

Claims

1. An isolated engineered polypeptide comprising the amino acid stretches essentially corresponding to a first and a second fragment of the penton base wherein the first fragment of the polypeptide is present between the first and second amino acid stretches forming the jellyroll fold domain in the full length penton base and wherein the second fragment of the polypeptide is present between the second and third fragments forming the jellyroll fold domain in the full length penton base, respectively, wherein the isolated engineered domain lacks the amino acid stretches forming the jellyroll fold domain of the adenovirus penton base, wherein optionally the first and/or second fragments of the polypeptide contain(s) one or more heterologous modification(s).
2. The polypeptide of claim 1 having the structure of the following general formula (I):

N-A-L-B-C (I)

wherein

A represents an amino acid stretch corresponding to the N-terminal amino acid stretch of the adenovirus penton base present between the first and the second amino acid stretch forming the jellyroll fold domain of the adenovirus penton base;

B represents an amino acid stretch corresponding to the C-terminal amino acid stretch of the adenovirus penton base inserted between the second and the third amino acid stretch forming the jellyroll fold domain of the adenovirus penton base;

L represents a chemical group selected from the group consisting of an amino acid, an oligopeptide and a polypeptide;

N may or may not be present, and, if present, represents a chemical group consisting of an amino acid, an oligopeptide and a polypeptide;

C: may or may not be present, and, if present, represents a chemical group consisting of an amino acid, an oligopeptide and a polypeptide;

wherein, optionally, fragment A and/or B contain(s) one or more heterologous modifications.

3. The polypeptide according to any one of claims 2 wherein the fragment A comprises an amino acid sequence selected from the group consisting of the amino acid sequences according to the following table and amino acid sequences having an identity of at least 85 %, more preferred at least 90 %, even more preferred 95 %, particularly preferred at least 98 %, most preferred at least 99 %, with the respective amino acid sequence shown in the following table:

Sequence based on penton base protomer of	Sequence according to UniProt Acc. No.	SEQ ID NO:	N-terminal amino acid selected from positions	C-terminal amino acid selected from positions
hAd3	Q2Y0H9	1	130 to 137	399 to 405
hAd2	P03276	2	130 to 137	426 to 432
hAd4	Q2KSF3	3	126 to 133	380 to 386
hAd5	P12538	4	130 to 137	426 to 432
hAd7	Q9JFT6	5	130 to 137	399 to 405
hAd11	D2DM93	6	130 to 137	416 to 422
hAd12	P36716	7	120 to 127	352 to 358
hAd17	F1DT65	8	117 to 124	371 to 377
hAd25	M0QUK0	9	125 to 133	389 to 395
hAd35	Q7T941	10	131 to 138	446 to 452
hAd37	Q912J1	11	117 to 124	373 to 379
hAd41	F8WQN4	12	128 to 135	362 to 368
gorAd	E5L3Q9	13	131 to 138	417 to 423
ChimpAd	G9G849	14	126 to 133	373 to 379
sAd18	H8PFZ9	15	128 to 135	354 to 360
sAd20	F6KSU4	16	127 to 134	359 to 365
sAd49	F2WTK5	17	128 to 135	357 to 363
rhAd51	A0A0A1EWW1	18	125 to 132	353 to 359
rhAd52	A0A0A1EWX7	19	125 to 132	351 to 357
rhAd53	A0A0A1EWZ7	20	126 to 133	352 to 358

wherein, optionally, fragment A contains one or more heterologous modifications.

4. The polypeptide of claim 2 or 3 wherein the fragment B comprises an amino acid sequence selected from the group consisting of the amino acid sequences according to the following table and amino acid sequences having an identity of at least 85 %, more preferred at least 90 %, even more preferred 95 %, particularly preferred at

least 98 %, most preferred at least 99 %, with the respective amino acid sequence shown in the following table:

Sequence based on penton base protomer of	Sequence according to UniProt Acc. No.	SEQ ID NO:	N-terminal amino acid selected from positions	C-terminal amino acid selected from positions
hAd3	Q2Y0H9	1	441 to 444	491 to 494
hAd2	P03276	2	468 to 471	518 to 521
hAd4	Q2KSF3	3	422 to 445	465 to 468
hAd5	P12538	4	468 to 471	491 to 494
hAd7	Q9JFT6	5	441 to 444	464 to 467
hAd11	D2DM93	6	458 to 461	481 to 484
hAd12	P36716	7	394 to 398	418 to 421
hAd17	F1DT65	8	414 to 417	438 to 441
hAd25	M0QUK0	9	441 to 444	454 to 457
hAd35	Q7T941	10	498 to 501	521 to 524
hAd37	Q912J1	11	415 to 418	438 to 441
hAd41	F8WQN4	12	405 to 408	438 to 441
gorAd	E5L3Q9	13	459 to 462	482 to 485
ChimpAd	G9G849	14	421 to 424	444 to 457
sAd18	H8PFZ9	15	396 to 399	419 to 422
sAd20	F6KSU4	16	401 to 404	424 to 427
sAd49	F2WTK5	17	399 to 402	422 to 425
rhAd51	A0A0A1EWW1	18	395 to 398	418 to 421
rhAd52	A0A0A1EWX7	19	393 to 396	416 to 419
rhAd53	A0A0A1EWZ7	20	394 to 397	417 to 420

wherein, optionally, fragment B contains one or more heterologous modifications.

