAACACCA	TCTGGCTGTT	TGGGCCGGCC
AAV2	CCACGAAAAA	GTTTCGGCAAG	AGGAACACCA	TCTGGCTGTT	TGGGCCTGCA
AAV3	CGCAAAAGAA	GTTTCGGGAAG	AGGAACACCA	TCTGGCTCTT	TGGGCCGGCC
AAV8	CTCAGAAAAA	GTTTCGGGAAA	CGCAACACCA	TCTGGCTGTT	TGGACCCGCC
AAV9	CACAAAAGAA	GTTTCGGGAAA	CGCAACACCA	TCTGGCTGTT	TGGGCCGGCC
AAV7	CCCAGAAAAA	GTTTCGGGAAG	CGCAACACCA	TCTGGCTGTT	TGGGCCCGCC
44_2					

Fig. 1AB

	1351				1400
42_2				GAA	TTCGCCCTTT
42_8				GAA	TTCGCCCTTT
42_15				GAA	TTCGCCCTTT
42_5b				GAA	TTCGCCCTTT
42_1b					
42_13				GAA	TTCGCCCTTT
42_3a				GAA	TTCGCCCTTT
42_4					
42_5a				GA	ATTGCCCTT
42_10					
42_3b					
42_11				GAA	TTCGCCCTTT
42_6b	GCCAAGGCCA	TTCTCGGCGG	CAGCAAGGTG	CGCGTGGACC	AAAAGTGCAA
43_1				GAA	TTCGCCCTTT
43_5				GAA	TTCGCCCTTT
43_12				GAA	TTCGCCCTT.
43_20				GAA	TTCGCCCTTT
43_21				GAA	TTCGCCCTT.
43_23				GAA	TTCGCCCTT.
43_25				GAA	TTCGCCCTTT
44_1				GAA	TTCGCCCTTT
44_5				GAA	TTCGCCCTTT
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4				GA	ATTGCCCTT
A3_5				GA	ATTGCCCTT
A3_7			A	GCGGCCGCGA	ATTGCCCTT
A3_3				GA	ATTGCCCTT
42_12				GAA	TTCGCCCTTT
AAV1	ACCACGGGCA	AGACCAACAT	CGCGGAAGCC	ATCGCCCACG	CCGTGCCCTT
AAV2	ACTACCGGGA	AGACCAACAT	CGCGGAGGCC	ATAGCCCACA	CTGTGCCCTT
AAV3	ACGACGGGTA	AAACCAACAT	CGCGGAAGCC	ATCGCCCACG	CCGTGCCCTT
AAV8	ACCACCGGCA	AGACCAACAT	TGCGGAAGCC	ATCGCCCACG	CCGTGCCCTT
AAV9	ACCACGGGAA	AGACCAACAT	CGCAGAAGCC	ATTGCCACG	CCGTGCCCTT
AAV7	ACCACCGGCA	AGACCAACAT	TGCGGAAGCC	ATCGCCCACG	CCGTGCCCTT
44_2				GA	ATTGCCCTT

Fig. 1AC

	1401				1450
42_2	.CTACGGCTG	CGTCAACTGG	ACCAATGAGA	ACTTTCCCTT	CAACGATTGC
42_8	.CTACGGCTG	CGTCAACTGG	ACCAATGAGA	ACTTTCCCTT	CAACGATTGC
42_15	.CTACGGCTG	CGTCAACTGG	ACCAATGAGA	ACTTTCCCTT	CAACGATTGC
42_5b	.CTACGGCTG	CGTCAACTGG	ACCAATGAGA	ACTTTCCCTT	CAACGATTGC
42_1b					
42_13	.CTACGGCTG	CGTCAACTGG	ACCAATGAGA	ACTTTCCCTT	CAACGATTGC
42_3a	.CTACGGCTG	CGTCAACTGG	ACCAATGAGA	ACTTTCCCTT	CAACGATTGC
42_4					
42_5a	.CTACGGCTG	CGTCAACTGG	ACCAATGAGA	ACTTTCCCTT	CAACGATTGC
42_10					
42_3b					
42_11	.CTACGGCTG	CGTCAACTGG	ACCAATGAGA	ACTTTCCCTT	CAACGATTGC
42_6b	.GTCTTCCGC	CCAGATCGAT	CCCACCCCGG	TGATCGTCAC	TTCCAACACC
43_1	.CTACGGCTG	CATCAACTGG	ACCAATGAGA	ACTTTCCCTT	CAACGATTGC
43_5	.CTACGGCTG	CGTCAACTGG	ACCAATGAGA	ACTTTCCCTT	CAACGATTGC
43_12	GGCTG	CGTCAACTGG	ACCAATGAGA	ACTTTCCCTT	CAACGATTGC
43_20	.CTACGGCTG	CGTCAACTGG	ACCAATGAGA	ACTTTCCCTT	CAACGATTGC
43_21	GGCTG	CGTCAACTGG	ACCAATGAGA	ACTTTCCCTT	CAACGATTGC
43_23	.CTACGGCTG	CGTCAACTGG	ACCAATGAGA	ACTTTCCCTT	CAACGATTGC
43_25	.CTACGGCTG	CGTCAACTGG	ACCAATGAGA	ACTTTCCCTT	CAACGATTGC
44_1	.CTACGGCTG	CGTCAACTGG	ACCAATGAGA	ACTTTCCCTT	CAACGATTGC
44_5	.CTACGGCTG	CGTCAACTGG	ACCAATGAGA	ACTTTCCCTT	CAACGATTGC
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4	TCTACGGCTG	CGTCAACTGG	ACCAATGAAA	ACTTTCCCTT	CAACGATTGC
A3_5	TCTACGGCTG	CGTCAACTGG	ACCAATGAAA	ACTTTCCCTT	CAACGATTGC
A3_7	TCTACGGCTG	CGTCAACTGG	ACCAATGAAA	ACTTTCCCTT	CAACGATTGC
A3_3	TCTACGGCTG	CGTCAACTGG	ACCAATGAAA	ACTTTCCCTT	CAACGATTGC
42_12	.CTACGGCTG	CGTCAACTGG	ACCAATGAGA	ACTTTCCCTT	CAACGATTGC
AAV1	.CTACGGCTG	CGTCAACTGG	ACCAATGAGA	ACTTTCCCTT	CAATGATTGC
AAV2	.CTACGGGTG	CGTAAACTGG	ACCAATGAGA	ACTTTCCCTT	CAACGACTGT
AAV3	.CTACGGCTG	CGTAAACTGG	ACCAATGAGA	ACTTTCCCTT	CAACGATTGC
AAV8	.CTACGGCTG	CGTCAACTGG	ACCAATGAGA	ACTTTCCCTT	CAATGATTGC
AAV9	.CTACGGCTG	CGTCAACTGG	ACCAATGAGA	ACTTTCCCTT	CAACGATTGC
AAV7	.CTACGGCTG	CGTCAACTGG	ACCAATGAGA	ACTTTCCCTT	CAACGATTGC
44_2	TCTACGGCTG	CGTCAACTGG	ACCAATGAGA	ACTTTCCCTT	CAACGATTGC

Fig. 1AD

	1451				1500
42_2	GTCGACAAGA	TGGTGATCTG	GTGGGAGGAG	GGCAAGATGA	CGGCCAAGGT
42_8	GTCGACAAGA	TGGTGATCTG	GTGGGAGGAG	GGCAAGATGA	CGGCCAAGGT
42_15	GTCGACAAGA	TGGTGATCTG	GTGGGAGGAG	GGCAAGATGA	CGGCCAAGGT
42_5b	GTCGACAAGA	TGGTGATCTG	GTGGGAGGAG	GGCAAGATGA	CGGCCAAGGT
42_1b					
42_13	GTCGACAAGA	TGGTGATCTG	GTGGGAGGAG	GGCAAGATGA	CGGCCAAGGT
42_3a	GTCGACAAGA	TGGTGATCTG	GTGGGAGGAG	GGCAAGATGA	CGGCCAAGGT
42_4					
42_5a	GTCGACAAGA	TGGTGATCTG	GTGGGAGGAG	GGCAAGATGA	CGGCCAAGGT
42_10					
42_3b					
42_11	GTCGACAAGA	TGGTGATCTG	GTGGGAGGAG	GGCAAGATGA	CGGCCAAGGT
42_6b	AACATGTGCG	CCGTGATTGA	CGGGAACAGC	ACCACCTTCG	AGCACCAGCA
43_1	GTCGACAAGA	TGGTGATCTG	GTGGGAGGAG	GGCAAGATGA	CGGCCAAGGT
43_5	GTCGACAAGA	TGGTGATCTG	GTGGGAGGAG	GGCAAGATGA	CGGCCAAGGT
43_12	GTCGACAAGA	TGGTGATCTG	GTGGGAGGAG	GGCAAGATGA	CGGCCAAGGT
43_20	GTCGACAAGA	TGGTGATCTG	GTGGGAGGAG	GGCAAGATGA	CGGCCAAGGT
43_21	GTCGACAAGA	TGGTGATCTG	GTGGGAGGAG	GGCAAGATGA	CGGCCAAGGT
43_23	GTCGACAAGA	TGGTGATCTG	GTGGGAGGAG	GGCAAGATGA	CGGCCAAGGT
43_25	GTCGACAAGA	TGGTGATCTG	GTGGGAGGAG	GGCAAGATGA	CGGCCAAGGT
44_1	GTCGACAAGA	TGTTGATCTG	GTGGGAGGAG	GGCAAGATGA	CGGCCAAGGT
44_5	GTCGACAAGA	TGGTGATCTG	GTGGGAGGAG	GGCAAGATGA	CGGCCAAGGT
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4	GTCGACAAGA	TGGTGATCTG	GTGGGAGGAG	GGAAAGATGA	CCGCCAAGGT
A3_5	GTCGACAAGA	TGGTGATCTG	GTGGGAGGAG	GGAAAGATGA	CCGCCAAGGT
A3_7	GTCGACAAGA	TGGTGATCTG	GTGGGAGGAG	GGAAAGATGA	CCGCCAAGGT
A3_3	GTCGACAAGA	TGGTGATCTG	GTGGGAGGAG	GGAAAGATGA	CCGCCAAGGT
42_12	GTCGACAAGA	TGGTGATCTG	GTGGGAGGAG	GGCAAGATGA	CGGCCAAGGT
AAV1	GTCGACAAGA	TGGTGATCTG	GTGGGAGGAG	GGCAAGATGA	CGGCCAAGGT
AAV2	GTCGACAAGA	TGGTGATCTG	GTGGGAGGAG	GGGAAGATGA	CCGCCAAGGT
AAV3	GTCGACAAGA	TGGTGATCTG	GTGGGAGGAG	GGCAAGATGA	CGGCCAAGGT
AAV8	GTCGACAAGA	TGGTGATCTG	GTGGGAGGAG	GGCAAGATGA	CGGCCAAGGT
AAV9	GTCGACAAGA	TGGTGATCTG	GTGGGAGGAG	GGCAAGATGA	CGGCCAAGGT
AAV7	GTCGACAAGA	TGGTGATCTG	GTGGGAGGAG	GGCAAGATGA	CGGCCAAGGT
44_2	GTCGACAAGA	TGGTGATCTG	GTGGGAGGAG	GGCAAGATGA	CGGCCAAGGT

Fig. 1AE

	1501				1550
42_2	CGTGGAGTCC	GCCAAGGCCA	TTCTCGGCGG	CAGCAAGGTG	CGCGTGGACC
42_8	CGTGGAGTCC	GCCAAGGCCA	TTCTCGGCGG	CAGCAAGGTG	CGCGTGGACC
42_15	CGTGGAGTCC	GCCAAGGCCA	TTCTCGGCGG	CAGCAAGGTG	CGCGTGGACC
42_5b	CGTGGAGTCC	GCCAAGGCCA	TTCTCGGCGG	CAGCAAGGTG	CGCGTGGACC
42_1b					
42_13	CGTGGAGTCC	GCCAAGGCCA	TTCTCGGCGG	CAGCAAGGTG	CGCGTGGACC
42_3a	CGTGGAGTCC	GCCAAGGCCA	TTCTCGGCGG	CAGCAAGGTG	CGCGTGGACC
42_4					
42_5a	CGTGGAGTCC	GCCAAGGCCA	TTCTCGGCGG	CAGCAAGGTG	CGCGTGGACC
42_10					
42_3b					
42_11	CGTGGAGTCC	GCCAAGGCCA	TTCTCGGCGG	CAGCAAGGTG	CGCGTGGACC
42_6b	GCCGTTGCAG	GACCGGATGT	TCAAATTTGA	ACTCACCCGC	CGTCTGGAGC
43_1	CGTGGAGTCC	GCCAAGGCCA	TTCTCGGCGG	CAGCAAGGTG	CGCGTGGACC
43_5	CGTGGAGTCC	GCCAAGGCCA	TTCTCGGCGG	CAGCAAGGTG	CGCGTGGACC
43_12	CGTGGAGTCC	GCCAAGGCCA	TTCTCGGCGG	CAGCAAGGTG	CGCGTGGACC
43_20	CGTGGAGTCC	GCCAAGGCCA	TTCTCGGCGG	CAGCAAGGTG	CGTGTGGACC
43_21	CGTGGAGTCC	GCCAAGGCCA	TTCTCGGCGG	CAGCAAGGTG	CGTGTGGACC
43_23	CGTGGAGTCC	GCCAAGGCCA	TTCTCGGCGG	CAGCAAGGTG	CGTGTGGACC
43_25	CGTGGAGTCC	GCCAAGGCCA	TTCTCGGCGG	CAGCAAGGTG	CGTGTGGACC
44_1	CGTGGAGTCC	GCCAAGGCCA	TTCTCGGCGG	CAGCAAAGTG	CGCGTGGACC
44_5	CGTGGAGTCC	GCCAAGGCCA	TTCTCGGCGG	CAGCAAAGTG	CGCGTGGACC
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4	CGTGGAATCT	GCCAAAGCCA	TTCTGGGTGG	AAGCAAGGTT	CGTGTGGACC
A3_5	CGTGGAATCT	GCCAAAGCCA	TTCTGGGTGG	AAGCAAGGTT	CGTGTGGACC
A3_7	CGTGGAATCT	GCCAAAGCCA	TTCTGGGTGG	AAGCAAGGTT	CGTGTGGACC
A3_3	CGTGGAATCT	GCCAAAGCCA	TTCTGGGTGG	AGGCAAGGTT	CGTGTGGACC
42_12	CGTGGAGTCC	GCCAAGGCCA	TTCTCGGCGG	CAGCAAGGTG	CGCGTGGACC
AAV1	CGTGGAGTCC	GCCAAGGCCA	TTCTCGGCGG	CAGCAAGGTG	CGCGTGGACC
AAV2	CGTGGAGTCG	GCCAAAGCCA	TTCTCGGAGG	AAGCAAGGTG	CGCGTGGACC
AAV3	CGTGGAGAGC	GCCAAGGCCA	TTCTGGGCGG	AAGCAAGGTG	CGCGTGGACC
AAV8	CGTGGAGTCC	GCCAAGGCCA	TTCTCGGCGG	CAGCAAGGTG	CGCGTGGACC
AAV9	CGTGGAGTCC	GCCAAGGCCA	TTCTCGGCGG	CAGCAAGGTG	CGCGTGGACC
AAV7	CGTGGAGTCC	GCCAAGGCCA	TTCTCGGCGG	CAGCAAGGTG	CGCGTGGACC
44_2	CGTGGAGTCC	GCCAAGGCCA	TTCTCGGCGG	CAGCAAAGTG	CGCGTGGACC

Fig. 1AF

	1551				1600
42_2	AAAAGTGCAA	GTCTTCCGCC	CAGATCGATC	CCACCCCCGT	GATCGTCACT
42_8	AAAAGTGCAA	GTCTTCCGCC	CAGATCGATC	CCACCCCCGT	GATCGTCACT
42_15	AAAAGTGCAA	GTCGTCCGCC	CAGATCGACC	CCACCCCCGT	GATCGTCACC
42_5b	AAAAGTGCAA	GTCGTCCGCC	CAGATCGACC	CCACCCCCGT	GATCGTCACC
42_1b					
42_13	AAAAGTGCAA	GTCGTCCGCC	CAGATCGATC	CCACCCCCGT	GATCGTCACT
42_3a	AAAAGTGCAA	GTCGTCCGCC	CAGATCGATC	CCACCCCCGT	GATCGTCACT
42_4					
42_5a	AAAAGTGCAA	GTCGTCCGCC	CAGATCGACC	CCACCCCCGT	GATCGTCACC
42_10					
42_3b					
42_11	AAAAGTGCAA	GTCTTCCGCC	CAGATCGATC	CCACCCCCGT	GATCGTCACT
42_6b	ATGACTTTGG	CAAGGTGACA	AAGCAGGAAG	TCAAAGAGTT	CTTCCGCTGG
43_1	AAAAGTGCAA	GTCGTCCGCC	CAGATCGACC	CCACCCCCGT	GATCGTCACC
43_5	AAAAGTGCAA	GTCGTCCGCC	CAGATCGACC	CCACCCCCGT	GATCGTCACC
43_12	AAAAGTGCAA	GTCGTCCGCC	CAGATCGACC	CCACCCCCGT	GATCGTCACC
43_20	AAAAGTGCAA	GTCTTCCGCC	CAGATCGATC	CCACCCCCGT	GATCGTCACC
43_21	AAAAGTGCAA	GTCTTCCGCC	CAGATCGATC	CCACCCCCGT	GATCGTCACC
43_23	AAAAGTGCAA	GTCTTCCGCC	CAGATCGATC	CCACCCCCGT	GATCGTCACC
43_25	AAAAGTGCAA	GTCTTCCGCC	CAGATCGATC	CCACCCCCGT	GATCGTCACC
44_1	AAAAGTGCAA	GCCGTCCGCC	CAGATCGACC	CCACCCCCGT	GATCGTCACC
44_5	AAAAGTGCAA	GTCGTCCGCC	CAGATCGACC	CCACCCCCGT	GATCGTCACC
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4	AGAAATGCAA	GTCTTCGGCC	CAGATCGACC	CGACTCCGGT	GATTGTCACC
A3_5	AGAAATGCAA	GTCTTCGGCC	CAGATCGACC	CGACTCCGGT	GATTGTCACC
A3_7	AGAAATGCAG	GTCTTCGGCC	CAGATCGACC	CGACTCCGGT	GATTGTCACC
A3_3	AGAAATGCAA	GTCTTCGGCC	CAGATCGACC	CGACTCCGGT	GATTGTCACC
42_12	AAAAGTGCAA	GTCGTCCGCC	CAGATCGACC	CCACCCCCGT	GATCGTCACC
AAV1	AAAAGTGCAA	GTCGTCCGCC	CAGATCGACC	CCACCCCCGT	GATCGTCACC
AAV2	AGAAATGCAA	GTCCTCGGCC	CAGATAGACC	CGACTCCCGT	GATCGTCACC
AAV3	AAAAGTGCAA	GTCATCGGCC	CAGATCGAAC	CCACTCCCGT	GATCGTCACC
AAV8	AAAAGTGCAA	GTCGTCCGCC	CAGATCGACC	CCACCCCCGT	GATCGTCACC
AAV9	AAAAGTGCAA	GTCGTCCGCC	CAGATCGACC	CCACTCCCGT	GATCGTCACC
AAV7	AAAAGTGCAA	GTCGTCCGCC	CAGATCGACC	CCACCCCCGT	GATCGTCACC
44_2	AAAAGTGCAA	GTCGTCCGCC	CAGATCGACC	CCACCCCCGT	GATCGTCACC

Fig. 1AG

	1601				1650
42_2	TCCAACACCA	ACATGTGCGC	TGTGATTGAC	GGGAACAGCA	CCACCTTCGA
42_8	TCCAACACCA	ACATGTGCGC	CGTGATTGAC	GGGAACAGCA	CCACCTTCGA
42_15	TCCAACACCA	ACATGTGCGC	CGTGATTGAC	GGGAACAGCA	CCACCTTCGA
42_5b	TCCAACACCA	ACATGTGCGC	CGTGATTGAC	GGGAACAGCA	CCACCTTCGA
42_1b					
42_13	TCCAACACCA	ACATGTGCGC	CGTGATTGAC	GGGAACAGCA	CCACCTTCGA
42_3a	TCCAACACCA	ACATGTGCGC	CGTGATTGAC	GGGAACAGCA	CCACCTTCGA
42_4					
42_5a	TCCAACACCA	ACATGTGCGC	CGTGATTGAC	GGGAACAGCA	CCACCTTCGA
42_10					
42_3b					
42_11	TCCAACACCA	ACATGTGCGC	CGTGATTGAC	GGGAACAGCA	CCACCTTCGA
42_6b	GCGCAGGATC	ACGTGACCGA	GGTGGCGCAT	GAGTTCTACG	TCAGAAAGGG
43_1	TCCAACACCA	ACATGTGCGC	CGTGATTGAC	GGGAACAGCA	CCACCTTCGA
43_5	TCCAACACCA	ACATGTGCGC	CGTGATTGAC	GGGAACAGCA	CCACCTTCGA
43_12	TCCAACACCA	ACATGTGCGC	CGTGATTGAC	GGGAACAGCA	CCACCTTCGA
43_20	TCCAACACCA	ACATGTGCGC	CGTGATTGAC	GGGAACAGCG	CCACCTTCGA
43_21	TCCAACACCA	ACATGTGCGC	CGTGATTGAC	GGGAACAGCA	CCACCTTCGA
43_23	TCCAACACCA	ACATGTGCGC	CGTGATTGAC	GGGAACAGCA	CCACCTTCGA
43_25	TCCAACACCA	ACATGTGCGC	CGTGATTGAC	GGGAACAGCA	CCACCTTCGA
44_1	TCCAACACCA	ACATGTGCGC	CGTGATTGAC	GGGAACAGCA	CCACCTTCGA
44_5	TCCAACACCA	ACATGTGCGC	CGTGATTGAC	GGGAACAGCA	CCACCTTCGA
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4	TCTAACACCA	ACATGTGCGC	CGTGATTGAC	GGAAACTCGA	CCACCTTCGA
A3_5	TCTAACACCA	ACATGTGCGC	CGTGATTGAC	GGAAACTCGA	CCACCTTCGA
A3_7	TCTAACACCA	ACATGTGCGC	CGTGATTGAC	GGAAACTCGA	CCACCTTCGA
A3_3	TCTAACACCA	ACATGTGCGC	CGTGATTGAC	GGAAACTCGA	CCACCTTCGA
42_12	TCCAACACCA	ACATGTGCGC	CGTGATTGAC	GGGAACAGCA	CCACCTTCGA
AAV1	TCCAACACCA	ACATGTGCGC	CGTGATTGAC	GGGAACAGCA	CCACCTTCGA
AAV2	TCCAACACCA	ACATGTGCGC	CGTGATTGAC	GGGAACAGCA	CCACCTTCGA
AAV3	TCCAACACCA	ACATGTGCGC	CGTGATTGAC	GGGAACAGCA	CCACCTTCGA
AAV8	TCCAACACCA	ACATGTGCGC	CGTGATTGAC	GGGAACAGCA	CCACCTTCGA
AAV9	TCCAACACCA	ACATGTGCGC	CGTGATTGAC	GGGAACAGCA	CCACCTTCGA
AAV7	TCCAACACCA	ACATGTGCGC	CGTGATTGAC	GGGAACAGCA	CCACCTTCGA
44_2	TCCAACACCA	ACATGTGCGC	CGTGATTGAC	GGGAACAGCA	CCACCTTCGA

Fig. 1AH

	1651				1700
42_2	GCACCAGCAG	CCGTTACAAG	ACCGGATGTT	CAAATTTGAA	CTCACCCGCC
42_8	GCACCAGCAG	CCGTTACAAG	ACCGGATGTT	CAAATTTGAA	CTCACCCGCC
42_15	GCACCAGCAG	CCGTTGCAGG	ACCGGATGTT	CAAATTTGAA	CTCACCCGCC
42_5b	GCACCAGCAG	CCGTTACAAG	ACCGGATGTT	CAAATTTGAA	CTCACCCGCC
42_1b					
42_13	GCACCAGCAG	CCGTTACAAG	ACCGGATGTT	CAAATTTGAA	CTCACCCGCC
42_3a	GCACCAGCAG	CCGTTACAAG	ACCGGATGTT	CAAATTTGAA	CTCACCCGCC
42_4					
42_5a	GCACCAGCAG	CCGTTGCAGG	ACCGGATGTT	CAAATTTGAA	CTCACCCGCC
42_10					
42_3b					
42_11	GCACCAGCAG	CCGTTACAAG	ACCGGATGTT	CAAATTTGAA	CTCACCCGCC
42_6b	TGGAGCCAAC	AAGAGACCCG	CCCCCGATGA	CGCGGATAAA	AGCGAGCCCA
43_1	GCACCAGCAG	CCGTTGCAGG	ACCGGATGTT	CAAGTTCGAA	CTCACCCGCC
43_5	GCACCAGCAG	CCGTTGCAGG	ACCGGATGTT	CAAGTTCGAA	CTCACCCGCC
43_12	GCACCAGCAG	CCGTTGCAGG	ACCGGATGTT	CAAGTTCGAA	CTCACCCGCC
43_20	GCACCAGCAG	CCGTTGCAGG	ACCGGATGTT	CAAATTTGAA	CTCACCCGCC
43_21	GCACCAGCAG	CCGTTGCAGG	ACCGGATGTT	CAAATTTGAA	CTCACCCGCC
43_23	GCACCAGCAG	CCGTTGCAGG	ACCGGATGTT	CAAATTTGAA	CTCACCCGCC
43_25	GCACCAGCAG	CCGTTGCAGG	ACCGGATGTT	CAAATTTGAA	CTCACCCGCC
44_1	GCACCAGCAG	CCGTTGCGGG	ACCGGATGTT	CAAGTTTGAA	CTCACCCGCC
44_5	GCACCAGCAG	CCGTTGCAGG	ACCGGATGTT	CAAGTTTGAA	CTCACCCGCC
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4	GCACCAGCAG	CCGTTGCAAG	ACCGGATGTT	CAAATTTGAA	CTTACCCGCC
A3_5	GCACCAGCAG	CCGTTGCAAG	ACCGGATGTT	CAAATTTGAA	CTTACCCGCC
A3_7	GCACCAGCAG	CCGTTGCAAG	ACCGGATGTT	CAAATTTGAA	CTTACCCGCC
A3_3	GCACCAGCAG	CCGTTGCAAG	ACCGGATGTT	CAAATTTGAA	CTTACCCGCC
42_12	GCACCAGCAG	CCGTTACAAG	ACCGGATGTT	CAAATTTGAA	CTCACCCGCC
AAV1	GCACCAGCAG	CCGTTGCAGG	ACCGGATGTT	CAAATTTGAA	CTCACCCGCC
AAV2	ACACCAGCAG	CCGTTGCAAG	ACCGGATGTT	CAAATTTGAA	CTCACCCGCC
AAV3	GCATCAGCAG	CCGCTGCAGG	ACCGGATGTT	TGAATTTGAA	CTTACCCGCC
AAV8	GCACCAGCAG	CCTCTCCAGG	ACCGGATGTT	TAAGTTCGAA	CTCACCCGCC
AAV9	GCACCAGCAG	CCTCTCCAGG	ACCGGATGTT	TAAGTTCGAA	CTCACCCGCC
AAV7	GCACCAGCAG	CCGTTGCAGG	ACCGGATGTT	CAAATTTGAA	CTCACCCGCC
44_2	GCACCAGCAG	CCGTTGCAGG	ACCGGATGTT	CAAGTTTGAA	CTCACCCGCC

Fig. 1AI

	1701				1750
42_2	GTCTGGAGCA	CGACTTTGGC	AAGGTGACAA	AGCAGGAAGT	CAAAGAGTTC
42_8	GTCTGGAGCA	CGACTTTGGC	AAGGTGACAA	AGCAGGAAGT	CAAAGAGTTC
42_15	GTCTGGAGCA	TGACTTTGGC	AAGGTGACAA	AGCAGGAAGT	CAAAGAGTTC
42_5b	GTCTGGAGCA	CGACTTTGGC	AAGGTGACAA	AGCAGGAAGT	CAAAGAGTTC
42_1b					
42_13	GTCTGGAGCA	TGACTTTGGC	AAGGTGACAA	AGCAGGAAGT	CAAAGAGTTC
42_3a	GTCTGGAGCA	TGACTTTGGC	AAGGTGACAA	AGCAGGAAGT	CAAAGAGTTC
42_4					
42_5a	GTCTGGAGCA	TGACTTTGGC	AAGGCGACAA	AGCAGGAAGT	CAAAGAGTTC
42_10					
42_3b					
42_11	GTCTGGAGCA	CGACTTTGGC	AAGGTGACAA	AGCAGGAAGT	CAAAGAGTTC
42_6b	AGCGGGCCTG	CCCCTCAGTC	GCGGATCCAT	CGACGTCAGA	CGCGGAAGGA
43_1	GTCTGGAGCA	CGACTTTGGC	AAGGTGACCA	AGCAGGAAGT	CAAAGAGTTC
43_5	GTCTGGAGCA	CGACTTTGGC	AAGGTGACCA	AGCAGGAAGT	CAAAGAGTTC
43_12	GTCTGGAGCA	CGACTTTGGC	AAGGTGACCA	AGCAGGAAGT	CAAAGAGTTC
43_20	GTCTGGAGCA	TGACTTTGGC	AAGGTGACGA	AGCAGGAAGT	CAAAGAGTTC
43_21	GTCTGGAGCA	TGACTTTGGC	AAGGTGACGA	AGCAGGAAGT	CAAAGAGTTC
43_23	GTCTGGAGCA	TGACTTTGGC	AAGGTGACGA	AGCAGGAAGT	CAAAGAGTTC
43_25	GTCTGGAGCA	TGACTTTGGC	AAGGTGACGA	AGCAGGAAGT	CAAAGGGTTC
44_1	GTCTGGAGCA	CGACTTTGGC	AAGGTGACAA	AGCAGGAAGT	CAGAGAGTTC
44_5	GTCTGGAGCA	CGACTTTGGC	AAGGTGACAA	AGCAGGAAGT	CAGAGAGTTC
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4	GTTTGGATCA	TGACTTTGGG	AAGGTCACCA	AGCAGGAAGT	CAAAGACTTT
A3_5	GTTTGGATCA	TGACTTTGGG	AAGGTCACCA	AGCAGGAAGT	CAAAGACTTT
A3_7	GTTTGGATCA	TGACTTTGGG	AAGGTCACCA	AGCAGGAAGT	CAAAGACTTT
A3_3	GTTTGGATCA	TGACTTTGGG	AAGGTCACCA	AGCAGGAAGT	CAAAGACTTT
42_12	GTCTGGAGCA	CGACTTTGGC	AAGGTGACAA	AGCAGGAAGT	CAAAGAGTTC
AAV1	GTCTGGAGCA	TGACTTTGGC	AAGGTGACAA	AGCAGGAAGT	CAAAGAGTTC
AAV2	GTCTGGATCA	TGACTTTGGG	AAGGTCACCA	AGCAGGAAGT	CAAAGACTTT
AAV3	GTTTGGACCA	TGACTTTGGG	AAGGTCACCA	AACAGGAAGT	AAAGGACTTT
AAV8	GTCTGGAGCA	CGACTTTGGC	AAGGTGACAA	AGCAGGAAGT	CAAAGAGTTC
AAV9	GTCTGGAGCA	CGACTTTGGC	AAGGTGACAA	AGCAGGAAGT	CAAAGAGTTC
AAV7	GTCTGGAGCA	CGACTTTGGC	AAGGTGACGA	AGCAGGAAGT	CAAAGAGTTC
44_2	GTCTGGAGCA	CGACTTTGGC	AAGGTGACAA	AGCAGGAAGT	CAGAGAGTTC

Fig. 1AJ

	1751				1800
42_2	TTCCGCTGGG	CGCAGGATCA	CGTGACCGAG	GTGGCGCATG	AGTTCTACGT
42_8	TTCCGCTGGG	CGCAGGATCA	CGTGACCGAG	GTGGCGCATG	AGTTCTACGT
42_15	TTCCGCTGGG	CGCAGGATCA	CGTGACCGAG	GTGGCGCATG	AGTTCTACGT
42_5b	TTCCGCTGGG	CGCAGGATCA	CGTGACCGAG	GTGGCGCATG	AGTTCTACGT
42_1b					
42_13	TTCCGCTGGG	CGCAGGATCA	CGTGACCGAG	GTGGCGCATG	AGTTCTACGT
42_3a	TTCCGCTGGG	CGCAGGATCA	CGTGACCGAG	GTGGCGCATG	AGTTCTACGT
42_4					
42_5a	TTCCGCTGGG	CGCAGGATCA	CGTGACCGAG	GTGGCGCATG	AGTTCTACGT
42_10					
42_3b					
42_11	TTCCGCTGGG	CGCAGGATCA	CGTGACCGAG	GTGGCGCATG	AGTTCTACGT
42_6b	GCTCCGGTGG	ACTTTGCCGA	CAGGTACCAA	AACAAATGTT	CTCGTCACGC
43_1	TTCCGCTGGG	CGCAGGATCA	CGTGACCGAG	GTGGCGCATG	AGTTCTACGT
43_5	TTCCGCTGGG	CGCAGGATCA	CGTGACCGAG	GTGGCGCATG	AGTTCTACGT
43_12	TTCCGCTGGG	CGCAGGATCA	CGTGACCGAG	GTGGCGCATG	AGTTCTACGT
43_20	TTCCGCTGGG	CGCAGGATCA	CGTGACCGAG	GTGGCGCATG	AGTTCCACGT
43_21	TTCCGCTGGG	CGCAGGATCA	CGTGACCGAG	GTGGCGCATG	AGTTCCACGT
43_23	TTCCGCTGGG	CGCAGGATCA	CGTGACCGAG	GTGGCGCATG	AGTTCCACGT
43_25	TTCCGCTGGG	CGCAGGATCA	CGTGACCGAG	GTGGCGCATG	AGTTCCACGT
44_1	TTCCGCTGGG	CGCAGGATCA	CGTGACCGAG	GTGGCGCACG	AGTTCTACGT
44_5	TTCCGCTGGG	CGCAGGATCA	CGTGACCGAG	GTGGCGCACG	AGTTCTACGT
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4	TTCCGGTGGG	CTCAAGATCA	CGTGACTGAG	GTGGAGCATG	AGTTCTACGT
A3_5	TTCCGGTGGG	CTCAAGATCA	CGTGACTGAG	GTGGAGCATG	AGTTCTACGT
A3_7	TTCCGGTGGG	CTCAAGATCA	CGTGACTGAG	GTGGAGCATG	AGTTCTACGT
A3_3	TTCCGGTGGG	CTCAAGATCA	CGTGACTGAG	GTGGAGCATG	AGTTCTACGT
42_12	TTCCGCTGGG	CGCAGGATCA	CGTGACCGAG	GTGGCGCATG	AGTTCTACGT
AAV1	TTCCGCTGGG	CGCAGGATCA	CGTGACCGAG	GTGGCGCATG	AGTTCTACGT
AAV2	TTCCGGTGGG	CAAAGGATCA	CGTGGTTGAG	GTGGAGCATG	AATTCTACGT
AAV3	TTCCGGTGGG	CTTCCGATCA	CGTGACTGAC	GTGGCTCATG	AGTTCTACGT
AAV8	TTCCGCTGGG	CCAGTGATCA	CGTGACCGAG	GTGGCGCATG	AGTTTACGT
AAV9	TTCCGCTGGG	CCAGTGATCA	CGTGACCGAG	GTGGCGCATG	AGTTTACGT
AAV7	TTCCGCTGGG	CCAGTGATCA	CGTGACCGAG	GTGGCGCATG	AGTTCTACGT
44_2	TTCCGCTGGG	CGCAGGATCA	CGTGACCGAG	GTGGCGCACG	AGTTCTACGT

Fig. 1AK

	1801					1850
						P40/TATA
42_2	CAGAAAGGGT	GGAGCCAACA	AGAGACCCGC	CCCCGATGAC	GCGGATAAAA	
42_8	CAGAAAGGGT	GGAGCCAACA	AGAGACCCGC	CCCCGATGAC	GCGGATAAAA	
42_15	CAGAAAGGGT	GGAGCCAACA	AGAGACCCGC	CCCCGATGAC	GCGGATAAAA	
42_5b	CAGAAAGGGT	GGAGCCAACA	AGAGACCCGC	CCCCGATGAC	GCGGATAAAA	
42_1b						
42_13	CAGAAAGGGT	GGAGCCAACA	AGAGACCCGC	CCCCGATGAC	GCGGATAAAA	
42_3a	CAGAAAGGGT	GGAGCCAACA	AGAGACCCGC	CCCCGATGAC	GCGGATAAAA	
42_4						
42_5a	CAGAAAGGGT	GGAGCCAACA	AGAGACCCGC	CCCCGATGAC	GCGGATAAAA	
42_10						
42_3b						
42_11	CAGAAAGGGT	GGAGCCAACA	AGAGACCCGC	CCCCGATGAC	GCGGATAAAA	
42_6b	GGGCATAGCG	CTGACGTAAA	TCACGTCATA	GGGGAGTGGT	CCTGTATTAG	
43_1	CAGAAAGGGC	GGAGCCAGCA	AAAGACCCGC	CCCCGATGAC	GCGGATATAA	
43_5	CAGAAAGGGC	GGAGCCAGCA	AAAGACCCGC	CCCCGATGAC	GCGGATATAA	
43_12	CAGAAAGGGC	GGAGCCAGCA	AAAGACCCGC	CCCCGATGAC	GCGGATATAA	
43_20	CAGAAAGGGT	GGAGCCAACA	AGAGACCCGC	CCCCGATGAC	GCGGATATAA	
43_21	CAGAAAGGGT	GGAGCCAACA	AGAGACCCGC	CCCCGATGAC	GCGGATATAA	
43_23	CAGAAAGGGT	GGCGCCAACA	AGAGACCCGC	CCCCGATGAC	GCGGATATAA	
43_25	CAGAAAGGGT	GGAGCCAACA	AGAGACCCGC	CCCCGATGAC	GCGGATATAA	
44_1	CAGAAAGGGT	GGAGCCAACA	AGAGACCCGC	CCCCGATGAC	GCGGATAAAA	
44_5	CAGAAAGGGT	GGAGCCAACA	AGAGACCCGC	CCCCGATGAC	GCGGATAAAA	
223_10						
223_2						
223_4						
223_5						
223_6						
223_7						
A3_4	CAAAAAGGGT	GGAGCCAAGA	AAAGGCCCGC	CCCCGATGAT	GTATATATAA	
A3_5	CAAAAAGGGT	GGAGCCAAGA	AAAGGCCCGC	CCCCGATGAT	GTATATATAA	
A3_7	CAAAAAGGGT	GGAGCCAAGA	AAAGGCCCGC	CCCCGATGAT	GTATATATAA	
A3_3	CAAAAAGGGT	GGAGCCAAGA	AAAGGCCCGC	CCCCGATGAT	GTATATATAA	
42_12	CAGAAAGGGT	GGAGCCAACA	AGAGACCCGC	CCCCGATGAC	GCGGATAAAA	
AAV1	CAGAAAGGGT	GGAGCCAACA	AAAGACCCGC	CCCCGATGAC	GCGGATAAAA	
AAV2	CAAAAAGGGT	GGAGCCAAGA	AAAGACCCGC	CCCCAGTGAC	GCAGATATAA	
AAV3	CAGAAAGGGT	GGAGCTAAGA	AACGCCCCGC	CTCCAATGAC	GCGGATGTAA	
AAV8	CAGAAAGGGC	GGAGCCAGCA	AAAGACCCGC	CCCCGATGAC	GCGGATAAAA	
AAV9	CAGAAAGGGC	GGAGCCAGCA	AAAGACCCGC	CCCCGATGAC	GCGGATAAAA	
AAV7	CAGAAAGGGC	GGAGCCAGCA	AAAGACCCGC	CCCCGATGAC	GCGGATATAA	
44_2	CAGAAAGGGT	GGAGCCAACA	AGAGACCCGC	CCCCGATGAC	GCGGATAAAA	
						P40/TATA

