variety of infectious agents. Studies conducted in experimental animals (e. g. rodents, canines and nonhuman primates) indicate that recombinant replication-defective human adenoviral vectors carrying transgenes encoding immunogens as well as other antigens elicit both humoral and cell-mediated immune responses against the transgene product. Generally speaking, investigators have reported success using human adenoviral vectors as vaccine carriers in non human experimental systems by either using immunization protocols that utilizes high doses of recombinant adenoviral vectors that are predicted to elicit immune responses; or by using immunization protocols which employ the sequential administration of adenoviral vectors that are derived from different serotypes but which carry the same transgene product as boosting immunizations (Mastrangeli, et. al., Human Gene Therapy, 7: 79-87 (1996)).

Vectors derived from species C adenoviruses (e.g. Ad5, Ad6 and ChAd3) are the most immunogenic (Colloca et al., Sci. Transl. Med. 4 (115), 2012). In particular, viral vectors based on human adenovirus type 5 (Ad5) have been developed for gene therapy and vaccine applications. Although Ad5-based vectors are extremely efficient in animal models, the presence of pre-existing neutralizing antibodies in humans against Ad5 wild type virus (in particular directed to the capsid as shown in Figure 1) has in clinical trials been demonstrated to reduce the efficiency of gene transduction (Moore JP et al. Science. 2008 May 9; 320(5877):753-5). Such antibodies are largely directed to the hypervariable regions of the hexon protein. Immunity in the general population limits the broad application of Ad vectored-vaccines based on Ad5. On the other hand, rare human adenoviruses are less immunogenic than Ad5 (Colloca et al., Sci. Transl. Med. 4 (115), 2012). Vectors based on non-human adenoviruses have a very low pre-existing immunity in the general human population (Farina et al., J. Virol. 75 (23), 11603-11613, 2001). Some non-human adenovirus vectors are known, but since immunity against these can develop in humans, there is an ongoing need for further adenovirus vectors with high immunogenicity and a low or absent pre-existing neutralizing antibodies in humans.

SUMMARY

In one aspect, the disclosure provides a polynucleotide encoding an adenovirus hexon protein comprising:

A) (i) a HVR1 comprising an amino acid sequence according to position 136 to 168 of SEQ ID NO: 2, or a variant thereof comprising up to two mutations,

F) (i) a HVR1 comprising an amino acid sequence according to position 136 to 168 of SEQ ID NO: 21, or a variant thereof comprising up to two mutations,

(ii) a HVR2 comprising an amino acid sequence according to position 187 to 201 of SEQ ID NO: 21, or a variant thereof comprising up to two mutations,

(iii) a HVR3 comprising an amino acid sequence according to position 219 to 225 of SEQ ID NO: 21, or a variant thereof comprising up to two mutations,

(iv) a HVR4 comprising an amino acid sequence according to position 257 to 267 of SEQ ID NO: 21, or a variant thereof comprising up to two mutations,

(v) a HVR5 comprising an amino acid sequence according to position 275 to 289 of SEQ ID NO: 21, or a variant thereof comprising up to two mutations,

(vi) a HVR6 comprising an amino acid sequence according to position 313 to 321 of SEQ ID NO: 21, or a variant thereof comprising up to two mutations, and

(vii) a HVR7 comprising an amino acid sequence according to position 430 to 455 of SEQ ID NO: 21, or a variant thereof comprising up to two mutations; or

G) (i) a HVR1 comprising an amino acid sequence according to position 136 to 168 of SEQ ID NO: 23, or a variant thereof comprising up to two mutations,

(ii) a HVR2 comprising an amino acid sequence according to position 187 to 201 of SEQ ID NO: 23, or a variant thereof comprising up to two mutations,

(iii) a HVR3 comprising an amino acid sequence according to position 219 to 225 of SEQ ID NO: 23, or a variant thereof comprising up to two mutations,

(iv) a HVR4 comprising an amino acid sequence according to position 257 to 268 of SEQ ID NO: 23, or a variant thereof comprising up to two mutations,

(v) a HVR5 comprising an amino acid sequence according to position 276 to 290 of SEQ ID NO: 23, or a variant thereof comprising up to two mutations,

(vi) a HVR6 comprising an amino acid sequence according to position 314 to 322 of SEQ ID NO: 23, or a variant thereof comprising up to two mutations, and

(vii) a HVR7 comprising an amino acid sequence according to position 431 to 456 of SEQ ID NO: 23, or a variant thereof comprising up to two mutations; wherein the polynucleotide encoding an adenovirus hexon protein according to G) further encodes for an adenovirus fiber protein according to SEQ ID NO: 6, or a variant thereof comprising up to two mutations.