5. The polypeptide according to any one of claims 2 to 4 characterized in that fragment A and/or B contain(s) one or more heterologous modifications wherein said one or more heterologous modifications is/are contained in the following sites:
- the RGD loop region of fragment A; and/or
 - the V-loop of fragment A; and/or
 - the floor region having the sequence (from N- to C-terminal)
 $X_1-X_2-X_3-X_4-X_5-X_6-D-X_7-X_8-X_9-S-Y-N-X_{10}-X_{11}-X_{12}-X_{13}-X_{14}-X_{15}-X_{16}$ (SEQ ID NO: 21)
of fragment A, wherein
 X_1 is I or L, and is preferably I;

- X₂ is selected from the group consisting of K, Q and E, and is preferably Q;
 X₃ is P or A, and is preferably P;
 X₄ is selected from the group consisting of L, V and I, and is preferably L
 X₅ is selected from the group consisting of T, E, A, K and L, and is preferably E;
 5 X₆ is selected from the group consisting of E, K, T and Q, and is preferably K;
 X₇ is selected from the group consisting of S, P and D, and is preferably S;
 X₈ is selected from the group consisting of K, T and S, and is preferably K;
 X₉ is selected from the group consisting of K, S, N, G and D, and is preferably S;
 X₁₀ is L or V, and is preferably V;
 10 X₁₁ is I or L, and is preferably I;
 X₁₂ is selected from the group consisting of S, E and P, and is preferably E;
 X₁₃ is no amino acid (i.e. not present) or is N, and is preferably no amino acid;
 X₁₄ is D or G, and is preferably D;
 X₁₅ is selected from the group consisting of S, K, Q and T, and is preferably K; and
 15 X₁₆ is selected from the group consisting of T, N, I, K and M, and is preferably I;
 and/or
 - the sequence (from N- to C-terminal) T-H-V-F-X₁₇-R-F-P (SEQ ID NO: 22) of
 fragment B wherein X₁₇ is D or N, and is preferably N.
- 20 6. The polypeptide of claim 5 wherein the N-terminus of the RGD loop region of
 fragment A is defined by the following sequence (from N-terminal to C-terminal):
 X₁₈-X₁₉-X₂₀-X₂₁-X₂₂-X₂₃-X₂₄-X₂₅-X₂₆ (SEQ ID NO: 23) wherein
 X₁₈ is selected from the group consisting of D, E and N, and is preferably D;
 X₁₉ is selected from the group consisting of V, L, and I, and is preferably V;
 25 X₂₀ is any amino acid, preferably selected from the group consisting of A, D, E, K, S,
 and T, and is more preferably T;
 X₂₁ is any amino acid, preferably selected from the group consisting of A, D, E, and K,
 and is more preferably A;
 X₂₂ is selected from the group consisting of F, Y, and W, and is preferably Y;
 30 X₂₃ is selected from the group consisting of A, D, E, N, and Q, is preferably E or Q,
 and is more preferably E;
 X₂₄ is any amino acid, preferably selected from the group consisting of A, D, E, N, and
 K, and is more preferably E;
 X₂₅ is selected from the group consisting of S or T, and is preferably S; and
 35 X₂₆ is any amino acid and constitutes the N-terminal amino acid of the RGD loop
 region