Fig. 1AL

	1851			P40 RNA	1900
42_2	GCGAGCCCAA	GCGGGCCTGC	CCCTCAGTCG	CGGATCCATC	GACGTCAGAC
42_8	GCGAGCCCAA	GCGGGCCTGC	CCCTCAGTCG	CGGATCCATC	GACGTCAGAC
42_15	GCGAGCCCAA	GCGGGCCTGC	CCCTCAGTCG	CGGATCCATC	GACGTCAGAC
42_5b	GCGAGCCCAA	GCGGGCCTGC	CCCTCAGTCG	CGGATCCATC	GACGTCAGAC
42_1b					
42_13	GCGAGCCCAA	GCGGGCCTGC	CCCTCAGTCG	CGGATCCATC	GACGTCAGAC
42_3a	GCGAGCCCAA	GCGGGCCTGC	CCCTCAGTCG	CGGATCCATC	GACGTCAGAC
42_4					
42_5a	GCGAGCCCAA	GCGGGCCCGC	CCCTCAGTCG	CGGATCCATC	GACGTCAGAC
42_10					
42_3b					
42_11	GCGAGCCCAA	GCGGGCCTGC	CCCTCAGTCG	CGGATCCATC	GACGTCAGAC
42_6b	CTGTCACGTG	AGTGCTTTTG	CGACATTTTG	C..ATCCATC	GACGTCAGAC
43_1	GCGAGCCCAA	GCGGGCCTGC	CCCTCAGTCG	CGGATCCATC	GACGTCAGAC
43_5	GCGAGCCCAA	GCGGGCCTGC	CCCTCAGTCG	CGGATCCATC	GACGTCAGAC
43_12	GCGAGCCCAA	GCGGGCCTGC	CCCTCAGTCG	CGGATCCATC	GACGTCAGAC
43_20	GCGAGCCCAA	GCGGGCCTGC	CCCTCAGTCG	CGGATCCATC	GACGTCAGAC
43_21	GCGAGCCCAA	GCGGGCCTGC	CCCTCAGTCG	CGGATCCATC	GACGTCAGAC
43_23	GCGAGCCCAA	GCGGGCCTGC	CCCTCAGTCG	CGGATCCATC	GACGTCAGAC
43_25	GCGAGCCCAA	GCGGGCCTGC	CCCTCAGTCG	CGGATCCATC	GACGTCAGAC
44_1	GCGAGCCCAA	GCGGGCCTGC	CCCTCAGTCG	CGGATCCATC	GACGTCAGAC
44_5	GCGAGCCCAA	GCGGGCCTGC	CCCTCAGTCG	CGGATCCATC	GACGTCAGAC
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4	ATGAGCCCAA	GCGGGCGCGC	GAGTCAGTTG	CGCAGCCATC	GACGTCAGAC
A3_5	ATGAGCCCAA	GCGGGCGCGC	GAGTCAGTTG	CGCAGCCATC	GACGTCAGAC
A3_7	ATGAGCCCAA	GCGGGCGCGC	GAGTCAGTTG	CGCAGCCATC	GACGTCAGAC
A3_3	ATGAGCCCAA	GCGGGCGCGC	GAGTCAGTTG	CGCAGCCATC	GACGTCAGAC
42_12	GCGAGCCCAA	GCGGGCCTGC	CCCTCAGTCG	CGGATCCATC	GACGTCAGAC
AAV1	GCGAGCCCAA	GCGGGCCTGC	CCCTCAGTCG	CGGATCCATC	GACGTCAGAC
AAV2	GTGAGCCCAA	ACGGGTGCGC	GAGTCAGTTG	CGCAGCCATC	GACGTCAGAC
AAV3	GCGAGCCCAA	ACGGGAGTGC	ACGTCAGTTG	CGCAGCCGAC	AACGTCAGAC
AAV8	GCGAGCCCAA	GCGGGCCTGC	CCCTCAGTCG	CGGATCCATC	GACGTCAGAC
AAV9	GCGAGCCCAA	GCGGGCCTGC	CCCTCAGTCG	CGGATCCATC	GACGTCAGAC
AAV7	GCGAGCCCAA	GCGGGCCTGC	CCCTCAGTCG	CGGATCCATC	GACGTCAGAC
44_2	GCGAGCCCAA	GCGGGCCTGC	CCCTCAGTCG	CGGATCCATC	GACGTCAGAC

P40 RNA

Fig. 1AM

	1901				1950
42_2	GCGGAAGGAG	CTCCGGTGGA	CTTTGCCGAC	AGGTACCAA	ACAAATGTTC
42_8	GCGGAAGGAG	CTCCGGTGGA	CTTTGCCGAC	AGGTACCAA	ACAAATGTTC
42_15	GCGGAAGGAG	CTCCGGTGGA	CTTTGCCGAC	AGGTACCAA	ACAAATGTTC
42_5b	GCGGAAGGAG	CTCCGGTGGA	CTTTGCCGAC	AGGTACCAA	ACAAATGTTC
42_1b					
42_13	GCGGAAGGAG	CTCCGGTGGA	CTTTGCCGAC	AGGTACCAA	ACAAATGTTC
42_3a	GCGGAAGGAG	CTCCGGTGGA	CTTTGCCGAC	AGGTACCAA	ACAAATGTTC
42_4					
42_5a	GCGGAAGGAG	CTCCGGTGGA	CTTTGCCGAC	AGGTACCAA	ACAAATGTTC
42_10					
42_3b					
42_11	GCGGAAGGAG	CTCCGGTGGA	CTTTGCCGAC	AGGTACCAA	ACAAATGTTC
42_6b	GCGGAAGGAG	CTCCGGTGGA	CTTTGCCGAC	AGGTACCAA	ACAAGTGTTC
43_1	GCGGAAGGAG	CTCCGGTGGA	CTTTGCCGAC	AGGTACCAA	ACAAATGTTC
43_5	GCGGAAGGAG	CTCCGGTGGA	CTTTGCCGAC	AGGTACCAA	ACAAATGTTC
43_12	GCGGAAGGAG	CTCCGGTGGA	CTTTGCCGAC	AGGTACCAA	ACAAATGTTC
43_20	GCGGAAGGAG	CTCCGGTGGA	CTTTGCCGAC	AGGTACCAA	ACAAATGTTC
43_21	GCGGAAGGAG	CTCCGGTGGA	CTTTGCCGAC	AGGTACCAA	ACAAATGTTC
43_23	GCGGAAGGAG	CTCCGGTGGA	CTTTGCCGAC	AGGTACCAA	ACAAATGTTC
43_25	GCGGAAGGAG	CTCCGGTGGA	CTTTGCCGAC	AGGTACCAA	ACAAATGTTC
44_1	GCGGAAGGAG	CTCCGGTGGA	CTTTGCCGAC	AGGTACCAA	ACAAATGTTC
44_5	GCGGAAGGAG	CTCCGGTGGA	CTTTGCCGAC	AGGTACCAA	ACAAATGTTC
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4	GCGGA...AG	CTTCGATAAA	CTACGCGGGC	AGGTACCAA	ACAAATGTTC
A3_5	GCGGA...AG	CTTCGATAAA	CTACGCGGAC	AGGTACCAA	ACAAATGTTC
A3_7	GCGGA...AG	CTTCGATAAA	CTACGCGGAC	AGGTACCAA	ACAAATGTTC
A3_3	GCGGA...AG	CTTCGATAAA	CTACGCGGAC	AGGTACCAA	ACAAATGTTC
42_12	GCGGAAGGAG	CTCCGGTGGA	CTTTGCCGAC	AGGTACCAA	ACAAATGTTC
AAV1	GCGGAAGGAG	CTCCGGTGGA	CTTTGCCGAC	AGGTACCAA	ACAAATGTTC
AAV2	GCGGA...AG	CTTCGATCAA	CTACGCAGAC	AGGTACCAA	ACAAATGTTC
AAV3	GCGGA...AG	CACCGGCGGA	CTACGCGGAC	AGGTACCAA	ACAAATGTTC
AAV8	GCGGAAGGAG	CTCCGGTGGA	CTTTGCCGAC	AGGTACCAA	ACAAATGTTC
AAV9	GCGGAAGGAG	CTCCGGTGGA	CTTTGCCGAC	AGGTACCAA	ACAAATGTTC
AAV7	GCGGAAGGAG	CTCCGGTGGA	CTTTGCCGAC	AGGTACCAA	ACAAATGTTC
44_2	GCGGAAGGAG	CTCCGGTGGA	CTTTGCCGAC	AGGTACCAA	ACAAATGTTC

Fig. 1AN

	1951				2000
42_2	TCGTCACGCG	GGCATGCTTC	AGATGCTGTT	TCCCTG.CAA	GACATGCGAG
42_8	TCGTCACGCG	GGCATGCTTC	AGATGCTGTT	TCCCTG.CAA	GACATGCGAG
42_15	TCGTCACGCG	GGCATGCTTC	AGATGCTGTT	TCCCTG.CAA	GACATGCGAG
42_5b	TCGTCACGCG	GGCATGCTTC	AGATGCTGTT	TCCCTG.CAA	GACATGCGAG
42_1b			GAATTC	GCCCTT....	.GGCTGCGTC
42_13	TCGTCACGCG	GGCATGCTTC	AGATGCTGTT	TCCCTG.CAA	GACATGCGAG
42_3a	TCGTCACGCG	GGCATGCTTC	AGATGCTGCT	TCCCTG.CAA	GACATGCGAG
42_4			GAATTC	GCCCTTTCTA	CGGCTGCGTC
42_5a	TCGTCACGCG	GGCATGCTTC	AGATGCTGTT	TCCCTG.CAA	AACATGCGAG
42_10			GAATTC	GCCCTTTCTA	CGGCTGCGTC
42_3b			GAATTC	GCCCTTTCTA	CGGCTGCGTC
42_11	TCGTCACGCG	GGCATGCTTC	AGATGCTGTT	TCCCTG.CAA	GACATGCGAG
42_6b	TCGTCACGCG	GGCATGCTTC	AGATGCTGTT	TCCCTG.CAA	GACATGCGAG
43_1	TCGTCACGCG	GGCATGCTTC	AGATGCTGTT	TCCCTG.CAA	AACGTGCGAG
43_5	TCGTCACGCG	GGCATGCTTC	AGACGCTGTT	TCCCTG.CAA	AACGTGCGAG
43_12	TCGTCACGCG	GGCATGCTCC	AGATGCTGTT	TCCCTG.CAA	AACGTGCGAG
43_20	TCGTCACGCG	GGCATGCTTC	AGATGCTGTT	TCCCTG.CAA	GACATGCGAG
43_21	TCGTCACGCG	GGCATGCTTC	AGATGCTGTT	TCCCTG.CAA	GACATGCGAG
43_23	TCGTCACGCG	GGCATGCTTC	AGATGCTGTT	TCCCTG.CAA	GACATGCGAG
43_25	TCGTCACGCG	GGCATGCTTC	AGATGCTGTT	TCCCTG.CAA	GACATGCGAG
44_1	TCGTCACGCG	GGCATGCTTC	AGATGCTGTT	TCCCTG.CAA	AACATGCGAG
44_5	TCGTCACGCG	GGCATGCTTC	AGATGCTGTT	TCCCTG.CAA	AACATGCGAG
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4	TCGTCACGTG	GGCATGAATC	TGATGCTGTT	TCCCTG.TCG	ACAATGCGAA
A3_5	TCGTCACGTG	GGCATGAATC	TGATGCTGTT	TCCCTG.TCG	ACAATGCGAA
A3_7	TCGTCACGTG	GGCATGAATC	TGATGCTGTT	TCCCTG.TCG	ACAATGCGAA
A3_3	TCGTCACGTG	GGCATGAATC	TGATGCTGTT	TCCCTG.TCG	ACAATGCGAA
42_12	TCGTCACGCG	GGCATGCTTC	AGATGCTGTT	TCCCTG.CAA	GACATGCGAG
AAV1	TCGTCACGCG	GGCATGCTTC	AGATGCTGTT	TCCCTG.CAA	GACATGCGAG
AAV2	TCGTCACGTG	GGCATGAATC	TGATGCTGTT	TCCCTG.CAG	ACAATGCGAG
AAV3	TCGTCACGTG	GGCATGAATC	TGATGCTTTT	TCCCTG.TAA	AACATGCGAG
AAV8	TCGTCACGCG	GGCATGCTTC	AGATGCTGTT	TCCCTG.CAA	AACGTGCGAG
AAV9	TCGTCACGCG	GGCATGCTTC	AGATGCTGCT	TCCCTG.CAA	AACGTGCGAG
AAV7	TCGTCACGCG	GGCATGATTC	AGATGCTGTT	TCCCTG.CAA	AACGTGCGAG
44_2	TCGTCACGCG	GGCATGCTTC	AGATGCTGTT	TCCCTG.CAA	AACATGCGAG

Fig. 1AO

	2001				2050
42_2	AGAATGAATC	AGAATTTCAA	CATTTGCTTC	ACGCACGGGA	CCAGAGACTG
42_8	AGAATGAATC	AGAATTTCAA	CATTTGCTTC	ACGCACGGGA	CCAGAGACTG
42_15	AGAATGAATC	AGAATTTCAA	CATTTGCTTC	ACGCGCGGGA	CCAGAGACTG
42_5b	AGAATGAATC	AGAATTTCAA	CATTTGCTTC	ACGCACGGGA	CCAGAGACTG
42_1b	A.ACTGGACC	A..ATGAGAA	CTTTCCCTTC	A.....A	CGATTGCGTC
42_13	AGAATGAATC	AGAATTTCAA	CATTTGCTTC	ACGCACGGGA	CCAGAGACTG
42_3a	AGAATGAATC	AGAATTTTCA	CATTTGCTTC	ACGCACGGGA	CCAGAGACTG
42_4	A.ACTGGACC	A..ATGAGAA	CTTTCCCTTC	A.....A	CGATTGCGTC
42_5a	AGAATGAATC	AGAATTTCAA	CATTTGCTTC	ACGCACGGGA	CCAGAGACTG
42_10	A.ACTGGACC	A..ATGAGAA	CTTTCCCTTC	A.....A	CGATTGCGTC
42_3b	A.ACTAGACC	A..ATGAGAA	CTTTCCCTTC	A.....A	CGATTGCGTC
42_11	AGAATGAATC	AGAATTTCAA	CATTTGCTTC	ACGCACGGGA	CCGGAGACTG
42_6b	AGAATGAATC	AGAATTTCAA	CATTTGCTTC	ACGCACGGGA	CCAGAGACTG
43_1	AAAATGAATC	AGAATTTCAA	CATTTGCTTC	ACGCACGGGG	TCAGAGACTG
43_5	AGAATGAATC	AGAATTTCAA	CATTTGCTTC	ACGCACGGGG	TCAGAGACTG
43_12	AGAATGAATC	AGAATTTCAA	CATTTGCTTC	ACGCACGGGG	TCAGAGACTG
43_20	AGAATGAATC	AGAATTTCAA	CATTTGCTTC	ACGCACGGGA	CCAGAGACTG
43_21	AGAATGAATC	AGAATTTCAA	CATTTGCTTC	ACGCACGGGA	CCAGAGACTG
43_23	AGAATGAATC	AGAATTTCAA	CATTTGCTTC	ACGCACGGGA	CCAGAGACTG
43_25	AGAATGAATC	AGAATTTCAA	CATTTGCTTC	ACGCACGGGA	CCAGAGACTG
44_1	AGAATGAATC	AGAATTTCAA	CATTTGCTTC	ACGCACGGGA	CCAGAGACTG
44_5	AGAATGAATC	AGAATTTCAA	CATTTGCTTC	ACGCACGGGA	CCAGAGACTG
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4	AGAATGAATC	AGAATTCAAA	TATCTGCTTC	ACACACGGGC	AAAAAGACTG
A3_5	AGAATGAATC	AGAATTCAAA	TATCTGCTTC	ACACACGGGC	AAAAAGACTG
A3_7	AGAATGAATC	AGAATTCAAA	TATCTGCTTC	ACACACGGGC	AAAAAGACTG
A3_3	AGAATGAATC	AGAATTCAAA	TATCTGCTTC	ACACACGGGC	AAAAAGACTG
42_12	AGAATGAATC	AGAATTTCAA	CATTTGCTTC	ACGCACGGGA	CCAGAGACTG
AAV1	AGAATGAATC	AGAATTTCAA	CATTTGCTTC	ACGCACGGGA	CGAGAGACTG
AAV2	AGAATGAATC	AGAATTCAAA	TATCTGCTTC	ACTCACGGAC	AGAAAGACTG
AAV3	AGAATGAATC	AAATTTCCAA	TGTCTGTTTT	ACGCATGGTC	AAAGAGACTG
AAV8	AGAATGAATC	AGAATTTCAA	CATTTGCTTC	ACACACGGGG	TCAGAGACTG
AAV9	AGAATGAATC	AGAATTTCAA	CATTTGCTTC	ACACACGGGG	TCAGAGACTG
AAV7	AGAATGAATC	AGAATTTCAA	CATTTGCTTC	ACACACGGGG	TCAGAGACTG
44_2	AGAATGAATC	AGAATTTCAA	CATTTGCTTC	ACGCACGGGA	CCAGAGACTG

Fig. 1AP

	2051				2100
42_2	TTCAGAATGT	TTCCCCGGCG	TGTCAGAATC	TCAACC....	..GGTCGTCA
42_8	TTCAGAATGT	TTCCCCGGCG	TGTCAGAATC	TCAACC....	..GGTCGTCA
42_15	TTCAGAATGT	TTCCCCGGCG	TGTCAGAATC	TCAACC....	..GGTCGTCA
42_5b	TTCAGAATGT	TTCCCCGGCG	TGTCAGAATC	TCAACC....	..GGTCGTCA
42_1b	GACAAGATGG	TGATCTGGTG	GG..AGGAGG	GCAAGA....	..TGACGGCC
42_13	TTCAGAATGT	TTCCCCGGCG	TGTCAGAATC	TCAACC....	..GGTCGTCA
42_3a	TTCAGAATGT	TTCCCCGGCG	TGTCAGAATC	TCAACC....	..GGTCGTCA
42_4	GACAAGATGG	TGATCTGGTG	GG..AGGAGG	GCAAGA....	..TGACGGCC
42_5a	TTCAGAATGT	TTCCCCGGCG	TGTCAGAATC	TCAACC....	..GGTCGTCA
42_10	GACAAGATGG	TGATCTGGTG	GG..AGGAGG	GCAAGA....	..TGACGGCC
42_3b	GACAAGATGG	TGATCTGGTG	GG..AGGAGG	GCAAGA....	..TGACGGCC
42_11	TTCAGAATGT	TTCCCCGGCG	TGTCAGAATC	TCAACC....	..GGTCGTCA
42_6b	TTCAGAATGT	TTCCCCGGCG	TGTCAGAATC	TCAACC....	..GGTCGTCA
43_1	CTCAGAATGT	TTCCCCGGTG	CATCAGAATC	TCAACC....	..GGTCGTCA
43_5	CTCAGAATGT	TTCCCCGGTG	CATCAGAATC	TCAACC....	..GGTCGTCA
43_12	CTCAGAATGT	TTCCCCGGTG	CATCAGAATC	TCAACC....	..GGTCGTCA
43_20	TTCAGAATGT	TTCCCCGGCG	TGTCAGAATC	TCAACC....	..GGTCGTCA
43_21	TTCAGAATGT	TTCCCCGGCG	TGTCAGAATC	TCAACC....	..GGTCGTCA
43_23	TTCAGAATGT	TTCCCCGGCG	TGTCAGAATC	TCAACC....	..GGTCGTCA
43_25	TTCAGAATGT	TTCCCCGGCG	TGTCAGAATC	TCAACC....	..GGTCGTCA
44_1	TTCAGAATGT	TTCCCCGGCG	TGTCAGAATC	TCAACC....	..GGTCGTCA
44_5	TTCAGAATGT	TTCCCCGGCG	TGTCAGAATC	TCAACC....	..GGTTGTCA
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4	TTTGGGAATGC	TTTCCCG...	TGTCAGAATC	TCAACCCGTT	TCTGTTCGTCA
A3_5	TTTGGGAATGC	TTTCCCG...	TGTCAGAATC	TCAACCCGTT	CCTGTTCGTCA
A3_7	TTTGGGAATGC	TTTCCCG...	TGTCAGAATC	TCAACCCGTT	TCTGTTCGTCA
A3_3	TTTGGGAATGC	TTTCCCG...	TGTCAGAATC	TCAACCCGTT	TCTGTTCGTCA
42_12	TTCAGAATGT	TTCCCCGGCG	TGTCAGAATC	TCAACC....	..GGTCGTCA
AAV1	TTCAGAGTGC	TTCCCCGGCG	TGTCAGAATC	TCAACC....	..GGTCGTCA
AAV2	TTTAGAGTGC	TTTCCCG...	TGTCAGAATC	TCAACCCGTT	TCTGTTCGTCA
AAV3	TGGGGAATGC	TTCCCTGGAA	TGTCAGAATC	TCAACCCGTT	TCTGTTCGTCA
AAV8	CTCAGAGTGT	TTCCCCGGCG	TGTCAGAATC	TCAACC....	..GGTCGTCA
AAV9	CTCAGAGTGT	TTCCCCGGCG	TGTCAGAATC	TCAACC....	..GGTCGTCA
AAV7	TTTAGAGTGT	TTCCCCGGCG	TGTCAGAATC	TCAACC....	..GGTCGTCA
44_2	TTCAGAATGT	TTCCCCGGCG	TGTCAGAATC	TCAACC....	..GGTCGTCA

Fig. 1AQ

	2101				2150
42_2	GAAAGAGGAC	GTATCGGAAA	CTCTGTGCCA	TTCATCATCT	GCTGGGG.CG
42_8	GAAAGAGGAC	GTATCGGAAA	CTCTGTGCCA	TTCATCATCT	GCTAGGG.CG
42_15	GAAAGAGGAC	GTATCGGAAA	CTCTGTGCCA	TTCATCATCT	GCTGGGG.CG
42_5b	GAAAGAGGAC	GTATCGGAAA	CTCTGTGCCA	TTCATCATCT	GCTGGGG.CG
42_1b	.AAGGTCGTG	GAGTCCGCCA	AG....GCCA	TTCATCATCT	GCTGGGG.CG
42_13	GAAAGAGGAC	GTATCGGAAA	CTCTGTGCCA	TTCATCATCT	GCTGGGG.CG
42_3a	GAAAGAGGAC	GTATCGGAAA	CTCTGTGCCA	TTCATCATCT	GCTGGGG.CG
42_4	.AAGGTCGTG	GAGTCCGCCA	AG....GCCA	TTCATCATCT	GCTGGGG.CG
42_5a	GAAAGAGGAC	GTATCGGAAA	CTCTGTGCCA	TTCATCATCT	GCTGGGG.CG
42_10	AA....GGTC	GTGAAGTCCG	CCAAG.GCCA	TTCATCATCT	GCTGGGG.CG
42_3b	AA....GGTC	GTGGAGTCCG	CCAAG.GCCA	TTCATCATCT	GCTGGGG.CG
42_11	GAAAGAGGAC	GTATCGGAAA	CTCTGTGCCA	TTCATCATCT	GCTGGGG.CG
42_6b	GAAAGAGGAC	GTATCGGAAA	CTCTGTGCCA	TTCATCATCT	GCTGGGG.CG
43_1	GAAAAAAAC	GTATCAGAAA	CTGTGTGCCA	TTCATCATCT	GCTGGGG.CG
43_5	GAAAAAAAC	GTATCAGAAA	CTGTGTGCCA	TTCATCATCT	GCTGGGG.CG
43_12	GAAAAAAAC	GTATCAGAAA	CTGTGTGCCA	TTCATCATCT	GCTGGGG.CG
43_20	GAAAGAGGAC	GTATCGGAAA	CTCTGTGCCA	TTCATCATCT	GCTGGGG.CG
43_21	GAAAGAGGAC	GTATCGGAAA	CTCTGTGCCA	TTCATCATCT	GCTGGGG.CG
43_23	GAAAGAGGAC	GTATCGGAAA	CTCTGTGCCA	TTCATCATCT	GCTGGGG.CG
43_25	GAAAGAGGAC	GTATCGGAAA	CTCTGTGCCA	TTCATCATCT	GCTGGGG.CG
44_1	GAAAAAAGAC	GTATCGGAAA	CTCTGTGCCA	TTCATCATCT	GCTGGGG.CG
44_5	GAAAAAAGAC	GTATCGGAAA	CTCTGTGCCA	TTCATCATCT	GCTGGGG.CG
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4	GAAAAACG..	.TATCAGAAA	CTTTGTTACA	TTCATCATAT	CATGGGA.AA
A3_5	GAAAAACG..	.TATCAGAAA	CTTTGTTACA	TTCATCATAT	CATGGGA.AA
A3_7	GAAAAACG..	.TATCAGAAA	CTTTGTTACA	TTCATCATAT	CATGGGA.AA
A3_3	GAAAAACG..	.TATCAGAAA	CTTTGTTACA	TTCATCATAT	CATGGGA.AA
42_12	GAAAGAGGAC	GTATCGGAAA	CTCTGTGCCA	TTCATCATCT	GCTGGGG.CG
AAV1	GAAAGAGGAC	GTATCGGAAA	CTCTGTGCCA	TTCATCATCT	GCTGGGG.CG
AAV2	AAAAGGCG..	.TATCAGAAA	CTGTGCTACA	TTCATCATAT	CATGGGA.AA
AAV3	AAAAGAAGAC	TTATCAGAAA	CTGTGTCCAA	TTCATCATAT	CCTGGGA.AG
AAV8	GAAAGAGGAC	GTATCGGAAA	CTCTGTGCCA	TTCATCATCT	GCTGGGG.CG
AAV9	GAAAGAGGAC	GTATCGGAAA	CTCTGTGCCA	TTCATCATCT	GCTGGGG.CG
AAV7	GAAAAAAGAC	GTATCGGAAA	CTCTGTGCCA	TTCATCATCT	GCTGGGG.CG
44_2	GAAAAAAGAC	GTATCGGAAA	CTCTGTGCCA	TTCATCATCT	GCTGGGGGGCG

Fig. 1AR

	2151				2200
42_2	GGCTCCCGAG	ATTGCTTGCT	CGGCCTGCGA	TCTGGTCAAC	GTGGACCTGG
42_8	GGCTCCCGAG	ATTGCTTGCT	CGGCCTGCGA	TCTGGTCAAC	GTGGACCTGG
42_15	GGCTCCCGAG	ATTGCTTGCT	CGGCCTGCGA	TCTGGTCAAC	GTGGACCTGG
42_5b	GGCTCCCGAG	ATTGCTTGCT	CGGCCTGCGA	TCTGGTCAAC	GTGGACCTGG
42_1b	GGCTCCCGAG	ATTGCTTGCT	CGGCCTGCGA	TCTGGTCAAC	GTGGACCTGG
42_13	GGCTCCCGAG	ATTGCTTGCT	CGGCCTGCGA	TCTGGTCAAC	GTGGACCTGG
42_3a	GGCTCCCGAG	ATTGCTTGCT	CGGCCTGCGA	TCTGGTCAAC	GTGGACCTGG
42_4	GGCTCCCGAG	ATTGCTTGCT	CGGCCTGCGA	TCTGGTCAAC	GTGGACCTGG
42_5a	GGCTCCCGAG	ATTGCTTGCT	CGGCCTGCGA	TCTGGTCAAC	GTGGACCTGG
42_10	GGCTCCCGAG	ATTGCTTGCT	CGGCCTGCGA	TCTGGTCAAC	GTGGACCTGG
42_3b	GGCTCCCGAG	ATTGCTTGCT	CGGCCTGCGA	TCTGGTCAAC	GTGGACCTGG
42_11	GGCTCCCGAG	ATTGCTTGCT	CGGCCTGCGA	TCTGGTCAAC	GTGGACCTGG
42_6b	GGCTCCCGAG	ATTGCTTGCT	CGGCCTGCGA	TCTGGTCAAC	GTGGACCTGG
43_1	GGCACCCGAG	ATTGCTTGCT	CGGCCTGCGA	TCTGGTCAAC	GTGGACCTGG
43_5	GGCACCCGAG	ATTGCTTGCT	CGGCCTGCGA	TCTGGTCAAC	GTGGACCTGG
43_12	GGCACCCGAG	ATTGCTTGCT	CGGCCTGCGA	TCTGGTCAAC	GTGGACCTGG
43_20	GGCTCCCGAG	ATTGCTTGCT	CGGCCTGCGA	TCTGGTCAAC	GTGGACCTGG
43_21	GGCTCCCGAG	ATTGCTTGCT	CGGCCTGCGA	TCTGGTCAAC	GTGGACCTGG
43_23	GGCTCCCGAG	ATTGCTTGCT	CGGCCTGCGA	TCTGGTCAAC	GTGGACCTGG
43_25	GGCTCCCGAG	ATTGCTTGCT	CGGCCTGCGA	TCTGGTCAAC	GTGGACCTGG
44_1	GGCACCCGAG	ATTGCTTGCT	CGGCCTGCGA	TCTGGTCAAC	GTGGACCTAG
44_5	GGCACCCGAG	ATTGCTTGCT	CGGCCTGCGA	TCTGGTCAAC	GTGGACCTAG
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4	AGAACCAGAC	...GCCTGCA	CTGCCTGCGA	CCTGGTAAAT	GTGGACTTGG
A3_5	AGTACCAGAC	...GCCTGCA	CTGCCTGCGA	CCTGGTAAAT	GTGGACTTGG
A3_7	AGTACCAGAC	...GCCTGCA	CTGCCTGCGA	CCTGGTAAAT	GTGGACTTGG
A3_3	AGTACCAGAC	...GCCTGCA	CTGCCTGCGA	CCTGGTAAAT	GTGGACTTGG
42_12	GGCTCCCGAG	ATTGCTTGCT	CGGCCTGCGA	TCTGGTCAAC	GTGGACCTGG
AAV1	GGCTCCCGAG	ATTGCTTGCT	CGGCCTGCGA	TCTGGTCAAC	GTGGACCTGG
AAV2	GGTGCCAGAC	...GCTTGCA	CTGCCTGCGA	TCTGGTCAAT	GTGGATTTGG
AAV3	GGCACCCGAG	ATTGCCTGTT	CGGCCTGCGA	TTTGGCCAAT	GTGGACTTGG
AAV8	GGCTCCCGAG	ATTGCTTGCT	CGGCCTGCGA	TCTGGTCAAC	GTGGACCTGG
AAV9	GGCTCCCGAG	ATTGCTTGCT	CGGCCTGCGA	TCTGGTCAAC	GTGGACCTGG
AAV7	GGCGCCCGAG	ATTGCTTGCT	CGGCCTGCGA	CCTGGTCAAC	GTGGACCTGG
44_2	GGCACCCGAG	ATTGCTTGCT	CGGCCTGCGA	TCTGGTCAAC	GTGGACCTAG

Fig. 1AS

2201

2250

			Rep 78 stop	vp1 start	
42_2	ATGACCGTGT	TTCTGAGCAA	TAAATGACTT	AAACCAGGTA	TGGCTGCCGA
42_8	ATGACTGTGT	TTCTGAGCAA	TAAATGACTT	AAACCAGGTA	TGGCTGCCGA
42_15	ATGACTGTGT	TTCTGAGCAA	TAAATGACTT	AAACCAGGTA	TGGCTGCCGA
42_5b	ATGACTGTGT	TTCTGAGCAA	TAAATGACTT	AAACCAGGTA	TGGCTGCCGA
42_1b	ATGACTGTGT	TTCTGAGCAA	TAAATGACTT	AAACCAGGTA	TGGCTGCCGA
42_13	ATGACTGTGT	TTCTGAGCAA	TAAATGACTT	AAACCAGGTA	TGGCTGCCGA
42_3a	ATGACTGTGT	TTCTGAGCAA	TAAATGACTT	AAACCAGGTA	TGGCTGCCGA
42_4	ATGACTGTGT	TTCTGAGCAA	TAAATGACTT	AAACCAGGTA	TGGCTGCCGA
42_5a	ATGACTGTGT	TTCTGAGCAA	TAAATGACTT	AAACCAGGTA	TGGCTGCCGA
42_10	ATGACTGTGT	TTCTGAGCAA	TAAATGACTT	AAACCAGGTA	TGGCTGCCGA
42_3b	ATGACTGTGT	TTCTGAGCAA	TAAATGACTT	AAACCAGGTA	TGGCTGCCGA
42_11	ATGACTGTGT	TTCTGAGCAA	TAAATGACTT	AAACCAGGTA	TGGCTGCCGA
42_6b	ATGACTGTGT	TTCTGAGCAA	TAAATGACTT	AAACCAGGTA	TGGCTGCCGA
43_1	ACGACTGTGT	TTCTGAGCAA	TAAATGACTT	AAACCAGGTA	TGGCTGCCGA
43_5	ACGACTGTGT	TTCTGAGCAA	TAAATGACTT	AAACCAGGTA	TGGCTGCCGA
43_12	ACGACTGTGT	TTCTGAGCAA	TAAATGACTT	AAACCAGGTA	TGGCTGCCGA
43_20	ATGACTGTGT	TTCTGAGCAA	TAAATGACTT	AAACCAGGTA	TGGCTGCCGA
43_21	ATGACTGTGT	TTCTGAGCAA	TAAATGACTT	AAACCAGGTA	TGGCTGCCGA
43_23	ATGACTGTGT	TTCTGAGCAA	TAAATGACTT	AAACCAGGTA	TGGCTGCCGA
43_25	ATGACTGTGT	TTCTGAGCAA	TAAATGACTT	AAACCAGGTA	TGGCTGCCGA
44_1	ATGACTGTGT	TTCTGAGCAA	TAAATGACTT	AAACCAGGTA	TGGCTGCCGA
44_5	ATGACTGTGT	TTCTGAGCAA	TAAATGACTT	AAACCAGGTA	TGGCTGCCGA
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4	ATGACTGTAT	TTCTGAGCAA	TAAATGACTT	AAATCAGGTA	TGGCTGCTGA
A3_5	ATGACTGTAT	TTCTGAGCAA	TAAATGACTT	AAATCAGGTA	TGGCTGCTGA
A3_7	ATGACTGTAT	TTCTGAGCAA	TAAATGACTT	AAATCAGGTA	TGGCTGCTGA
A3_3	ATGACTGTAT	TTCTGAGCAA	TAAATGACTT	AAATCAGGTA	TGGCTGCTGA
42_12	ATGACTGTGT	TTCTGAGCAA	TAAATGACTT	AAACCAGGTA	TGGCTGCCGA
AAV1	ATGACTGTGT	TTCTGAGCAA	TAAATGACTT	AAACCAGGTA	TGGCTGCCGA
AAV2	ATGACTGCAT	CTTTGAACAA	TAAATGATTT	AAATCAGGTA	TGGCTGCCGA
AAV3	ATGACTGTGT	TTCTGAGCAA	TAAATGACTT	AAACCAGGTA	TGGCTGCTGA
AAV8	ATGACTGTGT	TTCTGAGCAA	TAAATGACTT	AAACCAGGTA	TGGCTGCCGA
AAV9	ATGACTGTGT	TTCTGAGCAA	TAAATGACTT	AAACCAGGTA	TGGCTGCCGA
AAV7	ACGACTGCGT	TTCTGAGCAA	TAAATGACTT	AAACCAGGTA	TGGCTGCCGA
44_2	ATGACTGTGT	TTCTGAGCAA	TAAATGACTT	AAACCAGGTA	TGGCTGCCGA

Rep78 stop

vp1 start

Fig. 1AT

	2251				2300
				Rep68 stop	
42_2	TGGTTATCTT	CCAGATTGGC	TCGAGGACAA	CCTCTCTGAG	GGCATTCGCG
42_8	TGGTTATCTT	CCAGATTGGC	TCGAGGACAA	CCTCTCTGAG	GGCATTCGCG
42_15	TGGTTATCTT	CCAGATTGGC	TCGAGGACAA	CCTCTCTGAG	GGCATTCGCG
42_5b	TGGTTATCTT	CCAGATTGGC	TCGAGGACAA	CCTCTCTGAG	GGCATTCGCG
42_1b	TGGTTATCTT	CCAGATTGGC	TCGAGGACAA	CCTCTCTGAG	GGCATTCGCG
42_13	TGGTTATCTT	CCAGATTGGC	TCGAGGACAA	CCTCTCTGAG	GGCATTCGCG
42_3a	TGGTCATCTT	CCAGATTGGC	TCGAGGACAA	CCTCTCTGAG	GGCATTCGCG
42_4	TGGTTATCTT	CCAGATTGGC	TCGAGGACAA	CCTCTCTGAG	GGCATTCGCG
42_5a	TGGTTATCTT	CCAGATTGGC	TCGAGGACAA	CCTCTCTGAG	GGCATTCGCG
42_10	TGGTTATCTT	CCAGATTGGC	TCGAGGACAA	CCTCTCTGAG	GGCATTCGCG
42_3b	TGGTTATCTT	CCAGATTGGC	TCGAGGACAA	CCTCTCTGAG	GGCATTCGCG
42_11	TGGTTATCTT	CCAGATTGGC	TCGAGGACAA	CCTCTCTGAG	GGCATTCGCG
42_6b	TGGTTATCTT	CCAGATTGGC	TCGAGGACAA	CCTCTCTGAG	GGCATTCGCG
43_1	TGGTTATCTT	CCAGATTGGC	TTGAGGACAA	CCTCTCTGAG	GGCATTCGCG
43_5	TGGTTATCTT	CCAGATTGGC	TTGAGGACAA	CCTCTCTGAG	GGCATTCGCG
43_12	TGGTTATCTT	CCAGATTGGC	TTGAGGACAA	CCTCTCTGAG	GGCATTCGCG
43_20	TGGTTATCTT	CCAGATTGGC	TCGAGGACAA	CCTCTCTGAG	GGCATTCGCG
43_21	TGGTTATCTT	CCAGATTGGC	TCGAGGACAA	CCTCTCTGAG	GGCATTCGCG
43_23	TGGTTATCTT	CCAGATTGGC	TCGAGGACAA	CCTCTCTGAG	GGCATTCGCG
43_25	TGGTTATCTT	CCAGATTGGC	TCGAGGACAA	CCTCTCTGAG	GGCATTCGCG
44_1	TGGTTATCTT	CCAGATTGGC	TCGAGGACAA	CCTCTCTGAG	GGCATTCGCG
44_5	TGGTTATCTT	CCAGATTGGC	TCGAGGACAA	CCTCTCTGAG	GGCATTCGCG
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4	CGGTTATCTT	CCAGATTGGC	TCGAGGACAC	TCTCTCTGAA	GGAATCAGAC
A3_5	CGGTTATCTT	CCAGATTGGC	TCGAGGACAC	TCTCTCTGAA	GGAATCAGAC
A3_7	CGGTTATCTT	CCAGATTGGC	TCGAGGACAC	TCTCTCTGAA	GGAATCAGAC
A3_3	CGGTTATCTT	CCAGATTGGC	TCGAGGACAC	TCTCTCTGAA	GGAATCAGAC
42_12	TGGTTATCTT	CCAGATTGGC	TCGAGGACAA	CCTCTCTGAG	GGCATCCGCG
AAV1	TGGTTATCTT	CCAGATTGGC	TCGAGGACAA	CCTCTCTGAG	GGCATTCGCG
AAV2	TGGTTATCTT	CCAGATTGGC	TCGAGGACAC	TCTCTCTGAA	GGAATAAGAC
AAV3	CGGTTATCTT	CCAGATTGGC	TCGAGGACAA	CCTTTCTGAA	GGCATTCGTG
AAV8	TGGTTATCTT	CCAGATTGGC	TCGAGGACAA	CCTCTCTGAG	GGCATTCGCG
AAV9	TGGTTATCTT	CCAGATTGGC	TCGAGGACAA	CCTCTCTGAG	GGCATTCGCG
AAV7	TGGTTATCTT	CCAGATTGGC	TCGAGGACAA	CCTCTCTGAG	GGCATTCGCG
44_2	TGGTTATCTT	CCAGATTGGC	TCGAGGACAA	CCTCTCTGAG	GGCATTCGCG
				Rep 68 stop	

Fig. 1AU

	2301				2350
42_2	AGTGGTGGGA	CTTGAAACCT	GGAGCCCCGA	AACCCAAAGC	CAACCAGCAA
42_8	AGTGGTGGGA	CTTGAAACCT	GGAGCCCCGA	AACCCAAAGC	CAACCAGCAA
42_15	AGTGGTGGGA	CTTGAAACCT	GGAGCCCCGA	AACCCAAAGC	CAACCAGCAA
42_5b	AGTGGTGGGA	CTTGAAACCT	GGAGCCCCGA	AACCCAAAGC	CAACCAGCAA
42_1b	AGTGGTGGGA	CTTGAGACCT	GGAGCCCCGA	AACCCAAAGC	CAACCAGCAA
42_13	AGTGGTGGGA	CTTGAAACCT	GGAGCCCCGA	AACCCAAAGC	CAACCAGCAA
42_3a	AGTGGTGGGA	CTTGAAACCT	GGAGCCCCGA	AACCCAAAGC	CAACCAGCAA
42_4	AGTGGTGGGA	CTTGAAACCT	GGAGCCCCGA	AACCCAAAGC	CAACCAGCAA
42_5a	AGTGGTGGGA	CTTGAAACCT	GGAGCCCCGA	AACCCAAAGC	CAACCAGCAA
42_10	AGTGGTGGGA	CTTGAAACCT	GGAGCCCCGA	AACCCAAAGC	CAACCAGCAA
42_3b	AGTGGTGGGA	CTTGAAACCT	GGAGCCCCGA	AACCCAAAGC	CAACCAGCAA
42_11	AGTGGTGGGA	CTTGAAACCT	GGAGCCCCGA	AACCCAAAGC	CAACCAGCAA
42_6b	AGTGGTGGGA	CTTGAAACCT	GGAGCCCCGA	AACCCAAAGC	CAACCAGCAA
43_1	AGTGGTGGGA	CCTGAAACCT	GGAGCCCCGA	AACCCAAAGC	CAACCAGCAA
43_5	AGTGGTGGGA	CCTGAAACCT	GGAGCCCCGA	AACCCAAAGC	CAACCAGCAA
43_12	AGTGGTGGGA	CCTGAAACCT	GGAGCCCCGA	AACCCAAAGC	CAACCAGCAA
43_20	AGTGGTGGGA	CTTGAAACCT	GGAGCCCCGA	AACCCAAAGC	CAACCAGCAA
43_21	AGTGGTGGGA	CTTGAAACCT	GGAGCCCCGA	AACCCAAAGC	CAACCAGCAA
43_23	AGTGGTGGGA	CTTGAAACCT	GGAGCCCCGA	AACCCAAAGC	CAACCAGCAA
43_25	AGTGGTGGGA	CTTGAAACCT	GGAGCCCCGA	AACCCAAAGC	CAACCAGCAA
44_1	AGTGGTGGGA	CTTGAAACCT	GGAGCCCCGA	AACCCAAAGC	CAACCAGCAA
44_5	AGTGGTGGGA	CTTGAAACCT	GGAGCCCCGA	AACCCAAAGC	CAACCAGCAA
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4	AGTGGTGGAA	GCTCAAACCT	GGCCCACCAC	CGCCGAAACC	TAACCAACAA
A3_5	AGTGGTGGAA	GCTCAAACCT	GGCCCACCAC	CGCCGAAACC	TAACCAACAA
A3_7	AGTGGTGGAA	GCTCAAACCT	GGCCCACCAC	CGCCGAAACC	TAACCAACAA
A3_3	AGTGGTGGAA	GCTCAAACCT	GGCCCACCAC	CGCCGAAACC	TAACCAACAA
42_12	AGTGGTGGGA	CTTGAAACCT	GGAGCCCCGA	AACCCAAAGC	CAACCAGCAA
AAV1	AGTGGTGGGA	CTTGAAACCT	GGAGCCCCGA	AGCCCAAAGC	CAACCAGCAA
AAV2	AGTGGTGGAA	GCTCAAACCT	GGCCCACCAC	CACCAAAGCC	CGCAGAGCGG
AAV3	AGTGGTGGGC	TCTGAAACCT	GGAGTCCCTC	AACCCAAAGC	GAACCAACAA
AAV8	AGTGGTGGGC	GCTGAAACCT	GGAGCCCCGA	AGCCCAAAGC	CAACCAGCAA
AAV9	AGTGGTGGGC	GCTGAAACCT	GGAGCCCCGA	AGCCCAAAGC	CAACCAGCAA
AAV7	AGTGGTGGGA	CCTGAAACCT	GGAGCCCCGA	AACCCAAAGC	CAACCAGCAA
44_2	AGTGGTGGGA	CTTGAAACCT	GGAGCCCCGA	AACCCAAAGC	CAACCAGCAA