In another aspect, the disclosure provides an isolated hexon polypeptide encoded by the polynucleotide as defined in A), B), C), D), E) or F) as disclosed herein.

In another aspect, the present disclosure provides an isolated adenoviral capsid comprising hexon and preferably also fiber and/or penton proteins encoded by the polynucleotide as described herein. In an example, the disclosure provides an adenoviral capsid comprising hexon, fiber and penton proteins, wherein for A)-F) the hexon is the hexon encoded by the polynucleotide of the first example, and for G) the hexon and the fiber are the hexon and fiber encoded by the polynucleotide of the first example.

In yet another aspect, the disclosure provides an adenovirus (i) encoded by an polynucleotide as described herein, (ii) comprising a polynucleotide as described herein and/or (iii) comprising a hexon polypeptide as described herein or the capsid as described herein.

In another aspect, the disclosure provides a virus-like particle encoded by a polynucleotide as described herein. In an example, the disclosure provides a virus-like particle (i) encoded by a polynucleotide as described herein and/or (ii) comprising a hexon polypeptide as described herein or the capsid as described herein.

In yet another aspect, the disclosure provides a vector comprising a polynucleotide as described herein.

In yet another aspect, the disclosure provides a composition comprising (i) an adjuvant, (ii) a polynucleotide as described herein, a hexon polypeptide as described herein, an adenoviral capsid polypeptide as described herein, an adenovirus as described herein, a virus-like particle as described herein, or a vector as described herein, and optionally (iii) a pharmaceutically acceptable excipient.

In yet another aspect, the disclosure provides an isolated cell comprising a polynucleotide as described herein, a hexon polypeptide as described herein, an adenoviral capsid polypeptide as described herein, an adenovirus as described herein, a virus-like particle as described herein, or a vector of the sixth as described herein.

In a further aspect, the disclosure provides a polynucleotide as described herein, a hexon polypeptide as described herein, an adenoviral capsid as described herein, an adenovirus as described herein, a virus-like particle as described herein, a vector as described herein, the composition as described herein and/or the cell as described herein for use in therapy. In a further aspect, the disclosure provides a use of a polynucleotide as described herein, a hexon polypeptide as described herein, an adenoviral capsid as described herein, an adenovirus as described herein, a virus-like particle as described herein, a vector as described herein, the composition as described herein and/or the cell as described herein in the manufacture of a medicament for treating or preventing a disease, preferably coronavirus disease, more preferably Covid-19.

In another example, the disclosure provides a polynucleotide as described herein, a hexon polypeptide as described herein, an adenoviral capsid polypeptide as described herein, an adenovirus as described herein, a virus-like particle as described herein, a vector as described herein, a composition as described herein and/or a cell as described herein for use in treating or preventing a disease.

In a further aspect, the disclosure relates to an *in vitro* method for producing an adenovirus or an adenovirus-like particle, comprising the steps of

(i) expressing a polynucleotide as described herein in a cell such that an adenovirus or an adenovirus-like particle is assembled in the cell,

(ii) isolating the adenovirus or the adenovirus-like particle from the cell or the medium surrounding the cell.