7. The polypeptide of claim 5 or 6 wherein the C-terminus of the RGD loop region of fragment A is defined by the following sequence (from N-terminal to C-terminal):
 $X_{27}-X_{28}-X_{29}-X_{30}-X_{31}-X_{32}-X_{33}-X_{34}$ (SEQ ID NO: 24)
 Wherein
- 5 X_{27} is any amino acid and constitutes the C-terminal amino acid of the second RGD loop;
 X_{28} is selected from the group consisting of I, L and V, and is preferably I;
 X_{29} is selected from the group consisting of D, E, K, N, Q, and V, is preferably Q or K, and is more preferably Q;
- 10 X_{30} is selected from the group consisting of C, G and P, and is preferably P;
 X_{31} is selected from the group consisting of I, L and V, is preferably L or V and is more preferably L;
 X_{32} is selected from the group consisting of D, E, S and T, is preferably E or T and is more preferably E;
- 15 X_{33} is selected from the group consisting of D, E, , S and T, is preferably E, or T, and is more preferably K; and
 X_{34} is selected from the group consisting of D and E, and is preferably D;
8. The polypeptide according to any one of claims 5 to 7 wherein the N-terminus of the V loop of fragment A is defined by the following sequence (from N-terminal to C-terminal):
 $X_{35}-X_{36}-X_{37}-X_{38}-X_{39}-X_{40}-X_{41}-X_{42}$ (SEQ ID NO: 25)
 wherein
- 25 X_{35} is selected from the group consisting of F, Y, and W, and is preferably F;
 X_{36} is selected from the group consisting of H, K and R, and is preferably K;
 X_{37} is selected from the group consisting of A, V, I, and L, and is preferably A;
 X_{38} is selected from the group consisting of H, K, and R, and is preferably R;
 X_{39} is selected from the group consisting of A, V, I, and L, and is preferably V;
 X_{40} is selected from the group consisting of A, V, I, L and M, and is preferably M;
- 30 X_{41} is selected from the group consisting of A, V, I, and L, and is preferably V; and
 X_{42} is any amino acid and constitutes the N-terminal amino acid of the V loop.
9. The polypeptide according to any one of claims 5 to 8 wherein the C-terminus of the V loop of fragment A is defined by the following sequence (from N-terminal to C-terminal):
 $X_{43}-X_{44}-X_{45}-X_{46}-X_{47}-X_{48}-X_{49}$ (SEQ ID NO: 26)
 wherein
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- X₄₃ is any amino acid and constitutes the C-terminal amino acid of the V loop;
 X₄₄ is selected from the group consisting of F, Y, and W, and is preferably Y;
 X₄₅ is selected from the group consisting of D, E, S and T, is preferably E or T and is more preferably E;
- 5 X₄₆ is selected from the group consisting of F, Y, and W, and is preferably W;
 X₄₇ is selected from the group consisting of A, F, V, Y, and W, is preferably F or V and is more preferably F;
 X₄₈ is selected from the group consisting of D, E, S and T, is preferably D or E and is more preferably E; and
- 10 X₄₉ is selected from the group consisting of F, Y, and W, and is preferably F.
10. The polypeptide according to any one of claims 2 to 9 wherein the heterologous modification is selected from the group consisting of one or more single amino acid mutations in comparison to the wildtype sequence of fragment A and/or B, one or more replacements of wildtype amino acid stretches by one or more heterologous amino acids and/or amino acid stretches one or more insertions of heterologous amino acid stretches, one or more deletions of one or more amino acids and one or more amino acid modifications as well as any combination(s) thereof.
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- 20 11. The polypeptide according to any one of claims 2 to 10, wherein the heterologous modification provides a target specific binding entity.
12. The polypeptide of claim 11, wherein the target specific binding entity is selected from the group consisting of antigens, epitopes, CDRs, antibodies, antibody fragments such as an antigen binding (Fab) fragment, a Fab' fragment, a F(ab')₂ fragment, a heavy chain antibody, a single-domain antibody (sdAb), a single-chain fragment variable (scFv), a fragment variable (Fv), a VH domain, a VL domain, a single domain antibody, a nanobody, an IgNAR (immunoglobulin new antigen receptor), a di-scFv, a bispecific T-cell engager (BITEs), a dual affinity re-targeting (DART) molecule, a triple body, a diabody, a single-chain diabody, a paratope, an alternative scaffold protein, and a fusion protein thereof, a toxin and a venom.
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- 30
13. The polypeptide according to any one of claims 1 to 3 having one of the following amino acid sequences (from N- terminal to C-terminal):
- 35 MSYYHHHHHDYDIPTTENLYFQGAMSGIQPNVNEYMFSNKFARVMVSRKAPEGVTVNDTY
 DHKEDILKYEWFEFILPEGNFSATMTIDLMNNAIIDNYLEIGRQNGVLES DIGVKFDTRNFR
 L GWDPE TKLIMPGVYTYEAFHPDIVLLPGCGVDFTESRLSNLLGIRKRHPFQEGFKIMYEDLEG
 GNIPALLDVTAYEESKDDTTTETTTKKELKIQPLEKDSKRSYNVLEDKINTAYRSWYLSYNY

GNPEKGIRSWTLLTTS DVTTCGANGDSGNPVFSKSFYNEQAVYSQQLRQATSLTHVFNRFPENQ
ILIRPPAPTITTVSENV
(SEQ ID NO: 27)

5 GAMGSGIQPNVNEYMF SNKFKARVMVSRKAPEGVTVNDTYDHKEDILKYEWFEFILPEGNFSA
TMTIDLMNNAIIDNYLEIGRQNGVLESDIGVKFDTRNFRLGWDPEPKLIMPGVYTYEAFHPDI
VLLPGCGVDFTESRLSNLLGIRKRHPFQEGFKIMYEDLEGGNIPALLDVTAYEESKKDTTET
TTKKELKIQPLEKDSKRSYNVLEDKINTAYRSWYLSYNYGNPEKGIRSWTLLTTS DVTTCGAN
10 GDSGNPVFSKSFYNEQAVYSQQLRQATSLTHVFNRFPENQILIRPPAPTITTVSENV
(SEQ ID NO: 32)

MSYYHHHHHDYDIPTTENLYFQGTIMHTNMPNVNEFMYSNKFKARVMVSRKAPEGVTVNDTY
DHKEDILEYEWVEFELPEGNF SVTMTIDLMNNAIIDNYLAVGRQNGVLESDIGVKFDTRNFRL
15 GWDVPTELVM PGVYTNEAFHPDI VLLPGCGVDFTESRLSNLLGIRKRQPFQEGFQIMYEDLEG
GNIPALLDVDAYEKS KDTTETTTKKELKIQPVEKDSKDRSYNVLPDKINTAYRSWYLAYNY
GDPEKGVRSWTLLTTS DVTTCGVEQAELLPVYSKSFFNEQAVYSQQLRAFTSLTHVFNRFPENQ
ILVRPPAPTITTVSENV
(SEQ ID NO: 28)