Fig. 1AV

	2351				2400
42_2	AAGCAGGACG	ACGGCCGGGG	TCTGGTGCTT	CCTGGCTACA	AGTACCTCGG
42_8	AAGCAGGACG	ACGGCCGGGG	TCTGGTGCTT	CCTGGCTACA	AGTACCTCGG
42_15	AAGCAGGACG	ACGGCCGGGG	TCTGGTGCTT	CCTGGCTACA	AGTACCTCGG
42_5b	AAGCAGGACG	ACGGCCGGGG	TCTGGTGCTT	CCTGGCTACA	AGTACCTCGG
42_1b	AAGCAGGACG	ACGGCCGGGG	TCTGGTGCTT	CCTGGCTACA	AGTACCTCGG
42_13	AAGCAGGACG	ACGGCCGGGG	TCTGGTGCTT	CCTGGCTACA	AGTACCTCGG
42_3a	AAGCAGGACG	ACGGCCGGGG	TCTGGTGCTT	CCTGGCTACA	AGTACCTCGG
42_4	AAGCAGGACG	ACGGCCGGGG	TCTGGTGCTT	CCTGGCTACA	AGTACCTCGG
42_5a	AAGCAGGACG	ACGGCCGGGG	TCTGGTGCTT	CCTGGCTACA	AGTACCTCGG
42_10	AAGCAGGACG	ACGGCCGGGG	TCTGGTGCTT	CCTGGCTACA	AGTACCTCGG
42_3b	AAGCAGGACG	ACGGCCGGGG	TCTGGTGCTT	CCTGGCTACA	AGTACCTCGG
42_11	AAGCAGGACG	ACGGCCGGGG	TCTGGTGCTT	CCTGGCTACA	AGTACCTCGG
42_6b	AAGCAGGACG	ACGGCCGGGG	TCTGGTGCTT	CCTGGCTACA	AGTACCTCGG
43_1	AAGCAGGACG	ACGGCCGGGG	TCTGGTGCTT	CCTGGCTACA	AGTACCTCGG
43_5	AAGCAGGACG	ACGGCCGGGG	TCTGGTGCTT	CCTGGCTACA	AGTACCTCGG
43_12	AAGCAGGACG	ACGGCCGGGG	TCTGGTGCTT	CCTGGCTACA	AGTACCTCGG
43_20	AAGCAGGACG	ACGGCCGGGG	TCTGGTGCTT	CCTGGCTACA	AGTACCTCGG
43_21	AAGCAGGACG	ACGGCCGGGG	TCTGGTGCTT	CCTGGCTACA	AGTACCTCGG
43_23	AAGCAGGACG	ACGGCCGGGG	TCTGGTGCTT	CCTGGCTACA	AGTACCTCGG
43_25	AAGCAGGACG	ACGGCCGGGG	TCTGGTGCTT	CCTGGCTACA	AGTACCTCGG
44_1	AAGCAGGACG	ACGGCCGGGG	TCTGGTGCTT	CCTGGCTACA	AGTACCTCGG
44_5	AAGCAGGACG	ACGGCCGGGG	TCTGGTGCTT	CCTGGCTACA	AGTACCTCGG
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4	CACCGGGACG	ACAGTAGGGG	TCTTGTGCTT	CCTGGGTACA	AGTACCTCGG
A3_5	CACCGGGACG	ACAGTAGGGG	TCTTGTGCTT	CCTGGGTACA	AGTACCTCGG
A3_7	CACCGGGACG	ACAGTAGGGG	TCTTGTGCTT	CCTGGGTACA	AGTACCTCGG
A3_3	CACCGGGACG	ACAGTAGGGG	TCTTGTGCTT	CCTGGGTACA	AGTACCTCGG
42_12	AAGCAGGACG	ACGGCCGGGG	TCTGGTGCTT	CCTGGCTACA	AGTACCTCGG
AAV1	AAGCAGGACG	ACGGCCGGGG	TCTGGTGCTT	CCTGGCTACA	AGTACCTCGG
AAV2	CATAAGGACG	ACAGCAGGGG	TCTTGTGCTT	CCTGGGTACA	AGTACCTCGG
AAV3	CACCAGGACA	ACCGTCGGGG	TCTTGTGCTT	CCGGGTACA	AATACCTCGG
AAV8	AAGCAGGACG	ACGGCCGGGG	TCTGGTGCTT	CCTGGCTACA	AGTACCTCGG
AAV9	AAGCAGGACG	ACGGCCGGGG	TCTGGTGCTT	CCTGGCTACA	AGTACCTCGG
AAV7	AAGCAGGACA	ACGGCCGGGG	TCTGGTGCTT	CCTGGCTACA	AGTACCTCGG
44_2	AAGCAGGACG	ACGGCCGGGG	TCTGGTGCTT	CCTGGCTACA	AGTACCTCGG

Fig. 1AW

	2401				2450
42_2	ACCCTTCAAC	GGACTCGACA	AGGGAGAGCC	GGTCAACGAG	GCAGACGCCG
42_8	ACCCTTCAAC	GGACTCGACA	AGGGGGAGCC	CGTCAACGCG	GCGGACGCAG
42_15	ACCCTTCAAC	GGACTCGACA	AGGGGGAGCC	CGTCAACGCG	GCGGACGCAG
42_5b	ACCCTTCAAC	GGACTCGACA	AGGGAGAGCC	GGTCAACGAG	GCAGACGCCG
42_1b	ACCCTTCAAC	GGACTCGACA	AGGGAGAGCC	GGTCAACGAG	GCAGACGCCG
42_13	ACCCTTCAAC	GGACTCGACA	AGGGGGAGCC	CGTCAACGCG	GCGGACGCAG
42_3a	ACCCTTCAAC	GGACTCGACA	AGGGGGAGCC	CGTCAACGCG	GCGGACGCAG
42_4	ACCCTTCAAC	GGACTCGACA	AGGGAGAGCC	GGTCAACGAG	GCAGACGCCG
42_5a	ACCCTTCAAC	GGACTCGACA	AGGGAGAGCC	GGTCAACGAG	GCAGACGCCG
42_10	ACCCTTCAAC	GGACTCGACA	AGGGAGAGCC	GGTCAACGAG	GCAGACGCCG
42_3b	ACCCTTCAAC	GGACTCGACA	AGGGAGAGCC	GGTCAACGAG	GCAGACGCCG
42_11	ACCCTTCAAC	GGACTCGACA	AGGGAGAGCC	GGTCAACGCG	GCGGACGCAG
42_6b	ACCCTTCAAC	GGACTCGACA	AGGGAGAGCC	GGTCAACGAG	GCAGACGCCG
43_1	ACCCTTCAAC	GGACTCGACA	AGGGGGAGCC	CGTCAACGCG	GCGGACGCAG
43_5	ACCCTTCAAC	GGACTCGACA	AGGGGGAGCC	CGTCAACGCG	GCGGACGCAG
43_12	ACCCTTCAAC	GGACTCGACA	AGGGGGAGCC	CGTCAACGCG	GCGGACGCAG
43_20	ACCCTTCAAC	GGACTCGACA	AGGGGGAGCC	CGTCAACGCG	GCGGACGCAG
43_21	ACCCTTCAAC	GGACTCGACA	AGGGGGAGCC	CGTCAACGCG	GCGGACGCAG
43_23	ACCCTTCAAC	GGACTCGACA	AGGGGGAGCC	CGTCAACGCG	GCGGACGCAG
43_25	ACCCTTCAAC	GGACTCGACA	AGGGGGAGCC	CGTCAACGCG	GCGGACGCAG
44_1	ACCCTTCAAC	GGACTCGACA	AGGGGGAGCC	CGTCAACGCG	GCGGACGCAG
44_5	ACCCTTCAAC	GGACTCGACA	AGGGGGAGCC	CGTCAACGCG	GCGGACGCAG
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4	ACCCTTCAAC	GGACTCGACA	AAGGAGAGCC	GGTCAACGAG	GCAGACGCCG
A3_5	ACCCTTCAAC	GGACTCGACA	AAGGAGAGCC	GGTCAACGAG	GCAGACGCCG
A3_7	ACCCTTCAAC	GGACTCGACA	AAGGAGAGCC	GGTCAACGAG	GCAGACGCCG
A3_3	ACCCTTCAAC	GGACTCGACA	AAGGAGAGCC	GGTCAACGAG	GCAGACGCCG
42_12	ACCCTTCAAC	GGACTCGACA	AGGGAGAGCC	GGTCAACGAG	GCAGACGCCG
AAV1	ACCCTTCAAC	GGACTCGACA	AGGGGGAGCC	CGTCAACGCG	GCGGACGCAG
AAV2	ACCCTTCAAC	GGACTCGACA	AGGGAGAGCC	GGTCAACGAG	GCAGACGCCG
AAV3	ACCCGGTAAC	GGACTCGACA	AAGGAGAGCC	GGTCAACGAG	GCGGACGCGG
AAV8	ACCCTTCAAC	GGACTCGACA	AGGGGGAGCC	CGTCAACGCG	GCGGACGCAG
AAV9	ACCCTTCAAC	GGACTCGACA	AGGGGGAGCC	CGTCAACGCG	GCGGACGCAG
AAV7	ACCCTTCAAC	GGACTCGACA	AGGGGGAGCC	CGTCAACGCG	GCGGACGCAG
44_2	ACCCTTCAAC	GGACTCGACA	AGGGGGAGCC	CGTCAACGCG	GCGGACGCAG

Fig. 1AX

	2451				2500
42_2	CGGCCCTCGA	GCACG.ACAA	GGCCTACGAC	AAGCAGCTCG	AGCAGGGGGA
42_8	CGGCCCTCGA	GCACG.ACAA	GGCCTACGAC	CAGCAGCTCA	AAGCGGGTGA
42_15	CGGCCCTCGA	GCACG.ACAA	GGCCTACGAC	CAGCAGCTCA	AAGCGGGTGA
42_5b	CGGCCCTCGA	GCACG.ACAA	GGCCTACGAC	AAGCAGCTCG	AGCAGGGGGA
42_1b	CGGCCCTCGA	GCACG.ACAA	GGCCTACGAC	AAGCAGCTCG	AGCAGGGGGA
42_13	CGGCCCTCGA	GCACG.ACAA	GGCCTACGAC	CAGCAGCTCA	AAGCGGGTGA
42_3a	CGGCCCTCGA	GCACG.ACAA	GGCCTACGAC	CAGCAGCTCA	AAGCGGGTGA
42_4	CGGCCCTCGA	GCACG.ACAA	GGCCTACGAC	AAGCAGCTCG	AGCAGGGGGA
42_5a	CGGCCCTCGA	GCACG.ACAA	GGCCTACGAC	AAGCAGCTCG	AGCAGGGGGA
42_10	CGGCCCTCGA	GCACG.ACAA	GGCCTACGAC	AAGCAGCTCG	AGCAGGGGGA
42_3b	CGGCCCTCGA	GCACG.ACAA	GGCCTACGAC	AAGCAGCTCG	AGCAGGGGGA
42_11	CGGCCCTCGA	GCACG.ACAA	GGCCTACGAC	CAGCAGCTCA	AAGCGGGTGA
42_6b	CGGCCCTCGA	GCACG.ACAA	GGCCTACGAC	AAGCAGCTCG	AGCAGGGGGA
43_1	CGGCCCTCGA	GCACG.ACAA	GGCCTACGAC	CAGCAGCTCA	AAGCGGGTGA
43_5	CGGCCCTCGA	GCACG.ACAA	GGCCTACGAC	CAGCAGCTCA	AAGCGGGTGA
43_12	CGGCCCTCGA	GCACG.ACAA	GGCCTACGAC	CAGCAGCTCA	AAGCGGGTGA
43_20	CGGCCCTCGA	GCACG.ACAA	AGCCTACGAC	CAGCAGCTCA	AAGCGGGTGA
43_21	CGGCCCTCGA	GCACG.ACAA	AGCCTACGAC	CAGCAGCTCA	AAGCGGGTGA
43_23	CGGCCCTCGA	GCACG.ACAA	AGCCTACGAC	CAGCAGCTCA	AAGCGGGTGA
43_25	CGGCCCTCGA	GCACG.ACAA	AGCCTACGAC	CAGCAGCTCA	AAGCGGGTGA
44_1	CGGCCCTCGA	GCACG.ACAA	GGCCTACGAC	CAGCAGCTCA	AAGCGGGTGA
44_5	CGGCCCTCGA	GCACG.ACAA	GGCCTACGAC	CAGCAGCTCA	AAGCGGGTGA
223_10		CAA	GGCCTACGAC	CAGCAGCTCA	AAGCGGGTGA
223_2		CAA	GGCCTACGAC	CAGCAGCTCA	AAGCGGGTGA
223_4		CAA	GGCCTACGAC	CAGCAGCTCA	AAGCGGGTGA
223_5		CAA	GGCCTACGAC	CAGCAGCTCA	AAGCGGGTGA
223_6		CAA	GGCCTACGAC	CAGCAGCTCA	AAGCGGGTGA
223_7		CAA	GGCCTACGAC	CAGCAGCTCA	AAGCGGGTGA
A3_4	CGGCCCTCGA	GCACG.ACAA	AGCCTACGAC	CACCAGCTCA	AGCAAGGGGA
A3_5	CGGCCCTCGA	GCACG.ACAA	AGCCTACGAC	CACCAGCTCA	AGCAAGGGGA
A3_7	CGGCCCTCGA	GCACG.ACAA	AGCCTACGAC	CACCAGCTCA	AGCAAGGGGA
A3_3	CGGCCCTCGA	GCACG.ACAA	AGCCTACGAC	CACCAGCTCA	AGCAAGGGGA
42_12	CGGCCCTCGA	GCACG.ACAA	GGCCTACGAC	AAGCAGCTCG	AGCAGGGGGA
AAV1	CGGCCCTCGA	GCACG.ACAA	GGCCTACGAC	CAGCAGCTCA	AAGCGGGTGA
AAV2	CGGCCCTCGA	GCACGTACAA	AGCCTACGAC	CGGCAGCTCG	ACAGCGGAGA
AAV3	CAGCCCTCGA	ACACG.ACAA	AGCTTACGAC	CAGCAGCTCA	AGGCCGGTGA
AAV8	CGGCCCTCGA	GCACG.ACAA	GGCCTACGAC	CAGCAGCTGC	AGGCCGGTGA
AAV9	CGGCCCTCGA	GCACG.GCAA	GGCCTACGAC	CAGCAGCTGC	AGGCCGGTGA
AAV7	CGGCCCTCGA	GCACG.ACAA	GGCCTACGAC	CAGCAGCTCA	AAGCGGGTGA
44_2	CGGCCCTCGA	GCACG.ACAA	GGCCTACGAC	CAGCAGCTCA	AAGCGGGTGA

Fig. 1AY

	2501				2550
42_2	CAACCCGTAC	CTCAAGTACA	ACCACGCCGA	CGCCGAGTTT	CAGGAGCGTC
42_8	CAATCCGTAC	CTGCGGTATA	ACCACGCCGA	CGCCGAGTTT	CAGGAGCGTC
42_15	CAATCCGTAC	CTGCGGTATA	ACCACGCCGA	CGCCGAGTTT	CAGGAGCGTC
42_5b	CAACCCGTAC	CTCAAGTACA	ACCACGCCGA	CGCCGAGTTT	CAGGAGCGTC
42_1b	CAACCCGTAC	CTCAAGTACA	ACCACGCCGA	CGCCGAGTTT	CAGGAGCGTC
42_13	CAATCCGTAC	CTGCGGTATA	ACCACGCCGA	CGCCGAGTTT	CAGGAGCGTC
42_3a	CAATCCGTAC	CTGCGGTATA	ACCACGCCGA	CGCCGAGTTT	CAGGAGCGTC
42_4	CAACCCGTAC	CTCAAGTACA	ACCACGCCGA	CGCCGAGTTT	CAGGAGCGTC
42_5a	CAACCCGTAC	CTCAAGTACA	ACCACGCCGA	CGCCGAGTTT	CAGGAGCGTC
42_10	CAACCCGTAC	CTCAAGTACA	ACCACGCCGA	CGCCGAGTTT	CAGGAGCGTC
42_3b	CAACCCGTAC	CTCAAGTACA	ACCACGCCGA	CGCCGAGTTT	CAGGAGCGTC
42_11	CAATCCGTAC	CTGCGGTATA	ACCACGCCGA	CGCCGAGTTT	CAGGAGCGTC
42_6b	CAACCCGTAC	CTCAAGTACA	ACCACGCCGA	CGCCGAGTTT	CAGGAGCGTC
43_1	CAATCCGTAC	CTGCGGTATA	ACCACGCCGA	CGCCGAGTTT	CAGGAGCGTC
43_5	CAATCCGTAC	CTGCGGTATA	ACCACGCCGA	CGCCGAGTTT	CAGGAGCGTC
43_12	CAATCCGTAC	CTGCGGTATA	ACCACGCCGA	CGCCGAGTTT	CAGGAGCGTC
43_20	CAATCCGTAC	CTGCGGTATA	ATCACGCCGA	CGCCGAGTTT	CAGGAGCGTC
43_21	CAATCCGTAC	CTGCGGTATA	ATCACGCCGA	CGCCGAGTTT	CAGGAGCGTC
43_23	CAATCCGTAC	CTGCGGTATA	ATCACGCCGA	CGCCGAGTTT	CAGGAGCGTC
43_25	CAATCCGTAC	CTGCGGTATA	ATCACGCCGA	CGCCGAGTTT	CAGGAGCGTC
44_1	CAATCCGTAC	CTGCGGTATA	ACCACGCCGA	CGCCGAGTTT	CAGGAGCGTC
44_5	CAATCCGTAC	CTGCGGTATA	ACCACGCCGA	CGCCGAGTTT	CAGGAGCGTC
223_10	CAATCCGTAC	CTGCGGTATA	ACCACGCCGA	CGCCGAGTTT	CAGGAGCGTC
223_2	CAATCCGTAC	CTGCGGTATA	ACCACGCCGA	CGCCGAGTTT	CAGGAGCGTC
223_4	CAATCCGTAC	CTGCGGTATA	ACCACGCCGA	CGCCGAGTTT	CAGGAGCGTC
223_5	CAATCCGTAC	CTGCGGTATA	ACCACGCCGA	CGCCGAGTTT	CAGGAGCGTC
223_6	CAATCCGTAC	CTGCGGTATA	ACCACGCCGA	CGCCGAGTTT	CAGGAGCGTC
223_7	CAATCCGTAC	CTGCGGTATA	ACCACGCCGA	CGCCGAGTTT	CAGGAGCGTC
A3_4	CAACCCGTAC	CTCAAATACA	ACCACGCCGA	CGCTGAATTT	CAGGAGCGTC
A3_5	CAACCCGTAC	CTCAAATACA	ACCACGCCGA	CGCTGAATTT	CAGGAGCGTC
A3_7	CAACCCGTAC	CTCAAATACA	ACCACGCCGA	CGCTGAATTT	CAGGAGCGTC
A3_3	CAACCCGTAC	CTCAAATACA	ACCACGCCGA	CGCTGAATTT	CAGGAGCGTC
42_12	CAACCCGTAC	CTCAAGTACA	ACCACGCCGA	CGCCGAGTTT	CAGGAGCGTC
AAV1	CAATCCGTAC	CTGCGGTATA	ACCACGCCGA	CGCCGAGTTT	CAGGAGCGTC
AAV2	CAACCCGTAC	CTCAAGTACA	ACCACGCCGA	CGCCGAGTTT	CAGGAGCGTC
AAV3	CAACCCGTAC	CTCAAGTACA	ACCACGCCGA	CGCCGAGTTT	CAGGAGCGTC
AAV8	CAATCCGTAC	CTGCGGTATA	ACCACGCCGA	CGCCGAGTTT	CAGGAGCGTC
AAV9	CAATCCGTAC	CTGCGGTATA	ACCACGCCGA	CGCCGAGTTT	CAGGAGCGTC
AAV7	CAATCCGTAC	CTGCGGTATA	ACCACGCCGA	CGCCGAGTTT	CAGGAGCGTC
44_2	CAATCCGTAC	CTGCGGTATA	ACCACGCCGA	CGCCGAGTTT	CAGGAGCGTC

Fig. 1A2

	2551				2600
42_2	TTCAAGAAGA	TACGTCTTTT	GGGGGCAACC	TCGGGCGAGC	AGTCTTCCAG
42_8	TGCAAGAAGA	TACGTCTTTT	GGGGGCAACC	TCGGGCGAGC	AGTCTTCCAG
42_15	TGCAAGAAGA	TACGTCTTTT	GGGGGCAACC	TCGGGCGAGC	AGTCTTCCAG
42_5b	TTCAAGAAGA	TACGTCTTTT	GGGGGCAACC	TCGGGCGAGC	AGTCTTCCAG
42_1b	TTCAAGAAGA	TACGTCTTTT	GGGGGCAACC	TCGGGCGAGC	AGTCTTCCAG
42_13	TTCAAGAAGA	TACGTCTTTT	GGGGGCAACC	TCGGGCGAGC	AGTCTTCCAG
42_3a	TTCAAGAAGA	TACGTCTTTT	GGGGGCAACC	TCGGGCGAGC	AGTCTTCCAG
42_4	TTCAAGAAGA	TACGTCTTTT	GGGGGCAACC	TCGGGCGAGC	AGTCTTCCAG
42_5a	TTCAAGAAGA	TACGTCTTTT	GGGGGCAACC	TCGGGCGAGC	AGTCTTCCGG
42_10	TTCAAGAAGA	TACGTCTTTT	GGGGGCAACC	TCGGGCGAGC	AGTCTTCCAG
42_3b	TTCAAGAAGA	TACGTCTTTT	GGGGGCAACC	TCGGGCGAGC	AGTCTTCCAG
42_11	TTCAAGAAGA	TACGTCTTTT	GGGGGCAACC	TCGGGCGAGC	AGTCTTCCAG
42_6b	TTCAAGAAGA	TACGTCTTTT	GGGGGCAACC	TCGGGCGAGC	AGTCTTCCAG
43_1	TGCAAGAAGA	TACGTCTTTT	GGGGGCAACC	TCGGGCGAGC	AGTCTTCCAG
43_5	TGCAAGAAGA	TACGTCTTTT	GGGGGCAACC	TCGGGCGAGC	AGTCTTCCAG
43_12	TGCAAGAAGA	TACGTCTTTT	GGGGGCAACC	TCGGGCGAGC	AGTCTTCCAG
43_20	TGCAAGAAGA	TACGTCTTTT	GGGGGCAACC	TCGGGCGAGC	AGTCTTCCAG
43_21	TGCAAGAAGA	TACGTCTTTT	GGGGGCAACC	TCGGGCGAGC	AGTCTTCCAG
43_23	TGCAAGAAGA	TACGTCTTTT	GGGGGCAACC	TCGGGCGAGC	AGTCTTCCAG
43_25	TGCAAGAAGA	TACGTCTTTT	GGGGGCAACC	TCGGGCGAGC	AGTCTTCCAG
44_1	TGCAAGAAGA	TACGTCTTTT	GGGGGCAACC	TCGGGCGAGC	AGTCTTCCAG
44_5	TGCAAGAAGA	TACGTCTTTT	GGGGGCAACC	TCGGGCGAGC	AGTCTTCCAG
223_10	TTCAAGAAGA	TACGTCTTTT	GGGGGCAACC	TCGGGCGAGC	AGTCTTCCAG
223_2	TTCAAGAAGA	TACGTCTTTT	GGGGGCAACC	TCGGGCGAGC	AGTCTTCCAG
223_4	TTCAAGAAGA	TACGTCTTTT	GGGGGCAACC	TCGGGCGAGC	AGTCTTCCAG
223_5	TTCAAGAAGA	TACGTCTTTT	GGGGGCAACC	TCGGGCGAGC	AGTCTTCCAG
223_6	TTCAAGAAGA	TACGTCTTTT	GGGGGCAACC	TCGGGCGAGC	AGTCTTCCAG
223_7	TTCAAGAAGA	TACGTCTTTT	GGGGGCAACC	TCGGGCGAGC	AGTCTTCCAG
A3_4	TTCAAGAAGA	TACGTCTTTC	GGGGGCAACC	TCGGGCGAGC	AGTCTTCCAG
A3_5	TTCAAGAAGA	TACGTCTTTC	GGGGGCAACC	TCGGGCGAGC	AGTCTTCCAG
A3_7	TTCAAGAAGA	TACGTCTTTC	GGGGGCAACC	TCGGGCGAGC	AGTCTTCCAG
A3_3	TTCAAGAAGA	TACGTCTTTC	GGGGGCAACC	TCGGGCGAGC	AGTCTTCCAG
42_12	TTCAAGAAGA	TACGTCTTTT	GGGGGCAACC	TCGGGCGAGC	AGTCTTCCAG
AAV1	TGCAAGAAGA	TACGTCTTTT	GGGGGCAACC	TCGGGCGAGC	AGTCTTCCAG
AAV2	TTAAAGAAGA	TACGTCTTTT	GGGGGCAACC	TCGGGCGAGC	AGTCTTCCAG
AAV3	TTCAAGAAGA	TACGTCTTTT	GGGGGCAACC	TTGGCAGAGC	AGTCTTCCAG
AAV8	TGCAAGAAGA	TACGTCTTTT	GGGGGCAACC	TCGGGCGAGC	AGTCTTCCAG
AAV9	TGCAAGAAGA	TACGTCTTTT	GGGGGCAACC	TCGGGCGAGC	AGTCTTCCAG
AAV7	TGCAAGAAGA	TACGTCATTT	GGGGGCAACC	TCGGGCGAGC	AGTCTTCCAG
44_2	TGCAAGAAGA	TACGTCTTTT	GGGGGCAACC	TCGGGCGAGC	AGTCTTCCAG

Fig. 1AAA

	2601				2650
42_2	GCCAAGAAGC	GGGTTCTCGA	ACCTCTCGGT	CTGGTTGAGG	AAGGCGCTAA
42_8	GCCAAGAAGC	GGGTTCTCGA	ACCTCTCGGT	CTGGTTGAGG	AAGGCGCTAA
42_15	GCCAAGAAGC	GGGTTCTCGA	ACCTCTCGGT	CTGGTTGAGG	AAGGCGCTAA
42_5b	GCCAAGAAGC	GGGTTCTCGA	ACCTCTCGGT	CTGGTTGAGG	AAGGCGCTAA
42_1b	GCCAAGAAGC	GGGTTCTCGA	ACCTCTCGGT	CTGGTTGAGG	AAGGCGCTAA
42_13	GCCAAGAAGC	GGGTTCTCGA	ACCTCTCGGT	CTGGTTGAGG	AAGGCGCTAA
42_3a	GCCAAGAAGC	GGGTTCTCGA	ACCTCTCGGT	CTGGTTGAGG	AAGGCGCTAA
42_4	GCCAAGAAGC	GGGTTCTCGA	ACCTCTCGGT	CTGGTTGAGG	AAGGCGCTAA
42_5a	GCCAAGAAGC	GGGTTCTCGA	ACCTCTCGGT	CTGGTTGAGG	AAGGCGCTAA
42_10	GCCAAGAAGC	GGGTTCTCGA	ACCTCTCGGT	CTGGTTGAGG	AAGGCGCTAA
42_3b	GCCAAGAAGC	GGGTTCTCGA	ACCTCTCGGT	CTGGTTGAGG	AAGGCGCTAA
42_11	GCCAAGAAGC	GGGTTCTCGA	ACCTCTCGGT	CTGGTTGAGG	AAGGCGCTAA
42_6b	GCCAAGAAGC	GGGTTCTCGA	ACCTCTCGGT	CTGGTTGAGG	AAGGCGCTAA
43_1	GCCAAGAAGC	GGGTTCTCGA	ACCTCTCGGT	CTGGTTGAGG	AAGGCGCTAA
43_5	GCCAAGAAGC	GGGTTCTCGA	ACCTCTCGGT	CTGGTTGAGG	AAGGCGCTAA
43_12	GCCAAGAAGC	GGGTTCTCGA	ACCTCTCGGT	CTGGTTGAGG	AAGGCGCTAA
43_20	GCCAAGAAGC	GGGTTCTCGA	ACCTCTCGGT	CTGGTTGAGG	AAGGCGCTAA
43_21	GCCAAGAAGC	GGGTTCTCGA	ACCTCTCGGT	CTGGTTGAGG	AAGGCGCTAA
43_23	GCCAAGAAGC	GGGTTCTCGA	ACCTCTCGGT	CTGGTTGAGG	AAGGCGCTAA
43_25	GCCAAGAAGC	GGGTTCTCGA	ACCTCTCGGT	CTGGTTGAGG	AAGGCGCTAA
44_1	GCCAAGAAGC	GGGTTCTCGA	ACCTCTCGGT	CTGGTTGAGG	AAGGCGCTAA
44_5	GCCAAGAAGC	GGGTTCTCGA	ACCTCTCGGT	CTGGTTGAGG	AAGGCGCTAA
223_10	GCCAAAAAGC	GGGTTCTCGA	ACCTCTTGGT	CTGGTTGAGA	CGCCAGCTAA
223_2	GCCAAAAAGC	GGGTTCTCGA	ACCTCTTGGT	CTGGTTGAGA	CGCCAGCTAA
223_4	GCCAAAAAGC	GGGTTCTCGA	ACCTCTTGGT	CTGGTTGAGA	CGCCAGCTAA
223_5	GCCAAAAAGC	GGGTTCTCGA	ACCTCTTGGT	CTGGTTGAGA	CGCCAGCTAA
223_6	GCCAAAAAGC	GGGTTCTCGA	ACCTCTTGGT	CTGGTTGAGA	CGCCAGCTAA
223_7	GCCAAAAAGC	GGGTTCTCGA	ACCTCTTGGT	CTGGTTGAGA	CGCCAGCTAA
A3_4	GCCAAAAAGA	GGGTACTCGA	GCCTCTTGGT	CTGGTTGAGG	AAGCTGTTAA
A3_5	GCCAAAAAGA	GGGTACTCGA	GCCTCTTGGT	CTGGTTGAGG	AAGCTGTTAA
A3_7	GCCAAAAAGA	GGGTACTCGA	GCCTCTTGGT	CTGGTTGAGG	AAGCTGTTAA
A3_3	GCCAAAAAGA	GGGTACTCGA	GCCTCTTGGT	CTGGTTGAGG	AAGCTGTTAA
42_12	GCCAAGAAGC	GGGTTCTCGA	ACCTCTCGGT	CTGGTTGAGG	AAGGCGCTAA
AAV1	GCCAAGAAGC	GGGTTCTCGA	ACCTCTCGGT	CTGGTTGAGG	AAGGCGCTAA
AAV2	GCGAAAAAGA	GGGTTCTTGA	ACCTCTGGGC	CTGGTTGAGG	AACCTGTTAA
AAV3	GCCAAAAAGA	GGATCCTTGA	GCCTCTTGGT	CTGGTTGAGG	AAGCAGCTAA
AAV8	GCCAAGAAGC	GGGTTCTCGA	ACCTCTCGGT	CTGGTTGAGG	AAGGCGCTAA
AAV9	GCCAAGAAGC	GGGTTCTCGA	ACCTCTCGGT	CTGGTTGAGG	AAGGCGCTAA
AAV7	GCCAAGAAGC	GGGTTCTCGA	ACCTCTCGGT	CTGGTTGAGG	AAGGCGCTAA
44_2	GCCAAGAAGC	GGGTTCTCGA	ACCTCTCGGT	CTGGTTGAGG	AAGGCGCTAA

Fig. 1AAB

2651

2700

vp2 start
 42_2 GACGGCTCCT GGAAAGAAGA GACCCATAGA ...ATCCCCC
 42_8 GACGGCTCCT GGAAAGAAGA GACCGGTAGA GCCATCACCC CAGCGTTCTC
 42_15 GACGGCTCCT GGAAAGAAGA GACCGGTAGA GCCATCACCC CAGCGTTCTC
 42_5b GACGGCTCCT GGAAAGAAGA GACCGGTAGA GCCATCACCC CAGCGTTCTC
 42_1b GACGGCTCCT GGAAAGAAGA GACCCATAGA ...ATCCCCC
 42_13 GACGGCTCCT GGAAAGAAGA GACCCATAGA ...ATCCCCC
 42_3a GACGGCTCCT GGAAAGAAGA GACCCATAGA ...ATCCCCC
 42_4 GACGGCTCCT GGAAAGAAGA GACCCATAGA ...ATCCCCC
 42_5a GACGGCTCCT GGAAAGAAGA GACCCATAGA ...ATCCCCC
 42_10 GACGGCTCCT GGAAAGAAGA GACCCATAGA ...ATCCCCC
 42_3b GACGGCTCCT GGAAAGAAGA GACCCATAGA ...ATCCCCC
 42_11 GACGGCTCCT GGAAAGAAGA GACCCATAGA ...ATCCCCC
 42_6b GACGGCTCCT GGAAAGAAGA GACCGGTAGA GCCATCACCC CAGCGTTCTC
 43_1 GACGGCTCCT GGAAAGAAGA GACCGGTAGA GCCATCACCT CAGCGTTCCC
 43_5 GACGGCTCCT GGAAAGAAGA GACCGGTAGA GCCATCACCT CAGCGTTCCC
 43_12 GACGGCTCCT GGAAAGAAGA GACCGGTAGA GCCATCACCT CAGCGTTCCC
 43_20 GACGGCTCCT GGAAAGAAGA GACTGGTAGA GCAGTCGCCA CAAGAG...C
 43_21 GACGGCTCCT GGAAAGAAGA GACCGGTAGA GCAGTCGCCA CAAGAG...C
 43_23 GACGGCTCCT GGAAAGAAGA GACCGGTAGA GCAGTCGCCA CAAGAG...C
 43_25 GACGGCTCCT GGAAAGAAGA GACCGGTAGA GCAGTCGCCA CAAGAG...C
 44_1 GACGGCTCCT GGAAAGAAGA GACCGGTAGA GCCATCACCC CAGCGTTCTC
 44_5 GACGGCTCCT GGAAAGAAGA GACCGGTAGA GCCATCACCC CAGCGTTCTC
 223_10 GACGGCACCT GGAAAGAAGC GACCGGTAGA CTCGCCA... ..
 223_2 GACGGCACCT GGAAAGAAGC GACCGGTAGA CTCGCCA... ..
 223_4 GACGGCACCT GGAAAGAAGC GACCGGTAGA CTCGCCA... ..
 223_5 GACGGCACCT GGAAAGAAGC GACCGGTAGA CTCGCCA... ..
 223_6 GACGGCACCT GGAAAGAAGC GACCGGTAGA CTCGCCA... ..
 223_7 GACGGCACCT GGAAAGAAGC GACCGGTAGA CTCGCCA... ..
 A3_4 GACGGCTCCT GGAAAAAAGA GACCTATAGA GCAGTCTCCT GCAGAA...C
 A3_5 GACGGCTCCT GGAAAAAAGA GACCTATAGA GCAGTCTCCT GCAGAA...C
 A3_7 GACGGCTCCT GGAAAAAAGA GACCTATAGA GCAGTCTCCT GCAGAA...C
 A3_3 GACGGCTCCT GGAAAAAAGA GACCTATAGA GCAGTCTCCT GCAGAA...C
 42_12 GACGGCTCCT GGAAAGAAGA GACCGGTAGA GCCATCACCC CAGCGTTCTC
 AAV1 GACGGCTCCT GGAAAGAAAC GTCCGGTAGA GCAGTCGCCA CAAGAG...C
 AAV2 GACGGCTCCG GGAAAAAAGA GGCCGGTAGA GCACTCTCCT GTGGAG...C
 AAV3 AACGGCTCCT GGAAAGAAGG GGGCTGTAGA TCAGTCTCCT CAGGAA...C
 AAV8 GACGGCTCCT GGAAAGAAGA GACCGGTAGA GCCATCACCC CAGCGTTCTC
 AAV9 GACGGCTCCT GGAAAGAAGA GACCGGTAGA GCCATCACCC CAGCGTTCTC
 AAV7 GACGGCTCCT GCAAAGAAGA GACCGGTAGA GCCGTCACCT CAGCGTTCCC
 44_2 GACGGCTCCT GGAAAGAAGA GACCGGTAGA GCCATCACCC CAGCGTTCTC
 vp2 start

Fig. 1AAC

	2701				2750
42_2	..GACTCCTC	CACGGGCATC	GGCAAGAAAG	GCCAGCAGCC	CGCTAAAAAG
42_8	CAGACTCCTC	TACGGGCATC	GGCAAGACAG	GCCAGCAGCC	CGCGAAAAAG
42_15	CAGACTCCTC	TACGGGCATC	GGCAAGACAG	GCCAGCAGCC	CGCGAAAAAG
42_5b	CAGACTCCTC	TACGGGCATC	GGCAAGACAG	GCCAGCAGCC	CGCGAAAAAG
42_1b	..GACTCCTC	CACGGGCATC	GGCAAGAAAG	GCCAGCAGCC	CGCTAAAAAG
42_13	..GACTCCTC	CACGGGCATC	GGCAAGAAAG	GCCAGCAGCC	CGCTAAAAAG
42_3a	..GACTCCTC	CACGGGCATC	GGCAAGAAAG	GCCAGCAGCC	CGCTAAAAAG
42_4	..GACTCCTC	CACGGGCATC	GGCAAGAAAG	GCCAGCAGCC	CGCTAAAAAG
42_5a	..GACTCCTC	CACGGGCATC	GGCAAGAAAG	GCCAGCAGCC	CGCTAAAAAG
42_10	..GACTCCTC	CACGGGCATC	GGCAGGAAAG	GCCAGCAGCC	CGCTAAAAAG
42_3b	..GACTCCTC	CACGGGCATC	GGCAAGAAAG	GCCAGCAGCC	CGCTAAAAAG
42_11	..GACTCCTC	CACGGGCATC	GGCAAGAAAG	GCCAGCAGCC	CGCTAAAAAG
42_6b	CAGACTCCTC	TACGGGCATC	GGCAAGACAG	GCCAGCAGCC	CGCGAAAAAG
43_1	CCGACTCCTC	CACGGGCATC	GGCAAGAAAG	GCCACCAGCC	CGCGAGAAAG
43_5	CCGACTCCTC	CACGGGCATC	GGCAAGAAAG	GCCACCAGCC	CGCGAGAAAG
43_12	CCGACTCCTC	CACGGGCATC	GGCAAGAAAG	GCCACCAGCC	CGCGAGAAAG
43_20	CAGACTCCTC	CTCGGGCATC	GGCAAGACAG	GCCAGCAGCC	CGCTAAAAAG
43_21	CAGACTCCTC	CTCGGGCATC	GGCAAGACAG	GCCAGCAGCC	CGCTAAAAAG
43_23	CAGACTCCTC	CTCGGGCATC	GGCAAGACAG	GCCAGCAGCC	CGCTAAAAAG
43_25	CAGACTCCTC	CTCGGGCATC	GGCAAGACAG	GCCAGCAGCC	CGCTAAAAAG
44_1	CAGACTCCTC	TACGGGCATC	GGCAAGAAAG	GCCAGCAGCC	CGCGAAAAAG
44_5	CAGACTCCTC	TACGGGCATC	GGCAAGAAAG	GCCAGCAGCC	CGCGAAAAAG
223_10	..GACTCCAC	CTCGGGCATC	GGCAAGAAAG	GCCAGCAGCC	CGCGAAAAAG
223_2	..GACTCCAC	CTCGGGCATC	GGCAAGAAAG	GCCAGCAGCC	CGCGAAAAAG
223_4	..GACTCCAC	CTCGGGCATC	GGCAAGAAAG	GCCAGCAGCC	CGCGAAAAAG
223_5	..GACTCCAC	CTCGGGCATC	GGCAAGAAAG	GCCAGCAGCC	CGCGAAAAAG
223_6	..GACTCCAC	CTCGGGCATC	GGCAAGAAAG	GCCAGCAGCC	CGCGAAAAAG
223_7	..GACTCCAC	CTCGGGCATC	GGCAAGAAAG	GCCAGCAGCC	CGCGAAAAAG
A3_4	CGGACTCTTC	CTCGGGCATC	GGCGAATCAG	GCCAGCAGCC	CGCTAAGAAA
A3_5	CGGACTCTTC	CTCGGGCATC	GGCAAATCAG	GCCAGCAGCC	CGCTAAGAAA
A3_7	CGGACTCTTC	CTCGGGCATC	GGCAAATCAG	GCCAGCAGCC	CGCTAAGAAA
A3_3	CGGACTCTTC	CTCGGGCATC	GGCAAATCAG	GCCAGCAGCC	CGCTAAGAAA
42_12	CAGACTCCTC	TACGGGCATC	GGCAAGACAG	GCCAGCAGCC	CGCGAAAAAG
AAV1	CAGACTCCTC	CTCGGGCATC	GGCAAGACAG	GCCAGCAGCC	CGCTAAAAAG
AAV2	CAGACTCCTC	CTCGGGGAACC	GGAAAGGCGG	GCCAGCAGCC	TGCAAGAAAA
AAV3	CGGACTCATC	ATCTGGTGTT	GGCAAATCGG	GCAAACAGCC	TGCCAGAAAA
AAV8	CAGACTCCTC	TACGGGCATC	GGCAAGAAAG	GCCAACAGCC	CGCCAGAAAA
AAV9	CAGACTCCTC	TACGGGCATC	GGCAAGAAAG	GCCAACAGCC	CGCCAGAAAA
AAV7	CCGACTCCTC	CACGGGCATC	GGCAAGAAAG	GCCAGCAGCC	CGCCAGAAAG
44_2	CAGACTCCTC	TACGGGCATC	GGCAAGAAAG	GCCAGCAGCC	CGCGAAAAAG