CLAIMS

1. An isolated polynucleotide encoding an adenovirus hexon protein comprising:

A) (i) a HVR1 comprising an amino acid sequence according to position 136 to 168 of SEQ ID NO: 2, or a variant thereof comprising up to two mutations,

(ii) a HVR2 comprising an amino acid sequence according to position 187 to 201 of SEQ ID NO: 2, or a variant thereof comprising up to two mutations,

(iii) a HVR3 comprising an amino acid sequence according to position 219 to 225 of SEQ ID NO: 2, or a variant thereof comprising up to two mutations,

(iv) a HVR4 comprising an amino acid sequence according to position 257 to 268 of SEQ ID NO: 2, or a variant thereof comprising up to two mutations,

(v) a HVR5 comprising an amino acid sequence according to position 276 to 290 of SEQ ID NO: 2, or a variant thereof comprising up to two mutations,

(vi) a HVR6 comprising an amino acid sequence according to position 314 to 322 Y of SEQ ID NO: 2, or a variant thereof comprising up to two mutations, and

(vii) a HVR7 comprising an amino acid sequence according to position 431 to 456 of SEQ ID NO: 2, or a variant thereof comprising up to two mutations; or

B) (i) a HVR1 comprising an amino acid sequence according to position 136 to 168 of SEQ ID NO: 9, or a variant thereof comprising up to two mutations,

(ii) a HVR2 comprising an amino acid sequence according to position 187 to 201 of SEQ ID NO: 9, or a variant thereof comprising up to two mutations,

(iii) a HVR3 comprising an amino acid sequence according to position 219 to 225 of SEQ ID NO: 9, or a variant thereof comprising up to two mutations,

(iv) a HVR4 comprising an amino acid sequence according to position 257 to 268 of SEQ ID NO: 9, or a variant thereof comprising up to two mutations,

(v) a HVR5 comprising an amino acid sequence according to position 276 to 290 of SEQ ID NO: 9, or a variant thereof comprising up to two mutations,

(vi) a HVR6 comprising an amino acid sequence according to position 314 to 322 of SEQ ID NO: 9, or a variant thereof comprising up to two mutations, and

(vii) a HVR7 comprising an amino acid sequence according to position 431 to 456 of SEQ ID NO: 9, or a variant thereof comprising up to two mutations; or

C) (i) a HVR1 comprising an amino acid sequence according to position 136 to 163 of SEQ ID NO: 11, or a variant thereof comprising up to two mutations,

(ii) a HVR2 comprising an amino acid sequence according to position 182 to 196 of SEQ ID NO: 11, or a variant thereof comprising up to two mutations,

(iii) a HVR3 comprising an amino acid sequence according to position 214 to 220 of SEQ ID NO: 11, or a variant thereof comprising up to two mutations,

(iv) a HVR4 comprising an amino acid sequence according to position 252 to 262 of SEQ ID NO: 11, or a variant thereof comprising up to two mutations,

(v) a HVR5 comprising an amino acid sequence according to position 270 to 278 of SEQ ID NO: 11, or a variant thereof comprising up to two mutations,

(vi) a HVR6 comprising an amino acid sequence according to position 302 to 310 of SEQ ID NO: 11, or a variant thereof comprising up to two mutations, and

(vii) a HVR7 comprising an amino acid sequence according to position 419 to 442 of SEQ ID NO: 11, or a variant thereof comprising up to two mutations; or

D) (i) a HVR1 comprising an amino acid sequence according to position 136 to 168 of SEQ ID NO: 17, or a variant thereof comprising up to two mutations,

(ii) a HVR2 comprising an amino acid sequence according to position 187 to 201 of SEQ ID NO: 17, or a variant thereof comprising up to two mutations,

(iii) a HVR3 comprising an amino acid sequence according to position 219 to 225 of SEQ ID NO: 17, or a variant thereof comprising up to two mutations,

(iv) a HVR4 comprising an amino acid sequence according to position 257 to 267 of SEQ ID NO: 17, or a variant thereof comprising up to two mutations,

(v) a HVR5 comprising an amino acid sequence according to position 275 to 289 of SEQ ID NO: 17, or a variant thereof comprising up to two mutations,

(vi) a HVR6 comprising an amino acid sequence according to position 313 to 321 of SEQ ID NO: 17, or a variant thereof comprising up to two mutations, and

(vii) a HVR7 comprising an amino acid sequence according to position 430 to 455 of SEQ ID NO: 17, or a variant thereof comprising up to two mutations; or

E) (i) a HVR1 comprising an amino acid sequence according to position 136 to 168 of SEQ ID NO: 19, or a variant thereof comprising up to two mutations,