20 QGTIMHTNMPNVNEFMYSNKFKARVMVSRKAPEGVTVNDTYDHKEDILEYEWVEFELPEGNF
VTMTIDLMNNAIIDNYLAVGRQNGVLESDIGVKFDTRNFRLGWDVPTELVM PGVYTNEAFHPD
IVLLPGCGVDFTESRLSNLLGIRKRQPFQEGFQIMYEDLEGGNIPALLDVDAYEKS KDTTTE
TTKKELKIQPVEKDSKDRSYNVLPDKINTAYRSWYLAYNYGDPEKGVRSWTLLTTS DVTTCGV
25 EQAELLPVYSKSFFNEQAVYSQQLRAFTSLTHVFNRFPENQILVRPPAPTITTVSENV
(SEQ ID NO: 33)

14. An isolated engineered polypeptide comprising the large fragment of the alpha-helical
domain of an adenovirus penton base protein which polypeptide lacks the small
fragment of the alpha-helical domain and the jellyroll fold domain of the adenovirus
30 penton base protein, wherein said large fragment optionally contains one or more
heterologous modifications.

15. The polypeptide of claim 14 having, from N- to C-terminal, the structure of the
following general formula II:

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N-A-C (II)

wherein

- 40 A represents an amino acid stretch corresponding to the N-terminal amino acid
stretch of the adenovirus penton base present between the first and the
second amino acid stretch forming the jellyroll fold domain of the adenovirus
penton base;
- N may or may not be present, and, if present, represents a chemical group
consisting of an amino acid, an oligopeptide and a polypeptide;

C: may or may not be present, and, if present, represents a chemical group consisting of an amino acid, an oligopeptide and a polypeptide; wherein, optionally, fragment A contain one or more heterologous modifications.

- 5 16. The polypeptide of claim 15 wherein the fragment A comprises an amino acid sequence selected from the group consisting of the amino acid sequences according to the following table and amino acid sequences having an identity of at least 85 %, more preferred at least 90 %, even more preferred 95 %, particularly preferred at least 98 %, most preferred at least 99 %, with the respective amino acid sequence
- 10 shown in the following table:

Sequence based on penton base protomer of	Sequence according to UniProt Acc. No.	SEQ ID NO:	N-terminal amino acid selected from positions	C-terminal amino acid selected from positions
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hAd5	P12538	4	130 to 137	426 to 432
hAd7	Q9JFT6	5	130 to 137	399 to 405
hAd11	D2DM93	6	130 to 137	416 to 422
hAd12	P36716	7	120 to 127	352 to 358
hAd17	F1DT65	8	117 to 124	371 to 377
hAd25	M0QUK0	9	125 to 133	389 to 395
hAd35	Q7T941	10	131 to 138	446 to 452
hAd37	Q912J1	11	117 to 124	373 to 379
hAd41	F8WQN4	12	128 to 135	362 to 368
gorAd	E5L3Q9	13	131 to 138	417 to 423
ChimpAd	G9G849	14	126 to 133	373 to 379
sAd18	H8PFZ9	15	128 to 135	354 to 360
sAd20	F6KSU4	16	127 to 134	359 to 365
sAd49	F2WTK5	17	128 to 135	357 to 363
rhAd51	A0A0A1EWW1	18	125 to 132	353 to 359
rhAd52	A0A0A1EWX7	19	125 to 132	351 to 357
rhAd53	A0A0A1EWZ7	20	126 to 133	352 to 358

wherein, optionally, fragment A contains one or more heterologous modifications.

17. The polypeptide of claim 15 or 16 characterized in that fragment A contains one or more heterologous modifications wherein said one or more heterologous modifications is/are contained in the following sites:
- the RGD loop region of fragment A; and/or
 - the V-loop of fragment A; and/or
 - the floor region having the sequence (from N- to C-terminal)
 $X_1-X_2-X_3-X_4-X_5-X_6-D-X_7-X_8-X_9-S-Y-N-X_{10}-X_{11}-X_{12}-X_{13}-X_{14}-X_{15}-X_{16}$ (SEQ ID NO: 21)
of fragment A, wherein
- X_1 is I or L, and is preferably I;
- X_2 is selected from the group consisting of K, Q and E, and is preferably Q;
- X_3 is P or A, and is preferably P;
- X_4 is selected from the group consisting of L, V and I, and is preferably L
- X_5 is selected from the group consisting of T, E, A, K and L, and is preferably E;
- X_6 is selected from the group consisting of E, K, T and Q, and is preferably K;
- X_7 is selected from the group consisting of S, P and D, and is preferably S;
- X_8 is selected from the group consisting of K, T and S, and is preferably K;
- X_9 is selected from the group consisting of K, S, N, G and D, and is preferably S;
- X_{10} is L or V, and is preferably V;
- X_{11} is I or L, and is preferably I;
- X_{12} is selected from the group consisting of S, E and P, and is preferably E;
- X_{13} is no amino acid (i.e. not present) or is N, and is preferably no amino acid;
- X_{14} is D or G, and is preferably D;
- X_{15} is selected from the group consisting of S, K, Q and T, and is preferably K; and
- X_{16} is selected from the group consisting of T, N, I, K and M, and is preferably I;
- and/or
- the sequence (from N- to C-terminal) T-H-V-F- X_{17} -R-F-P (SEQ ID NO: 22) of fragment B wherein X_{17} is D or N, and is preferably N.
18. The polypeptide of claim 17 wherein the N-terminus of the RGD loop region of fragment A is defined by the following sequence (from N-terminal to C-terminal):
 $X_{18}-X_{19}-X_{20}-X_{21}-X_{22}-X_{23}-X_{24}-X_{25}-X_{26}$ (SEQ ID NO: 23) wherein
- X_{18} is selected from the group consisting of D, E and N, and is preferably D;
- X_{19} is selected from the group consisting of V, L, and I, and is preferably V;
- X_{20} is any amino acid, preferably selected from the group consisting of A, D, E, K, S, and T, and is more preferably T;
- X_{21} is any amino acid, preferably selected from the group consisting of A, D, E, and K, and is more preferably A;