Fig. 1AAD

	2751				2800
42_2	AAGCTCAACT	TTGGGCAGAC	TGGCGACTCA	GAGTCAGTGC	CCGACCCCCA
42_8	AGACTCAACT	TTGGGCAGAC	TGGCGACTCA	GAGTCAGTGC	CCGACCCTCA
42_15	AGACTCAACT	TTGGGCAGAC	TGGCGACTCA	GAGTCAGTGC	CCGACCCTCA
42_5b	AGACTCAACT	TTGGGCAGAC	TGGCGACTCA	GAGTCAGTGC	CCGACCCTCA
42_1b	AGACTCAACT	TTGGGCAGAC	TGGCGACTCA	GAGTCAGTGC	CCGACCCTCA
42_13	AAGCTCAACT	TTGGGCAGAC	TGGCGACTCA	GAGTCAGTGC	CCGACCCTCA
42_3a	AAGCTCAACT	TTGGGCAGAC	TGGCGACTCA	GAGTCAGTGC	CCGACCCTCA
42_4	AAGCTCAACT	TTGGGCAGAC	TGGCGACTCA	GAGTCAGTGC	CCGACCCTCA
42_5a	AAGCTCAACT	TTGGGCAGAC	TGGCGACTCA	GAGTCAGTGC	CCGACCCCCA
42_10	AAGCTCAACT	TTGGGCAGAC	TGGCGACTCA	GAGTCAGTGC	CCGACCCTCA
42_3b	AAGCTCAACT	TTGGGCAGAC	TGGCGACTCA	GAGTCAGTGC	CCGACCCTCA
42_11	AAGCTCAACT	TTGGGCAGAC	TGGCGACTCA	GAGTCAGTGC	CCGACCCTCA
42_6b	AGACTCAACT	TTGGGCAGAC	TGGCGACTCA	GAGTCAGTGC	CCGACCCTCA
43_1	AGACTGAACT	TTGGGCAGAC	TGGCGACTCG	GAGTCAGTCC	CCGACCCTCA
43_5	AGACTGAACT	TTGGGCAGAC	TGGCGACTCG	GAGTCAGTCC	CCGACCCTCA
43_12	AGACTGAACT	TTGGGCAGAC	TGGCGACTCG	GAGTCAGTCC	CCGACCCTCA
43_20	AGACTCAATT	TTGGTCAGAC	TGGCGACTCA	GAGTCAGTCC	CCGACCCACA
43_21	AGACTCAATT	TTGGTCAGAC	TGGCGACTCA	GAGTCAGTCC	CCGACCCACA
43_23	AGACTCAATT	TTGGTCAGAC	TGGCGACTCA	GAGTCAGTCC	CCGACCCACA
43_25	AGACTCAATT	TTGGTCAGAC	TGGCGACTCA	GAGTCAGTCC	CCGACCCACA
44_1	AGACTCAACT	TTGGGCAGAC	TGGCGACTCA	GAGTCAGTGC	CCGACCCTCA
44_5	AGACTCAACT	TTGGGCAGAC	TGGCGACTCA	GAGTCAGTGC	CCGACCCTCA
223_10	AGACTCAACT	TTGGGCAGAC	TGGCGACTCA	GAGTCAGTCC	CCGACCCTCA
223_2	AGACTCAACT	TTGGGCAGAC	TGGCGACTCA	GAGTCAGTCC	CCGACCCTCA
223_4	AGACTCAACT	TTGGGCAGAC	TGGCGACTCA	GAGCCAGTCC	CCGACCCTCA
223_5	AGACTCAACT	TTGGGCAGAC	TGGCGACTCA	GAGCCAGTCC	CCGACCCTCA
223_6	AGACTCAACT	TTGGGCAGAC	TGGCGACTCA	GAGTCAGTCC	CCGACCCTCA
223_7	AGACTCAACT	TTGGGCAGAC	TGGCGACTCA	GAGTCAGTCC	CCGACCCTCA
A3_4	AGACTCAATT	TTGGTCAGAC	TGGCGACACA	GAGTCAGTCC	CAGACCCTCA
A3_5	AGACTCAATT	TTGGTCAGAC	TGGCGACACA	GAGTCAGTCC	CAGACCCTCA
A3_7	AGACTCAATT	TTGGTCAGAC	TGGCGACACA	GAGTCAGTCC	CAGACCCTCA
A3_3	AGACTCAATT	TTGGTCAGAC	TGGCGACACA	GAGTCAGTCC	CAGGCCCTCA
42_12	AGACTCAACT	TTGGGCAGAC	TGGCGACTCA	GAGTCAGTGC	CCGACCCTCA
AAV1	AGACTCAATT	TTGGTCAGAC	TGGCGACTCA	GAGTCAGTCC	CCGATCCACA
AAV2	AGATTGAATT	TTGGTCAGAC	TGGAGACGCA	GAATCAGTAC	CTGACCCCCA
AAV3	AGACTAAATT	TCGGTCAGAC	TGGAGACTCA	GAGTCAGTCC	CAGACCCTCA
AAV8	AGACTCAATT	TTGGTCAGAC	TGGCGACTCA	GAGTCAGTTC	CAGACCCTCA
AAV9	AGACTCAATT	TTGGTCAGAC	TGGCGACTCA	GAGTCAGTTC	CAGACCCTCA
AAV7	AGACTCAATT	TCGGTCAGAC	TGGCGACTCA	GAGTCAGTCC	CCGACCCTCA
44_2	AGACTCAACT	TTGGGCAGAC	TGGCGACTCA	GAGTCAGTGC	CCGACCCTCA

Fig. 1AAE

	2801				2850	
						vp3 start
42_2	ACCTCTCGGA	GAACCTCCCG	CCGCGCCCTC	AGGTCTGGGA	TCTGGTACAA	
42_8	ACCAATCGGA	GAACCCCCCG	CAGGCCCTC	TGGTCTGGGA	TCTGGTACAA	
42_15	ACCAATCGGA	GAACCCCCCG	CAGGCCCTC	TGGTCTGGGA	TCTGGTACAA	
42_5b	ACCAATCGGA	GAACCCCCCG	CAGGCCCTC	TGGTCTGGGA	TCTGGTACAA	
42_1b	ACCAATCGGA	GAACCCCCCG	CAGGCCCTC	TGGTCTGGGA	TCTGGCACAA	
42_13	ACCAATCGGA	GAACCCCCCG	CAGGCCCTC	TGGTCTGGGA	TCTGGTACAA	
42_3a	ACCAATCGGA	GAACCCCCCG	CAGGCCCTC	TGGTCTGGGA	TCTGGTACAA	
42_4	ACCAATCGGA	GAACCCCCCG	CAGGCCCTC	TGGTCTGGGA	TCTGGTACAA	
42_5a	ACCTCTCGGA	GAACCTCCCG	CCGCGCCCTC	AGGTCTGGGA	TCTGGTACAA	
42_10	ACCAATCGGA	GAACCCCCCG	CAGGCCCTC	TGGTCTGGGA	TCTGGTACAA	
42_3b	ACCAATCGGA	GAACCCCCCG	CAGGCCCTC	TGGTCTGGGA	TCTGGTACAA	
42_11	ACCAATCGGA	GAACCCCCCG	CAGGCCCTC	TGGTCTGGGA	TCTGGTACAA	
42_6b	ACCAATCGGA	GAACCCCCCG	CAGGCCCTC	TGGTCTGGGA	TCTGGTACAA	
43_1	ACCAATCGGA	GAACCACCAG	CAGGCCCTC	TGGTCTGGGA	TCTGGTACAA	
43_5	ACCAATCGGA	GAACCACCAG	CAGGCCCTC	TGGTCTGGGA	TCTGGTACAA	
43_12	ACCAATCGGA	GAACCACCAG	CAGGCCCTC	TGGTCTGGGA	TCTGGTACAA	
43_20	ACCTCTCGGA	GAACCTCCAG	CAGGCCCTC	AGGTCTGGGA	CCTAATACAA	
43_21	ACCTCTCGGA	GAACCTCCAG	CAGGCCCTC	AGGTCTGGGA	CCTAATACAA	
43_23	ACCTCTCGGA	GAACCTCCAG	CAGGCCCTC	AGGTCTGGGA	CCTAATACAA	
43_25	ACCTCTCGGA	GAACCTCCAG	CAGGCCCTC	AGGTCTGGGA	CCTAATACAA	
44_1	ACCAATCGGA	GAACCCCCCG	CAGGCCCTC	TGGTCTGGGA	TCTGGTACAA	
44_5	ACCAATCGGA	GAACCCCCCG	CAGGCCCTC	TGGTCTGGGA	TCTGGTACAA	
223_10	ACCAATCGGA	GAACCACCAG	CAGGCCCTC	TGGTCTGGGA	TCTGGTACAA	
223_2	ACCAATCGGA	GAACCACCAG	CAGGCCCTC	TGGTCTGGGA	TCTGGTACAA	
223_4	ACCAATCGGA	GAACCACCAG	CAGGCCCTC	TGGTCTGGGA	TCTGGTACAA	
223_5	ACCAATCGGA	GAACCACCAG	CAGGCCCTC	TGGTCTGGGA	TCTGGTACAA	
223_6	ACCAATCGGA	GAACCACCAG	CAGGCCCTC	TGGTCTGGGA	TCTGGTACAA	
223_7	ACCAATCGGA	GAACCACCAG	CAGGCCCTC	TGGTCTGGGA	TCTGGTACAA	
A3_4	ACCAATCGGA	GAACCCCCCG	CAGGCCCTC	TGGTGTGGGA	TCTAATACAA	
A3_5	ACCAATCGGA	GAACCCCCCG	CAGGCCCTC	TGGTGTGGGA	TCTAATACAA	
A3_7	ACCAATCGGA	GAACCCCCCG	CAGGCCCTC	TGGTGTGGGA	TCTAATACAA	
A3_3	ACCAATCGGA	GAACCCCCCG	CAGGCCCTC	TGGTGTGGGA	TCTAATACAA	
42_12	ACCAATCGGA	GAACCCCCCG	CAGGCCCTC	TGGTCTGGGA	TCTGGTACAA	
AAV1	ACCTCTCGGA	GAACCTCCAG	CAACCCCCGC	TGCTGTGGGA	CCTACTACAA	
AAV2	GCCTCTCGGA	CAGCCACCAG	CAGGCCCTC	TGGTCTGGGA	ACTAATACGA	
AAV3	ACCTCTCGGA	GAACCACCAG	CAGCCCCCAC	AAGTTTGGGA	TCTAATACAA	
AAV8	ACCTCTCGGA	GAACCTCCAG	CAGCGCCCTC	TGGTGTGGGA	CCTAATACAA	
AAV9	ACCTCTCGGA	GAACCTCCAG	CAGCGCCCTC	TGGTGTGGGA	CCTAATACAA	
AAV7	ACCTCTCGGA	GAACCTCCAG	CAGCGCCCTC	TAGTGTGGGA	TCTGGTACAG	
44_2	ACCAATCGGA	GAACCCCCCG	CAGGCCCTC	TGGTCTGGGA	TCTGGTACAA	vp3 start

Fig. 1AAF

	2851				2900
	vp3 start codon				
42_2	TGGCTGCAGG	CGGTGGCGCA	CCAATGGCAG	ACAATAACGA	AGGCGCCGAC
42_8	TGGCTGCAGG	CGGTGGCGCT	CCAATGGCAG	ACAATAACGA	AGGCGCCGAC
42_15	TGGCTGCAGG	CGGTGGCGCT	CCAATGGCAG	ACAATAACGA	AGGCGCCGAC
42_5b	TGGCTGCAGG	CGGTGGCGCT	CCAATGGCAG	ACAATAACGA	AGGCGCCGAC
42_1b	TGGCTGCAGG	CGGTGGCGCT	CCAATGGCAG	ACAATAACGA	AGGCGCCGAC
42_13	TGGCTGCAGG	CGGTGGCGCT	CCAATGGCAG	ACAATAACGA	AGGCGCCGAC
42_3a	TGGCTGCAGG	CGGTGGCGCT	CCAATGGCAG	ACAATAACGA	AGGCGCCGAC
42_4	TGGCTGCAGG	CGGTGGCGCT	CCAATGGCAG	ACAATAACGA	AGGCGCCGAC
42_5a	TGGCTGCAGG	CGGTGGCGCA	CCAATGGCAG	ACAATAACGA	AGGCGCCGAC
42_10	TGGCTGCAGG	CGGTGGCGCT	CCAATGGCAG	ACAATAACGA	AGGCGCCGAC
42_3b	TGGCTGCAGG	CGGTGGCGCT	CCAATGGCAG	ACAATAACGA	AGGCGCCGAC
42_11	TGGCTGCAGG	CGGTGGCGCT	CCAATGGCAG	ACAATAACGA	AGGCGCCGAC
42_6b	TGGCTGCAGG	CGGTGGCGCT	CCAATGGCAG	ACAATAACGA	AGGCGCCGAC
43_1	TGGCTGCAGG	CGGTGGCGCT	CCAATGGCAG	ACAATAACGA	AGGCGCCGAC
43_5	TGGCTGCAGG	CGGTGGCGCT	CCAATGGCAG	ACAATAACGA	AGGCGCCGAC
43_12	TGGCTGCAGG	CGGTGGCGCT	CCAATGGCAG	ACAATAACGA	AGGCGCCGAC
43_20	TGGCTTCAGG	CGGTGGCGCT	CCAATGGCAG	ACAATAACGA	AGGCGCCGAC
43_21	TGGCTTCAGG	CGGTGGCGCT	CCAATGGCAG	ACAATAACGA	AGGCGCCGAC
43_23	TGGCTTCAGG	CGGTGGCGCT	CCAATGGCAG	ACAATAACGA	AGGCGCCGAC
43_25	TGGCTTCAGG	CGGTGGCGCT	CCAATGGCAG	ACAATAACGA	AGGCGCCGAC
44_1	TGGCTGCAGG	CGGTGGCGCT	CCAATGGCAG	ACAATAACGA	AGGCGCCGAC
44_5	TGGCTGCAGG	CGGTGGCGCT	CCAATGGCAG	ACAATAACGA	AGGCGCCGAC
223_10	TGGCTGCAGG	CGGTGGCGCA	CCAATGGCTG	ACAATAACGA	GGGCGCCGAC
223_2	TGGTTGCAGG	CGGTGGCGCA	CCAATGGCTG	ACAATAACGA	GGGCGCCGAC
223_4	TGGCTGCAGG	CGGTGGCGCA	CCAATGGCTG	ACAATAACGA	GGGCGCCGAC
223_5	TGGCTGCAGG	CGGTGGCGCA	CCAATGGCTG	ACAATAACGA	GGGCGCCGAC
223_6	TGGCTGCAGG	CGGTGGCGCA	CCAATGGCTG	ACAATAGCGA	GGGCGCCGAC
223_7	TGGCTGCAGG	CGGTGGCGCA	CCAATGGCTG	ACAATAACGA	GGGCGCCGAC
A3_4	TGGCTTCAGG	CGGTGGGGCA	CCAATGGCAG	ACGATAACGA	AGGCGCCGAC
A3_5	TGGCTTCAGG	CGGTGGGGCA	CCAATGGCAG	ACAATAACGA	AGGCGCCGAC
A3_7	TGGCTTCAGG	CGGTGGGGCA	CCAATGGCAG	ACAATAACGA	AGGCGCCGAC
A3_3	TGGCTTCAGG	CGGTGGGGCA	CCAATGGCAG	ACAATAACGA	AGGCGCCGAC
42_12	TGGCTGCAGG	CGGTGGCGCT	CCAATGGCAG	ACAATAACGA	AGGCGCCGAC
AAV1	TGGCTTCAGG	CGGTGGCGCA	CCAATGGCAG	ACAATAACGA	AGGCGCCGAC
AAV2	TGGCTACAGG	CAGTGGCGCA	CCAATGGCAG	ACAATAACGA	GGGCGCCGAC
AAV3	TGGCTTCAGG	CGGTGGCGCA	CCAATGGCAG	ACAATAACGA	GGGTGCCGAT
AAV8	TGGCTGCAGG	CGGTGGCGCA	CCAATGGCAG	ACAATAACGA	AGGCGCCGAC
AAV9	TGGCTGCAGG	CGGTGGCGCA	CCAATGGCAG	ACAATAACGA	AGGCGCCGAC
AAV7	TGGCTGCAGG	CGGTGGCGCA	CCAATGGCAG	ACAATAACGA	AGGTGCCGAC
44_2	TGGCTGCAGG	CGGTGGCGCT	CCAATGGCAG	ACAATAACGA	AGGCGCCGAC
	vp3 start codon (cont'd)				

Fig. 1AAG

	2901				2950
42_2	GGAGTGGGTA	ATGCCTCCGG	AAATTGGCAT	TGCGATTCCA	CATGGCTGGG
42_8	GGAGTGGGTA	GTTCTCAGG	AAATTGGCAT	TGCGATTCCA	CATGGCTGGG
42_15	GGAGTGGGTA	GTTCTCAGG	AAATTGGCAT	TGCGATTCCA	CATGGCTGGG
42_5b	GGAGTGGGTA	GTTCTCAGG	AAATTGGCAT	TGCGATTCCA	CATGGCTGGG
42_1b	GGAGTGGGTA	GTTCTCAGG	AAATTGGCAT	TGCGATTCCA	CATGGCTGGG
42_13	GGAGTGGGTA	GTTCTCAGG	AAATTGGCAT	TGCGATTCCA	CATGGCTGGG
42_3a	GGAGTGGGTA	GTTCTCAGG	AAATTGGCAT	TGCGATTCCA	CATAGCTGGG
42_4	GGAGTGGGTA	ATGCCTCCGG	AAATTGGCAT	TGCGATTCCA	CATGGCTGGG
42_5a	GGAGTGGGTA	ATGCCTCCGG	AAATTGGCAT	TGCGATTCCA	CATGGCTGGG
42_10	GGAGTGGGTA	ATGCCTCCGG	AAATTGGCAT	TGCGATTCCA	CATGGCTGGG
42_3b	GGAGTGGGTA	ATGCCTCCGG	AAATTGGCAT	TGCGATTCCA	CATGGCTGGG
42_11	GGAGTGGGTA	ATGCCTCCGG	AAATTGGCAT	TGCGATTCCA	CATGGCTGGG
42_6b	GGAGTGGGTA	GTTCTCAGG	AAATTGGCAT	TGCGATTCCA	CATGGCTGGG
43_1	GGAGTGGGTA	GTTCTCAGG	AAATTGGCAT	TGCGATTCCA	CATGGCTGGG
43_5	GGAGTGGGTA	GTTCTCAGG	AAATTGGCAT	TGCGATTCCA	CATGGCTGGG
43_12	GGAGTGGGTA	GTTCTCAGG	AAATTGGCAT	TGCGATTCCA	CATGGCTGGG
43_20	GGAGTGGGTA	ATTCCTCGGG	AAATTGGCAT	TGCGATTCCA	CATGGCTGGG
43_21	GGAGTGGGTA	ATTCCTCGGG	AAATTGGCAT	TGCGATTCCA	CATGGCTGGG
43_23	GGAGTGGGTA	ATTCCTCGGG	AAATTGGCAT	TGCGATTCCA	CATGGCTGGG
43_25	GGAGTGGGTA	ATTCCTCGGG	AAATTGGCAT	TGCGATTCCA	CATGGCTGGG
44_1	GGAGTGGGTA	GTTCTCAGG	AAATTGGCAT	TGCGATTCCA	CATGGCTGGG
44_5	GGAGTGGGTA	GTTCTCAGG	AAATTGGCAT	TGCGATTCCA	CATGGCTGGG
223_10	GGAGTGGGTA	ATGCCTCAGG	AAATTGGCAT	TGCGATTCCA	CATGGCTGGG
223_2	GGAGTGGGTA	ATGCCTCAGG	AAATTGGCAT	TGCGATTCCA	CATGGCTGGG
223_4	GGAGTGGGTA	ATGCCTCAGG	AAATTGGCAT	TGCGATTCCA	CACGGCTGGG
223_5	GGAGTGGGTA	ATGCCTCAGG	AAATTGGCAT	TGCGATTCCA	CACGGCTGGG
223_6	GGAGTGGGTA	ATGCCTCAGG	AAATTGGCAT	TGCGATTCCA	CATGGCTGGG
223_7	GGAGTGGGTA	ATGCCTCAGG	AAATTGGCAT	TGCGATTCCA	CATGGCTGGG
A3_4	GGAGTGGGTA	ATTCCTCGGG	AAATTGGCAT	TGCGATTCCA	CATGGATGGG
A3_5	GGAGTGGGTA	ATTCCTCGGG	AAATTGGCAT	TGCGATTCCA	CATGGATGGG
A3_7	GGAGTGGGTA	ATTCCTCGGG	AAATTGGCAT	TGCGATTCCA	CATGGATGGG
A3_3	GGAGTGGGTA	ATTCCTCGGG	AAATTGGCAT	TGCGATTCCA	CATGGATGGG
42_12	GGAGTGGGTA	GTTCTCAGG	AAATTGGCAT	TGCGATTCCA	CATGGCTGGG
AAV1	GGAGTGGGTA	ATGCCTCAGG	AAATTGGCAT	TGCGATTCCA	CATGGCTGGG
AAV2	GGAGTGGGTA	ATTCCTCCGG	AAATTGGCAT	TGCGATTCCA	CATGGATGGG
AAV3	GGAGTGGGTA	ATTCCTCAGG	AAATTGGCAT	TGCGATTCCC	AATGGCTGGG
AAV8	GGAGTGGGTA	GTTCTCAGG	AAATTGGCAT	TGCGATTCCA	CATGGCTGGG
AAV9	GGAGTGGGTA	ATTCCTCGGG	AAATTGGCAT	TGCGATTCCA	CATGGCTGGG
AAV7	GGAGTGGGTA	ATGCCTCAGG	AAATTGGCAT	TGCGATTCCA	CATGGCTGGG
AAV10	GGTA	ATTCCTCCGG	AAATTGGCAT	TGCGATTCCA	CATGGCTGGG
AAV11	GGTA	ATTCCTCCGG	AAATTGGCAT	TGCGATTCCA	CATGGCTGGG
AAV12	GGTA	ATTCCTCCGG	AAATTGGCAT	TGCGATTCCA	CATGGCTGGG
44_2	GGAGTGGGTA	GTTCTCAGG	AAATTGGCAT	TGCGATTCCA	CATGGCTGGG

FIG. 1AAH

	2951				3000
42_2	CGACAGAGTC	ATCACCACCA	GCACCCGCAC	CTGGGGCCCTG	CCCACCTACA
42_8	CGACAGAGTC	ATCACCACCA	GCACCCGAAC	CTGGGGCCCTC	CCCACCTACA
42_15	CGACAGAGTC	ATCACCACCA	GCACCCGAAC	CTGGGGCCCTC	CCCACCTACA
42_5b	CGACAGAGTC	ATCACCACCA	GCACCCGAAC	CTGGGGCCCTC	CCCACCTACA
42_1b	CGACAGAGTC	ATCACCACCA	GCACCCGAAC	CTGGGGCCCTC	CCCACCTACA
42_13	CGACAGAGTC	ATCACCACCA	GCACCCGAAC	CTGGGGCCCTC	CCCACCTACA
42_3a	CGACAGAGTC	ATCACCACCA	GCACCCGAAC	CTGGGGCCCTC	CCCACCTACA
42_4	CGACAGAGTC	ATCACCACCA	GCACCCGCAC	CTGGGGCCCTG	CCCACCTACA
42_5a	CGACAGAGTC	ATCACCACCA	GCACCCGCAC	CTGGGGCCCTG	CCCACCTACA
42_10	CGACAGAGTC	ATCACCACCA	GCACCCGCAC	CTGGGGCCCTG	CCCACCTACA
42_3b	CGACAGAGTC	ATCACCACCA	GCACCCGCAC	CTGGGGCCCTG	CCCACCTACA
42_11	CGACAGAGTC	ATCACCACCA	GCACCCGCAC	CTGGGGCCCTG	CCCACCTACA
42_6b	CGACAGAGTC	ATCACCACCA	GCACCCGAAC	CTGGGGCCCTC	CCCACCTACA
43_1	CGACAGAGTC	ATCACCACCA	GCACCCGAAC	CTGGGGCCCTG	CCCACCTACA
43_5	CGACAGAGTC	ATCACCACCA	GCACCCGAAC	CTGGGGCCCTG	CCCACCTACA
43_12	CGACAGAGTC	ATCACCACCA	GCACCCGAAC	CTGGGGCCCTG	CCCACCTACA
43_20	GGACAGAGTC	ATCACCACCA	GCACCCGAAC	CTGGGGCCCTG	CCCACCTACA
43_21	GGACAGAGTC	ATCACCACCA	GCACCCGAAC	CTGGGGCCCTG	CCCACCTACA
43_23	GGACAGAGTC	ATCACCACCA	GCACCCGAAC	CTGGGGCCCTG	CCCACCTACA
43_25	GGACAGAGTC	ATCACCACCA	GCACCCGAAC	CTGGGGCCCTG	CCCACCTACA
44_1	CGACAGAGTC	ATCACCACCA	GCACCCGAAC	CTGGGGCCCTC	CCCACCTACA
44_5	CGACAGAGTC	ATCACCACCA	GCACCCGAAC	CTGGGGCCCTC	CCCACCTACA
223_10	CGACAGAGTC	ATCACCACCA	GCACCCGAAC	CTGGGGCCCTG	CCCACCTACA
223_2	CGACAGAGTC	ATCACCACCA	GCACCCGAAC	CTGGGGCCCTG	CCCACCTACA
223_4	CGACAGAGTC	ATCACCACCA	GCACCCGAAC	CTGGGGCCCTG	CCCACCTACA
223_5	CGACAGAGTC	ATCACCACCA	GCACCCGAAC	CTGGGGCCCTG	CCCACCTACA
223_6	CGACAGAGTC	ATCACCACCA	GCACCCGAAC	CTGGGGCCCTG	CCCACCTACA
223_7	CGACAGAGTC	ATCACCACCA	GCACCCGAAC	CTGGGGCCCTG	CCCACCTACA
A3_4	CGACAGAGTT	ATCACCACCA	GCACAAGAAC	CTGGGGCCCTC	CCCACCTACA
A3_5	CGACAGAGTT	ATCACCACCA	GCACAAGAAC	CTGGGGCCCTC	CCCACCTACA
A3_7	CGACAGAGTT	ATCACCACCA	GCACAAGAAC	CTGGGGCCCTC	CCCACCTACA
A3_3	CGACAGAGTT	ATCACCACCA	GCACAAGAAC	CTGGGGCCCTC	CCCACCTACA
42_12	CGACAGAGTC	ATCACCACCA	GCACCCGAAC	CTGGGGCCCTC	CCCACCTACA
AAV1	CGACAGAGTC	ATCACCACCA	GCACCCGCAC	CTGGGGCCCTG	CCCACCTACA
AAV2	CGACAGAGTC	ATCACCACCA	GCACCCGAAC	CTGGGGCCCTG	CCCACCTACA
AAV3	CGACAGAGTC	ATCACCACCA	GCACCCGAAC	CTGGGGCCCTG	CCCACCTACA
AAV8	CGACAGAGTC	ATCACCACCA	GCACCCGAAC	CTGGGGCCCTG	CCCACCTACA
AAV9	GGACAGAGTC	ATCACCACCA	GCACCCGAAC	CTGGGGCATTG	CCCACCTACA
AAV7	CGACAGAGTC	ATTACCACCA	GCACCCGAAC	CTGGGGCCCTG	CCCACCTACA
AAV10	CGACAGAGTC	ATCACCACCA	GCACCCGAAC	CTGGGGCCCTG	CCCACCTACA
AAV11	CGACAGAGTC	ATCACCACCA	GCACCCGAAC	CTGGGGCCCTG	CCAACCTACA
AAV12	CGACCGAGTC	ATTACCACCA	GCACCCGGAC	TTGGGGCCCTG	CCCACCTACA
44_2	CGACAGAGTC	ATCACCACCA	GCACCCGAAC	CTGGGGCCCTC	CCCACCTACA

Fig. 1AAI

	3001				3050
42_2	ACAACCACCT	CTACAAGCAG	ATATCAA..G	TCAGAGCGGG	GCT....ACC
42_8	ACAACCACCT	CTACAAGCAA	ATCTCCAACG	GGACATCGGG	AGGAAGCACC
42_15	ACAACCACCT	CTACAAGCAA	ATCTCCAACG	GGACATCGGG	AGGAAGCACC
42_5b	ACAACCACCT	CTACAAGCAA	ATCTCCAACG	GGACATCGGG	AGGAAGCACC
42_1b	ACAACCACCT	CTACAAGCAA	ATCTCCAACG	GGACATCGGG	AGGAAGCACC
42_13	ACAACCACCT	CTACAAGCAA	ATCTCCAACG	GGACATCGGG	AGGAAGCACC
42_3a	ACAACCACCT	CTACAAGCAA	ATCTCCAACG	GGACATCGGG	AGGAAGCACC
42_4	ACAACCACCT	CTACAAGCAG	ATATCAA...	.GTCAGAGCG	GGGC..TACC
42_5a	ACAACCACCT	CTACAAGCAG	ATATCAA...	.GTCAGAGCG	GGGC..TACC
42_10	ACAACCACCT	CTACAAGCAG	ATATCAA..G	TCAGAGCGGG	GCTA....CC
42_3b	ACAACCACCT	CTACAAGCAG	ATATCAA..G	TCAGAGCGGG	GCTA....CC
42_11	ACAACCACCT	CTACAAGCAG	ATATCAA..G	TCAGAGCGGG	GCTA....CC
42_6b	ACAACCACCT	CTACAAGCAA	ATCTCCAACG	GGACATCGGG	AGGAAGCACC
43_1	ACAACCATCT	CTACAAGCAA	ATCTCCAACG	GGACATCGGG	AGGAAGCACT
43_5	ACAACCATCT	CTACAAGCAA	ATCTCCAACG	GGACATCGGG	AGGAAGCACT
43_12	ACAACCATCT	CTACAAGCAA	ATCTCCAACG	GGACATCGGG	AGGAAGCACT
43_20	ACAACCACCT	CTACAAGCAA	ATCTCCAACG	GCACCTCGGG	AGGAAGCACC
43_21	ACAACCACCT	CTACAAGCAA	ATCTCCAACG	GCACCTCGGG	AGGAAGCACC
43_23	ACAACCACCT	CTACAAGCAA	ATCTCCAACG	GCACCTCGGG	AGGAAGCACC
43_25	ACAACCACCT	CTACAAGCAA	ATCTCCAACG	GCACCTCGGG	AGGAAGCACC
44_1	ACAACCACCT	CTACAAGCAA	ATCTCCAACG	GGACTTCGGG	AGGAAGCACC
44_5	ACAACCACCT	CTACAAGCAA	ATCTCCAACG	GGACTTCGGG	AGGAAGCACC
223_10	ACAACCACCT	CTACAAGCAA	ATCTCCAGTC	AGTCAGCAGG	GAG...CACC
223_2	ACAACCACCT	CTACAAGCAA	ATCTCCAGTC	AGTCAGCAGG	GAG...CACC
223_4	ACAACCACCT	CTACAAGCAA	ATCTCCAGTC	AGTCAGCAGG	GAG...CACC
223_5	ACAACCACCT	CTACAAGCAA	ATCTCCAGTC	AGTCAGCAGG	GAG...CACC
223_6	ACAACCACCT	CTACAAGCAA	ATCTCCAGTC	AGTCAGCAGG	GAG...CACC
223_7	ACAACCACCT	CTACAAGCAA	ATCTCCAGTC	AGTCAGCAGG	GAG...CACC
A3_4	ATAATCACCT	CTACAAGCAA	ATCTCCA...	GCGAATCGGG	AGC...CACC
A3_5	ATAATCACCT	CTACAAGCAA	ATCTCCA...	GCGAATCGGG	AGC...CACC
A3_7	ATAATCGCCT	CTACAAGCAA	ATCTCCA...	GCGAATCGGG	AGC...CACC
A3_3	ATAATCACCT	CTACAAGCAA	ATCTCCA...	GCGAATCGGG	AGC...CACC
42_12	ACAACCACCT	CTACAAGCAA	ATCTCCAACG	GGACATCGGG	AGGAAGCACC
AAV1	ATAACCACCT	CTACAAGCAA	ATCTCCAGTG	CTTCAACGGG	.GG..CCAGC
AAV2	ACAACCACCT	CTACAAACAA	ATTTCCA...	GCCAATCAGG	AGC...CTCG
AAV3	ACAACCATCT	CTACAAGCAA	ATCTCCA...	GCCAATCAGG	AGC...TTCA
AAV8	ACAACCACCT	CTACAAGCAA	ATCTCCAACG	GGACATCGGG	AGGAGCCACC
AAV9	ACAACCACCT	CTACAAGCAA	ATCTCCAATG	GAACATCGGG	AGGAAGCACC
AAV7	ACAACCACCT	CTACAAGCAA	ATCTCCAGTG	AAACTGCAGG	TAG...TACC
AAV10	ACAACCACAT	CTACAAGCAA	ATCTCCAGCG	AGACAGGAGC	CACCAACGAC
AAV11	ACAACCACCT	CTACAAACAA	ATCTCCAGCG	CTTCAACGGG	GGCCAGCAAC
AAV12	ACAACCACCT	CTACAAGCAA	ATCTCCAGCC	AATCGGGTGC	CACCAACGAC
44_2	ACAACCACCT	CTACAAGCAA	ATCTCCAACG	GGACTTCGGG	AGGAAGCACC

Fig. 1AAJ

	3051				3100
42_2	AACGACAACC	ACTTCTTCGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
42_8	AACGACAACA	CCTACTTCGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
42_15	AACGACAACA	CCTACTTCGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
42_5b	AACGACAACA	CCTACTTCGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
42_1b	AACGACAACA	CCTACTTCGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
42_13	AACGACAACA	CCTACTTCGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
42_3a	AACGACAACA	CCTACTTCGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
42_4	AACGACAACC	ACTTCTTCGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
42_5a	AACGACAACC	ACTTCTTCGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
42_10	AACGACAACC	ACTTCTTCGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
42_3b	AACGACAACC	ACTTCTTCGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
42_11	AACGACAACC	ACTTCTTCGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
42_6b	AACGACAACA	CCTACTTCGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
43_1	AACGACAACA	CCTACTTTGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
43_5	AACGACAACA	CCTACTTTGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
43_12	AACGACAACA	CCTACTTTGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
43_20	AACGACAACA	CCTATTTTGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
43_21	AACGACAACA	CCTATTTTGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
43_23	AACGACAACA	CCTATTTTGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
43_25	AACGACAACA	CCTATTTTGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
44_1	AACGACAACA	CCTACTTCGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
44_5	AACGACAACA	CCTACTTCGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
223_10	AACGATAACG	TCTATTTTCGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
223_2	AACGATAACG	TCTATTTTCGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
223_4	AACGATAACG	TCTATTTTCGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
223_5	AACGATAACG	TCTATTTTCGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
223_6	AACGATAACG	TCTATTTTCGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
223_7	AACGATAACG	TCTATTTTCGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
A3_4	AACGACAACC	ACTACTTCGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
A3_5	AACGACAACC	ACTACTTCGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
A3_7	AACGACAACC	ACTACTTCGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
A3_3	AACGACAACC	ACTACTTCGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
42_12	AACGACAACA	CCTACTTCGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
AAV1	AACGACAACC	ACTACTTCGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
AAV2	AACGACAATC	ACTACTTTGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
AAV3	AACGACAACC	ACTACTTTGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
AAV8	AACGACAACA	CCTACTTCGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
AAV9	AACGACAACA	CCTACTTTGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
AAV7	AACGACAACA	CCTACTTCGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
AAV10	AACCACTACT	TCGGCTACAG	C.....ACC	CCCTGGGGGT	ATTTTGACTT
AAV11	...GACAACC	ACTACTTTGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT
AAV12	AACCACTACT	TCGGCTA...	...CAGCACC	CCCTGGGGGT	ATTTTGACTT
44_2	AACGACAACA	CCTACTTCGG	CTACAGCACC	CCCTGGGGGT	ATTTTGACTT

Fig. 1AAK

	3101				3150
42_2	TAACAGATTC	CACTGCCACT	TCTCACCACG	TGACTGGCAG	CGACTCATCA
42_8	TAACAGATTC	CACTGCCACT	TCTCACCACG	TGACTGGCAG	CGACTCATCA
42_15	TAACAGATTC	CACTGCCACT	TCTCACCACG	TGACTGGCAG	CGACTCATCA
42_5b	TAACAGATTC	CACTGCCACT	TCTCACCACG	TGACTGGCAG	CGACTCATCA
42_1b	TAACAGATTC	CACTGCCACT	TCTCACCACG	TGACTGGCAG	CGACTCATCA
42_13	TAACAGATTC	CACTGCCACT	TCTCACCACG	TGACTGGCAG	CGACTCATCA
42_3a	TAACAGATTC	CACTGCCACT	TCTCACCACG	TGACTGGCAG	CGACTCATCA
42_4	CAACAGATTC	CACTGCCACT	TCTCACCACG	TGACTGGCAG	CGACTCATCA
42_5a	CAACAGATTC	CACTGCCACT	TCTCACCACG	TGACTGGCAG	CGACTCATCA
42_10	CAACAGATTC	CACTGCCACT	TCTCACCACG	TGACTGGCAG	CGACTCATCA
42_3b	CAACAGATTC	CACTGCCACT	TCTCACCACG	TGACTGGCAG	CGACTCATCA
42_11	CAACAGATTC	CACTGCCACT	TCTCACCACG	TGACTGGCAG	CGACTCATCA
42_6b	TAACAGATTC	CACTGCCACT	TCTCACCACG	TGACTGGCAG	CGACTCATCA
43_1	CAACAGATTC	CACTGCCACT	TCTCACCACG	TGACTGGCAG	CGACTCATCA
43_5	CAACAGATTC	CACTGCCACT	TCTCACCACG	TGACTGGCAG	CGACTCATCA
43_12	CAACAGATTC	CACTGCCACT	TCTCACCACG	TGACTGGCAG	CGACTCATCA
43_20	CAACAGATTC	CACTGTCACT	TTTCACCACG	TGACTGGCAA	CGACTCATCA
43_21	CAACAGATTC	CACTGTCACT	TTTCACCACG	TGACTGGCAA	CGACTCATCA
43_23	CAACAGATTC	CACTGTCACT	TTTCACCACG	TGACTGGCAA	CGACTCATCA
43_25	CAACAGATTC	CACTGTCACT	TTTCACCACG	TGACTGGCAA	CGACTCATCA
44_1	TAACAGATTC	CACTGCCACT	TCTCACCACG	TGACTGGCAG	CGACTCATCA
44_5	TAACAGATTC	CACTGCCACT	TCTCACCACG	TGACTGGCAG	CGACTCATCA
223_10	CAACAGATTC	CATTGCCACT	TCTCACCACG	TGACTGGCAG	CGACTTATCA
223_2	CAACAGATTC	CATTGCCACT	TCTCACCACG	TGACTGGCAG	CGACTTATCA
223_4	CAACAGATTC	CATTGCCACT	TCTCACCACG	TGACTGGCAG	CGACTTATCA
223_5	CAACAGATTC	CATTGCCACT	TCTCACCACG	TGACTGGCAG	CGACTTATCA
223_6	CAACAGATTC	CATTGCCACT	TCTCACCACG	TGACTGGCAG	CGACTTATCA
223_7	CAACAGATTC	CATTGCCACT	TCTCACCACG	TGACTGGCAG	CGACTTATCA
A3_4	TAACAGATTC	CACTGTCACT	TCTCACCACG	TGACTGGCAG	CGACTCATCA
A3_5	TAACAGATTC	CACTGTCACT	TCTCACCACG	TGACTGGCAG	CGACTCATCA
A3_7	TAACAGATTC	CACTGTCACT	TCTCACCACG	TGACTGGCAG	CGACTCATCA
A3_3	TAACAGATTC	CACTGTCACT	TCTCACCACG	TGACTGGCAG	CGACTCATCA
42_12	TAACAGATTC	CACTGCCACT	TCTCACCACG	TGACTGGCAG	CGACTCATCA
AAV1	CAACAGATTC	CACTGCCACT	TTTCACCACG	TGACTGGCAG	CGACTCATCA
AAV2	CAACAGATTC	CACTGCCACT	TTTCACCACG	TGACTGGCAA	AGACTCATCA
AAV3	TAACAGATTC	CACTGCCACT	TCTCACCACG	TGACTGGCAG	CGACTCATTA
AAV8	TAACAGATTC	CACTGCCACT	TTTCACCACG	TGACTGGCAG	CGACTCATCA
AAV9	CAACAGATTC	CACTGCCACT	TCTCACCACG	TGACTGGCAG	CGACTCATCA
AAV7	TAACAGATTC	CACTGCCACT	TCTCACCACG	TGACTGGCAG	CGACTCATCA
AAV10	TAACAGATTC	CACTGCCACT	TTTCACCACG	TGACTGGCAG	CGACTCATCA
AAV11	TAACAGATTC	CACTGCCACT	TCTCACCACG	TGACTGGCAG	CGACTCATCA
AAV12	CAACAGATTC	CACTGCCATT	TCTCACCACG	TGACTGGCAG	CGACTCATCA
44_2	TAACAGATTC	CACTGCCACT	TCTCACCACG	TGACTGGCAG	CGACTCATCA