(ii) a HVR2 comprising an amino acid sequence according to position 187 to 201 of SEQ ID NO: 19, or a variant thereof comprising up to two mutations,

(iii) a HVR3 comprising an amino acid sequence according to position 219 to 225 of SEQ ID NO: 19, or a variant thereof comprising up to two mutations,

(iv) a HVR4 comprising an amino acid sequence according to position 257 to 268 of SEQ ID NO: 19, or a variant thereof comprising up to two mutations,

(v) a HVR5 comprising an amino acid sequence according to position 276 to 290 of SEQ ID NO: 19, or a variant thereof comprising up to two mutations,

(vi) a HVR6 comprising an amino acid sequence according to position 314 to 322 of SEQ ID NO: 19, or a variant thereof comprising up to two mutations, and

(vii) a HVR7 comprising an amino acid sequence according to position 431 to 456 of SEQ ID NO: 19, or a variant thereof comprising up to two mutations; or

F) (i) a HVR1 comprising an amino acid sequence according to position 136 to 168 of SEQ ID NO: 21, or a variant thereof comprising up to two mutations,

(ii) a HVR2 comprising an amino acid sequence according to position 187 to 201 of SEQ ID NO: 21, or a variant thereof comprising up to two mutations,

(iii) a HVR3 comprising an amino acid sequence according to position 219 to 225 of SEQ ID NO: 21, or a variant thereof comprising up to two mutations,

(iv) a HVR4 comprising an amino acid sequence according to position 257 to 267 of SEQ ID NO: 21, or a variant thereof comprising up to two mutations,

(v) a HVR5 comprising an amino acid sequence according to position 275 to 289 of SEQ ID NO: 21, or a variant thereof comprising up to two mutations,

(vi) a HVR6 comprising an amino acid sequence according to position 313 to 321 of SEQ ID NO: 21, or a variant thereof comprising up to two mutations, and

(vii) a HVR7 comprising an amino acid sequence according to position 430 to 455 of SEQ ID NO: 21, or a variant thereof comprising up to two mutations; or

G) (i) a HVR1 comprising an amino acid sequence according to position 136 to 168 of SEQ ID NO: 23, or a variant thereof comprising up to two mutations,

(ii) a HVR2 comprising an amino acid sequence according to position 187 to 201 of SEQ ID NO: 23, or a variant thereof comprising up to two mutations,

(iii) a HVR3 comprising an amino acid sequence according to position 219 to 225 of SEQ ID NO: 23, or a variant thereof comprising up to two mutations,

(iv) a HVR4 comprising an amino acid sequence according to position 257 to 268 of SEQ ID NO: 23, or a variant thereof comprising up to two mutations,

(v) a HVR5 comprising an amino acid sequence according to position 276 to 290 of SEQ ID NO: 23, or a variant thereof comprising up to two mutations,

(vi) a HVR6 comprising an amino acid sequence according to position 314 to 322 of SEQ ID NO: 23, or a variant thereof comprising up to two mutations, and

(vii) a HVR7 comprising an amino acid sequence according to position 431 to 456 of SEQ ID NO: 23, or a variant thereof comprising up to two mutations; wherein the

polynucleotide encoding an adenovirus hexon protein according to G) further encodes for an adenovirus fiber protein according to SEQ ID NO: 6, or a variant thereof comprising up to two mutations.

2. The isolated polynucleotide of claim 1, wherein the hexon protein according to
A) comprises an amino acid sequence according to SEQ ID NO: 2, or a variant thereof having at least 80% sequence identity,
B) comprises an amino acid sequence according to SEQ ID NO: 9, or a variant thereof having at least 80% sequence identity,
C) comprises an amino acid sequence according to SEQ ID NO: 11, or a variant thereof having at least 80% sequence identity,
D) comprises an amino acid sequence according to SEQ ID NO: 17, or a variant thereof having at least 80% sequence identity, and/or
E) comprises an amino acid sequence according to SEQ ID NO: 19, or a variant thereof having at least 80% sequence identity,
F) comprises an amino acid sequence according to SEQ ID NO: 21, or a variant thereof having at least 80% sequence identity, and/or
G) comprises an amino acid sequence according to SEQ ID NO: 23, or a variant thereof having at least 80% sequence identity.