- X₂₂ is selected from the group consisting of F, Y, and W, and is preferably Y;
 X₂₃ is selected from the group consisting of A, D, E, N, and Q, is preferably E or Q,
 and is more preferably E;
 X₂₄ is any amino acid, preferably selected from the group consisting of A, D, E, N, and
 5 K, and is more preferably E;
 X₂₅ is selected from the group consisting of S or T, and is preferably S; and
 X₂₆ is any amino acid and constitutes the N-terminal amino acid of the RGD loop
 region
- 10 19. The polypeptide of claim 17 or 18 wherein the C-terminus of the RGD loop region of
 fragment A is defined by the following sequence (from N-terminal to C-terminal):
 X₂₇-X₂₈-X₂₉-X₃₀-X₃₁-X₃₂-X₃₃-X₃₄ (SEQ ID NO: 24)
 Wherein
 X₂₇ is any amino acid and constitutes the C-terminal amino acid of the second RGD
 15 loop;
 X₂₈ is selected from the group consisting of I, L and V, and is preferably I;
 X₂₉ is selected from the group consisting of D, E, K, N, Q, and V, is preferably Q or K,
 and is more preferably Q;
 X₃₀ is selected from the group consisting of C, G and P, and is preferably P;
 20 X₃₁ is selected from the group consisting of I, L and V, is preferably L or V and is more
 preferably L;
 X₃₂ is selected from the group consisting of D, E, S and T, is preferably E or T and is
 more preferably E;
 X₃₃ is selected from the group consisting of D, E, , S and T, is preferably E, or T, and
 25 is more preferably K; and
 X₃₄ is selected from the group consisting of D and E, and is preferably D;
20. The polypeptide according to any one of claims 17 to 19 wherein the N-terminus of
 the V loop of fragment A is defined by the following sequence (from N-terminal to C-
 30 terminal):
 X₃₅-X₃₆-X₃₇-X₃₈-X₃₉-X₄₀-X₄₁-X₄₂ (SEQ ID NO: 25)
 wherein
 X₃₅ is selected from the group consisting of F, Y, and W, and is preferably F;
 X₃₆ is selected from the group consisting of H, K and R, and is preferably K;
 35 X₃₇ is selected from the group consisting of A, V, I, and L, and is preferably A;
 X₃₈ is selected from the group consisting of H, K, and R, and is preferably R;

X₃₉ is selected from the group consisting of A, V, I, and L, and is preferably V;
 X₄₀ is selected from the group consisting of A, V, I, L and M, and is preferably M;
 X₄₁ is selected from the group consisting of A, V, I, and L, and is preferably V; and
 X₄₂ is any amino acid and constitutes the N-terminal amino acid of the V loop.

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21. The polypeptide according to any one of claims 17 to 20 wherein the C-terminus of the V loop of fragment A is defined by the following sequence (from N-terminal to C-terminal):

X₄₃-X₄₄-X₄₅-X₄₆-X₄₇-X₄₈-X₄₉ (SEQ ID NO: 26)

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wherein

X₄₃ is any amino acid and constitutes the C-terminal amino acid of the V loop;
 X₄₄ is selected from the group consisting of F, Y, and W, and is preferably Y;
 X₄₅ is selected from the group consisting of D, E, S and T, is preferably E or T and is more preferably E;

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X₄₆ is selected from the group consisting of F, Y, and W, and is preferably W;
 X₄₇ is selected from the group consisting of A, F, V, Y, and W, is preferably F or V and is more preferably F;

X₄₈ is selected from the group consisting of D, E, S and T, is preferably D or E and is more preferably E; and

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X₄₉ is selected from the group consisting of F, Y, and W, and is preferably F.

22. The polypeptide according to any one of claims 15 to 21 wherein the heterologous modification is selected from the group consisting of one or more single amino acid mutations in comparison to the wildtype sequence of fragment A, one or more replacements of wildtype amino acid stretches by one or more heterologous amino acids and/or amino acid stretches one or more insertions of heterologous amino acid stretches, one or more deletions of one or more amino acids and one or more amino acid modifications as well as any combination(s) thereof.