Fig. 1AAL

	3151				3200
42_2	ACAACAACTG	GGGATTCCGG	CCCAGAAAGC	TGCGGTTCAA	GTTGTTCAAC
42_8	ACAACAACTG	GGGATTCCGG	CCCAAGAGAC	TCAACTTCAA	GCTCTTCAAC
42_15	ACAACAACTG	GGGATTCCGG	CCCAAGAGAC	TCAACTTCAA	GCTCTTCAAC
42_5b	ACAACAACTG	GGGATTCCGG	CCCAAGAGAC	TCAACTTCAA	GCTCTTCAAC
42_1b	ACAACAACTG	GGGATTCCGG	CCCAAGAGAC	TCAACTTCAA	GCTCTTCAAC
42_13	ACAACAACTG	GGGATTCCGG	CCCAAGAGAC	TCAACTTCAA	GCTCTTCAAC
42_3a	ACAACAGCTG	GGGATTCCGG	CCCAAGAGAC	TCAACTTCAA	GCTCTTCAAC
42_4	ACAACAACTG	GGGATTCCGG	CCCAAGAGAC	TCAACTTCAA	GCTCTTCAAC
42_5a	ACAACAACCG	GGGATTCCGG	CCCAGAAAGC	TGCGGTTCAA	GTTGTTCAAC
42_10	ACAACAACTG	GGGATTCCGG	CCCAGAAAGC	TGCGGTTCAA	GTTGTTCAAC
42_3b	ACAACAACTG	GGGATTCCGG	CCCAGAAAGC	TGCGGTTCAA	GTTGTTCAAC
42_11	ACAACAACTG	GGGATTCCGG	CCCAGAAAGC	TGCGGTTCAA	GTTGTTCAAC
42_6b	ACAACAACTG	GGGATTCCGG	CCCAGAAAGC	TGCGGTTCAA	GTTGTTCAAC
43_1	ACAATAACTG	GGGATTCCGG	CCCAAGAGAC	TCAACTTCAA	GCTCTTCAAC
43_5	ACAATAACTG	GGGATTCCGG	CCCAAGAGAC	TCAACTTCAA	GCTCTTCAAC
43_12	ACAATAACTG	GGGATTCCGG	CCCAAGAGAC	TCAACTTCAA	GCTCTTCAAC
43_20	ACAACAATTG	GGGATTCCGG	CCCAAAAGAC	TCAACTTCAA	GCTGTTCAAC
43_21	ACAACAATTG	GGGATTCCGG	CCCAAAAGAC	TCAACTTCAA	GCTGTTCAAC
43_23	ACAACAATTG	GGGATTCCGG	CCCAAAAGAC	TCAACTTCAA	GCTGTTCAAC
43_25	ACAACAATTG	GGGATTCCGG	CCCAAAAGAC	TCAACTTCAA	GCTGTTCAAC
44_1	ACAACAACTG	GGGATTCCGG	CCCAAGAGAC	TCAACTTCAA	GCTCTTCAAC
44_5	ACAACAACTG	GGGATTCCGG	CCCAAGAGAC	CCAAC TTCAA	GCTCTTCAAC
223_10	ACAACAACTG	GGGATTCCGG	CCCAAGAAGC	TCAACTTCAA	GCTCTTCAAC
223_2	ACAACAACTG	GGGATTCCGG	CCCAAGAAGC	TCAACTTCAA	GCTCTTCAAC
223_4	ACAACAACTG	GGGATTCCGG	CCCAAGAAGC	TCAACTTCAA	GCTCTTCAAC
223_5	ACAACAACTG	GGGATTCCGG	CCCAAGAAGC	TCAACTTCAA	GCTCTTCAAC
223_6	ACAACAACTG	GGGATTCCGG	CCCAAGAAGC	TCAACTTCAA	GCTCTTCAAC
223_7	ACAACAACTG	GGGATTCCGG	CCCAAGAAGC	TCAACTTCAA	GCTCTTCAAC
A3_4	ACAACAACTG	GGGATTTAGA	CCCAAGAAAC	TCAATTTCAA	GCTCTTCAAC
A3_5	ATAACAACTG	GGGATTTAGA	CCCAAGAAAC	TCAATTTCAA	GCTCTTCAAC
A3_7	ACAACAACTG	GGGATTTAGA	CCCAAGAAAC	TCAATTTCAA	GCTCTTCAAC
A3_3	ACAACAACTG	GGGATTTAGA	CCCAAGAAAC	TCAATTTCAA	GCTCTTCAAC
42_12	ACAACAACTG	GGGATTCCGG	CCCAAGAGAC	TCAACTTCAA	GCTCTTCAAC
AAV1	ACAACAATTG	GGGATTCCGG	CCCAAGAGAC	TCAACTTCAA	ACTCTTCAAC
AAV2	ACAACAACTG	GGGATTCCGA	CCCAAGAGAC	TCAACTTCAA	GCTCTTTAAC
AAV3	ACAACAACTG	GGGATTCCGG	CCCAAGAAAC	TCAGCTTCAA	GCTCTTCAAC
AAV8	ACAACAACTG	GGGATTCCGG	CCCAAGAGAC	TCAGCTTCAA	GCTCTTCAAC
AAV9	ACAACAACTG	GGGATTCCGG	CCAAAGAGAC	TCAACTTCAA	GCTGTTCAAC
AAV7	ACAACAACTG	GGGATTCCGG	CCCAAGAAGC	TGCGGTTCAA	GCTCTTCAAC
AAV10	ACAACAACTG	GGGATTC			
AAV11	ACAACAACTG	GGGATTC			
AAV12	ACAACAACTG	GGGATTC			
44_2	ACAACAACTG	GGGATTCCGG	CCCAAGAGAC	TCAACTTCAA	GCTCTTCAAC

Fig. 1AAM

	3201				3250
42_2	ATCCAGGTCA	AGGAGGTCAC	GACGAACGAC	GGCGTTACGA	CCATCGCTAA
42_8	ATCCAGGTCA	AGGAGGTCAC	GCAGAATGAA	GGCACCAAGA	CCATCGCCAA
42_15	ATCCAGGTCA	AGGAGGTCAC	GCAGAATGAA	GGCACCAAGA	CCATCGCCAA
42_5b	ATCCAGGTCA	AGGAGGTCAC	GCAGAATGAA	GGCACCAAGA	CCATCGCCAA
42_1b	ATCCAGGTCA	AGGAGGTCAC	GCAGAATGAA	GGCACCAAGA	CCATCGCCAA
42_13	ATCCAGGTCA	AGGAGGTCAC	GCAGAATGAA	GGCACCAAGA	CCATCGCCAA
42_3a	ATCCAGGTCA	AGGAGGTCAC	GCAGAATGAA	GGCACCAAGA	CCATCGCCAA
42_4	ATCCAGGTCA	AGGAGGTCAC	GCAGAATGAA	GGCACCAAGA	CCATCGCCAA
42_5a	ATCCAGGTCA	AGGAGGTCAC	GACGAACGAC	GGCGTTACGA	CCATCGCTAA
42_10	ATCCAGGTCA	AGGAGGTCAC	GACGAACGAC	GGCGTTACGA	CCATCGCCAA
42_3b	ATCCAGGTCA	AGGAGGTCAC	GACGAACGAC	GGCGTTACGA	CCATCGCTAA
42_11	ATCCAGGTCA	AGGAGGTCAC	GACGAACGAC	GGCGTTACGA	CCATCGCTAA
42_6b	ATCCAGGTCA	AGGAGGTCAC	GACGGACGAC	GGCGTTACGA	CCATCGCTAA
43_1	ATCCAGGTCA	AGGAGGTCAC	GCAGAATGAA	GGCACCAAGA	CCATCGCCAA
43_5	ATCCAGGTCA	AGGAGGTCAC	GCAGAATGAA	GGCACCAAGA	CCATCGCCAA
43_12	ATCCAGGTCA	AGGAGGTCAC	GCAGAATGAA	GGCACCAAGA	CCATCGCCAA
43_20	ATCCAGGTCA	AGGAAGTCAC	GACGAACGAA	GGCACCAAGA	CCATCGCCAA
43_21	ATCCAGGTCA	AGGAAGTCAC	GACGAACGAA	GGCACCAAGA	CCATCGCCAA
43_23	ATCCAGGTCA	AGGAAGTCAC	GACGAACGAA	GGCACCAAGA	CCATCGCCAA
43_25	ATCCAGGTCA	AGGAAGTCAC	GACGAACGAA	GGCACCAAGA	CCATCGCCAA
44_1	ATCCAGGTCA	AGGAGGTCAC	GCAGAATGAA	GGCACCAAGA	CCATCGCCAA
44_5	ATCCAGGTCA	AGGAGGTCAC	GCAGAATGAA	GGCACCAAGA	CCATCGCCAA
223_10	ATCCAGGTCA	AGGAGGTCAC	GACGAATGAC	GGTGTACAA	CCATCGCTAA
223_2	ATCCAGGTCA	AGGAGGTCAC	GACGAATGAC	GGTGTACAA	CCATCGCTAA
223_4	ATCCAGGTCA	AGGAGGTCAC	GACGAATGAC	GGCGTCACAA	CCATCGCTAA
223_5	ATCCAGGTCA	AGGAGGTCAC	GACGAATGAC	GGCGTCACAA	CCATCGCTAA
223_6	ATCCAGGTCA	AGGAGGTCAC	GACGAATGAC	GGTGTACAA	CCATCGCTAA
223_7	ATCCAGGTCA	AGGAGGTCAC	GACGAATGAC	GGCGTCACAA	CCATCGCTAA
A3_4	ATCCAAGTCA	AGGAGGTCAC	GCAGAATGAT	GGAACCACGA	CCATCGCCAA
A3_5	ATCCAAGTCA	AGGAGGTCAC	GCAGAATGAT	GGAACCACGA	CCATCGCCAA
A3_7	ATCCAAGTCA	AGGAGGTCAC	GCAGAATGAT	GGAACCACGA	CCATCGCCAA
A3_3	ATCCAAGTCA	AGGAGGTCAC	GCAGAATGAT	GGAACCACGA	CCATCGCCAA
42_12	ATCCAGGTCA	AGGAGGTCAC	GCAGAATGAA	GGCACCAAGA	CCATCGCCAA
AAV1	ATCCAAGTCA	AGGAGGTCAC	GACGAATGAT	GGCGTCACAA	CCATCGCTAA
AAV2	ATTCAAGTCA	AAGAGGTCAC	GCAGAATGAC	GGTACGACGA	CGATTGCCAA
AAV3	ATCCAAGTTA	GAGGGGTCAC	GCAGAACGAT	GGCACGACGA	CTATTGCCAA
AAV8	ATCCAGGTCA	AGGAGGTCAC	GCAGAATGAA	GGCACCAAGA	CCATCGCCAA
AAV9	ATCCAGGTCA	AGGAGGTTAC	GACGAACGAA	GGCACCAAGA	CCATCGCCAA
AAV7	ATCCAGGTCA	AGGAGGTCAC	GACGAATGAC	GGCGTTACGA	CCATCGCTAA
44_2	ATCCAGGTCA	AGGAGGTCAC	GCAGAATGAA	GGCACCAAGA	CCATCGCCAA

Fig. 1AAN

	3251				3300
42_2	TAACCTTACC	AGCACGATTC	AGGTCTTCTC	GGACTCGGAG	TACCAACTGC
42_8	TAACCTTACC	AGCACGATTC	AGGTCTTTAC	GGACTCGGAA	TACCAGCTCC
42_15	TAACCTTACC	AGCACGATTC	AGGTCTTTAC	GGACTCGGAA	TACCAGCTCC
42_5b	TAACCTTACC	AGCACGATTC	AGGTCTTTAC	GGACTCGGAA	TACCAGCTCC
42_1b	TAACCTTACC	AGCACGATTC	AGGTCTTTAC	GGACTCGGAA	TACCAGCTCC
42_13	TAACCTTACC	AGCACGATTC	AGGTCTTTAC	GGACTCGGAA	TACCAGCTCC
42_3a	TAACCTTACC	AGCACGATTC	AGGTCTTTAC	GGACTCGGAA	TACCAGCTCC
42_4	TAACCTTACC	AGCACGATTC	AGGTCTTTAC	GGACTCGGAA	TACCGGCTCC
42_5a	TAACCTTACC	AGCACGATTC	AGGTCTTCTC	GGACTCGGAG	TACCAACTGC
42_10	TAACCTTACC	AGCACGATTC	AGGTCTTCTC	GGACTCGGAG	TACCAACTGC
42_3b	TAACCTTACC	AGCACGATTC	AGGTCTTCTC	GGACTCGGAG	TACCAACTGC
42_11	TAACCTTACC	AGCACGATTC	AGGTCTTCTC	GGACTCGGAG	TACCAACTGC
42_6b	TAACCTTACC	AGCACGATTC	AGGTCTTCTC	GGACTCGGAG	TACCAACTGC
43_1	TAACCTTACC	AGCACGATTC	AGGTGTTTAC	GGACTCGGAA	TACCAGCTCC
43_5	TAACCTTACC	AGCACGATTC	AGGTGTTTAC	GGACTCGGAA	TACCAGCTCC
43_12	TAACCTTACC	AGCACGATTC	AGGTGTTTAC	GGACTCGGAA	TACCAGCTCC
43_20	TAATCTCACC	AGCACCGTGC	AGGTCTTTAC	GGACTCGGAG	TACCAGTTAC
43_21	TAATCTCACC	AGCACCGTGC	GGGTCTTTAC	GGACTCGGAG	TACCAGTTAC
43_23	TAATCTCACC	AGCACCGTGC	AGGTCTTTAC	GGACTTGGAG	TACCAGTTAC
43_25	TAATCTCACC	AGCACCGTGC	AGGTCTTTAC	GGACTCGGAG	TACCAGTTAC
44_1	TAACCTTACC	AGCACGATTC	AGGTCTTTAC	GGACTCGGAA	TACCAGCTCC
44_5	TAACCTTACC	AGCACGATTC	AGGTCTTTAC	GGACTCGGAA	TACCAGCTCC
223_10	TAACCTTACC	AGCACGGTTC	AGGTCTTTTC	GGACTCGGAA	TATCAACTGC
223_2	TAACCTTACC	AGCACGGTTC	AGGTCTTTTC	GGACTCGGAA	TATCAACTGC
223_4	TAACCTTACC	AGCACGGTTC	AGGTCTTTTC	GGACTCGGAA	TATCAACTGC
223_5	TAACCTTACC	AGCACGGTTC	AGGTCTTTTC	GGACTCGGAA	TATCAACTGC
223_6	TAACCTTACC	AGCACGGTTC	AGGTCTTTTC	GGACTCGGAA	TATCAACTGC
223_7	TAACCTTACC	AGCACGGTTC	AGGTCTTTTC	GGACCCGGAA	TATCAACTGC
A3_4	TAACCTTACC	AGCACGGTGC	AGGTCTTCAC	AGACTCTGAG	TACCAGCTGC
A3_5	TAACCTTACC	AGCACGGTGC	AGGTCTTCAC	AGACTCTGAG	TACCAGCTGC
A3_7	TAACCTTACC	AGCACGGTGC	AGGTCTTCAC	AGACTCTGAG	TACCAGCTGC
A3_3	TAACCTTACC	AGCGCGGTGC	AGGTCTTCAC	AGACTCTGAG	TACCAGCTGC
42_12	TAACCTTACC	AGCACGATTC	AGGTCTTTAC	GGACTCGGAA	TACCAGCTCC
AAV1	TAACCTTACC	AGCACGGTTC	AAGTCTTCTC	GGACTCGGAG	TACCAGCTTC
AAV2	TAACCTTACC	AGCACGGTTC	AGGTGTTTAC	TGACTCGGAG	TACCAGCTCC
AAV3	TAACCTTACC	AGCACGGTTC	AAGTGTTTAC	GGACTCGGAG	TATCAGCTCC
AAV8	TAACCTCACC	AGCACCATCC	AGGTGTTTAC	GGACTCGGAG	TACCAGCTGC
AAV9	TAACCTTACC	AGCACCGTCC	AGGTCTTTAC	GGACTCGGAG	TACCAGCTAC
AAV7	TAACCTTACC	AGCACGATTC	AGGTATTCTC	GGACTCGGAA	TACCAGCTGC
44_2	TAACCTTACC	AGCACGATTC	AGGTCTTTAC	GGACTCGGAA	TACCAGCTCC

Fig. 1AAO

	3301				3350
42_2	CGTACGTCCT	CGGCTCTGCG	CACCAGGGCT	GCCTCCCTCC	GTTCCCTGCG
42_8	CGTACGTCCT	CGGCTCTGCG	CACCAGGGCT	GCCTGCCTCC	GTTCCCGGCG
42_15	CGTACGTCCT	CGGCTCTGCG	CACCAGGGCT	GCCTGCCTCC	GTTCCCGGCG
42_5b	CGTACGTCCT	CGGCTCTGCG	CACCAGGGCT	GCCTGCCTCC	GTTCCCGGCG
42_1b	CGTACGTCCT	CGGCTCTGCG	CACCAGGGCT	GCCTGCCTCC	GTTCCCGGCG
42_13	CGTACGTCCT	CGGCTCTGCG	CACCAGGGCT	GCCTGCCTCC	GTTCCCGGCG
42_3a	CGTACGTCCT	CGGCTCTGCG	CACCAGGGCT	GCCTGCCTCC	GTTCCCGGCG
42_4	CGTACGTCCT	CGGCTCTGCG	CACCAGGGCT	GCCTGCCTCC	GTTCCCGGCG
42_5a	CGTACGTCCT	CGGCTCTGCG	CACCAGGGCT	GCCTCCCTCC	GTTCCCTGCG
42_10	CGTACGTCCT	CGGCTCTGCG	CACCAGGGCT	GCCTCCCTCC	GTTCCCTGCG
42_3b	CGTACGTCCT	CGGCTCTGCG	CACCAGGGCT	GCCTCCCTCC	GTTCCCTGCG
42_1	CGTACGTCCT	CGGCTCTGCG	CACCAGGGCT	GCCTCCCTCC	GTTCCCTGCG
42_6b	CGTACGTCCT	CGGCTCTGCG	CACCAGGGCT	GCCTCCCTCC	GTTCCCTGCG
43_1	CGTACGTCCC	CGGCTCTGCG	CACCAGGGCT	GCCTCCCTCC	GTTCCCGGCG
43_5	CGTACGTCCT	CGGCTCTGCG	CACCAGGGCT	GCCTCCCTCC	GTTCCCGGCG
43_12	CGTACGTCCT	CGGCTCTGCG	CACCAGGGCT	GCCTCCCTCC	GTTCCCGGCG
43_20	CGTACGTGCT	AGGATCCGCT	CACCAGGGAT	GTCTGCCTCC	GTTCCCGGCG
43_21	CGTACGTGCT	AGGATCCGCT	CACCAGGGAT	GTCTGCCTCC	GTTCCCGGCG
43_23	CGTACGTGCT	AGGATCCGCT	CACCAGGGAT	GTCTGCCTCC	GTTCCCGGCG
43_25	CGTACGTGCT	AGGATCCGCT	CACCAGGGAT	GTCTGCCTCC	GTTCCCGGCG
44_1	CGTACGTCCT	CGGCTCTGCG	CACCAGGGCT	GCCTGCCTCC	GTTCCCGGCG
44_5	CGTACGTCCT	CGGCTCTGCG	CACCAGGGCT	GCCTGCCTCC	GTTCCCGGCG
223_10	CGTACGTCCT	CGGCTCCGCG	CACCAGGGCT	GCCTGCCTCC	GTTCCCGGCA
223_2	CGTACGTCCT	CGGCTCCGCG	CACCAGGGCT	GCCTGCCTCC	GTTCCCGGCA
223_4	CGTACGTCCT	CGGCTCCGCG	CACCAGGGCT	GCCTGCCTCC	GTTCCCGGCA
223_5	CGTACGTCCT	CGGCTCCGCG	CACCAGGGCT	GCCTGCCTCC	GTTCCCGGCA
223_6	CGTACGTCCT	CGGCTCCGCG	CACCAGGGCT	GCCTGCCTCC	GTTCCCGGCA
223_7	CGTACGTCCT	CGGCTCCGCG	CACCAGGGCT	GCCTGCCTCC	GTTCCCGGCA
A3_4	CCTACGTCCT	CGGTTCGGCT	CACCAGGGCT	GCCTTCCGCC	GTTCCCAGCA
A3_5	CCTACGTCCT	CGGTTCGGCT	CACCAGGGCT	GCCTTCCGCC	GTTCCCAGCA
A3_7	CCTACGTCCT	CGGTTCGGCT	CACCAGGGCT	GCCTTCCGCC	GTTCCCAGCA
A3_3	CCTACGTCCT	CGGTTCGGCT	CACCAGGGCT	GCCTTCCGCC	GTTCCCAGCA
42_12	CGTACGTCCT	CGGCTCTGCG	CACCAGGGCT	GCCTGCCTCC	GTTCCCGGCG
AAV1	CGTACGTCCT	CGGCTCTGCG	CACCAGGGCT	GCCTCCCTCC	GTTCCCGGCG
AAV2	CGTACGTCCT	CGGCTCGGCG	CATCAAGGAT	GCCTCCCGCC	GTTCCCAGCA
AAV3	CGTACGTGCT	CGGGTCGGCG	CACCAAGGCT	GTCTCCCGCC	GTTTCCAGCG
AAV8	CGTACGTTCT	CGGCTCTGCC	CACCAGGGCT	GCCTGCCTCC	GTTCCCGGCG
AAV9	CGTACGTCCT	AGGCTCTGCC	CACCAAGGAT	GCCTGCCACC	GTTTCCTGCA
AAV7	CGTACGTCCT	CGGCTCTGCG	CACCAGGGCT	GCCTGCCTCC	GTTCCCGGCG
44_2	CGTACGTCCT	CGGCTCTGCG	CACCAGGGCT	GCCTGCCTCC	GTTCCCGGCG

Fig. 1AAP

	3351				3400
42_2	GACGTGTTCA	TGATTCCTCA	GTACGGATAT	CTGACTCTAA	ACAACGGCAG
42_8	GACGTCTTCA	TGATTCCTCA	GTACGGGTAC	CTGACTCTGA	ACAACGGCAG
42_15	GACGTCTTCA	TGATTCCTCA	GTACGGGTAC	CTGACTCTGA	ACAACGGCAG
42_5b	GACGTCTTCA	TGATTCCTCA	GTACGGGTAC	CTGACTCTGA	ACAACGGCAG
42_1b	GACGTCTTCA	TGATTCCTCA	GTACGGGTAC	CTGACTCTGA	ACAACGGCAG
42_13	GACGTCTTCA	TGATTCCTCA	GTACGGGTAC	CTGACTCTGA	ACAACGGCAG
42_3a	GACGTCTTCA	TGATTCCTCA	GTACGGGTAC	CTGACTCTGA	ACAACGGCAG
42_4	GACGTCTTCA	TGATTCCTCA	GTACGGGTAC	CTGACTCTGA	ACAACGGCAG
42_5a	GACGTGTTCA	TGATTCCTCA	GTACGGATAT	CTGACTCTAA	ACAACGGCAG
42_10	GACGTGTTCA	TGATTCCTCA	GTACGGATAT	CTGACTCTAA	ACAACGGCAG
42_3b	GACGTGTTCA	TGATTCCTCA	GTACGGATAT	CTGACTCTAA	ACAACGGCAG
42_1	GACGTGTTCA	TGATTCCTCA	GTACGGATAT	CTGACTCTAA	ACAACGGCAG
42_6b	GACGTGTTCA	TGATTCCTCA	GTACGGATAT	CTGACTCTAA	ACAACGGCAG
43_1	GACGTCTTCA	TGATTCCTCA	GTACGGGTAT	CTGACCCTAA	ACAATGGCAG
43_5	GACGTCTTCA	TGATTCCTCA	GTACGGGTAT	CTGACCCTAA	ACAATGGCAG
43_12	GACGTCTTCA	TGATTCCTCA	GTACGGGTAT	CTGACCCTAA	ACAATGGCAG
43_20	GACGTCTTCA	CGGTTCCCTCA	GTACGGCTAT	TTAACTTTAA	ACAATGGAAG
43_21	GACGTCTTCA	TGGTTCCTCA	GTACGGCTAT	TTAACTTTAA	ACAATGGAAG
43_23	GACGTCTTCA	TGGTTCCTCA	GTACGGCTAT	TTAACTTTAA	ACAATGGAAG
43_25	GACGTCTTCA	TGGTTCCTCA	GTACGGCTAT	TTAACTTTAA	ACAATGGAAG
44_1	GACGTCTTCA	TGATTCCTCA	GTACGGGTAC	CTGACTCTGA	ACAATGGCAG
44_5	GACGTCTTCA	TGATTCCTCA	GTACGGGTAC	CTGACTCTGA	ACAATGGCAG
223_10	GACGTGTTCA	TGATTCCGCA	GTACGGATAC	CTGACTCTGA	ACAATGGCAG
223_2	GACGTGTTCA	TGATTCCGCA	GTACGGATAC	CTGACTCTGA	ACAATGGCAG
223_4	GACGTGTTCA	TGATTCCGCA	GTACGGATAC	CTGACTCTGA	ACAATGGCAG
223_5	GACGTGTTCA	TGATTCCGCA	GTACGGATAC	CTGACTCTGA	ACAATGGCAG
223_6	GACGTGTTCA	TGATTCCGCA	GTACGGATAC	CTGACTCTGA	ACAATGGCAG
223_7	GACGTGTTCA	TGATTCCGCA	GTACGGATAC	CTGACTCTGA	ACAATGGCAG
A3_4	GACGTCTTCA	TGATTCCTCA	GTACGGCTAC	TTGACTCTGA	ACAATGGCAG
A3_5	GACGTCTTCA	TGATTCCTCA	GTACGGCTAC	TTGACTCTGA	ACAATGGCAG
A3_7	GACGTCTTCA	TGATTCCTCA	GTACGGCTAC	TTGACTCTGA	ACAATGGCAG
A3_3	GACGTCTTCA	TGATTCCTCA	GTACGGCTAC	TTGACTCTGA	ACAATGGCAG
42_12	GACGTCTTCA	TGATTCCTCA	GTACGGGTAC	CTGACTCTGA	ACAACGGCAG
AAV1	GACGTGTTCA	TGATTCCGCA	ATACGGCTAC	CTGACGCTCA	ACAATGGCAG
AAV2	GACGTCTTCA	TGGTGCCACA	GTATGGATAC	CTCACCCTGA	ACAACGGGAG
AAV3	GACGTCTTCA	TGGTCCCTCA	GTATGGATAC	CTCACCCTGA	ACAACGGGAG
AAV8	GACGTGTTCA	TGATTCCTCA	GTACGGCTAC	CTAACACTCA	ACAACGGTAG
AAV9	GACGTCTTCA	TGGTTCCTCA	GTACGGCTAC	CTGACGCTCA	ACAATGGAAG
AAV7	GACGTCTTCA	TGATTCCTCA	GTACGGCTAC	CTGACTCTCA	ACAATGGCAG
44_2	GACGTCTTCA	TGATTCCTCA	GTACGGGTAC	CTGACTCTGA	ACAATGGCAG

Fig. 1AAQ

	3401				3450
42_2	TCAGTCTGTG	GGACGTTCCCT	CCTTCTACTG	CCTGGAGTAC	TTTCCTTCTC
42_8	TCAGGCCGTG	GGCCGTTCCCT	CCTTCTACTG	CCTGGAGTAC	TTTCCTTCTC
42_15	TCAGGCCGTG	GGCCGTTCCCT	CCTTCTACTG	CCTGGAGTAC	TTTCCTTCTC
42_5b	TCAGGCCGTG	GGCCGTTCCCT	CCTTCTACTG	CCTGGAGTAC	TTTCCTTCTC
42_1b	TCAGGCCGTG	GGCCGTTCCCT	CCTTCTACTG	CCTGGAGTAC	TTTCCTTCTC
42_13	TCAGGCCGTG	GGCCGTTCCCT	CCTTCTACTG	CCTGGAGTAC	TTTCCTTCTC
42_3a	TCAGGCCGTG	GGCCGTTCCCT	CCTTCTACTG	CCTGGAGTAC	TTTCCTTCTC
42_4	TCAGGCCGTG	GGCCGTTCCCT	CCTTCTACTG	CCTGGAGTAC	TTTCCTTCTC
42_5a	TCAGTCTGTG	GGACGTTCCCT	CCTTCTACTG	CCTGGAGTAC	TTTCCTTCTC
42_10	TCAGTCTGTG	GGACGTTCCCT	CCTTCTACTG	CCTGGAGTAC	TTTCCTTCTC
42_3b	TCAGTCTGTG	GGACGTTCCCT	CCTTCTACTG	CCTGGAGTAC	TTTCCTTCTC
42_11	TCAGTCTGTG	GGACGTTCCCT	CCTTCTACTG	CCTGGAGTAC	TTTCCTTCTC
42_6b	TCAGTCTGTG	GGACGTTCCCT	CCTTCTACTG	CCTGGAGTAC	TTTCCTTCTC
43_1	TCAGGCTGTG	GGCCGTTCCCT	CCTTCTACTG	CCTGGAATAC	TTCCCTTCTC
43_5	TCAGGCTGTG	GGCCGTTCCCT	CCTTCTACTG	CCTGGAATAC	TTCCCTTCTC
43_12	TCAGGCTGTG	GGCCGTTCCCT	CCTTCTACTG	CCTGGAATAC	TTCCCTTCTC
43_20	CCAAGCCCTG	GGACGTTCCCT	CCTTCTACTG	TCTGGAGTAT	TTCCCATCGC
43_21	CCAAGCCCTG	GGACGTTCCCT	CCTTCTACTG	TCTGGAGTAT	TTCCCATCGC
43_23	CCAAGCCCTG	GGACGTTCCCT	CCTTCTACTG	TCTGGAGTAT	TTCCCATCGC
43_25	CCAAGCCCTG	GGACGTTCCCT	CCTTCTACTG	TCTGGAGTAT	TTCCCATCGC
44_1	TCAGGCCGTG	GGCCGTTCCCT	CCTTCTACTG	CCTGGAGTAC	TTTCCTTCTC
44_5	TCAGGCCGTG	GGCCGTTCCCT	CCTTCTACTG	CCTGGAGTAC	TTTCCTTCTC
223_10	CCAATCGGTA	GGCCGTTCCCT	CCTTCTACTG	CCTGGAGTAC	TTTCCTTCTC
223_2	CCAATCGGTA	GGCCGTTCCCT	CCTTCTACTG	CCTGGAGTAC	TTTCCTTCTC
223_4	CCAATCGGTA	GGCCGTTCCCT	CCTTCTACTG	CCTGGAGTAC	TTTCCTTCTC
223_5	CCAATCGGTA	GGCCGTTCCCT	CCTTCTACTG	CCTGGAGTAC	TTTCCTTCTC
223_6	CCAATCGGTA	GGCCGTTCCCT	CCTTCTACTG	CCTGGAGTAC	TTTCCTTCTC
223_7	CCAATCGGTA	GGCCGTTCCCT	CCTTCTACTG	CCTGGAGTAC	TTTCCTTCTC
A3_4	CCAAGCGGTA	GGACGTTCTT	CATTCTACTG	TCTAGAGTAT	TTTCCCTCTC
A3_5	CCAAGCGGTA	GGACGTTCTT	CATTCTACTG	TCTAGAGTAT	TTTCCCTCTC
A3_7	CCAAGCGGTA	GGACGTTCTT	CATTCTACTG	TCTAGAGTAT	TTTCCCTCTC
A3_3	CCAAGCGGTA	GGACGTTCTT	CATTCTACTG	TCTAGAGTAT	TTTCCCTCTC
42_12	TCAGGCCGTG	GGCCGTTCCCT	CCTTCTACTG	CCTGGAGTAC	TTTCCTTCTC
AAV1	CCAAGCCGTG	GGACGTTTCAT	CCTTTTACTG	CCTGGAATAT	TTCCCTTCTC
AAV2	TCAGGCAGTA	GGACGCTCTT	CATTTTACTG	CCTGGAGTAC	TTTCCTTCTC
AAV3	TCAAGCGGTG	GGACGCTCAT	CCTTTTACTG	CCTGGAGTAC	TTCCCTTCGC
AAV8	TCAGGCCGTG	GGACGCTCCT	CCTTCTACTG	CCTGGAATAC	TTTCCTTCGC
AAV9	TCAAGCGTTA	GGACGTTCTT	CTTTCTACTG	TCTGGAATAC	TTCCCTTCTC
AAV7	TCAGTCTGTG	GGACGTTCCCT	CCTTCTACTG	CCTGGAGTAC	TTCCCTTCTC
44_2	TCAGGCCGTG	GGCCGTTCCCT	CCTTCTACTG	CCTGGAGTAC	TTTCCTTCTC

Fig. 1AAR

	3451				3500
42_2	AGATGCTGAG	AACGGGCAAT	AACTTTGAAT	TCAGCTACAC	CTTTGAGGAA
42_8	AAATGCTGAG	AACGGGCAAC	AACTTTGAGT	TCAGCTACCA	GTTTGAGGAC
42_15	AAATGCGGAG	AACGGGCAAC	AACTTTGAGT	TCAGCTACCA	GTTTGAGGAC
42_5b	AAATGCTGAG	AACGGGCAAC	AACTTTGAGT	TCAGCTACCA	GTTTGAGGAC
42_1b	AAATGCTGAG	AACGGGCAAC	AACTTTGAGT	TCAGCTACCA	GTTTGAGGAC
42_13	AAATGCTGAG	AACGGGCAAC	AACTTTGAGT	TCAGCTACCA	GTTTGAGGAC
42_3a	AAATGCTGAG	AACGGGCAAC	AACTTTGAGT	TCAGCTACCA	GTTTGAGGAC
42_4	AAATGCTGAG	AACGGGCAAC	AACTTTGAGT	TCAGCTACCA	GTTTGAGGAC
42_5a	AGATGCTGAG	AACGGGCAAT	AACTTTGAAT	TCAGCTACCA	GTTTGAGGAC
42_10	AGATGCTGAG	AACGGGCAAT	AACTTTGAAT	TCAGCTACAC	CTTTGAGGAA
42_3b	AGATGCTGAG	AACGGGCAAT	AACTTTGAAT	TCAGCTACAC	CTTTGAGGAA
42_11	AGATGCTGAG	AACGGGCAAT	AACTTTGAAT	TCAGCTACAC	CTTTGAGGAA
42_6b	AGATGCTGAG	AACGGGCAAT	AACTTTGAAT	TCAGCTACAC	CTTTGAGGAA
43_1	AAATGCTGAG	GACGGGCAAC	AACTTTGAAT	TCAGCTACAC	CTTCGAGGAC
43_5	AAATGCTGAG	GACGGGCAAC	AACTTTGAAT	TCAGCTACAC	CTTCGAGGAC
43_12	AAATGCTGAG	GACGGGCAAC	AACTTTGAAT	TCAGCTACAC	CTTCGAGGAC
43_20	AGATGCTGAG	AACCGGCAAC	AACTTTCAGT	TCAGCTACAC	CTTCGAGGAC
43_21	AGATGCTGAG	AACCGGCAAC	AACTTTCAGT	TCAGCTACAC	CTTCGAGGAC
43_23	AGATGCCGAG	AACCGGCAAC	AACTTTCAGT	TCAGCTACAC	CTTCGAGGAC
43_25	AGATGCTGAG	AACCGGCAAC	AACTTTCAGT	TCAGCTACAC	CTTCGAGGAC
44_1	AAATGCTGAG	AACGGGCAAC	AACTTTGAGT	TCAGCTACCA	GTTTGAGGAC
44_5	AAATGCTGAG	AACGGGCAAC	AACTTTGAGT	TCAGCTACCA	GTTTGAGGAC
223_10	AGATGCTGAG	AACGGGCAAC	AACTTCACCT	TTAGCTACAC	CTTCGAGGAC
223_2	AGATGCTGAG	AACGGGCAAC	AACTTCACCT	TTAGCTACAC	CTTCGAGGAC
223_4	AGATGCTGAG	AACGGGCAAC	AACTTCACCT	TTAGCTACAC	CTTCGAGGAC
223_5	AGATGCTGAG	AACGGGCAAC	AACTTCACCT	TTAGCTACAC	CTTCGAGGAC
223_6	AGATGCTGAG	AACGGGCAAC	AACTTCACCT	TTAGCTACAC	CTTCGAGGAC
223_7	AGATGCTGAG	AACGGGCAAC	AACTTCACCT	TTAGCTACAC	CTTCGAGGAC
A3_4	AGATGCTGAG	GACGGGAAAC	AACTTCACCT	TCAGCTACAC	TTTTGAAGAC
A3_5	AGATGCTGAG	GACGGGAAAC	AACTTCACCT	TCAGCTACAC	TTTTGAAGAC
A3_7	AGATGCTGAG	GACGGGAAAC	AACTTCACCT	TCAGCTACAC	TTTTGAAGAC
A3_3	AGATGCTGAG	GACGGGAAAC	AACTTCACCT	TCAGCTACAC	TTTTGAAGAC
42_12	AAATGCTGAG	AACGGGCAAC	AACTTTGAGT	TCAGCTACCA	GTTTGAGGAC
AAV1	AGATGCTGAG	AACGGGCAAC	AACTTTACCT	TCAGCTACAC	CTTTGAGGAA
AAV2	AGATGCTGCG	TACCGGAAAC	AACTTTACCT	TCAGCTACAC	TTTTGAGGAC
AAV3	AGATGCTAAG	GACTGGAAAT	AACTTCCAAT	TCAGCTATAC	CTTCGAGGAT
AAV8	AGATGCTGAG	AACCGGCAAC	AACTTCCAGT	TTACTTACAC	CTTCGAGGAC
AAV9	AGATGCTGAG	AACCGGCAAC	AACTTTCAGT	TCAGCTACAC	TTTCGAGGAC
AAV7	AGATGCTGAG	AACGGGCAAC	AACTTTGAGT	TCAGCTACAG	CTTCGAGGAC
44_2	AAATGCTGAG	AACGGGCAAC	AACTTTGAGT	TCAGCTACCA	GTTTGAGGAC

Fig. 1AAS

	3501				3550
42_2	GTGCCTTTCC	ACAGCAGCTA	TGCGCACAGC	CAGAGCCTGG	ACCGGCTGAT
42_8	GTGCCTTTTC	ACAGCAGCTA	CGCGCACAGC	CAAAGCCTGG	ACCGGCTGAT
42_15	GTGCCTTTTC	ACAGCAGCTA	CGCGCATAGC	CAAAGCCTGG	ACCGGCTGAT
42_5b	GTGCCTTTTC	ACAGCAGCTA	CGCGCACAGC	CAAAGCCTGG	ACCGGCTGAT
42_1b	GTGCCTTTTC	ACAGCAGCTA	TGCGCACAGC	CAAAGCCTGG	ACCGGCTGAT
42_13	GTGCCTTTTC	ACAGCAGCTA	TGCGCACAGC	CAAAGCCTGG	ACCGGCTGAT
42_3a	GTGCCTTTTC	ACAGCAGCTA	CGCGCACAGC	CAAAGCCTGG	ACCGGCTGAT
42_4	GTGCCTTTTC	ACAGCAGCTA	CGCGCACAGC	CAAAGCCTGG	ACCGGCTGAT
42_5a	GTGCCCTTTC	ACAGCAGCTA	CGCGCACAGC	CAAAGCCTGG	ACCGGCTGAT
42_10	GTGCCTTTCC	ACAGCAGCTA	TGCGCACAGC	CAGAGCCTGG	ACCGGCTGAT
42_3b	GTGCCTTTCC	ACAGCAGCTA	TGCGCACAGC	CAGAGCCTGG	ACCGGCTGAT
42_11	GTGCCTTTCC	ACAGCAGCTA	TGCGCACAGC	CAGAGCCTGG	ACCGGCTGAT
42_6b	GTGCCTTTCC	ACAGCAGCTA	TGCGCATAGC	CAGAGCCTGG	ACCGGCTGAT
43_1	GTGCCTTTCC	ACAGCAGCTA	CGCGCACAGC	CAGAGCCTGG	ACCGGCTGAT
43_5	GTGCCTTTCC	ACAGCAGCTA	CGCGCACAGC	CAGAGCCTGG	ACCGGCTGAT
43_12	GTGCCTTTCC	ACAGCAGCTA	CGCGCACAGC	CAGAGCCTGG	ACCGGCTGAT
43_20	GTGCCTTTCC	ACAGCAGCTA	CGCGCACAGC	CAGAGCCTGG	ACAGGCTGAT
43_21	GTGCCTTTCC	ACAGCAGCTA	CGCGCACAGC	CAGAGCCTGG	ACAGGCTGAT
43_23	GTGCCTTTCC	ACAGCAGCTA	CGCGCACAGC	CAGAGCCTGG	ACAGGCTGAT
43_25	GTGCCTTTCC	ACAGCAGCTA	CGCGCACAGC	CAGAGCCTGG	ACAGGCTGAT
44_1	GTGCCTTTTC	ACAGCAGCTA	CGCGCACAGC	CAAAGCCTGG	ACCGGCTGAT
44_5	GTGCCTTTTC	ACAGCAGCTA	CGCGCACAGC	CAAAGCCTGG	ACCGGCTGAT
223_10	GTGCCTTTCC	ACAGCAGCTA	CGCGCACAGC	CAGAGTCTGG	ACCGGCTGAT
223_2	GTGCCTTTCC	ACAGCAGCTA	CGCGCACAGC	CAGAGTCTGG	ACCGGCTGAT
223_4	GTGCCTTTCC	ACAGCAGCTA	CGCGCACAGC	CAGAGTCTGG	GCCGGCTGAT
223_5	GTGCCTTTCC	ACAGCAGCTA	CGCGCACAGC	CAGAGTCTGG	GCCGGCTGAT
223_6	GTGCCTTTCC	ACAGCAGCTA	CGCGCACAGC	CAGAGTCTGG	ACCGGCTGAT
223_7	GTGCCTTTCC	ACAGCAGCTA	CGCGCACAGC	CAGAGTCTGG	ACCGGCTGAT
A3_4	GTGCCTTTCC	ACAGCAGCTA	CGCGCACAGC	CAGAGTCTGG	ATCGGCTGAT
A3_5	GTGCCTTTCC	ACAGCAGCTA	CGCGCACAGC	CAGAGTCTGG	ATCGGCTGAT
A3_7	GTGCCTTTCC	ACAGCAGCTA	CGCGCACAGC	CAGAGTCTGG	ATCGGCTGAT
A3_3	GTGCCTTTCC	ACAGCAGCTA	CGCGCACAGC	CAGAGTCTGG	ATCGGCTGAT
42_12	GTGCCTTTTC	ACAGCAGCTA	CGCGCACAGC	CAAAGCCTGG	ACCGGCTGAC
AAV1	GTGCCTTTCC	ACAGCAGCTA	CGCGCACAGC	CAGAGCCTGG	ACCGGCTGAT
AAV2	GTTCTTTCC	ACAGCAGCTA	CGCTCACAGC	CAGAGTCTGG	ACCGTCTCAT
AAV3	GTACCTTTTC	ACAGCAGCTA	CGCTCACAGC	CAGAGTTTGG	ATCGCTTGAT
AAV8	GTGCCTTTCC	ACAGCAGCTA	CGCCACAGC	CAGAGCTTGG	ACCGGCTGAT
AAV9	GTGCCTTTCC	ACAGCAGCTA	CGCACACAGC	CAGAGTCTAG	ATCGACTGAT
AAV7	GTGCCTTTCC	ACAGCAGCTA	CGCACACAGC	CAGAGCCTGG	ACCGGCTGAT
44_2	GTGCCTTTTC	ACAGCAGCTA	CGCGCACAGC	CAAAGCCTGG	ACCGGCTGAT