3. The isolated polynucleotide of any one of claims 1 to 2, further encoding an adenoviral fiber protein comprising with respect to
A) an amino acid sequence according to SEQ ID NO: 3 or SEQ ID NO: 6, or a variant thereof having at least 80% sequence identity,
B), D), E) and/or F) an amino acid sequence according to SEQ ID NO: 6, or a variant thereof having at least 80% sequence identity, and/or
C) an amino acid sequence according to SEQ ID NO: 12 or SEQ ID NO: 15, or a variant thereof having at least 80% sequence identity.

4. The isolated polynucleotide of any one of claims 1 to 3, further encoding an adenoviral penton protein comprising with respect to
A) an amino acid sequence according to SEQ ID NO: 4 or SEQ ID NO: 7, or a variant thereof having at least 80% sequence identity,

B), D), E), F) and/or G) an amino acid sequence according to SEQ ID NO: 7, or a variant thereof having at least 80% sequence identity, and/or
C) an amino acid sequence according to SEQ ID NO: 13, or a variant thereof having at least 80% sequence identity.

5. The isolated polynucleotide of any one of claims 1 to 4, wherein the adenovirus comprises a non-adenoviral gene, protein or fragment thereof, and wherein the non-adenoviral gene or protein optionally is a coronaviral gene or protein, preferably a SARS-CoV-2 gene or protein.

6. The isolated polynucleotide of claim 5, wherein the non-adenoviral gene or protein is a coronaviral gene or protein, and wherein the coronaviral gene or protein is a spike gene or protein, preferably comprising a sequence according to SEQ ID NO: 30 or a variant thereof having at least 80% amino acid sequence identity.

7. An isolated hexon polypeptide encoded by the polynucleotide as defined in claim 1 A), B), C), D), E) or F) or in claim 2 A), B), C), D), E) or F).

8. An isolated adenoviral capsid comprising hexon and preferably also fiber and/or penton proteins encoded by the polynucleotide of any one of claims 1-4.

9. An adenovirus (i) encoded by a polynucleotide of any one of claims 1-6, (ii) comprising a polynucleotide of any of claims 1-6 and/or (iii) comprising a hexon polypeptide of claim 7 or an adenoviral capsid of claim 8.

10. A virus-like particle encoded by a polynucleotide of any one of claims 1-6.

11. A vector comprising a polynucleotide of any one of claims 1-6.

12. A composition comprising (i) an adjuvant, (ii) a polynucleotide of any one of claims 1-6, a hexon polypeptide of claim 7, an adenoviral capsid polypeptide of claim 8, an adenovirus of claim 9, a virus-like particle of claim 10, or a vector of claim 11, and optionally (iii) a pharmaceutically acceptable excipient.

13. An isolated cell comprising a polynucleotide of any one of claims 1-6, a hexon polypeptide of claim 7, an adenoviral capsid of claim 8, an adenovirus of claim 9, a virus-like particle of claim 10, or a vector of claim 11.

14. A polynucleotide of any one of claims 1-6, a hexon polypeptide of claim 7, an adenoviral capsid of claim 8, an adenovirus of claim 9, a virus-like particle of claim 10, a vector of claim 11, the composition of claim 12 and/or the cell of claim 13 for use in therapy.

15. Use of a polynucleotide of any one of claims 1-6, a hexon polypeptide of claim 7, an adenoviral capsid of claim 8, an adenovirus of claim 9, a virus-like particle of claim 10, a vector of claim 11, the composition of claim 12 and/or the cell of claim 13 in the manufacture of a medicament for treating or preventing a disease, preferably coronavirus disease, more preferably Covid-19.

16. An *in vitro* method for producing an adenovirus or an adenovirus-like particle, comprising the steps of

(i) expressing a polynucleotide of any one of claims 1-6 in a cell such that an adenovirus or an adenovirus-like particle is assembled in the cell,

(ii) isolating the adenovirus or the adenovirus-like particle from the cell or the medium surrounding the cell.