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- 30 23. The polypeptide according to any one of claims 15 to 22, wherein the heterologous modification provides a target specific binding entity.

24. The polypeptide of claim 23, wherein the target specific binding entity is selected from the group consisting of antigens, epitopes, CDRs, antibodies, antibody fragments such as an antigen binding (Fab) fragment, a Fab' fragment, a F(ab')₂ fragment, a heavy chain antibody, a single-domain antibody (sdAb), a single-chain fragment variable (scFv), a fragment variable (Fv), a VH domain, a VL domain, a single domain

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antibody, a nanobody, an IgNAR (immunoglobulin new antigen receptor), a di-scFv, a bispecific T-cell engager (BITEs), a dual affinity re-targeting (DART) molecule, a triple body, a diabody, a single-chain diabody, a paratope, an alternative scaffold protein, and a fusion protein thereof, a toxin and a venom.

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25. A nucleic acid encoding a polypeptide according to any one of the preceding claims.

26. A vector comprising the nucleic acid of claim 25.

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27. The vector of claim 26 containing the nucleic acid of claim 15 within an expression cassette.

28. A recombinant host cell comprising the nucleic acid of claim 24 or the vector of claim 26 or 27.

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29. A method for the production of a polypeptide according to any one of claims 1 to 24 comprising the step of culturing the host cell of claim 28 containing the vector of claim 28 under conditions allowing the expression of said polypeptide.

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30. The method of claim 29 further comprising the step of purifying the polypeptide from the cultured host cells.

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31. An engineered adenovirus penton base protein comprising the polypeptide according to any one of claims 5 to 12 fused to the multimerization domain (jellyroll fold domain) of an adenovirus penton base protein.

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32. The penton base protein of claim 31 having, from N- to C-terminal, the structure of the following general formula III:

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D-A-E-B-F (III)

wherein A and B are the fragments of the alpha-helical crown domain as defined in any one of claims 2 to 4, and D, E and F are the amino acid sequences of an adenovirus penton base forming the multimerization (jellyroll fold) domain, wherein one or more heterologous modifications is/are present in the floor region of fragment A and/or in the B loop of fragment B.

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33. An engineered adenovirus penton base protein comprising the polypeptide according to any one of claim 15 to 24 fused to the multimerization domain (jellyroll fold domain) of an adenovirus penton base protein.

5

34. The penton base of claim 33 having, from N- to C-terminal, the structure of the following general formula IV:



10

wherein A is the large fragment of the alpha-helical crown domain as defined in any one of claims 15 or 16, and D, E and F are the amino acid sequences of an adenovirus penton base forming the multimerization (jellyroll fold) domain, wherein, optionally and preferably, one or more heterologous modifications is/are present in the floor region of fragment A, and wherein Li is a linker selected from peptides, oligopeptides, polypeptides, proteins and protein complexes.

15

35. A penton base of claim 32 or 34 wherein fragment D of general formula (III) or (IV) has the following consensus sequence (SEQ ID NO: 34):

20 (U)₁₋₄₇ PTJ₁GRNSIRY SJ₂J₃X₄PJ₅J₆DTT J₇J₈YLV DNKSA DIASLNYQND
 HSNFJ₅TTVJ₉Q NNDJ₁₀J₁₁PJ₁₂EAJ₁₃ TQTINJ₁₄DJ₁₅RS RWGJ₁₆J₁₇LKTIJ₁₈
 J₁₉TZ₁Z₂Z₃Z₄Z₅Z₆Z₇Z₈ Z₉Z₁₀Z₁₁Z₁₂Z₁₃Z₁₄Z₁₅

wherein: fragment D ends on the C-terminal side before Z₁ at residue T or at an amino acid from Z₁ to Z₁₅

25

U is any or no amino acid

J₁ is E or G

J₂ is E or S

J₃ is L or V

J₄ is A or S

30

J₅ is L or Q

J₆ is Y or E

J₇ is R or K

J₈ is V or L

J₉ is V or I

35

J₁₀ is F or Y

J₁₁ is T or S

J₁₂ is A or T or I or G

J₁₃ is S or G

- J₁₄ is F or L
 J₁₅ is E or D
 J₁₆ is A or G
 J₁₇ is D or Q
 5 J₁₈ is L or M
 J₁₉ is H or R
 Z₁ , if present, is N
 Z₂ , if present, is M
 Z₃ , if present, is P
 10 Z₄ , if present, is N
 Z₅ , if present, is V or I
 Z₆ , if present, is N
 Z₇ , if present, is E or D
 Z₈ , if present, is Y or F
 15 Z₉ , if present, is M
 Z₁₀ , if present, is F or S or Y
 Z₁₁ , if present, is T or S
 Z₁₂ , if present, is S or N
 Z₁₃ , if present, is K
 20 Z₁₄ , if present, is F
 Z₁₆ , if present, is K.