Fig. 1AAT

	3551				3600
42_2	GAATCCCCTC	ATCGACCAGT	ACCTGTACTA	CCTGGCCCGG	ACCCAGAGCA
42_8	GAATCCCCTC	ATCGACCAGT	ACCTGTACTA	CCTGTCTCGG	ACTCAGTCCA
42_15	GAATCCCCTC	ATCGACCAGT	ACCTGTACTA	CCTGTCTCGG	ACTCAGTCCA
42_5b	GAATCCCCTC	ATCGACCAGT	ACCTGTACTA	CCTGTCTCGG	ACTCAGTCCA
42_1b	GAATCCCCTC	ATCGACCAGT	ACCTGTACTA	CCTGTCTCGG	ACTCAGTCCA
42_13	GAATCCCCTC	ATCGACCAGT	ACCTGTACTA	CCTGTCTCGG	ACTCAGTCCA
42_3a	GAATCCCCTC	ATCGACCAGT	ACCTGTACTA	CCTGTCTCGG	ACTCAGTCCA
42_4	GAATCCCCTC	ATCGACCAGT	ACCTGTACTA	CCTGTCTCGG	ACTCAGTCCA
42_5a	GAATCCCCTC	ATCGACCAGT	ACCTGTACTA	CCTGTCTCGG	ACTCAGTCCA
42_10	GAATCCCCTC	ATCGACCAGT	ACCTGTACTA	CCTGGCCCGG	ACCCAGAGCA
42_3b	GAATCCCCTC	ATCGACCAGT	ACCTGTACTA	CCTGGCCCGG	ACCCAGAGCA
42_11	GAATCCCCTC	ATCGACCAGT	ACCTGTACTA	CCTGGCCCGG	ACCCAGAGCA
42_6b	GAATCCCCTC	ATCGACCAGT	ACCTGTACTA	CCTGGCCCGG	ACCCAGAGCA
43_1	GAATCCTCTC	ATCGACCAGT	ACCTGTATTA	CTTATCCAGA	ACTCAGTCCA
43_5	GAATCCTCTC	ATCGACCAGT	ACCTGTATTA	CTTATCCAGA	ACTCAGTCCA
43_12	GAATCCTCTC	ATCGACCAGT	ACCTGTATTA	CTTATCCAGA	ACTCAGTCCA
43_20	GAATCCCCTC	ATCGACCAGT	ACCTGTACTA	CCTGGTCAGA	ACGCAAACGA
43_21	GAATCCCCTC	ATCGACCAGT	ACCTGTACTA	CCTGGTCAGA	ACGCAAACGA
43_23	GAATCCCCTC	ATCGACCAGT	ACCTGTACTA	CCTGGTCAGA	ACGCAAACGA
43_25	GAATCCCCTC	ATCGACCAGT	ACCTGTACTA	CCTGGTCAGA	ACGCAAACGA
44_1	GAATCCCCTC	ATCGACCAGT	ACCTGTACTA	CCTGTCTCGG	ACTCAGTCCA
44_5	GAATCCCCTC	ATCGACCAGT	ACCTGTACTA	CCTGTCTCGG	ACTCAGTCCA
223_10	GAATCCCCTC	ATCGACCAGT	ACCTGTACTA	CTTGGCCAGA	ACACAGAGCA
223_2	GAATCCCCTC	ATCGACCAGT	ACCTGTACTA	CTTGGCCAGA	ACACAGAGCA
223_4	GAATCCCCTC	ATCGACCAGT	ACCTGTACTA	CTTGGCCAGA	ACACAGAGCA
223_5	GAATCCCCTC	ATCGACCAGT	ACCTGTACTA	CTTGGCCAGA	ACACAGAGCA
223_6	GAATCCCCTC	ATCGACCAGT	ACCTGTACTA	CTTGGCCAGA	ACACAGAGCA
223_7	GAATCCCCTC	ATCGACCAGT	ACCTGTACTA	CTTGGCCAGA	ACACAGAGCA
A3_4	GAATCCTCTC	ATTGACCAGT	ACCTGTATTA	CCTGAGCAAA	ACTCAGGGTA
A3_5	GAATCCTCTC	ATTGACCAGT	ACCTGTATTA	CCTGAGCAAA	ACTCAGGGTA
A3_7	GAATCCTCTC	ATTGACCAGT	ACCTGTATTA	CCTGAGCAAA	ACTCAGGGTA
A3_3	GAATCCTCTC	ATTGACCAGT	ACCTGTATTA	CCTGAGCAAA	ACTCAGGGTA
42_12	GAATCCCCTC	ATCGACCAGT	ACCTGTACTA	CCTGGCCCGG	ACCCAGAGCA
AAV1	GAATCCTCTC	ATCGACCAAT	ACCTGTATTA	CCTGAACAGA	ACTCAA.AT
AAV2	GAATCCTCTC	ATCGACCAGT	ACCTGTATTA	CTTGAGCAGA	ACAAACACTC
AAV3	GAATCCTCTT	ATTGATCAGT	ATCTGTACTA	CCTGAACAGA	ACGCAAGGAA
AAV8	GAATCCTCTG	ATTGACCAGT	ACCTGTACTA	CTTGTCTCGG	ACTCAAACAA
AAV9	GAATCCCCTC	ATCGACCAGT	ACCTATACTA	CCTGGTCAGA	ACACAGACAA
AAV7	GAATCCCCTC	ATCGACCAGT	ACTTGTACTA	CCTGGCCAGA	ACACAGAGTA
44_2	GAATCCCCTC	ATCGACCAGT	ACCTGTACTA	CCTGTCTCGG	ACTCAGTCCA

Fig. 1AAU

	3601				3650
42_2	CTACGG..GG	TCCACAAGGG	AGCTGCA.GT	TCCA.....	TCAGGCTGGG
42_8	CGGGA...GG	TACCGCAGGA	ACTCAGCAGT	TGCTATTTTC	TCAGGCCGGG
42_15	CGGGA...GG	TACCGCAGGA	ACTCAGCAGT	TGCTATTTTC	TCAGGCCGGG
42_5b	CGGGA...GG	TACCGCAGGA	ACTCAGCAGT	TGCTATTTTC	TCAGGCCGGG
42_1b	CGGGA...GG	TACCGCAGGA	ACTCAGCAGT	TGCTATTTTC	TCAGGCCGGG
42_13	CGGGA...GG	TACCGCAGGA	ACTCAGCAGT	TGCTATTTTC	TCAGGCCGGG
42_3a	CGGGA...GG	TACCGCAGGA	ACTCAGCAGT	TGCTATTTTC	TCAGGCCGGG
42_4	CGGGA...GG	TACCGCAGGA	ACTCAGCAGT	TGCTATTTTC	TCAGGCCGGG
42_5a	CGGGA...GG	TACCGCAGGA	ACTCAGCAGT	TGCTATTTTC	TCAGGCCGGG
42_10	CTACG...GG	GTCCACAAGG	GAGCTGCAGT	TCCA.....	TCAGGCTGGG
42_3b	CTACG...GG	GTCCACAAGG	GAGCTGCAGT	TCCA.....	TCAGGCTGGG
42_11	CTACG...GG	GTCCACAAGG	GAGCTGCAGT	TCCA.....	TCAGGCTGGG
42_6b	CTACG...GG	GTCCACAAGG	GAGCTGCAGT	TCCA.....	TCAGGCTGGG
43_1	CAGGA...GG	AACTCAAGGT	ACTCAGCAAT	TGTTATTTTC	TCAAGCCGGG
43_5	CAGGA...GG	AACTCAAGGT	ACTCAGCAAT	TGTTATTTTC	TCAAGCCGGG
43_12	CAGGA...GG	AACTCAAGGT	ACTCAGCAAT	TGTTATTTTC	TCAAGCCGGG
43_20	CT.....GG	AACTGGAGGG	ACGCAGACTC	TGGCATTTCAG	CCAAGCGGGT
43_21	CT.....GG	AACTGGAGGG	ACGCAGACTC	TGGCATTTCAG	CCAAGCGGGT
43_23	CT.....GG	AACTGGAGGG	ACGCAGACTC	TGGCATTTCAG	CCAAGCGGGT
43_25	CT.....GG	AACTGGAGGG	ACGCAGACTC	TGGCATTTCAG	CCAAGCGGGT
44_1	CGGGA...GG	TACCGCAGGA	ACTCAGCAGT	TGCTATTTTC	TCAGGCCGGG
44_5	CGGGA...GG	TACCGCAGGA	ACTCAGCAGT	TGCTATTTTC	TCAGGCCGGG
223_10	ACGCAGGAGG	TACTGCTGGC	AATCGGGAAC	TGCAGTTTTC	TCAGGGCGGA
223_2	ACGCAGGAGG	TACTGCTGGC	AATCGGGAAC	TGCAGTTTTC	TCAGGGCGGA
223_4	ACGCAGGAGG	TACTGCTGGC	AATCGGGAAC	TGCAGTTTTC	TCAGGGCGGA
223_5	ACGCAGGAGG	TACTGCTGGC	AATCGGGAAC	TGCAGTTTTC	TCAGGGCGGA
223_6	ACGCAGGAGG	TACTGCTGGC	AATCGGGAAC	TGCAGTTTTC	TCAGGGCGGA
223_7	ACGCAGGAGG	TACTGCTGGC	AATCGGGAAC	TGCAGTTTTC	TCAGGGCGGA
A3_4	CAAG...TGG	AACAACGCAG	CAATCGAGAC	TGCAGTTCAG	CCAAGCTGGG
A3_5	CAAG...TGG	AACAACGCAG	CAATCGAGAC	TGCAGTTCAG	CCAAGCTGGG
A3_7	CAAG...TGG	AACAACGCAG	CAATCGAGAC	TGCAGTTCAG	CCAAGCTGGG
A3_3	CAAG...TGG	AACAACGCAG	CAATCGAGAC	TGCAGTTCAG	CCAAGCTGGG
42_12	CTACG...GG	GTCCACAAGG	GGGCTGCAGT	TCCA.....	TCAGGCTGGG
AAV1	CAGTCC..GG	AAGTGCCCAA	AACAAGGACT	TGCTGTTTAG	CCGTGGGTCT
AAV2	CAAG...TGG	AACCACCACG	CAGTCAAGGC	TTCAGTTTTC	TCAGGCCGGA
AAV3	CAACCTCTGG	AACAACCAAC	CAATCACGGC	TGCTTTTTAG	CCAGGCTGGG
AAV8	CAGGAG..GC	.ACGGCAAAT	ACGCAGACTC	TGGGCTTCAG	CCAAGGTGGG
AAV9	CTGGA.....	.ACTGGGGGA	ACTCAAACCT	TGGCATTTCAG	CCAAGCAGGC
AAV7	ACCCAGGAGG	CACAGCTGGC	AATCGGGAAC	TGCAGTTTTC	CCAGGGCGGG
44_2	CGGGA...GG	TACCGCAGGA	ACTCAGCAGT	TGCTATTTTC	TCAGGCCGGG

Fig. 1AAV

	3651				3700
42_2	CCCAACACCA	TGGCCGAGCA	ATCAAAGAAC	TGGCTGCCCCG	GACCCTGTTA
42_8	CCTAATAACA	TGTCGGCTCA	GGCCAAAAAC	TGGCTACCCG	GGCCCTGCTA
42_15	CCTAATAACA	TGTCGGCTCA	GGCCAAAAAC	TGGCTACCCG	GGCCCTGCTA
42_5b	CCTAATAACA	TGTCGGCTCA	GGCCAAAAAC	TGGCTACCCG	GGCCCTGCTA
42_1b	CCTAATAACA	TGTCGGCTCA	GGCCAAAAAC	TGGCTACCCG	GGCCCTGCTA
42_13	CCTAATAACA	TGTCGGCTCA	GGCCAAAAAC	TGGCTACCCG	GGCCCTGCTA
42_3a	CCTAATAACA	TGTCGGCTCA	GGCCAAAAAC	TGGCTACCCG	GGCCCTGCTA
42_4	CCTAATAACA	TGTCGGCTCA	GGCCAAAAAC	TGGCTACCCG	GGCCCTGCTA
42_5a	CCTAATAACA	TGTCGGCTCA	GGCCAAAAAC	TGGCTACCCG	GGCCCTGCTA
42_10	CCCAACACCA	TGGCCGAGCA	ATCAAAGAAC	TGGCTGCCCCG	GACCCTGTTA
42_3b	CCCAACACCA	TGGCCGAGCA	ATCAAAGAAC	TGGCTGCCCCG	GACCCTGTTA
42_11	CCCAACACCA	TGGCCGAGCA	ATCAAAGAAC	TGGCTGCCCCG	GACCCTGTTA
42_6b	CCCAACACCA	TGGCCGAGCA	ATCAAAGAAC	TGGCTGCCCCG	GACCCTGTTA
43_1	CCCGCAAACA	TGTCGGCTCA	GGCCAAGAAC	TGGCTACCTG	GACCGTGTTA
43_5	CCCGCAAACA	TGTCGGCTCA	GGCCAAGAAC	TGGCTACCTG	GACCGTGTTA
43_12	CCCGCAAACA	TGTCGGCTCA	GGCCAAGAAC	TGGCTACCTG	GACCGTGTTA
43_20	CCTAGCTCAA	TGGCCAACCA	GGCTAGAAAT	TGGGTGCCCCG	GACCTTGCTA
43_21	CCTAGCTCAA	TGGCCAACCA	GGCTAGAAAT	TGGGTGCCCCG	GACCTTGCTA
43_23	CCTAGCTCAA	TGGCCAACCA	GGCTAGAAAT	TGGGTGCCCCG	GACCTTGCTA
43_25	CCTAGCTCAA	TGGCCAACCA	GGCTAGAAAT	TGGGTGCCCCG	GACCTTGCTA
44_1	CCTAATAACA	TGTCGGCTCA	GGCCAAAAAC	TGGCTACCCG	GGCCCTGCTA
44_5	CCTAATAACA	TGTCGGCTCA	GGCCAAAAAC	TGGCTACCCG	GGCCCTGCTA
223_10	CCTACCACCA	TGGCCGAACA	AGCAAAGAAC	TGGCTGCCCCG	GACCTTGCTT
223_2	CCTACCACCA	TGGCCGAACA	AGCAAAGAAC	TGGCTGCCCCG	GACCTTGCTT
223_4	CCTACCACCA	TGGCCGAACA	AGCAAAGAAC	TGGCTGCCCCG	GACCTTGCTT
223_5	CCTACCACCA	TGGCCGAACA	AGCAAAGAAC	TGGCTGCCCCG	GACCTTGCTT
223_6	CCTACCACCA	TGGCCGAACA	AGCAAAGAAC	TGGCTGCCCCG	GACCTTGCTT
223_7	CCTACCACCA	TGGCCGAACA	AGCAAAGAAC	TGGCTGCCCCG	GACCTTGCTT
A3_4	CCTAGCTCCA	TGGCTCAGCA	GGCCAAAAAC	TGGCTACCGG	GACCCAGCTA
A3_5	CCTAGCTCCA	TGGCTCAGCA	GGCCAAAAAC	TGGCTACCGG	GACCCAGCTA
A3_7	CCTAGCTCCA	TGGCTCAGCA	GGCCAAAAAC	TGGCTACCGG	GACCCAGCTA
A3_3	CCTAGCTCCA	TGGCTCAGCA	GGCCAAAAAC	TGGCTACCGG	GACCCAGCTA
42_12	CCCAACACCA	TGGCCGAGCA	ATCAAAGAAC	TGGCTGCCCCG	GACCCTGTTA
AAV1	CCAGCTGGCA	TGTCTGTTCA	GCCCAAAAAAC	TGGCTACCTG	GACCCTGTTA
AAV2	GCGAGTGACA	TTCGGGACCA	GTCTAGGAAC	TGGCTTCCTG	GACCCTGTTA
AAV3	CCTCAGTCTA	TGTCTTTGCA	GGCCAGAAAT	TGGCTACCTG	GGCCCTGCTA
AAV8	CCTAATACAA	TGGCCAATCA	GGCAAAGAAC	TGGCTGCCAG	GACCCTGTTA
AAV9	CCTAGCTCAA	TGGCCAATCA	GGCTAGAAAC	TGGGTACCCG	GGCCTTGCTA
AAV7	CCTTCAACTA	TGGCCGAACA	AGCCAAGAAAT	TGGTTACCTG	GACCTTGCTT
44_2	CCTAATAACA	TGTCGGCTCA	GGCCAAAAAC	TGGCTACCCG	GGCCCTGCTA

Fig. 1AAW

	3701				3750
42_2	TCGGCAGCAG	AGACTGTCAA	AAAACATAGA	CAGCAACAAC	AACAGTAACT
42_8	CCGGCAGCAA	CGCGTCTCCA	CGACACTGTC	GCAAAATAAC	AACAGCAACT
42_15	CCGGCAGCAA	CGCGTCTCCA	CGACACTGTC	GCAAAATAAC	AACAGCAACT
42_5b	CCGGCAGCAA	CGCGTCTCCA	CGACACTGTC	GCAAAATAAC	AACAGCAACT
42_1b	CCGGCAGCAA	CGCGTCTCCA	CGACAGTGTC	GCAAAATAAC	AACAGCAACT
42_13	CCGGCAGCAA	CGCGTCTCCA	CGACAGTGTC	GCAAAATAAC	AACAGCAACT
42_3a	CCGGCAGCAA	CGCGTCTCCA	CGACACTGTC	GCAAAATAAC	AACAGCAACT
42_4	CCGGCAGCAA	CGCGTCTCCA	CGACACTGTC	GCAAAATAAC	AACAGCAACT
42_5a	CCGGCAGCAA	CGCGTCTCCA	CGACACTGTC	GCAAAATAAC	AACAGCAACT
42_10	TCGGCAGCAG	AGACTGTCAA	AAAACATAGA	CAGCAACAAC	AACAGTAACT
42_3b	TCGGCAGCAG	AGACTGTCAA	AAAACATAGA	CAGCAACAAC	ACCAGTAACT
42_11	TCGGCGGCAG	AGACTGTCAA	AAGACATAGA	CAGCAACAAC	AACAGTAACT
42_6b	TCGGCAGCAG	AGACTGTCAA	AAAACATAGA	CAGCAACAAC	AACAGTAACT
43_1	CCGTCAGCAA	CGAGTTTCCA	CGACACTGTC	GCAAAACAAC	AACAGCAATT
43_5	CCGTCAGCAA	CGAGTTTCCA	CGACACTGTC	GCAAAACAAC	AACAGCAATT
43_12	CCGTCAGCAA	CGAGTTTCCA	CGACACTGTC	GCAAAACAAC	AACAGCAATT
43_20	CCGGCAGCAG	CGCGTCTCCA	CGACAACCAA	CCAGAACAAC	AACAGCAACT
43_21	CCGGCAGCAG	CGCGTCTCCA	CGACAACCAA	CCAGAGCAAC	AACAGCAACT
43_23	CCGGCAGCAG	CGCGTCTCCA	CGACAACCAA	CCAGAACAAC	AACAGCAACT
43_25	CCGGCAGCAG	CGCGTCTCCA	CGACAACCAA	CCAGAACAAC	AACAGCAACT
44_1	CCGGCAGCAA	CGCGTCTCCA	CGACACTGTC	GCAAAATAAC	AACAGCAACT
44_5	CCGGCAGCAA	CGCGTCTCCA	CGACACTGTC	GCAAAATAAC	AACAGCAACT
223_10	CCGGCAACAG	AGAGTATCCA	AGACGCTGGA	TCAAAATAAC	AACAGCAACT
223_2	CCGGCAACAG	AGAGTATCCA	AGACGCTGGA	TCAAAATAAC	AACAGCAACT
223_4	CCGGCAACAG	AGAGTATCCA	AGACGCTGGA	TCAAAATAAC	AACAGCAACT
223_5	CCGGCAACAG	AGAGTATCCA	AGACGCTGGA	TCAAAATAAC	AACAGCAACT
223_6	CCGGCAACAG	AGAGTATCCA	AGACGCTGGA	TCAAAATAAC	AACAGCAACT
223_7	CCGGCAACAG	AGAGTATCCA	AGACGCTGGA	TCAAAATAAC	AACAGCAACT
A3_4	CCGACAGCAG	CGAATGTCTA	AGACGGCTAA	TGACAACAAC	AACAGTGAAT
A3_5	CCGACAGCAG	CGAATGTCTA	AGACGGCTAA	TGACAACAAC	AACAGTGAAT
A3_7	CCGACAGCAG	CGAATGTCTA	AGACGGCTAA	TGACAACAAC	AACAGTGAAT
A3_3	CCGACAGCAG	CGAATGTCTA	AGACGGCTAA	TGACAACAAC	AACAGTGAAT
42_12	TCGGCAGCAG	AGACTGTCAA	AAAACATAGA	CAGCAACAAC	AACAGTAACT
AAV1	TCGGCAGCAG	CGCGTTTCTA	AAACAAAAAC	AGACAACAAC	AACAGCAATT
AAV2	CCGCCAGCAG	CGAGTATCAA	AGACATCTGC	GGATAACAAC	AACAGTGAAT
AAV3	CCGGCAACAG	AGACTTTCAA	AGACTGCTAA	CGACAACAAC	AACAGTAACT
AAV8	CCGCCAACAA	CGCGTCTCAA	CGACAACCGG	GCAAAACAAC	AATAGCAACT
AAV9	CCGTCAGCAG	CGCGTCTCCA	CAACCACCAA	CCAAAATAAC	AACAGCAACT
AAV7	CCGGCAACAA	AGAGTCTCCA	AAACGCTGGA	TCAAAACAAC	AACAGCAACT
44_2	CCGGCAGCAA	CGCGTCTCCA	CGACACTGTC	GCAAAATAAC	AACAGCAACT

Fig. 1AAX

	3751				3800
42_2	TTGCCTGGAC	CGGGGCCACT	AAATACCATC	TGAATGGTAG	AAATTCATTA
42_8	TTGCTTGGAC	CGGTGCCACC	AAGTATCATC	TGAATGGCAG	AGACTCTCTG
42_15	TTGCTTGGAC	CGGTGCCACC	AAGTATCATC	TGAATGGCAG	AGACTCTCTG
42_5b	TTGCTTGGAC	CGGTGCCACC	AAGTATCATC	TGAATGGCAG	AGACTCTCTG
42_1b	TTGCTTGGAC	CGGTGCCACC	AAGTATCATC	TGAATGGCAG	AGACTCTCTG
42_13	TTGCTTGGAC	CGGTGCCACC	AAGTATCATC	TGAATGGCAG	AGACTCTCTG
42_3a	TTGCTTGGAC	CGGTGCCACC	AAGTATCATC	TGAATGGCAG	AGACTCTCTG
42_4	TTGCTTGGAC	CGGTGCCACC	AAGTATCATC	TGAATGGCAG	AGACTCTCTG
42_5a	TTGCTTGGAC	CGGTGCCACC	AAGTATCATC	TGAATGGCAG	AGACTCTCTG
42_10	TTGCCTGGAC	CGGGGCCACT	AAATACCATC	TGAATGGTAG	AAATTCATTA
42_3b	TTGCCTGGAC	CGGGGCCACT	AAATACCATC	TGAATGGTAG	AAATTCATTA
42_11	TTGCCTGGAC	CGGGGCCACT	AAATACCATC	TGAATGGTAG	AAATTCATTA
42_6b	TTGCCTGGAC	CGGGGCCACT	AAATACCATC	TGAATGGTAG	AAATTCATTA
43_1	TTGCTTGGAC	CGGTGCCACC	AAGTATCACC	TGAATGGCAG	AGACTCCCTG
43_5	TTGCTTGGAC	CGGTGCCACC	AAGTATCACC	TGAATGGCAG	AGACTCCCTG
43_12	TTGCTTGGAC	CGGTGCCACC	AAGTATCACC	TGAATGGCAG	AGACTCCCTG
43_20	TTGCCTGGAC	GGGAGCTGCC	AAGTTTAAGC	TGAACGGCCG	AGACTCTCTA
43_21	TTGCCTGGAC	GGGAGCTGCC	AAGTTTAAGC	TGAACGGCCG	AGACTCTCTA
43_23	TTGCCTGGAC	GGGAGCTGCC	AAGTTTAAGC	TGAACGGCCG	AGACTCTCTA
43_25	TTGCCTGGAC	GGGAGCTGCC	AAGTTTAAGC	TGAACGGCCG	AGACTCTCTA
44_1	TTGCCTGGAC	CGGTGCCACC	AAGTATCATC	TGAATGGCAG	AGACTCTCTG
44_5	TTGCCTGGAC	CGGTGCCACC	AAGTATCATC	TGAATGGCAG	AGACTCTCTG
223_10	TTGCCTGGAC	TGGTGCCACA	AAATACCATT	TAAATGGAAG	AAATTCATTG
223_2	TTGCCTGGAC	TGGTGCCACA	AAATACCATT	TAAATGGAAG	AAATTCATTG
223_4	TTGCCTGGAC	TGGTGCCACA	AAATACCATT	TAAATGGAAG	AAATTCATTG
223_5	TTGCCTGGAC	TGGTGCCACA	AAATACCATT	TAAATGGAAG	AAATTCATTG
223_6	TTGCCTGGAC	TGGTGCCACA	AAATACCATT	TAAATGGAAG	AAATTCATTG
223_7	TTGCCTGGAC	TGGTGCCACA	AAATACCATT	TAAATGGAAG	AAATTCATTG
A3_4	TTGCTTGGAC	TGCAGCCACC	AAATATTACC	TGAATGGAAG	AAATTCTCTG
A3_5	TTGCTTGGAC	TGCAGCCACC	AAATATTACC	TGAATGGAAG	AAATTCTCTG
A3_7	TTGCTTGGAC	TGCAGCCACC	AAATATTACC	TGAATGGAAG	AAATTCTCTG
A3_3	TTGCTTGGAC	TGCAGCCACC	AAATATTACC	TGAATGGAAG	AAATTCTCTG
42_12	TTGCCTGGAC	CGGGGCCACT	AAATACCATC	TGAATGGTAG	AAATTCATTA
AAV1	TTACCTGGAC	TGGTGCTTCA	AAATATAACC	TCAATGGGCG	TGAATCCATC
AAV2	ACTCGTGGAC	TGGAGCTACC	AAGTACCACC	TCAATGGCAG	AGACTCTCTG
AAV3	TTCCTTGGAC	AGCGGCCAGC	AAATATCATC	TCAATGGCCG	CGACTCGCTG
AAV8	TTGCCTGGAC	TGCTGGGACC	AAATACCATC	TGAATGGAAG	AAATTCATTG
AAV9	TTGCGTGGAC	GGGAGCTGCT	AAATTCAAGC	TGAACGGGAG	AGACTCGCTA
AAV7	TTGCTTGGAC	TGGTGCCACC	AAATATCACC	TGAACGGCAG	AAACTCGTTG
44_2	TTGCCTGGAC	CGGTGCCACC	AAGTATCATC	TGAATGGCAG	AGACTCTCTG

Fig. 1AAY

	3801				3850
42_2	ACCAACCCCG	GCGTAGCCAT	GGCCACCAAC	AAGGACGACG	AGGACCAGTT
42_8	GTAAATCCCG	GTGTCGCTAT	GGCAACGCAC	AAGGACGACG	AAGAGCGATT
42_15	GTAAATCCCG	GTGTCGCTAT	GGCAACGCAC	AAGGACGACG	AAGAGCGATT
42_5b	GTAAATCCCG	GTGTCGCTAT	GGCAACGCAC	AAGGACGACG	AAGAGCGATT
42_1b	GTAAATCCCG	GTGTCGCTAT	GGCAACGCAC	AAGGGCGACG	AAGAGCGATT
42_13	GTAAATCCCG	GTGTCGCTAT	GGCAACGCAC	AAGGGCGACG	AAGAGCGATT
42_3a	GTAAATCCCG	GTGTCGCTAT	GGCAACGCAC	AAGGACGACG	AAGAGCGATT
42_4	GTAAATCCCG	GTGTCGCTAT	GGCAACGCAC	AAGGACGACG	AAGAGCGATT
42_5a	GTAAATCCCG	GTGTCGCTAT	GGCAACGCAC	AAGGACGACG	AAGAGCGATT
42_10	ACCAACCCCG	GCGTAGCCAT	GGCCACCAAC	AAGGACGACG	AGGACCAGTT
42_3b	ACCAACCCCG	GCGTAGCCAT	GGCCACCAAC	AAGGACGACG	AGGACCAGTT
42_11	ACCAACCCCG	GCGTAGCCAT	GGCCACCAAC	AAGGACGACG	AGGACCAGTT
42_6b	ACCAACCCCG	GCGTAGCCAT	GGCCACCAAC	AAGGACGACG	AGGACCAGTT
43_1	GTTAATCCCG	GCGTTGCCAT	GGCTACCCAC	AAGGACGACG	AGGAGCGCTT
43_5	GTTAATCCCG	GCGTTGCCAT	GGCTACCCAC	AAGGACGACG	AGGAGCGCTT
43_12	GTTAATCCCG	GCGTTGCCAT	GGCTACCCAC	AAGGACGACG	AGGAGCGCTT
43_20	ATGAATCCGG	GCGTGGCAAT	GGCTTCCCAC	AAGGATGACG	ACGACCGCTT
43_21	ATGAATCCGG	GCGTGGCAAT	GGCTTCCCAC	AAGGATGACG	ACGACCGCTT
43_23	ATGAATCCGG	GCGTGGCAAT	GGCTTCCCAC	AAGGATGACG	ACGACCGCTT
43_25	ATGAATCCGG	GCGTGGCAAT	GGCTTCCCAC	AAGGATGACG	ACGACCGCTT
44_1	GTAAATCCCG	GTGTCGCTAT	GGCAACCCAC	AAGGACGACG	AAGAGCGATT
44_5	GTAAATCCCG	GTGTCGCTAT	GGCAACCCAC	AAGGACGACG	AAGAGCGATT
223_10	GTTAATCCCG	GTGTCGCCAT	GGCAACCCAC	AAGGACGACG	AGGAACGCTT
223_2	GTTAATCCCG	GTGTCGCCAT	GGCAACCCAC	AAGGACGACG	AGGAACGCTT
223_4	GTTAATCCCG	GTGTCGCCAT	GGCAACCCAC	AAGGACGACG	AGGAACGCTT
223_5	GTTAATCCCG	GTGTCGCCAT	GGCAACCCAC	AAGGACGACG	AGGAACGCTT
223_6	GTTAATCCCG	GTGTCGCCAT	GGCAACCCAC	AAGGACGACG	AGGAACGCTT
223_7	GTTAATCCCG	GTGTCGCCAT	GGCAACCCAC	AAGGACGACG	AGGAACGCTT
A3_4	GTCAATCCCG	GGCCCCCAAT	GGCCAGTCAC	AAGGACGATG	AGGAAAAGTA
A3_5	GTCAATCCCG	GGCCCCCAAT	GGCCAGTCAC	AAGGACGATG	AGGAAAAGTA
A3_7	GTCAATCCCG	GGCCCCCAAT	GGCCAGTCAC	AAGGACGATG	AGGAAAAGTA
A3_3	GTCAATCCCG	GGCCCCCAGT	GGCCAGTCAC	AAGGACGATG	AGGAAAAGTA
42_12	ACCAACCCCG	GCGTAGCCAT	GGCCACCAAC	AAGGACGACG	AGGACCAGTT
AAV1	ATCAACCCTG	GCACTGCTAT	GGCCTCACAC	AAAGACGACG	AAGACAAGTT
AAV2	GTGAATCC..	GGCC...AT	GGCAAGCCAC	AAGGACGATG	AAGAAAAGTT
AAV3	GTGAATCCAG	GACCAGCTAT	GGCCAGTCAC	AAGGACGATG	AAGAAAATT
AAV8	GCTAATCCTG	GCATCGCTAT	GGCAACACAC	AAAGACGACG	AGGAGCGTTT
AAV9	ATGAATCCTG	GCGTGGCTAT	GGCATCGCAC	AAAGACGACG	AGGACCGCTT
AAV7	GTTAATCCCG	GCGTCGCCAT	GGCAACTCAC	AAGGACGACG	AGGACCGCTT
44_2	GTAAATCCCG	GTGTCGCTAT	GGCAACCCAC	AAGGACGACG	AAGAGCGATT

Fig. 1AAZ

	3851				3900
42_2	CTTTCCCATC	AACGGAGTGC	TGGTTTTTGG	CGAAACGGGG	GCTGCCAACA
42_8	TTTTCATCC	AGCGGAGTCT	TGATGTTTGG	GAAACAGGGA	GCTGGAAA..
42_15	TTTTCATCC	AGCGGAGTCT	TGATGTTTGG	GAAACAGGGA	GCTGGAAA..
42_5b	TTTTCATCC	AGCGGAGTCT	TGATGTTTGG	GAAACAGGGA	GCTGGAAA..
42_1b	TTTTCATCC	AGCGGAGTCT	TGATGTTTGG	GAAACAGGGA	GCTGGAAA..
42_13	TTTTCATCC	AGCGGAGTCT	TGATGTTTGG	GAAACAGGGA	GCTGGAAA..
42_3a	TTTTCATCC	AGCGGAGTCT	TGATGTTTGG	GAAACAGGGA	GCTGGAAA..
42_4	TTTTCATCC	AGCGGAGTCT	TGATGTTTGG	GAAACAGGGA	GCTGGAAA..
42_5a	TTTTCATCC	AGCGGAGTCT	TGATGTTTGG	GAAACAGGGA	GCTGGAAA..
42_10	CTTTCCCATC	AACGGAGTGC	TGGTTTTTGG	CAAAACGGGG	GCTGCCAACA
42_3b	CTTTCCCATC	AACGGAGTGC	TGGTTTTTGG	CAAAACGGGG	GCTGCCAACA
42_11	CTTTCCCATC	AACGGAGTGC	TGGTTTTTGG	CAAAACGGGG	GCTGCCAACA
42_6b	CTTTCCCATC	AACGGAGTGC	TGGTTTTTGG	CAAAACGGGG	GCTGCCAACA
43_1	CTTCCCGTCA	AGCGGAGTTC	TAATGTTTGG	CAAGCAGGGG	GCTGGAAA..
43_5	CTTCCCGTCA	AGCGGAGTTC	TAATGTTTGG	CAAGCAGGGG	GCTGGAAA..
43_12	CTTCCCGTCA	AGCGGAGTTC	TAATGTTTGG	CAAGCAGGGG	GCTGGAAA..
43_20	CTTCCCTTCG	AGCGGGGTCC	TGATTTTTGG	CAAGCAAGGA	GCCGGGAA..
43_21	CTTCCCTTCG	AGCGGGGTCC	TGATTTTTGG	CAAGCAAGGA	GCCGGGAA..
43_23	CTTCCCTTCG	AGCGGGGTCC	TGATTTTTGG	CAAGCAAGGA	GCCGGGAA..
43_25	CTTCCCTTCG	AGCGGGGTCC	TGATTTTTGG	CAAGCAAGGA	GCCGGGAA..
44_1	TTTTCGTCC	AGCGGAGTCT	TAATGTTTGG	GAAACAGGGA	GCTGGAAA..
44_5	TTTTCGTCC	AGCGGAGTCT	TAATGTTTGG	GAAACAGGGA	GCTGGAAA..
223_10	CTTCCCTTCG	AGCGGAGTTC	TAATTTTTGG	CAAAACTGGA	GCAGCTAATA
223_2	CTCCCTTCG	AGCGGAGTTC	TAATTTTTGG	CAAAACTGGA	GCAGCTAATA
223_4	CTTCCCTTCG	AGCGGAGTTC	TAATTTTTGG	CAAAACTGGA	GCAGCTAATA
223_5	CTTCCCTTCG	AGCGGAGTTC	TAATTTTTGG	CAAAACTGGA	GCAGCTAATA
223_6	CTTCCCTTCG	AGCGGAGTTC	TAATTTTTGG	CAAAACTGGA	GCAGCTAATA
223_7	CTTCCCTTCG	AGCGGAGTTC	TAATTTTTGG	CAAAACTGGA	GCAGCTAATA
A3_4	TTTCCCATG	CACGGAAATC	TCATCTTTGG	AAAACAAGGC	ACAGGAAC..
A3_5	TTTCCCATG	CACGGAAATC	TCATCTTTGG	AAAACAAGGC	ACAGGAAC..
A3_7	TTTCCCATG	CACGGAAATC	TCATCTTTGG	AAAACAAGGC	ACAGGAAC..
A3_3	TTTCCCATG	CACGGAAATC	TCATCTTTGG	AAAACAAGGC	ACAGGAAC..
42_12	CTTTCCCATC	AACGGAGTGC	TGGTTTTTGG	CAAAACGGGG	GCTGCCAACA
AAV1	CTTTCCCATG	AGCGGTGTCA	TGATTTTTGG	AAAAGAGAGC	GCCGGAGC..
AAV2	TTTTCCTCAG	AGCGGGGTTC	TCATCTTTGG	GAAGCAAGGC	TCAGAGAA..
AAV3	TTTCCCTATG	CACGGCAATC	TAATATTTGG	CAAAGAAGGG	ACAACGGC..
AAV8	TTTTCCAGT	AACGGGATCC	TGATTTTTGG	CAAACAAAAT	GCTGCCAG..
AAV9	CTTTCCATCA	AGTGGCGTTC	TCATATTTGG	CAAGCAAGGA	GCCGGGAA..
AAV7	TTTCCCATCC	AGCGGAGTCC	TGATTTTTGG	AAAAACTGGA	GCAACTAACA
44_2	TTTTCGTCC	AGCGGAGTCT	TAATGTTTGG	GAAACAGGGA	GCTGGAAA..