36. The penton base of claim 35 wherein the fragment D comprises an amino acid sequence selected from the group consisting of the amino acid sequences of the following table and amino acid sequences having an identity of at least 85 %, more preferred at least 90 %, even more preferred 95 %, particularly preferred at least 98 %, most preferred at least 99 %, with the respective amino acid sequence shown in the following table:

Sequence based on penton base protomer of	Sequence according to UniProt Acc. No.	SEQ ID NO:	N-terminal amino acid selected from positions	C-terminal amino acid selected from positions
hAd3	Q2Y0H9	1	1 to 48	129 to 144
hAd2	P03276	2	1 to 48	129 to 144
hAd4	Q2KSF3	3	1 to 44	125 to 140
hAd5	P12538	4	1 to 48	129 to 144
hAd7	Q9JFT6	5	1 to 48	129 to 144

hAd11	D2DM93	6	1 to 48	129 to 144
hAd12	P36716	7	1 to 38	119 to 134
hAd17	F1DT65	8	1 to 35	116 to 131
hAd25	M0QUK0	9	1 to 43	124 to 139
hAd35	Q7T941	10	1 to 49	130 to 145
hAd37	Q912J1	11	1 to 35	116 to 131
hAd41	F8WQN4	12	1 to 46	127 to 142
gorAd	E5L3Q9	13	1 to 49	130 to 145
ChimpAd	G9G849	14	1 to 44	125 to 140
sAd18	H8PFZ9	15	1 to 46	127 to 142
sAd20	F6KSU4	16	1 to 45	126 to 141
sAd49	F2WTK5	17	1 to 48	127 to 142
rhAd51	A0A0A1EWW1	18	1 to 43	124 to 139
rhAd52	A0A0A1EWX7	19	1 to 43	124 to 139
rhAd53	A0A0A1EWZ7	20	1 to 44	125 to 140

37. The penton base according to any of claims 32 to 36 fragment E of general formula (III) or (IV) has the following sequence (SEQ ID NO: 35):

5 $Z_{17}Z_{18}Z_{19}Z_{20}Z_{21}Z_{22}Z_{23}Z_{24}Z_{25}Z_{26}Z_{27}QVYWSLPDJ_{20}MJ_{21}DPVTFRSTJ_{22}QJ_{23}J_{24}NJ_{25}PVVGJ_{26}ELZ_{28}Z_{29}Z_{30}$

wherein: fragment E begins on the N-terminal side at an amino acid from Z_{17} to Z_{27} or at amino acid Q after Z_{27} ;

10 amino acid stretch B ends on the C-terminal side before Z_{28} at amino acid L or at an amino acid from Z_{28} to Z_{30} ;

Z_{17} , if present, is L or S

Z_{18} , if present, is T or P or C

Z_{19} , if present, is T or P

Z_{20} , if present, is P or S or A or R

15 Z_{21} , if present, is N or D

Z_{22} , if present, is G or V

Z_{23} , if present, is H or T

Z_{24} , if present, is C

Z_{25} , if present, is G

20 Z_{26} , if present, is A or V or S

Z_{27} , if present, is E or Q

J_{20} is L or M

J_{21} is Q or K

- 5
- J₂₂ is Q or R or S
 J₂₃ is V or I
 J₂₄ is S or N
 J₂₅ is Y or F
 J₂₆ is A or V
 Z₂₈ , if present, is M or L
 Z₂₉ , if present, is P
 Z₃₀ , if present, is V or F.

- 10 38. The penton base of claim 37 wherein the fragment E comprises an amino acid sequence selected from the group consisting of the amino acid sequences of the following table and amino acid sequences having an identity of at least 85 %, more preferred at least 90 %, even more preferred 95 %, particularly preferred at least 98 %, most preferred at least 99 %, with the respective amino acid sequence shown in the following table:
- 15

Sequence based on penton base protomer of	Sequence according to UniProt Acc. No.	SEQ ID NO:	N-terminal amino acid selected from positions	C-terminal amino acid selected from positions
hAd3	Q2Y0H9	1	398 to 409	440 to 443
hAd2	P03276	2	425 to 436	467 to 470
hAd4	Q2KSF3	3	379 to 390	421 to 444
hAd5	P12538	4	425 to 436	467 to 470
hAd7	Q9JFT6	5	398 to 409	440 to 443
hAd11	D2DM93	6	415 to 426	457 to 460
hAd12	P36716	7	351 to 362	393 to 397
hAd17	F1DT65	8	370 to 381	413 to 416
hAd25	M0QUK0	9	388 to 399	440 to 443
hAd35	Q7T941	10	445 to 456	497 to 500
hAd37	Q912J1	11	372 to 383	414 to 417
hAd41	F8WQN4	12	362 to 373	404 to 407
gorAd	E5L3Q9	13	416 to 427	458 to 461
ChimpAd	G9G849	14	372 to 383	420 to 423
sAd18	H8PFZ9	15	353 to 364	395 to 398
sAd20	F6KSU4	16	358 to 369	400 to 403
sAd49	F2WTK5	17	356 to 367	398 to 401
rhAd51	A0A0A1EWW1	18	352 to 363	394 to 397

rhAd52	A0A0A1EWX7	19	350 to 361	392 to 395
rhAd53	A0A0A1EWZ7	20	351 to 362	393 to 396

39. The penton base according to any one of claims 32 to 38 wherein fragment F of general formula (III) or (IV) has the following sequence (SEQ ID NO: 36):

Z₃₁Z₃₂Z₃₃ALTDHGT LPLRSSIJ₂₇GV QRVTJ₂₈TDARR RTCPYVYKA LGIVJ₃₀PJ₃₁VLS SRTF

5 wherein: fragment F begins on the N-terminal side at an amino acid from Z₃₁ to Z₃₃ or at amino acid A after Z₃₃;

Z₃₁ , if present, is N

Z₃₂ , if present, is V

Z₃₃ , if present, is P

10 J₂₇ is R or S or G

J₂₈ is V or I

J₂₉ is Y or H

J₃₀ is A or S

J₃₁ is R or K

15

40. The penton base of claim 39 wherein fragment F comprises an amino acid sequence selected from the group consisting of the amino acid sequences of the following table and amino acid sequences having an identity of at least 85 %, more preferred at least 90 %, even more preferred 95 %, particularly preferred at least 98 %, most preferred at least 99 %, with the respective amino acid sequence shown in the following table:

20

Sequence based on penton base protomer of	Sequence according to UniProt Acc. No.	SEQ ID NO:	N-terminal amino acid selected from positions	C-terminal amino acid position
hAd3	Q2Y0H9	1	492 to 495	544
hAd2	P03276	2	519 to 522	571
hAd4	Q2KSF3	3	466 to 469	535
hAd5	P12538	4	492 to 495	571
hAd7	Q9JFT6	5	465 to 468	544
hAd11	D2DM93	6	482 to 485	561
hAd12	P36716	7	419 to 422	497
hAd17	F1DT65	8	438 to 441	517
hAd25	M0QUK0	9	455 to 458	534
hAd35	Q7T941	10	522 to 525	561

hAd37	Q912J1	11	439 to 442	519
hAd41	F8WQN4	12	439 to 432	508
gorAd	E5L3Q9	13	483 to 486	875
ChimpAd	G9G849	14	445 to 458	532
sAd18	H8PFZ9	15	420 to 423	508
sAd20	F6KSU4	16	425 to 428	512
sAd49	F2WTK5	17	423 to 426	511
rhAd51	A0A0A1EWW1	18	419 to 422	505
rhAd52	A0A0A1EWX7	19	417 to 420	503
rhAd53	A0A0A1EWZ7	20	418 to 421	504

41. A pentameric complex of the engineered adenovirus penton base protein according to any one of claims 32 to 40.
- 5 42. A virus-like particle (VLP) comprising 12 pentameric complexes of claim 41.
43. The polypeptide according to any one of claims 1 to 24 or the VLP of claim 42 for use as a medicament.
- 10 44. A pharmaceutical composition comprising a polypeptide according to any one of claims 1 to 24 or the engineered adenovirus penton base protein according to any one of claims 32 to 40 or the VLP of claim 42, optionally together with at least one pharmaceutically acceptable carrier, excipient and/or diluent.
- 15 45. A method for producing the VLP of claim 42 comprising the step of incubating a solution of a penton base according to any one of claims 32 to 40 under conditions allowing the assembly of the polypeptide into a VLP.
46. The polypeptide according to any one of claims 1 to 24 or the VLP of claim 42 for use in the treatment and/or prevention of an infectious disease, an immune disease, tumour or cancer.
- 20 47. A method of identifying a binding sequence to a target molecule comprising the steps of:
 - 25 (ia) preparing a library of vectors each containing a nucleotide sequence encoding a polypeptide having a candidate binding sequence in an expression cassette, each polypeptide encoded by said nucleotide sequence comprising a candidate

- binding sequence as a heterologous modification in one or more of RGD loop region and/or V loop and/or floor region and/or B loop as defined in any one of claims 5 to 9, wherein the candidate binding sequence encoded by the nucleotide sequence in each vector is different such that the vectors contain a randomized library of nucleotide sequences encoding randomized candidate binding sequences; or
- 5 (ib) preparing a library of vectors each containing a nucleotide sequence encoding a polypeptide having a candidate binding sequence in an expression cassette, each polypeptide encoded by said nucleotide sequence comprising a candidate binding sequence as a heterologous modification in one or more of RGD loop region and/or V loop and/or floor region as defined in any one of claims 17 to 21, wherein the candidate binding sequence encoded by the nucleotide sequence in each vector is different such that the vectors contain a randomized library of nucleotide sequences encoding randomized candidate binding sequences
- 10 (ii) expressing the polypeptides encoded by the nucleotide sequences from the library of vectors of step (ia) or (ib) in a host cell or a cell-free system, preferably cell free system;
- 15 (iii) contacting the polypeptides expressed in step (ii), optionally after purification from the host cells or the cell-free system, preferably cell free system, with the target molecule; and
- 20 (iv) detecting which polypeptide(s) have/has bound to the target molecule.
48. The method of claim 47 further comprising the step of determining the dissociation constant(s) (K_d) of the polypeptide(s) bound to the target molecule.
- 25