Fig. 1AAAA

	3901			3950
42_2	AGACAACGCT	GGAA.....	AACGTGCTAA	TGACCAGCGA GGAGGAGATC
42_8	AGACAACG.T	GGACTATAGC	AGCGTTATGC	TAACCAGTGA GGAAGAAATC
42_15	AGACAACG.T	GGACTATAGC	AGCGTTATGC	TAACCAGTGA GGAAGAAATC
42_5b	AGACAACG.T	GGACTATAGC	AGCGTTATGC	TAACCAGTGA GGAAGAAATC
42_1b	AGACAACG.T	GGACTATAGC	AGCGTTATGC	TAACCAGTGA GGAAGAAATC
42_13	AGACAACG.T	GGACTATAGC	AGCGTTATGC	TAACCAGTGA GGAAGAAATC
42_3a	AGACAACG.T	GGACTATAGC	AGCGTTATGC	TAACCAGTGA GGAAGAAATC
42_4	AGACAACG.T	GGACTATAGC	AGCGTTATGC	TAACCAGTGA GGAAGAAATC
42_5a	AGACAACG.T	GGACTATAGC	AGCGTTATGC	TAACCAGTGA GGAAGAAATC
42_10	AGACAACGCT	GGAA.....	AACGTGCTAA	TGACCAGCGA GGAGGAGATC
42_3b	AGACAACGCT	GGAA.....	AACGTGCTAA	TGACCAGCGA GGAGGAGATC
42_11	AGACAACGCT	GGAA.....	AACGTGCTAA	TGACCAGCGA GGAGGAGATC
42_6b	AGACAACGCT	GGAA.....	AACGTGCTAA	TGACCAGCGA GGAGGAGATC
43_1	AGACAATG.T	GGACTACAGC	AGCGTGATGC	TCACCAGCGA AGAAGAAATT
43_5	AGACAATG.T	GGACTACAGC	AGCGTGATGC	TCACCAGCGA AGAAGAAATT
43_12	AGACAATG.T	GGACTACAGC	AGCGTGATGC	TCACCAGCGA AGAAGAAATT
43_20	CGATGGAG.T	GGATTACAGC	CAAGTGCTGA	TTACAGATGA GGAAGAAATC
43_21	CGATGGAG.T	GGATTACAGC	CAAGTGCTGA	TTACAGATGA GGAAGAAATC
43_23	CGATGGAG.T	GGATTACAGC	CAAGTGCTGA	TTACAGATGA GGAAGAAATC
43_25	CGATGGAG.T	GGATTACAGC	CAAGTGCTGA	TTACAGATGA GGAAGAAATC
44_1	AGACAACG.T	GGACTATAGC	AGCGTTATGC	TAACCAGTGA GGAAGAAATT
44_5	AGACAACG.T	GGACTATAGC	AGCGTTATGC	TAACCAGTGA GGAAGAAATT
223_10	AAACTACATT	AGAA.....	AACGTGCTCA	TGACAAATGA AGAAGAAATT
223_2	AAACTACATT	AGAA.....	AACGTGCTCA	TGACAAATGA AGAAGAAATT
223_4	AAACTACATT	AGAA.....	AACGTGCTCA	TGACAAATGA AGAAGAAATT
223_5	AAACTACATT	AGAA.....	AACGTGCTCA	TGACAAATGA AGAAGAAATT
223_6	AAACTACATT	AGAA.....	AACGTGCTCA	TGACAAATGA AGAAGAAATT
223_7	AAACTACATT	AGAA.....	AACGTGCTCA	TGACAAATGA AGAAGAAATT
A3_4	TACCAATG.T	GGACATTGAA	TCAGTGCTTA	TTACAGACGA AGAAGAAATC
A3_5	TACCAATG.T	GGACATTGAA	TCAGTGCTTA	TTACAGACGA AGAAGAAATC
A3_7	TACCAATG.T	GGACATTGAA	TCAGTGCTTA	TTACAGACGA AGAAGAAATC
A3_3	TACCAATG.T	GGACATTGAA	TCAGTGCTTA	TTACAGACGA AGAAGAAATC
42_12	AGACAACGCT	GGAA.....	AACGTGCTAA	TGACCAGCGA GGAGGAGATC
AAV1	TTCAAACA.C	TGCATTGGAC	AATGTCATGA	TTACAGACGA AGAGGAAATT
AAV2	AACAAATG.T	GAACATTGAA	AAGGTCATGA	TTACAGACGA AGAGGAAATC
AAV3	AAGTAACG.C	AGAATTAGAT	AATGTAATGA	TTACGGATGA AGAAGAGATT
AAV8	AGACAATG.C	GGATTACAGC	GATGTCATGC	TCACCAGCGA GGAAGAAATC
AAV9	CGATGGAG.T	CGACTACAGC	CAGGTGCTGA	TTACAGATGA GGAAGAAATT
AAV7	AAACTACATT	GGAA.....	AATGTGTTAA	TGACAAATGA AGAAGAAATT
44_2	AGACAACG.T	GGACTATAGC	AGCGTTATGC	TAACCAGTGA GGAAGAAATT

Fig. 1AAAB

	3951				4000
42_2	AAAACCACCA	ATCCCGTGGC	TACAGAAGAA	TACGGTGTGG	TCTCCAGCAA
42_8	AAAACCACCA	ACCCAGTGGC	CACAGAACAG	TACGGCGTGG	TGGCCGATAA
42_15	AAAACCACCA	ACCCAGTGGC	CACAGAACAG	TACGGCGTGG	TGGCCGATAA
42_5b	AAAACCACCA	ACCCAGTGGC	CACAGAACAG	TACGGCGTGG	TGGCCGATAA
42_1b	AAAACCACCA	ACCCAGTGGC	CACAGAACAG	TACGGCGTGG	TGGCCGATAA
42_13	AAAACCACCA	ACCCAGTGGC	CACAGAACAG	TACGGCGTGG	TGGCCGATAA
42_3a	AAAACCACCA	ACCCAGTGGC	CACAGAACAG	TACGGCGTGG	TGGCCGATAA
42_4	AAAACCACCA	ACCCAGTGGC	CACAGAACAG	TACGGCGTGG	TGGCCGATAA
42_5a	AAAACCACCA	ACCCAGTGGC	CACAGAACAG	TACGGCGTGG	TGGCCGATAA
42_10	AAAACCACCA	ATCCCGTGGC	TACAGAAGAA	TACGGTGTGG	TCTCCAGCAA
42_3b	AAAACCACCA	ATCCCGTGGC	TACAGAACAG	TACGGTGTGG	TCTCCAGCAA
42_11	AAAACCACCA	ATCCCGTGGC	TACAGAAGAA	TACGGTGTGG	TCTCCAGCAA
42_6b	AAAACCACCA	ATCCCGTGGC	TACAGAAGAA	TACGGTGTGG	TCTCCAGCAA
43_1	AAAAC TACTA	ACCCAGTGGC	TACAGAGCAG	TATGGTGTGG	TGGCAGACAA
43_5	AAAAC TACTA	ACCCAGTGGC	TACAGAGCAG	TATGGTGTGG	TGGCAGACAA
43_12	AAAAC TACTA	ACCCAGTGGC	TACAGAGCAG	TATGGTGTGG	TGGCAGACAA
43_20	AAGGCTACCA	ACCCCGTGGC	CACAGAAGAA	TATGGAGCAG	TGGCCATCAA
43_21	AAGGCTACCA	ACCCCGTGGC	CACAGAAGAA	TATGGAGCAG	TGGCCATCAA
43_23	AAGGCTACCA	ACCCCGTGGC	CACAGAAGAA	TATGGAGCAG	TGGCCATCAA
43_25	AAGGCTACCA	ACCCCGTGGC	CACAGAAGAA	TATGGAGCAG	TGGCCATCAA
44_1	AAAACCACCA	ACCCAGTGGC	CACGGAACAG	TACGGCGTGG	TGGCCGATAA
44_5	AAAACCACCA	ACCCAGTGGC	CACAGAACAG	TACGGCGTGG	TGGCCGATAA
223_10	CGTCCTACCA	ACCCGGTAGC	TACCGAGGAA	TACGGGATTG	TAAGCAGCAA
223_2	CGTCCTACCA	ACCCGGTAGC	TACCGAGGAA	TACGGGATTG	TAAGCAGCAA
223_4	CGTCCTACCA	ACCCGGTAGC	TACCGAGGAA	TACGGGATTG	TAAGCAGCAA
223_5	CGTCCTACCA	ACCCGGTAGC	TACCGAGGAA	TACGGGATTG	TAAGCAGCAA
223_6	CGTCCTACCA	ACCCGGTAGC	TACCGAGGAA	TACGGGATTG	TAAGCAGCAA
223_7	CGTCCTACCA	ACCCGGTAGC	TACCGAGGAA	TACGGGATTG	TAAGCAGCAA
A3_4	AGAACA ACTA	ATCCTGTGGC	TACAGAACAA	TACGGACAGG	TTGCCACCAA
A3_5	AGAACG ACTA	ATCCTGTGGC	TACAGAACAA	TACGGACAGG	TTGCCACCAA
A3_7	AGAACA ACTA	ATCCTGTGGC	TACAGAACAA	TACGGACAGG	TTGCCACCAA
A3_3	AGAACA ACTA	ATCCTGTGGC	TACAGAACAA	TACGGACAGG	TTGCCACCAA
42_12	AAAACCACCA	ATCCCGTGGC	TACAGAAGAA	TACGGTGTGG	TCTCCAGCAA
AAV1	AAAGCCACTA	ACCCTGTGGC	CACCGAAAGA	TTTGGGACCG	TGGCAGTCAA
AAV2	GGAACAACCA	ATCCCGTGGC	TACGGAGCAG	TATGGTTCTG	TATCTACCAA
AAV3	CGTACCACCA	ATCCTGTGGC	AACAGAGCAG	TATGGAACTG	TGGCAAATAA
AAV8	AAAACC ACTA	ACCCTGTGGC	TACAGAGGAA	TACGGTATCG	TGGCAGATAA
AAV9	AAAGCCACCA	ACCCTGTAGC	CACAGAGGAA	TACGGAGCAG	TGGCCATCAA
AAV7	CGTCCTACTA	ATCCTGTAGC	CACGGAAGAA	TACGGGATAG	TCAGCAGCAA
44_2	AAAACCACCA	ACCCAGTGGC	CACAGAACAG	TACGGCGTGG	TGGCCGATAA

Fig. 1AAAC

	4001				4050
42_2	CCTGCAATCG	TCTACGGCCG	GACCCCAGAC	ACAGACTGTC	AACAGCCAGG
42_8	CCTGCAACAG	CAAAACGCCG	CTCCTATTGT	AGGGGCCGTC	AACAGTCAAG
42_15	CCTGCAACAG	CAAAACGCCG	CTCCTATTGT	AGGGGCCGTC	AACAGTCAAG
42_5b	CCTGCAACAG	CAAAACGCCG	CTCCTATTGT	AGGGGCCGTC	AACAGTCAAG
42_1b	CCTGCAACAG	CAAAACGCCG	CTCCTATTGT	AGGGGCCGTC	AACAGTCAAG
42_13	CCTGCAACAG	CAAAACGCCG	CTCCTATTGT	AGGGGCCGTC	AACAGTCAAG
42_3a	CCTGCAACAG	CAAAACGCCG	CTCCTATTGT	AGGGGCCGTC	AACAGTCAAG
42_4	CCTGCAACAG	CAAAACGCCG	CTCCTATTGT	AGGGGCCGTC	AACAGTCAAG
42_5a	CCTGCAACAG	CAAAACGCCG	CTCCTATTGT	AGGGGCCGTC	AACAGTCAAG
42_10	CCTGCAATCG	TCTACGGCCG	GACCCCAGAC	ACAGACTGTC	AACAGCCAGG
42_3b	CCTGCAATCG	TCTACGGCCG	GACCCCAGAC	ACAGACTGTC	AACAGCCAGG
42_11	CCTGCAATCG	TCTACGGCCG	GACCCCAGAC	ACAGACTGTC	AACAGCCAGG
42_6b	CCTGCAATCG	TCTACGGCCG	GACCCCAGAC	ACAGACTGTC	AACAGCCAGG
43_1	CCTGCAGCAG	ACCAACGGAG	CTCCCATTGT	GGGAACTGTC	AACAGCCAGG
43_5	CCTGCAGCAG	ACCAACGGAG	CTCCCATTGT	GGGAACTGTC	AACAGCCAGG
43_12	CCTGCAGCAG	ACCAACGGAG	CTCCCATTGT	GGGAACTGTC	AACAGCCAGG
43_20	CAACCAGGCC	GCCAATACGC	AGGCGCAGAC	CGGACTCGTG	CACAACCAGG
43_21	CAACCAGGCC	GCCAATACGC	AGGCGCAGAC	CGGACTCGTG	CACAACCAGG
43_23	CAACCAGGCC	GCCAATACGC	AGGCGCAGAC	CGGACTCGTG	CACAACCAGG
43_25	CAACCAGGCC	GCCAATACGC	AGGCGCAGAC	CGGACTCGTG	CACAACCAGG
44_1	CCTGCAACAG	CAAAACGCCG	CTCCTATTGT	AGGGGCCGTC	AACAGTCAAG
44_5	CCTGCAACAG	CAAAACGCCG	CTCCTATTGT	AGGGGCCGTC	AACAGTCAAG
223_10	CTTGCAGGCG	GCTAGCACCG	CAGCCCAGAC	ACAAGTTGTT	AACAACCAGG
223_2	CTTGCAGGCG	GCTAGCACCG	CAGCCCAGAC	ACAAGTTGTT	AACAACCAGG
223_4	CTTGCAGGCG	GCTAGCACCG	CAGCCCAGAC	ACAAGTTGTT	AACAACCAGG
223_5	CTTGCAGGCG	GCTAGCACCG	CAGCCCAGAC	ACAAGTTGTT	AACAACCAGG
223_6	CTTGCAGGCG	GCTAGCACCG	CAGCCCAGAC	ACAAGTTGTT	AACAACCAGG
223_7	CTTGCAGGCG	GCTAGCACCG	CAGCCCAGAC	ACAAGTTGTT	AACAACCAGG
A3_4	CCATCAGAGT	CAGGACACCA	CAGCTTCCTA	TGGAAGTGTG	GACAGCCAGG
A3_5	CCGTCAAGAGT	CAGAACACCA	CAGCTTCCTA	TGGAAGTGTG	GACAGCCAGG
A3_7	CCATCAGAGT	CAGAACACCA	CAGCTTCCTA	TGGAAGTGTG	GACAGCCAGG
A3_3	CCATCAGAGT	CAGAACACCA	CAGCTTCCTA	TGGAAGTGTG	GACAGCCAGG
42_12	CCTGCAATCG	TCTACGGCCG	GACCCCAGAC	ACAGACTGTC	AACAGCCAGG
AAV1	TTTCCAGAGC	AGCAGCACAG	ACCCTGCGAC	CGGAGATGTG	CATGCTATGG
AAV2	CCTCCAGAGA	GGCAACAGAC	AAGCAGCTAC	CGCAGATGTG	AACACACAAG
AAV3	CTTGCAGAGC	TCAAATACAG	CTCCCACGAC	TGGAAGTGTG	AATCATCAGG
AAV8	CTTGCAGCAG	CAAAACACGG	CTCCTCAAAT	TGGAAGTGTG	AACAGCCAGG
AAV9	CAACCAGGCC	GCTAACACGC	AGGCGCAAAC	TGGACTTGTG	CATAACCAGG
AAV7	CTTACAAGCG	GCTAATACTG	CAGCCCAGAC	ACAAGTTGTC	AACAACCAGG
44_2	CCTGCAACAG	CAAAACGCCG	CTCCTATTGT	AGGGGCCGTC	AACAGTCAAG

Fig. 1AAAD

	4051				4100
42_2	GGGCTCTGCC	CGGCATGGTC	TGGCAGAACC	GGGACGTGTA	CCTGCAGGGT
42_8	GAGCCTTACC	TGGCATGGTC	TGGCAGAACC	GGGACGTGTA	CCTGCAGGGT
42_15	GAGCCTTACC	TGGCATGGTC	TGGCAGAACC	GGGACGTGTA	CCTGCAGGGT
42_5b	GAGCCTTACC	TGGCATGGTC	TGGCAGAACC	GGGACGTGTA	CCTGCAGGGT
42_1b	GAGCCTTACC	TGGCATGGTC	TGGCAGAACC	GGGACGTGTA	CCTGCAGGGT
42_13	GAGCCTTACC	TGGCATGGTC	TGGCAGAACC	GGGACGTGTA	CCTGCAGGGT
42_3a	GAGCCTTACC	TGGCATGGTC	TGGCAGAACC	GGGACGTGTA	CCTGCAGGGT
42_4	GAGCCTTACC	TGGCATGGTC	TGGCAGAACC	GGGACGTGTA	CCTGCAGGGT
42_5a	GAGCCTTACC	TGGCATGGCC	TGGCAGAACC	GGGACGTGTA	CCTGCAGGGT
42_10	GGGCTCTGCC	CGGCATGGTC	TGGCAGAACC	GGGACGTGTA	CCTGCAGGGT
42_3b	GGGCTCTGCC	CGGCATGGTC	TGGCAGAACC	GGGACGTGTA	CCTGCAGGGT
42_11	GGGCTCTGCC	CGGCATGGTC	TGGCAGAACC	GGGACGTGTA	CCTGCAGGGT
42_6b	GGGCTCTGCC	CGGCATGGTC	TGGCAGAACC	GGGACGTGTA	CCTGCAGGGT
43_1	GGGCCTTACC	TGGTATGGTC	TGGCAAACC	GGGACGTGTA	CCTGCAGGGC
43_5	GGGCCTTACC	TGGTATGGTC	TGGCAAACC	GGGACGTGTA	CCTGCAGGGC
43_12	GGGCCTTACC	TGGTATGGTC	TGGCAAACC	GGGACGTGTA	CCTGCAGGGC
43_20	GGGTGATTCC	CGGCATGGTG	TGGCAGAATA	GAGACGTGTA	CCTGCAGGGT
43_21	GGGTGATTCC	CGGCATGGTG	TGGCAGAATA	GAGACGTGTA	CCTGCAGGGT
43_23	GGGTGATTCC	CGGCATGGTG	TGGCAGAATA	GAGACGTGTA	CCTGCAGGGT
43_25	GGGTGATTCC	CGGCATGGTG	TGGCAGAATA	GAGACGTGTA	CCTGCAGGGT
44_1	GAGCCTTACC	TGGCATGGTC	TGGCAGAACC	GGGACGTGTA	CCTGCAGGGT
44_5	GAGCCTTACC	TGGCATGGTC	TGGCAGAACC	GGGACGTGTA	CCTGCAGGGT
223_10	GAGCCTTACC	TGGCATGGTC	TGGCAGAACC	GGGACGTGTA	CCTGCAAGGT
223_2	GAGCCTTACC	TGGCATGGTC	TGGCAGAACC	GGGACGTGTA	CCTGCAAGGT
223_4	GAGCCTTACC	TGGCATGGTC	TGGCAGAACC	GGGACGTGTA	CCTGCAAGGT
223_5	GAGCCTTACC	TGGCATGGTC	TGGCAGAACC	GGGACGTGTA	CCTGCAAGGT
223_6	GAGCCTTACC	TGGCATGGTC	TGGCAGAACC	GGGACGTGTA	CCTGCAAGGT
223_7	GAGCCTTACC	TGGCATGGTC	TGGCAGAACC	GGGACGTGTA	CCTGCAAGGT
A3_4	GAATCTTACC	TGGAATGGTG	TGGCAGGACC	GCGATGTCTA	TCTTCAAGGT
A3_5	GAATCTTACC	TGGAATGGTG	TGGCAGGACC	GCGATGTCTA	TCTTCAAGGT
A3_7	GAATCTTACC	TGGAATGGTG	TGGCAGGACC	GCGATGTCTA	TCTTCAAGGT
A3_3	GAATCTTACC	TGGAATGGTG	TGGCAGGACC	GCGATGTCTA	TCTTCAAGGT
42_12	GGGCTCTGCC	CGGCATGGTC	TGGCAGAACC	GGGACGTGTA	CCTGCAGGGT
AAV1	GAGCATTACC	TGGCATGGTG	TGGCAAGATA	GAGACGTGTA	CCTGCAGGGT
AAV2	GCGTTCTTCC	AGGCATGGTC	TGGCAGGACA	GAGATGTGTA	CCTTCAGGGG
AAV3	GGGCCTTACC	TGGCATGGTG	TGGCAAGATC	GTGACGTGTA	CCTTCAAGGA
AAV8	GGGCCTTACC	CGGTATGGTC	TGGCAGAACC	GGGACGTGTA	CCTGCAGGGT
AAV9	GAGTTATTCC	TGGTATGGTC	TGGCAGAACC	GGGACGTGTA	CCTGCAGGGC
AAV7	GAGCCTTACC	TGGCATGGTC	TGGCAGAACC	GGGACGTGTA	CCTGCAGGGT
44_2	GAGCCTTACC	TGGCATGGTC	TGGCAGAACC	GGGACGTGTA	CCTGCAGGGT

Fig. 1AAAE

	4101				4150
42_2	CCC.ATCTGG	GCCAAAATTC	CTCACACGGA	CGGCAACTTT	CACCCGTCTC
42_8	CCT.ATCTGG	GCCAAGATTC	CTCACACGGA	CGGCAACTTT	CATCCTTCGC
42_15	CCT.ATCTGG	GCCAAGATTC	CTCACACGGA	CGGCAACTTT	CATCCTTCGC
42_5b	CCT.ATCTGG	GCCAAGATTC	CTCACACGGA	CGGCAACTTT	CATCCTTCGC
42_1b	CCT.ATCTGG	GCCAAGATTC	CTCACACGGA	CGGCAACTTT	CATCCTTCGC
42_13	CCT.ATCTGG	GCCAAGATTC	CTCACACGGA	CGGCAACTTT	CATCCTTCGC
42_3a	CCT.ATCTGG	GCCAAGATTC	CTCACACGGA	CGGCAACTTT	CATCCTTCGC
42_4	CCT.ATCTGG	GCCAAGATTC	CTCACACGGA	CGGCAACTTT	CATCCTTCGC
42_5a	CCT.ATCTGG	GCCAAGATTC	CTCACACGGA	CGGCAACTTT	CATCCTTCGC
42_10	CCC.ATCTGG	GCCAAAATTC	CTCACACGGA	CGGCAACTTT	CACCCGTCTC
42_3b	CCC.ATCTGG	GCCAAAATTC	CTCACACGGA	CGGCAACTTT	CACCCGTCTC
42_11	CCC.ATCTGG	GCCAAAATTC	CTCACACGGA	CGGCAACTTT	CACCCGTCTC
42_6b	CCC.ATCTGG	GCCAAAATTC	CTCACACGGA	CGGCAACTTT	CACCCGTCTC
43_1	CCC.ATCTGG	GCCAAAATTC	CTCACACGGA	CGGCAACTTT	CATCCTTCGC
43_5	CCC.ATCTGG	GCCAAAATTC	CTCACACGGA	CGGCAACTTT	CATCCTTCGC
43_12	CCC.ATCTGG	GCCAAAATTC	CTCACACGGA	CGGCAACTTT	CATCCTTCGC
43_20	CCC.ATCTGG	GCCAAAATTC	CTCACACGGA	CGGCAACTTT	CACCCGTCTC
43_21	CCC.ATCTGG	GCCAAAATTC	CTCACACGGA	CGGCAACTTT	CACCCGTCTC
43_23	CCC.ATCTGG	GCCAAAATTC	CTCACACGGA	CGGCAACTTT	CACCCGTCTC
43_25	CCC.ATCTGG	GCCAAAATTC	CTCACACGGA	CGGCAACTTT	CACCCGTCTC
44_1	CCT.ATCTGG	GCCAAGATTC	CTCACACGGA	CGGAAACTTT	CATCCCTCGC
44_5	CCT.ATCTGG	GCCAAGATTC	CTCACACGGA	CGGAAACTTT	CATCCCTCGC
223_10	CCC.ATTTGG	GCCAAGATTC	CTCACACGGA	CGGCAACTTT	CACCCGTCTC
223_2	CCC.ATTTGG	GCCAAGATTC	CTCACACGGA	CGGCAACTTT	CACCCGTCTC
223_4	CCC.ATTTGG	GCCAAGATTC	CTCACACGGA	CGGCAACTTT	CACCCGTCTC
223_5	CCC.ATTTGG	GCCAAGATTC	CTCACACGGA	CGGCAACTTT	CACCCGTCTC
223_6	CCC.ATTTGG	GCCAAGATTC	CTCACACGGA	CGGCAACTTT	CACCCGTCTC
223_7	CCC.ATTTGG	GCCAAGATTC	CTCACACGGA	CGGCAACTTT	CACCCGTCTC
A3_4	CCC.ATTTGG	GCCAAAATTC	CTCACACGGA	CGGCAACTTT	CATCCTTCGC
A3_5	CCC.ATTTGG	GCCAAAATTC	CTCACACGGA	CGGCAACTTT	CATCCTTCGC
A3_7	CCC.ATTTGG	GCCAAAATTC	CTCACACGGA	CGGCAACTTT	CATCCTTCGC
A3_3	CCC.ATTTGG	GCCAAAATTC	CTCACACGGA	CGGCAACTTT	CATCCTTCGC
42_12	CCC.ATCTGG	GCCAAAATTC	CTCACACGGA	CGGCAACTTT	CACCCGTCTC
AAV1	CCC.ATTTGG	GCCAAAATTC	CTCACACGGA	TGGCAACTTT	CACCCGTCTC
AAV2	CCC.ATCTGG	GCAAAGATTC	CACACACGGA	CGGCAACTTT	CACCCGTCTC
AAV3	CCT.ATCTGG	GCAAAGATTC	CTCACACGGA	TGGCAACTTT	CATCCTTCGC
AAV8	CCC.ATCTGG	GCCAAGATTC	CTCACACGGA	CGGCAACTTT	CACCCGTCTC
AAV9	CCCTATTTGG	GCTAAAATAC	CTCACACGGA	TGGCAACTTT	CACCCGTCTC
AAV7	CCC.ATCTGG	GCCAAGATTC	CTCACACGGA	TGGCAACTTT	CACCCGTCTC
44_2	CCT.ATCTGG	GCCAAGATTC	CTCACACGGA	CGGAAACTTT	CATCCCTCGC

Fig. 1AAAF

	4151				4200
42_2	CCCTGATGGG	CGGATTTGGA	CTCAAACACC	CGCCTCCTCA	AATTCTCATC
42_8	CGCTGATGGG	AGGCTTTGGA	CTGAAACACC	CGCCTCCTCA	GATCCTGATT
42_15	CGCTGATGGG	AGGCTTTGGA	CTGAAACACC	CGCCTCCTCA	GATCCTGATT
42_5b	CGCTGATGGG	AGGCTTTGGA	CTGAAACACC	CGCCTCCTCA	GATCCTGATT
42_1b	CGCTGATGGG	AGGCTTTGGA	CTGAAACACC	CGCCTCCTCA	GATCCTGATT
42_13	CGCTGATGGG	AGGCTTTGGA	CTGAAACACC	CGCCTCCTCA	GATCCTGATT
42_3a	CGCTGATGGG	AGGCTTTGGA	CTGAAACACC	CGCCTCCTCA	GATCCTGATT
42_4	CGCTGATGGG	AGGCTTTGGA	CTGAAACACC	CGCCTCCTCA	GATCCTGATT
42_5a	CGCTGATGGG	AGGCTTTGGA	CTGAAACACC	CGCCTCCTCA	GATCCTGATT
42_10	CCCTGATGGG	CGGATTTGGA	CTCAAACACC	CGCCTCCTCA	AATTCTCATC
42_3b	CCCTGATGGG	CGGATTTGGA	CTCAAACACC	CGCCTCCTCA	AATTCTCATC
42_11	CCCTGATGGG	CGGATTTGGA	CTCAAACACC	CGCCTCCTCA	AATTCTCATC
42_6b	CCCTGATGGA	CGGATTTGGA	CTCAAACACC	CGCCTCCTCA	AATTCTCATC
43_1	CGCTGATGGG	AGGCTTTGGA	CTGAAACACC	CGCCTCCTCA	GATCCTGGTG
43_5	CGCTGATGGG	AGGCTTTGGA	CTGAAACACC	CGCCTCCTCA	GATCCTGGTG
43_12	CGCTGATGGG	AGGCTTTGGA	CTGAAACACC	CGCCTCCTCA	GATCCTGGTG
43_20	CCCTGATGGG	CGGCTTTGGA	CTGAAGCACC	CGCCTCCTCA	AATTCTCATC
43_21	CCCTGATGGG	CGGCTTTGGA	CTGAAGCACC	CGCCTCCTCA	AATTCTCATC
43_23	CCCTGATGGG	CGGCTTTGGA	CTGAAGCACC	CGCCTCCTCA	AATTCTCATC
43_25	CCCTGATGGG	CGGCTTTGGA	CTGAAGCACC	CGCCTCCTCA	AATTCTCATC
44_1	CGCTGATGGG	AGGCTTTGGA	CTGAAACACC	CGCCTCCTCA	GATCCTGATT
44_5	CGCTGATGGG	AGGCTTTGGA	CTGAAACACC	CGCCTCCTCA	GATCCTGATT
223_10	CTCTAATGGG	TGGCTTTGGA	CTGAAACACC	CGCCTCCCCA	GATCCTGATC
223_2	CTCTAATGGG	TGGCTTTGGA	CTGAAACACC	CGCCTCCCCA	GATCCTGATC
223_4	CTCTAATGGG	TGGCTTTGGA	CTGAAACACC	CGCCTCCCCA	GATCCTGATC
223_5	CTCTAATGGG	TGGCTTTGGA	CTGAAACACC	CGCCTCCCCA	GATCCTGATC
223_6	CTCTAATGGG	TGGCTTTGGA	CTGAAACACC	CGCCTCCCCA	GATCCTGATC
223_7	CTCTAATGGG	TGGCTTTGGA	CTGAAACACC	CGCCTCCCCA	GATCCTGATC
A3_4	CGCTCATGGG	AGGCTTTGGA	CTGAAACACC	CTCCTCCCCA	GATCCTGATC
A3_5	CGCTCATGGG	AGGCTTTGGA	CTGAAACACC	CTCCTCCCCA	GATCCTGATC
A3_7	CGCTCATGGG	AGGCTTTGGA	CTGAAACACC	CTCCTCCCCA	GATCCTGATC
A3_3	CGCTCATGGG	AGGCTTTGGA	CTGAAACACC	CTCCTCCCCA	GATCCTGATC
42_12	CCCTGATGGG	CGGATTTGGA	CTCAAACACC	CGCCTCCTCA	AATTCTCATC
AAV1	CTCTTATGGG	CGGCTTTGGA	CTCAAGAACC	CGCCTCCTCA	GATCCTCATC
AAV2	CCCTCATGGG	TGGATTCGGA	CTTAAACACC	CTCCTCCACA	GATTCTCATC
AAV3	CTCTGATGGG	AGGCTTTGGA	CTGAAACATC	CGCCTCCTCA	AATCATGATC
AAV8	CGCTGATGGG	CGGCTTTGGC	CTGAAACATC	CTCCGCCTCA	GATCCTGATC
AAV9	CTCTGATGGG	TGGATTTGGA	CTGAAACACC	CACCTCCACA	GATTCTAATT
AAV7	CTTTGATGGG	CGGCTTTGGA	CTTAAACATC	CGCCTCCTCA	GATCCTGATC
44_2	CGCTGATGGG	AGGCTTTGGA	CTGAAACACC	CGCCTCCTCA	GATCCTGATT

Fig. 1AAAG

	4201				4250
42_2	AAAAACACCC	CGGTACCTGC	TAATCCTCCA	GAGGTGTTTA	CTCCTGCCAA
42_8	AAGAATACAC	CTGTTCCCGC	GGATCCTCCA	ACTACCTTCA	GTCAAGCCAA
42_15	AAGAATACAC	CTGTTCCCGC	GGATCCTCCA	ACTACCTTCA	GTCAAGCCAA
42_5b	AAGAATACAC	CTGTTCCCGC	GGATCCTCCA	ACTACCTTCA	GTCAAGCCAA
42_1b	AAGAATACAC	CTGTTCCCGC	GGATCCTCCA	ACTACCTTCA	GTCAAGCCAA
42_13	AAGAATACAC	CTGTTCCCGC	GGATCCTCCA	ACTACCTTCA	GTCAAGCCAA
42_3a	AAGAATACAC	CTGTTCCCGC	GGATCCTCCA	ACTACCTTCA	GTCAAGCCAA
42_4	AAGAATACAC	CTGTTCCCGC	GGATCCTCCA	ACTACCTTCA	GTCAAGCCAA
42_5a	AAGAATACAC	CTGTTCCCGC	GGATCCTCCA	ACTACCTTCA	GTCAAGCCAA
42_10	AAAAACACCC	CGGTACCTGC	TAATCCTCCA	GAGGTGTTTA	CTCCTGCCAA
42_3b	AAAAACACCC	CGGTACCTGC	TAATCCTCCA	GAGGTGTTTA	CTCCTGCCAA
42_11	AAAAACACCC	CGGTACCTGC	TAATCCTCCA	GAGGTGTTTA	CTCCTGCCAA
42_6b	AAAAACACCC	CGGTACCTGC	TAATCCTCCA	GAGGTGTTTA	CTCCTGCCAA
43_1	AAAAACACTC	CTGTTCCCTGC	GGATCCTCCG	ACCACCTTCA	GCCAGGCCAA
43_5	AAAAACACTC	CTGTTCCCTGC	GGATCCTCCG	ACCACCTTCA	GCCAGGCCAA
43_12	AAAAACACTC	CTGTTCCCTGC	GGATCCTCCG	ACCACCTTCA	GCCAGGCCAA
43_20	AAGAACACAC	CGGTTCCAGC	GGACCCGCCG	CTTACCTTCA	ACCAGGCCAA
43_21	AAGAACACAC	CGGTTCCAGC	GGACCCGCCG	CTTACCTTCA	ACCAGGCCAA
43_23	AAGAACACAC	CGGTTCCAGC	GGACCCGCCG	CTTACCTTCA	ACCAGGCCAA
43_25	AAGAACACAC	CGGTTCCAGC	GGACCCGCCG	CTTACCTTCA	ACCAGGCCAA
44_1	AAGAATACAC	CTGTTCCCGC	GGATCCTCCA	ACTACCTTCA	GTCAAGCTAA
44_5	AAGAATACAC	CTGTTCCCGC	GGATCCTCCA	ACTACCTTCA	GTCAAGCTAA
223_10	AAAAACACAC	CGGTACCTGC	TAATCCTCCA	GAAGTGTTTA	CTCCTGCCAA
223_2	AAAAACACGC	CGGTACCTGC	TAATCCTCCA	GAAGTGTTTA	CTCCTGCCAA
223_4	AAAAACACAC	CGGTACCTGC	TAATCCTCCA	GAAGTGTTTA	CTCCTGCCAA
223_5	AAAAACACAC	CGGTACCTGC	TAATCCTCCA	GAAGTGTTTA	CTCCTGCCAA
223_6	AAAAACACAC	CGGTACCTGC	TAATCCTCCA	GAAGTGTTTA	CTCCTGCCAA
223_7	AAAAACACAC	CGGTACCTGC	TAATCCTCCA	GAAGTGTTTA	CTCCTGCCAA
A3_4	AAAAACACAC	CTGTGCCAGC	GAATCCCGCG	ACCACTTTCA	CTCCTGGAAA
A3_5	AAAAACACAC	CTGTGCCAGC	GAATCCCGCG	ACCACTTTCA	CTCCTGGAAA
A3_7	AAAAACACAC	CTGTGCCAGC	GAATCCCGCG	ACCACTTTCA	CTCCTGGAAA
A3_3	AAAAACACAC	CTGTGCCAGC	GAATCCCGCG	ACCACTTTCA	CTCCTGGAAA
42_12	A...A.....				
AAV1	AAAAACACGC	CTGTTCCCTGC	GAATCCTCCG	GCGGAGTTTT	CAGCTACAAA
AAV2	AAGAACACCC	CGGTACCTGC	GAATCCTTCG	ACCACCTTCA	GTGCGGCAAA
AAV3	AAAAATACTC	CGGTACCGGC	AAATCCTCCG	ACGACTTTCA	GCCCGGCCAA
AAV8	AAGAACACGC	CTGTACCTGC	GGATCCTCCG	ACCACCTTCA	ACCAGTCAAA
AAV9	AAAAATACAC	CAGTGCCGGC	AGATCCTCCT	CTTACCTTCA	ATCAAGCCAA
AAV7	AAGAACACTC	CCGTTCCCGC	TAATCCTCCG	GAGGTGTTTA	CTCCTGCCAA
44_2	AAGAATACAC	CTGTTCCCGC	GGATCCTCCA	ACTACCTTCA	GTCAAGCTAA

Fig. 1AAAH

	4251				4300
42_2	GTTTGCCTCA	TTTATCACGC	AGTACAGCAC	CGGCCA.GGT	CAGCGTGGAG
42_8	GCTGGCGTCG	TTCATCACGC	AGTACAGCAC	CGGACA.GGT	CAGCGTGGAA
42_15	GCTGGCGTCG	TTCATCACGC	AGTACAGCAC	CGGACA.GGT	CAGCGTGGAA
42_5b	GCTGGCGTCG	TTCATCACGC	AGTACAGCAC	CGGACA.GGT	CAGCGTGGAA
42_1b	GCTGGCGTCG	TTCATCACGC	AGTACAGCAC	CGGACA.GGT	CAGCGTGGAA
42_13	GCTGGCGTCG	TTCATCACGC	AGTACAGCAC	CGGACA.GGT	CAGCGTGGAA
42_3a	GCTGGCGTCG	TTCATCACGC	AGTACAGCAC	CGGACA.GGT	CAGCGTGGAA
42_4	GCCGGCGTCG	TTCATCACGC	AGTACAGCAC	CGGACA.GGT	CAGCGTGGAA
42_5a	GCTGGCGTCG	TTCATCACGC	AGTACAGCAC	CGGACA.GGT	CAGCGTGGAA
42_10	GTTTGCCTCA	TTTATCACGC	AGTACAGCAC	CGGCCA.GGT	CAGCGTGGAG
42_3b	GTTTGCCTCA	TTTATCACGC	AGTACAGCAC	CGGCCA.GGT	CAGCGTGGAG
42_11	GTTTGCCTCA	TTTATCACGC	AGTACAGCAC	CGGCCA.GGT	CAGCGTGGAG
42_6b	GTTTGCCTCA	TTTATCACGC	AGTACAGCAC	CGGCCA.GGT	CAGCGTGGAG
43_1	GCTGGCTTCT	TTTATCACGC	AGTACAGCAC	CGGACA.GGT	CAGCGTGGAA
43_5	GCTGGCTTCT	TTTATCACGC	AGTACAGCAC	CGGACA.GGT	CAGCGTGGAA
43_12	GCTGGCTTCT	TTTATCACGC	AGTACAGCAC	CGGACA.GGT	CAGCGTGGAA
43_20	GCTGAACTCT	TTCATCACGC	AGTACAGCAC	CGGACA.GGT	CAGCGTGGAA
43_21	GCTGAACTCT	TTCATCACGC	AGTACAGCAC	CGGACA.GGT	CAGCGTGGAA
43_23	GCTGAACTCT	TTCATCACGC	AGTACAGCAC	CGGACA.GGT	CAGCGTGGAA
43_25	GCTGAACTCT	TTCATCACGC	AGTACAGCAC	CGGACA.GGT	CAGCGTGGAA
44_1	GCTGGCGTCG	TTCATCACGC	AGTACAGCAC	CGGACA.GGT	CAGCGTGGAA
44_5	GCTGGCGTCG	TTCATCACGC	AGTACAGCAC	CGGACA.GGT	CAGCGTGGAA
223_10	GTTTGCTTCC	TTCATCACGC	AGTACAGCAC	CGGGCA.AGT	CAGCGTTGAG
223_2	GTTTGCTTCC	TTCATCACGC	AGTACAGCAC	CGGGCA.AGT	CAGCGTTGAG
223_4	GTTTGCTTCC	TTCATCACGC	AGTACAGCAC	CGGGCA.AGT	CAGCGTTGAG
223_5	GTTTGCTTCC	TTCATCACGC	AGTACAGCAC	CGGGCA.AGT	CAGCGTTGAG
223_6	GCTTGCTTCC	TTCATCACGC	AGTACAGCAC	CGGGCA.AGT	CAGCGTTGAG
223_7	GATTGCTTCC	TTCATCACGC	AGTACAGCAC	CGGGCA.AGT	CAGCGTTGAG
A3_4	GTTTGCTTCG	TTCATTACCC	AGTATTCCAC	CGGACA.GGT	CAGCGTGGAA
A3_5	GTTTGCTTCG	TTCATTACCC	AGTATTCCAC	CGGACA.GGT	CAGCGTGGAA
A3_7	GTTTGCTTCG	TTCATTACCC	AGTATTCCAC	CGGACA.GGT	CAGCGTGGAA
A3_3	GTTTGCTTCG	TTCATTACCC	AGTATTCCAC	CGGACA.GGT	CAGCGTGGAA
42_12					
AAV1	GTTTGCTTCA	TTCATCACCC	AATACTCCAC	AGGACA.AGT	GAGTGTGGAA
AAV2	GTTTGCTTCC	TTCATCACAC	AGTACTCCAC	GGGACACGGT	CAGCGTGGAG
AAV3	GTTTGCTTCA	TTTATCACTC	AGTACTCCAC	TGGACA.GGT	CAGCGTGGAA
AAV8	GCTGAACTCT	TTCATCACGC	AATACAGCAC	CGGACA.GGT	CAGCGTGGAA
AAV9	GCTGAACTCT	TTCATCACGC	AGTACAGCAC	GGGACA.AGT	CAGCGTGGAA
AAV7	GTTTGCTTCG	TTCATCACAC	AGTACAGCAC	CGGACA.AGT	CAGCGTGGAA
44_2	GCTGGCGTCG	TTCATCACGC	AGTACAGCAC	CGGACA.GGT	CAGCGTGGAA

Fig. 1AAAI

	4301				4350
42_2	ATCGAGTGGG	AACTGCAGAA	AGAAAACAGC	AAACGCTGGA	ATCCAGAGAT
42_8	ATTGAATGGG	AGCTGCAGAA	AGAGAACAGC	AAGCGCTGGA	ACCCAGAGAT
42_15	ATTGAATGGG	AGCTGCAGAA	AGAGAACAGC	AAGCGCTGGA	ACCCAGAGAT
42_5b	ATTGAATGGG	AGCTGCAGAA	AGAGAACAGC	AAGCGCTGGA	ACCCAGAGAT
42_1b	ATTGAATGGG	AGCTGCAGAA	AGAGAACAGC	AAGCGCTGGA	ACCCAGAGAT
42_13	ATTGAATGGG	AGCTGCAGAA	AGAGAACAGC	AAGCGCTGGA	ACCCAGAGAT
42_3a	ATTGAATGGG	AGCTGCAGAA	AGAGAACAGC	AAGCGCTGGA	ACCCAGAGAT
42_4	ATTGAATGGG	AGCTGCAGAA	AGAGAACAGC	AAGCGCTGGA	ACCCAGAGAT
42_5a	ATTGAATGGG	AGCTGCAGAA	AGAGAACAGC	AAGCGCTGGA	ACCCAGAGAT
42_10	ATCGAGTGGG	AACTGCAGAA	AGAAAACAGC	AAACGCTGGA	ATCCAGAGAT
42_3b	ATCGAGTGGG	AACTGCAGAA	AGAAAACAGC	AAACGCTGGA	ATCCAGAGAT
42_11	ATCGAGTGGG	AACTGCAGAA	AGAGAACAGC	AAACGCTGGA	ATCCAGAGAT
42_6b	ATCGAGTGGG	AACTGCAGAA	AGAAAACAGC	AAACGCTGGA	ATCCAGAGAT
43_1	ATCGAATGGG	AGCTGCAGAA	AGAAAACAGC	AAGCGCTGGA	ACCCAGAGAT
43_5	ATCGAATGGG	AGCTGCAGAA	AGAAAACAGC	AAGCGCTGGA	ACCCAGAGAT
43_12	ATCGAATGGG	AGCTGCAGAA	AGAAAACAGC	AAGCGCTGGA	ACCCAGAGAT
43_20	ATCGAGTGGG	AGCTGCAGAA	AGAAAACAGC	AAACGCTGGA	ATCCAGAGAT
43_21	ATCGAGTGGG	AGCTGCAGAA	AGAAAACAGC	AAACGCTGGA	ATCCAGAGAT
43_23	ATCGAGTGGG	AGCTGCAGAA	AGAAAACAGC	AAACGCTGGA	ATCCAGAGAT
43_25	ATCGAGTGGG	AGCTGCAGAA	AGAAAACAGC	AAACGCTGGA	ATCCAGAGAT
44_1	ATTGAATGGG	AGCTGCAGAA	AGAAAACAGC	AAACGCTGGA	ACCCAGAGAT
44_5	ATTGAATGGG	AGCTGCAGAA	AGAAAACAGC	AAACGCTGGA	ACCCAGAGAT
223_10	ATCGAGTGGG	AGCTGCAGAA	AGAGAACAGC	AAGCGCTGGA	ACCCAGAGAT
223_2	ATCGAGTGGG	AGCTGCAGAA	AGAGAACAGC	AAGCGCTGGA	ACCCAGAGAT
223_4	ATCGAATGGG	AGCTGCAGAA	AGAGAACAGC	AAGCGCTGGA	ACCCAGAGAT
223_5	ATCGAATGGG	AGCTGCAGAA	AGAGAACAGC	AAGCGCTGGA	ACCCAGAGAT
223_6	ATCGAGTGGG	AGCTGCAGAA	AGAGAACAGC	AAGCGCTGGA	ACCCAGAGAT
223_7	ATCGAGTGGG	AGCTGCAGAA	AGAGAACAGC	AAGCGCTGGA	ACCCAGAGAT
A3_4	ATAGAGTGGG	AGCTGCAGAA	AGAAAACAGC	AAACGCTGGA	ACCCAGAAAT
A3_5	ATAGAGTGGG	AGCTGCAGAA	AGAAAACAGC	AAACGCTGGA	ACCCGGAAAT
A3_7	ATAGAGTGGG	AGCTGCAGAA	AGAAAACAGC	AAACGCTGGA	ACCCAGAAAT
A3_3	ATAGAGTGGG	AGCTGCAGAA	AGAAAACAGC	AAACGCTGGA	ACCCAGAAAT
42_12					
AAV1	ATTGAATGGG	AGCTGCAGAA	AGAAAACAGC	AAGCGCTGGA	ATCCCGAAGT
AAV2	ATCGAGTGGG	AGCTGCAGAA	GGAAAACAGC	AAACGCTGGA	ATCCCGAAAT
AAV3	ATTGAGTGGG	AGCTACAGAA	AGAAAACAGC	AAACGTTGGA	ATCCAGAGAT
AAV8	ATTGAATGGG	AGCTGCAGAA	GGAAAACAGC	AAGCGCTGGA	ACCCCGAGAT
AAV9	ATCGAGTGGG	AGCTGCAGAA	AGAAAACAGC	AAGCGCTGGA	ATCCAGAGAT
AAV7	ATCGAGTGGG	AGCTGCAGAA	GGAAAACAGC	AAGCGCTGGA	ACCCGGAGAT
44_2	ATTGAATGGG	AGCTGCAGAA	AGAAAACAGC	AAACGCTGGA	ACCCAGAGAT

Fig. 1AAAJ

	4351				4400
42_2	TCAGTACACC	TCAAATTATG	CCAAGTCTAA	TAAT.GTGGA	ATTTGCTGTC
42_8	TCAGTATACT	TCCAACACTACT	ACAAATCTAC	AAAT.GTGGA	CTTTGCTGTC
42_15	TCAGTATACT	TCCAACACTACT	ACAAATCTAC	AAAT.GTGGA	CTTTGCTGTC
42_5b	TCAGTATACT	TCCAACACTACT	ACAAATCTAC	AAAT.GTGGA	CTTTGCTGTC
42_1b	TCAGTATACT	TCCAACACTACT	ACAAATCTAC	AAAT.GTGGA	CTTTGCTGTC
42_13	TCAGTATACT	TCCAACACTACT	ACAAATCTAC	AAAT.GTGGA	CTTTGCTGTC
42_3a	TCAGTATACT	TCCAACACTACT	ACAAATCTAC	AAAT.GTGGA	CTTTGCTGTC
42_4	TCAGTATACT	TCCAACACTACT	ACAAATCTAC	AAAT.GTGGA	CTTTGCTGTC
42_5a	TCAGTATACT	TCCAACACTACT	ACAAATCTAC	AAAT.GTGGA	CTTTGCTGTC
42_10	TCAGTACACC	TCAAATTATG	CCAAGTCTAA	TAAT.GTGGA	ATTTGCTGTC
42_3b	TCAGTACACC	TCAAATTATG	CCAAGTCTAA	TAAT.GTGGA	ATTTGCTGTC
42_11	TCAGTACACC	TCAAATTATG	CCAAGTCTAA	TAAT.GTGGA	ATTTGCTGTC
42_6b	TCAGTACACC	TCAAATTATG	CCAAGTCTAA	TAAT.GTGGA	ATTTGCTGTC
43_1	TCAGTATACT	TCCAACACTACT	ACAAATCTAC	AAAT.GTGGA	CTTTGCTGTC
43_5	TCAGTATACT	TCCAACACTACT	ACAAATCTAC	AAAT.GTGGA	CTTTGCTGTC
43_12	TCAGTATACT	TCCAACACTACT	ACAAATCTAC	AAAT.GTGGA	CTTTGCTGTC
43_20	TCAATACACT	TCCAACACTACT	ACAAATCTAC	AAAT.GTGGA	CTTTGCTGTC
43_21	TCAATACACT	TCCAACACTACT	ACAAATCTAC	AAAT.GTGGA	CTTTGCTGTC
43_23	TCAATACACT	TCCAACACTACT	ACAAATCTAC	AAAT.GTGGA	CTTTGCTGTC
43_25	TCAATACACT	TCCAACACTACT	ACAAATCTAC	AAAT.GTGGA	CTTTGCTGTC
44_1	TCAATACACT	TCCAACACTACT	ACAAATCTAC	AAAT.GTGGA	CTTCGCTGTT
44_5	TCAATACACT	TCCAACACTACT	ACAAATCTAC	AAAT.GTGGA	CTTTGCTGTT
223_10	TCAGTACACC	TCCAACCTTTG	ACAAACAGAC	TGGA.GTGGA	CTTTGCTGTT
223_2	TCAGTACACC	TCCAACCTTTG	ACAAACAGAC	TGGA.GTGGA	CTTTGCTGTT
223_4	TCAGTACACC	TCCAACCTTTG	ACAAACAGAC	TGGA.GTGGA	CTTTGCTGTT
223_5	TCAGTACACC	TCCAACCTTTG	ACAAACAGAC	TGGA.GTGGA	CTTTGCTGTT
223_6	TCAGTACACC	TCCAACCTTTG	ACAAACAGAC	TGGA.GTGGA	CTTTGCTGTT
223_7	TCAGTACACC	TCCAACCTTTG	ACAAACAGAC	TGGA.GTGGA	CTTTGCTGTT
A3_4	TCAGTACACC	TCCAACACTACA	ACAAGTCGGT	GAAT.GTGGA	GTTTACCGTG
A3_5	TCAGTACACC	TCCAACACTACA	ACAAGTCGGT	GAAT.GTGGA	GTTTACCGTG
A3_7	TCAGTACACC	TCCAACACTACA	ACAAGTCGGT	GAAT.GTGGA	GTTTACCGTG
A3_3	TCAGTACACC	TCCAACACTACA	ACAAGTCGGT	GAAT.GTGGA	GTTTACCGTG
42_12	...GTATACT	TCCAACACTACT	ACAAATCTAC	AAAT.GTGGA	CTTTGCTGTC
AAV1	GCAGTACACA	TCCAATTATG	CAAAATCTGC	CAAC.GTTGA	TTTTACTGTG
AAV2	TCAGTACACT	TCCAACACTACA	ACAAGTCTGT	TAATCGTGGA	CTT.ACCGTG
AAV3	TCAGTACACT	TCCAACACTACA	ACAAGTCTGT	TAAT.GTGGA	CTTTACTGTA
AAV8	CCAGTACACC	TCCAACACTACT	ACAAATCTAC	AAGT.GTGGA	CTTTGCTGTT
AAV9	CCAGTATACT	TCAAACACTACT	ACAAATCTAC	AAAT.GTGGA	CTTTGCTGTC
AAV7	TCAGTACACC	TCCAACCTTTG	AAAAGCAGAC	TGGT.GTGGA	CTTTGCCGTT
44_2	TCAATACACT	TCCAACACTACT	ACAAATCTAC	AAAT.GTGGA	CTTTGCTGTT

Fig. 1AAAK

	4401				4450
42_2	AACAACGAAG	GGGTTTATAC	TGAGCCTCGC	CCCATTTGGCA	CCCGTTACCT
42_8	AATACTGAGG	GTACTTATTC	AGAGCCTCGC	CCCATTTGGCA	CCCGTTACCT
42_15	AATACTGAGG	GTACTTATTC	AGAGCCTCGC	CCCATTTGGCA	CCCGTTACCT
42_5b	AATACTGAGG	GTACTTATTC	AGAGCCTCGC	CCCATTTGGCA	CCCGTTACCT
42_1b	AATACTGAGG	GTACTTATTC	AGAGCCTCGC	CCCATTTGGCA	CCCGTTACCT
42_13	AATACTGAGG	GTACTTATTC	AGAGCCTCGC	CCCATTTGGCA	CCCGTTACCT
42_3a	AATACTGAGG	GTACTTATTC	AGAGCCTCGC	CCCATTTGGCA	CCCGTTACCT
42_4	AATACTGAGG	GTACTTATTC	AGAGCCTCGC	CCCATTTGGCA	CCCGTTACCT
42_5a	AATACTGAGG	GTACTTATTC	AGAGCCTCGC	CCCATTTGGCA	CCCGTTACCT
42_10	AACAACGAAG	GGGTTTATAC	TGAGCCTCGC	CCCATTTGGCA	CCCGTTACCT
42_3b	AACAACGAAG	GGGTTTATAC	TGAGCCTCGC	CCCATTTGGCA	CCCGTTACCT
42_11	AACAACGAAG	GGGTTTATAC	TGAGCCTCGC	CCCATTTGGCA	CCCGTTACCT
42_6b	AACAACGAAG	GGGTTTATAC	TGAGCCTCGC	CCCATTTGGCA	CCCGTTACCT
43_1	AATACTGAGG	GTACTTATTC	AGAGCCTCGC	CCCATTTGGCA	CTCGTTATCT
43_5	AATACCGAGG	GTACTTATTC	AGAGCCTCGC	CCCATTTGGCA	CTCGTTATCT
43_12	AATACTGAGG	GTACTTATTC	AGAGCCTCGC	CCCATTTGGCA	CTCGTTATCT
43_20	AACACGGAAG	GAGTTTATAG	CGAGCCTCGC	CCCATTTGGCA	CCCGTTACCT
43_21	AACACGGAAG	GAGTTTATAG	CGAGCCTCGC	CCCATTTGGCA	CCCGTTACCT
43_23	AACACGGAAG	GAGTTTATAG	CGAGCCTCGC	CCCATTTGGCA	CCCGTTACCT
43_25	AACACGGAGG	GGGTTTATAG	CGAGCCTCGC	CCCATTTGGCA	CCCGTTACCT
44_1	AACACAGATG	GCACTTATTC	TGAGCCTCGC	CCCATTTGGCA	CCCGTTACCT
44_5	AACACAGATG	GCACTTATTC	TGAGCCTCGC	CCCATTTGGCA	CCCGTTACCT
223_10	GACAGCCAGG	GTGTTTACTC	TGAGCCT...		
223_2	GACAGCCAGG	GTGTTTACTC	TGAGCCT...		
223_4	GACAGCCAGG	GTGTTTACTC	TGAGCCT...		
223_5	GACAGCCAGG	GTGTTTACTC	TGAGCCT...		
223_6	GACAGCCAGG	GTGTTTACTC	TGAGCCT...		
223_7	GACAGCCAGG	GTGTTTACTC	TGAGCCT...		
A3_4	GACGCAAACG	GTGTTTATTC	TGAACCCCGC	CCTATTGGCA	CTCGTTACCT
A3_5	GACGCAAACG	GTGTTTATTC	TGAACCCCGC	CCTATTGGCA	CTCGTTACCT
A3_7	GACGCAAACG	GTGTTTATTC	TGAACCCCGC	CCTATTGGCA	CTCGTTACCT
A3_3	GACGCAAACG	GTGTTTATTC	TGAACCCCGC	CCTATTGGCA	CTCGTTACCT
42_12	AATACTGAGG	GTACTTATTC	AGAGCCTCGC	CCCATTTGGCA	CCCGTTACCT
AAV1	GACAACAATG	GACTTTATAC	TGAGCCTCGC	CCCATTTGGCA	CCCGTTACCT
AAV2	GATACTAATG	GCGTGTATTC	AGAGCCTCGC	CCCATTTGGCA	CCAGATACCT
AAV3	GACACTAATG	GTGTTTATAG	TGAACCTCGC	CCTATTGGAA	CCCGGTATCT
AAV8	AATACAGAAG	GCGTGTACTC	TGAACCCCGC	CCCATTTGGCA	CCCGTTACCT
AAV9	AATACCGAAG	GTGTTTACTC	TGAGCCTCGC	CCCATTTGGTA	CTCGTTACCT
AAV7	GACAGCCAGG	GTGTTTACTC	TGAGCCTCGC	CCTATTGGCA	CTCGTTACCT
44_2	AACACAGATG	GCACTTATTC	TGAGCCTCGC	CCCATCGGCA	CCCGTTACCT

Fig. 1AAAL

	4451				4500
		<u>VP1-3 stop</u>		<u>Poly A signal</u>	
42_2	CACCCGTAAC	CTGTAATTGC	CTGTTAATCA	ATAAACCGGT	TAATTCGTTT
42_8	CACCCGTAAC	CTGTAATTGC	CTGTTAATCA	ATAAACCGGC	TAATTCGTTT
42_15	CACCCGTAAC	CTGTAATTGC	CTGTTAATCA	ATAAACCGGT	TAATTCGTTT
42_5b	CACCCGTAAC	CTGTAATTGC	CTGTTAATCA	ATAAACCGGT	TAATTCGTTT
42_1b	CACCCGTAAC	CTGTAATTGC	CTGTTAATCA	ATAAACCGGT	TGATTCGTTT
42_13	CACCCGTAGC	CTGTAATTGC	CTGTTAATCA	ATAAACCGGT	TGATTCGTTT
42_3a	CACCCGTAAC	CTGTAATTGC	CTGTTAATCA	ATAAACCGGT	TAATTCGTTT
42_4	CACCCGTAAC	CTGTAATTGC	CTGTTAATCA	ATAAACCGGT	TAATTCGTTT
42_5a	CACCCGTAAC	CTGTAATTGC	CTGTTAATCA	ATAAACCGGT	TAATTCGTTT
42_10	CACCCGTAAC	CTGTAATTGC	CTGTTAATCA	ATAAACCGGT	TAATTCGTTT
42_3b	CACCCGTAAC	CTGTAATTGC	CTGTTAATCA	ATAAACCGGT	TAATTCGTTT
42_11	CACCCGTAAC	CTGTAATTAC	TTGTTAATCA	ATAAACCGGT	TGATTCGTTT
42_6b	CACCCGTAAC	CTGTAATTGC	CTGTTAATCA	ATAAACCGGT	TAATTCGTTT
43_1	CACCCGTAAT	CTGTAATTGC	TTGTTAATCA	ATAAACCGGT	
43_5	CACCCGTAAT	CTGTAATTGC	TTGTTAATCA	ATAAACCGGT	TAATTCGTTT
43_12	CACCCGTAAT	CTGTAATTGC	TTGTTAATCA	ATAAACCGGT	TAATTCGTTT
43_20	CACCCGCAAC	CTGTAATTAC	ATGTTAATCA	ATAAACCGGT	TAATTCGTTT
43_21	CACCCGCAAC	CTGTAATTAC	ATGTTAATCA	ATAAACCGGT	TAATTCGTTT
43_23	CACCCGCAAC	CTGTAATTAC	ATGTTAATCA	ATAAACCGGT	TAATTCGTTT
43_25	CACCCGCAAC	CTGTAATTAC	ATGTTAATCA	ATAAACCGGT	TAATTCGTTT
44_1	CACCCGTAAT	CTGTAATTGC	TCGTTAATCA	ATAAACCGGT	TGATTCGTTT
44_5	CACCCGTAAT	CTGTAATTGC	TTGTTAATCA	ATAAACCGGT	TGATTCGTTT
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4	TACCCGGAAC	TTGTAATTTT	CTGTTAATGA	ATAAACCGAT	TTATGCGTTT
A3_5	TACCCGGAAC	TTGTAATTTT	CTGTTAATGA	ATAAACCGAT	TTATGCGTTT
A3_7	TACCCGGAAC	TTGTAATTTT	CTGTTAATGA	ATAAACCGAT	TTATGCGTTT
A3_3	TACCCGGAAC	TTGTAATTTT	CTGTTAATGA	ATAAGCCGAT	TTATGCGTTT
42_12	CACCCGTAAC	CTGTAATTGC	CTGTTAATCA	ATAAACCGGT	TAATTCGTTT
AAV1	TACCCGTCCC	CTGTAATTAC	GTGTTAATCA	ATAAACCGGT	TGATTCGTTT
AAV2	GACTCGTAAT	CTGTAATTGC	TTGTTAATCA	ATAAACCGTT	TAATTCGTTT
AAV3	CACACGAAAC	TTGTGAATCC	TGGTTAATCA	ATAAACCGTT	TAATTCGTTT
AAV8	CACCCGTAAT	CTGTAATTGC	CTGTTAATCA	ATAAACCGGT	TGATTCGTTT
AAV9	CACCCGTAAT	TTGTAATTGC	CTGTTAATCA	ATAAACCGGT	TAATTCGTTT
AAV7	CACCCGTAAT	CTGTAATTGC	ATGTTAATCA	ATAAACCGGT	TGATTCGTTT
44_2	CACCCGTAAT	CTGTAATTGC	TTGTTAATCA	ATAAACCGGT	TGATTCGTTT
		<u>vp1-3 stop</u>		<u>PolyA signal</u>	

Fig. 1AAAM

	4501				4550
42_2	CAGTTGAACT	TTGGTCTC.T	GCGAAGGGCG	AATTC.....	
42_8	CAGTTGAACT	TTGGTCTC.T	GCGAAGGGCG	AATTC.....	
42_15	CAGTTGAACT	TTGGTCTC.T	GCGAAGGGCG	AATTC.....	
42_5b	CAGTTGAACT	TTGGTCTC.T	GCGAAGGGCG	AATTCGTTTA	AACCTGCAGG
42_1b	CAGTTGAACT	TTGGTCTC..	...AAGGGCG	AATTC.....	
42_13	CAGTTGAACT	TTGGTCTC.T	GCGAAGGGCG	AATTC.....	
42_3a	CAGTTGAACT	TTGGTCTC.T	GCGAAGGGCG	AATTC.....	
42_4	CAGTTGAACT	TTGGTCTC.T	GCGAAGGGCG	AATTC.....	
42_5a	CAGTTGAACT	TTGGTCTC.T	GCGAAGGGCG	AATTC.....	
42_10	CAGTTGAACT	TTGGTC....	...AAGGGCG	AATTC.....	
42_3b	CAGTTGAACT	TTGGTCTC.T	GCGAAGGGCG	AATTC.....	
42_11	CAGTTGAACT	TTGGTCTC.T	GCGAAGGGCG	AATTC.....	
42_6b	CAGTTGAACT	TTGGTCTC.T	GCGAAGGGCG	AATTC.....	
43_1					
43_5	CAGTTGAACT	TTGGTCTC.T	GCGAAGGGCG	AATTCGTTTA	AACCTGCAGG
43_12	CAGTTGAACT	TTGGTCTC.T	GCGAAGGGCG	AATTC.....	
43_20	CAGTTGAACT	TTGGTCTC.T	GCGAAGGGCG	AATTC.....	
43_21	CAGTTGAACT	TTGGTCTC.T	GCGAAGGGCG	AATTC.....	
43_23	CAGTTGAACT	TTGGTCTC.T	GCGAAGGGCG	AATTC.....	
43_25	CAGTTGAACT	TTGGTCTC.T	GCGAAGGGCG	AATTC.....	
44_1	CAGTTGAACT	TTGGTCTC.T	GCGAAGGGCG	AATTC.....	
44_5	CAGTTGAACT	TTGGTCTC.T	GCGAAGGGCG	AATTC.....	
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4	CAGTTGAACT	TTGGTCTC.T	GCGAAGGGCG	AATTCGC.GG	CCGCTA....
A3_5	CAGTTGAACT	TTGGTCTC.T	GCGAAGGGCG	AATTC.....	
A3_7	CAGTTGAACT	TTGGTCTC.T	GCGAAGGGCG	AATTC.....	
A3_3	CAGTTGAACT	TTGGTCTC.T	GCGAAGGGCG	AATTCGT.TT	AAACCT....
42_12	CAGTTGAACT	TTGGTCTC.T	GCGAAGGGCG	AATTC.....	
AAV1	CAGTTGAACT	TTGGTCTCCT	GTCCTTCTTA	TCTTATCGGT	TACCATGGTT
AAV2	CAGTTGAACT	TTGGTCTC.T	GCGTATTTCT	..TTCTT.AT	CTAGTTTCCA
AAV3	CAGTTGAACT	TTGGCTCT.T	GTGCACTTCT	TTATCTTTAT	CTTGTTTCCA
AAV8	CAGTTGAACT	TTGGTCTC.T	GCG.....		
AAV9	CAGTTGAACT	TTGGTCTC.T	GCG.....		
AAV7	CAGTTGAACT	TTGGTCTCCT	GTGCTTCTTA	TCTTATCGGT	TTCCATAGCA
44_2	CAGTTGAACT	TTGGTCTC.T	GCGAAGGGCG	AATTC.....	

Fig. 1AAAN

	4551				4600
42_2					
42_8					
42_15					
42_5b	ACTAGTCCCT	TTAGTGAGGG	TTAATTCTGA	G.....	
42_1b					
42_13					
42_3a					
42_4					
42_5a					
42_10					
42_3b					
42_11					
42_6b					
43_1					
43_5	AC.....				
43_12					
43_20					
43_21					
43_23					
43_25					
44_1					
44_5					
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4					
A3_5					
A3_7					
A3_3					
42_12					
AAV1	ATAGCTTACA	CATTAAGTGC	TTGGTTGCGC	T.....	
AAV2	TGGCTAC...	GTAGATAAGT	AGC.....		
AAV3	TGGCTACTGC	GTAGATAAGC	AGCGGCCTGC	GGCGCTTGCG	CTTCGCGGTT
AAV8					
AAV9					
AAV7	ACTGGTTACA	CATTAAGTGC	TTGGGTGCGC	TTCACGATAA	GAACACTGAC
44_2					

Fig. 1AAAO

	4601				4650
42_2					
42_8					
42_15					
42_5b	CTTGGC	GTAATCATGG	GTCATAG...		
42_1b					
42_13					
42_3a					
42_4					
42_5a					
42_10					
42_3b					
42_11					
42_6b					
43_1					
43_5					
43_12					
43_20					
43_21					
43_23					
43_25					
44_1					
44_5					
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4					
A3_5					
A3_7					
A3_3					
42_12					
AAV1	TCGCGA	TAAAAGACTT	ACGTCATCGG	GTTACCCCTA	GTGATGGAGT
AAV2	ATGGCG	GGTTAATCAT	TAACCTACAAG	GA.ACCCCTA	GTGATGGAGT
AAV3	TACAACTGCT	GGTTAATATT	TAACCTCTCGC	CATACCTCTA	GTGATGGAGT
AAV8					
AAV9					
AAV7			..GTCACCGC	GGTACCCCTA	GTGATGGAGT
44_2					

Fig. 1AAAP

	4651				4700
42_2					
42_8					
42_15					
42_5b					
42_1b					
42_13					
42_3a					
42_4					
42_5a					
42_10					
42_3b					
42_11					
42_6b					
43_1					
43_5					
43_12					
43_20					
43_21					
43_23					
43_25					
44_1					
44_5					
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4					
A3_5					
A3_7					
A3_3					
42_12					
AAV1	TGCCCACTCC	CTCTCTGCGC	GCTCGCTCGC	TCGGTGGGGC	CTGCGGACCA
AAV2	TGGCCACTCC	CTCTCTGCGC	GCTCGCTCGC	TCACTGAGGC	CGGGCGACCA
AAV3	TGGCCACTCC	CTCTATGCGC	ACTCGCTCGC	TCGGTGGGGC	CTGGCGACCA
AAV8					
AAV9					
AAV7	TGGCCACTCC	CTCTATGCGC	GCTCGCTCGC	TCGGTGGGGC	CTGCGGACCA
44_2					

Fig. 1AAAQ

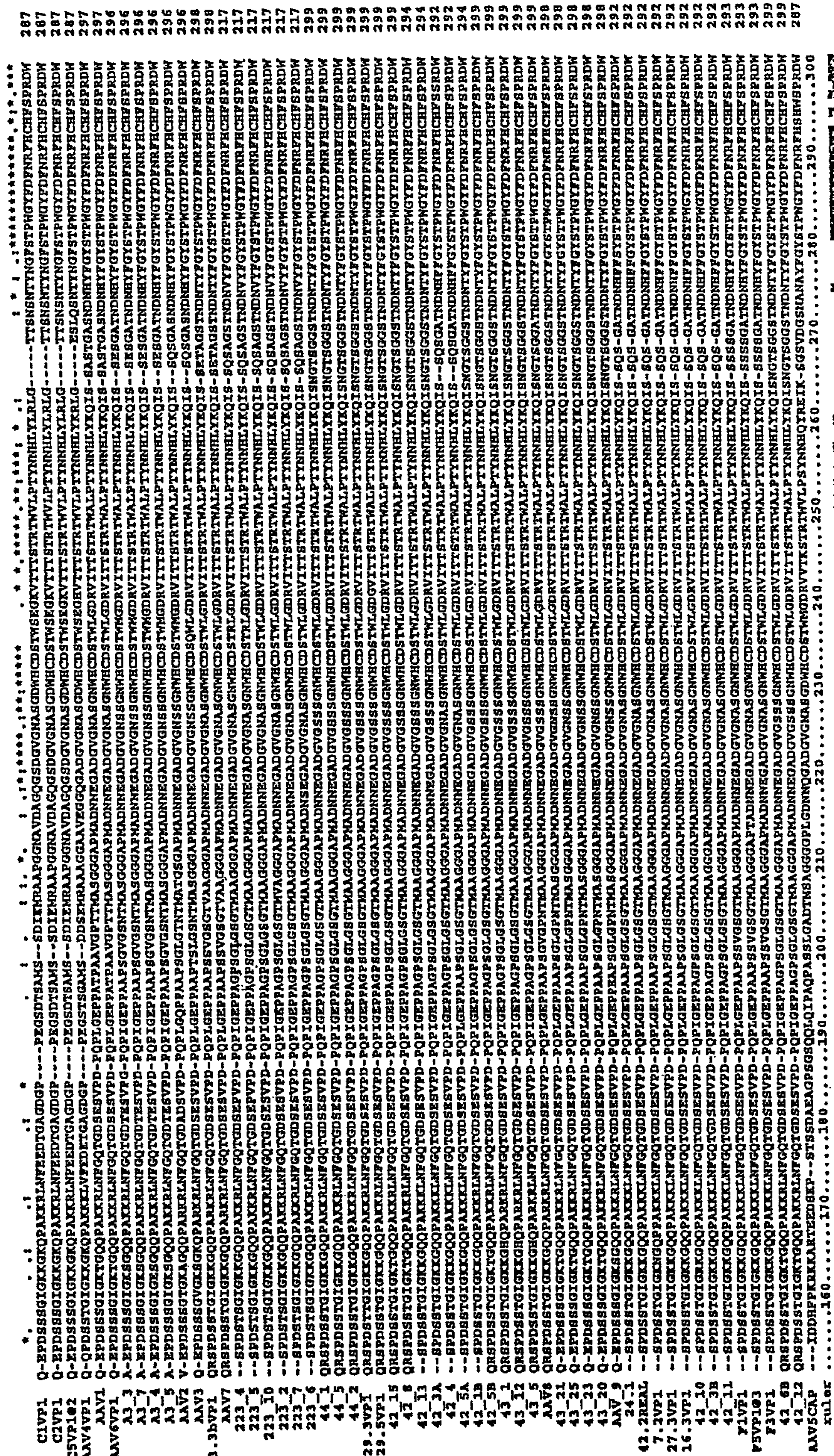
	4701				4750
42_2					
42_8					
42_15					
42_5b					
42_1b					
42_13					
42_3a					
42_4					
42_5a					
42_10					
42_3b					
42_11					
42_6b					
43_1					
43_5					
43_12					
43_20					
43_21					
43_23					
43_25					
44_1					
44_5					
223_10					
223_2					
223_4					
223_5					
223_6					
223_7					
A3_4					
A3_5					
A3_7					
A3_3					
42_12					
AAV1	AAGGTCCGCA	GACGGCAGAG	CTCTGCTCTG	CCGGCCCCAC	CGAGCGAGCG
AAV2	AAGGTCGCCC	GACGCCCCGG	CTTTGCCCGG	GCGGCCTCAG	TGAGCGAGCG
AAV3	AAGGTCGCCA	GACGGACGTG	CTTTGCACGT	CCGGCCCCAC	CGAGCGAGCG
AAV8					
AAV9					
AAV7	AAGGTCCGCA	GACGGCAGAG	CTCTGCTCTG	CCGGCCCCAC	CGAGCGAGCG
44_2					

Fig. 1AAAR

	4751		4774
42_2			
42_8			
42_15			
42_5b			
42_1b			
42_13			
42_3a			
42_4			
42_5a			
42_10			
42_3b			
42_11			
42_6b			
43_1			
43_5			
43_12			
43_20			
43_21			
43_23			
43_25			
44_1			
44_5			
223_10			
223_2			
223_4			
223_5			
223_6			
223_7			
A3_4			
A3_5			
A3_7			
A3_3			
42_12			
AAV1	AGCGCGCAGA	GAGGGAGTGG	GCAA
AAV2	AGCGCGCAGA	GAGGGAGTGG	CCAA
AAV3	AGTGCGCATA	GAGGGAGTGG	CCAA
AAV8			
AAV9			
AAV7	AGCGCGCATA	GAGGGAGTGG	CCAA
44_2			

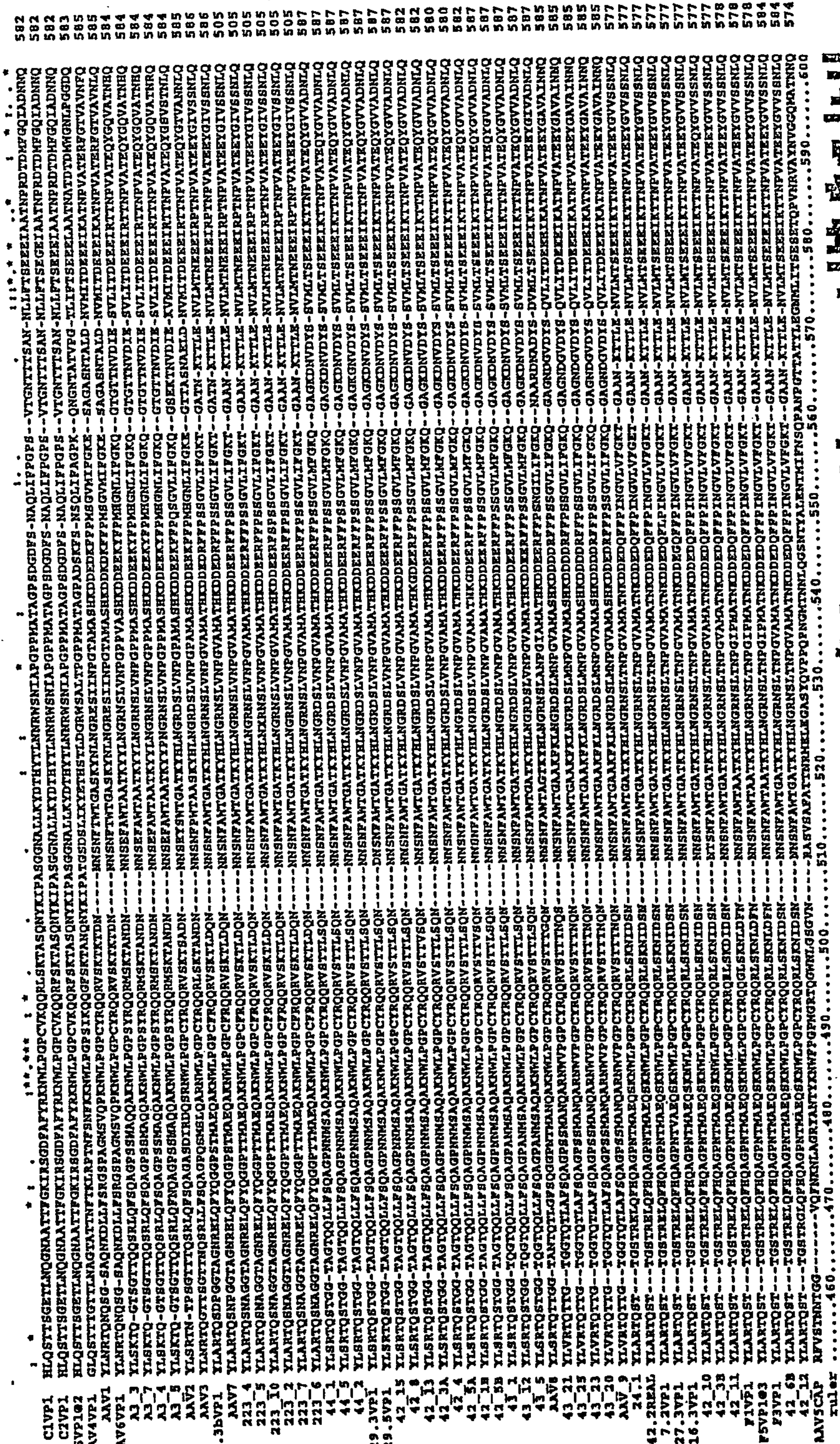
97/105

Fig. 2B



99/105

Fig. 2D



101/105

Fig. 2F

C1VP1	L	733
C2VP1	L	733
CSVP102	L	733
AAV4VP1	L	734
AAV1	L	736
NAV6VP1	L	736
A3_3	L	735
A3_7	L	735
A3_4	L	735
A3_5	L	735
AAV2	L	735
AAV3	L	736
3.3bVP1	L	737
AAV7	L	737
223_4	-	644
223_5	-	644
223_10	-	644
223_2	-	644
223_7	-	644
223_6	-	644
44_1	L	738
44_5	L	738
44_2	L	738
29.3VP1	L	738
29.5VP1	L	738
42_15	L	738
42_8	L	738
42_13	L	733
42_3A	L	733
42_4	L	731
42_5A	L	731
42_18	L	733
42_5B	L	738
43_1	L	738
43_12	L	738
43_5	L	738
AAV8	L	738
43_21	L	736
43_25	L	736
43_23	L	736
43_20	L	736
AAV_9	L	736
24_1	L	728
62.2BHAL	L	728
7.2VP1	L	728
27.3VP1	L	728
16.3VP1	L	728
42_10	L	728
42_38	L	728
42_11	L	728
F2VP1	L	729
F5VP103	L	729
F3VP1	L	729
42_6B	L	735
42_12	L	685
AAV5CAP	L	724
ruler	.	

Fig. 3A

Met Pro Gly Phe Tyr Glu Ile Val Ile Lys Val Pro Ser Asp Leu Asp
 1 5 10 15
 Glu His Leu Pro Gly Ile Ser Asp Ser Phe Val Asn Trp Val Ala Glu
 20 25 30
 Lys Glu Trp Glu Leu Pro Pro Asp Ser Asp Met Asp Leu Asn Leu Ile
 35 40 45
 Glu Gln Ala Pro Leu Thr Val Ala Glu Lys Leu Gln Arg Asp Phe Leu
 50 55 60
 Val Gln Trp Arg Arg Val Ser Lys Ala Pro Glu Ala Leu Phe Phe Val
 65 70 75 80
 Gln Phe Glu Lys Gly Glu Ser Tyr Phe His Leu His Val Leu Val Glu
 85 90 95
 Thr Thr Gly Val Lys Ser Met Val Leu Gly Arg Phe Leu Ser Gln Ile
 100 105 110
 Arg Glu Lys Leu Val Gln Thr Ile Tyr Arg Gly Val Glu Pro Thr Leu
 115 120 125
 Pro Asn Trp Phe Ala Val Thr Lys Thr Arg Asn Gly Ala Gly Gly Gly
 130 135 140
 Asn Lys Val Val Asp Glu Cys Tyr Ile Pro Asn Tyr Leu Leu Pro Lys
 145 150 155 160
 Thr Gln Pro Glu Leu Gln Trp Ala Trp Thr Asn Met Glu Glu Tyr Ile
 165 170 175
 Ser Ala Cys Leu Asn Leu Ala Glu Arg Lys Arg Leu Val Ala Gln His
 180 185 190
 Leu Thr His Val Ser Gln Thr Gln Glu Gln Asn Lys Glu Asn Leu Asn
 195 200 205
 Pro Asn Ser Asp Ala Pro Val Ile Arg Ser Lys Thr Ser Ala Arg Tyr
 210 215 220

Fig. 3B

Met Glu Leu Val Gly Trp Leu Val Asp Arg Gly Ile Thr Ser Glu Lys
 225 230 235 240
 Gln Trp Ile Gln Glu Asp Gln Ala Ser Tyr Ile Ser Phe Asn Ala Ala
 245 250 255
 Ser Asn Ser Arg Ser Gln Ile Lys Ala Ala Leu Asp Asn Ala Gly Lys
 260 265 270
 Ile Met Ala Leu Thr Lys Ser Ala Pro Asp Tyr Leu Val Gly Pro Ser
 275 280 285
 Leu Pro Ala Asp Ile Lys Thr Asn Arg Ile Tyr Arg Ile Leu Glu Leu
 290 295 300
 Asn Gly Tyr Asp Pro Ala Tyr Ala Gly Ser Val Phe Leu Gly Trp Ala
 305 310 315 320
 Gln Lys Lys Phe Gly Lys Arg Asn Thr Ile Trp Leu Phe Gly Pro Ala
 325 330 335
 Thr Thr Gly Lys Thr Asn Ile Ala Glu Ala Ile Ala His Ala Val Pro
 340 345 350
 Phe Tyr Gly Cys Val Asn Trp Thr Asn Glu Asn Phe Pro Phe Asn Asp
 355 360 365
 Cys Val Asp Lys Met Val Ile Trp Trp Glu Glu Gly Lys Met Thr Ala
 370 375 380
 Lys Val Val Glu Ser Ala Lys Ala Ile Leu Gly Gly Ser Lys Val Arg
 385 390 395 400
 Val Asp Gln Lys Cys Lys Ser Ser Ala Gln Ile Asp Pro Thr Pro Val
 405 410 415
 Ile Val Thr Ser Asn Thr Asn Met Cys Ala Val Ile Asp Gly Asn Ser
 420 425 430
 Thr Thr Phe Glu His Gln Gln Pro Leu Gln Asp Arg Met Phe Lys Phe
 435 440 445

Fig. 3C

Glu Leu Thr Arg Arg Leu Glu His Asp Phe Gly Lys Val Thr Lys Gln
 450 455 460

Glu Val Lys Glu Phe Phe Arg Trp Ala Ser Asp His Val Thr Glu Val
 465 470 475 480

Ala His Glu Phe Tyr Val Arg Lys Gly Gly Ala Ser Lys Arg Pro Ala
 485 490 495

Pro Asp Asp Ala Asp Ile Ser Glu Pro Lys Arg Ala Cys Pro Ser Val
 500 505 510

Ala Asp Pro Ser Thr Ser Asp Ala Glu Gly Ala Pro Val Asp Phe Ala
 515 520 525

Asp Arg Tyr Gln Asn Lys Cys Ser Arg His Ala Gly Met Ile Gln Met
 530 535 540

Leu Phe Pro Cys Lys Thr Cys Glu Arg Met Asn Gln Asn Phe Asn Ile
 545 550 555 560

Cys Phe Thr His Gly Val Arg Asp Cys Leu Glu Cys Phe Pro Gly Val
 565 570 575

Ser Glu Ser Gln Pro Val Val Arg Lys Lys Thr Tyr Arg Lys Leu Cys
 580 585 590

Ala Ile His His Leu Leu Gly Arg Ala Pro Glu Ile Ala Cys Ser Ala
 595 600 605

Cys Asp Leu Val Asn Val Asp Leu Asp Asp Cys Val Ser Glu Gln
 610 615 620