

WHAT IS CLAIMED IS:

1. An AAV vector comprising an Anc80 capsid protein and one or more
 5 transgenes selected from the group consisting of TMC1, TMC2, MYO7A, USCH1C,
 CDH23, PCDH15, SANS, CIB2, USH2A, VLGR1, WHRN, CLRN1, PDZD7.
2. A method of delivering a transgene to one or more cells in the inner ear in
 a subject, the method comprising:
 10 administering an adeno-associated virus (AAV) to the inner ear in a subject,
 wherein the AAV comprises an Anc80 capsid protein and a transgene.
3. The method of claim 2, wherein the one or more cells in the inner ear are
 selected from the group consisting of inner hair cells (IHCs) and outer hair cells (OHCs).
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4. The method of claim 3, wherein the transgene is delivered to at least 80%
 of inner hair cells and at least 80% of outer hair cells.
5. The method of claim 2, wherein the one or more cells in the inner ear are
 20 selected from the group consisting of spiral ganglion neurons, vestibular hair cells,
 vestibular ganglion neurons, supporting cells, and cells in the stria vascularis.
6. The method of claim 2, wherein the transgene is selected from the group
 consisting of ACTG1, ADCY1, ATOH1, ATP6V1B1, BDNF, BDP1, BSND,
 25 DATSPER2, CABP2, CD164, CDC14A, CDH23, CEACAM16, CHD7, CCDC50,
 CIB2, CLDN14, CLIC5, CLPP, CLRN1, COCH, COL2A1, COL4A3, COL4A4,
 COL4A5, COL9A1, COL9A2, COL11A1, COL11A2, CRYM, DCDC2, DFNA5,
 DFNB31, DFNB59, DIAPH1, EDN3, EDNRB, ELMOD3, EMOD3, EPS8, EPS8L2,
 ESPN, ESRRB, EYA1, EYA4, FAM65B, FOXI1, GIPC3, GJB2, GJB3, GJB6, GPR98,
 30 GRHL2, GPSM2, GRXCR1, GRXCR2, HARS2, HGF, HOMER2, HSD17B4, ILDR1,
 KARS, KCNE1, KCNJ10, KCNQ1, KCNQ4, KITLG, LARS2, LHFPL5, LOXHD1,
 LRTOMT, MARVELD2, MCM2, MET, MIR183, MIRN96, MITF, MSRB3, MT-RNR1,
 MT-TS1, MYH14, MYH9, MYO15A, MYO1A, MYO3A, MYO6, MYO7A, NARS2,

NDP, NF2, NT3, OSBPL2, OTOA, OTOF, OTOG, OTOGL, P2RX2, PAX3, PCDH15,
PDZD7, PJVK, PNPT1, POLR1D, POLR1C, POU3F4, POU4F3, PRPS1, PTPRQ, RDX,
S1PR2, SANS, SEMA3E, SERPINB6, SLC17A8, SLC22A4, SLC26A4, SLC26A5,
SIX1, SIX5, SMAC/DIABLO, SNAI2, SOX10, STRC, SYNE4, TBC1D24, TCOF1,
5 TECTA, TIMM8A, TJP2, TNC, TMC1, TMC2, TMIE, TMEM132E, TMPRSS3, TRPN,
TRIOBP, TSPEAR, USH1C, USH1G, USH2A, USH2D, VLGR1, WFS1, WHRN, and
XIAP.

7. The method of claim 2, wherein the transgene encodes a neurotrophic
10 factor.

8. The method of claim 7, wherein the neurotrophic factor is selected from
the group consisting of GDNF, BDNF, NT3, and HSP70.

9. The method of claim 2, wherein the transgene encodes an antibody or
15 fragment thereof.

10. The method of claim 2, wherein the transgene encodes an
immunomodulatory protein.
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11. The method of claim 2, wherein the transgene encodes an anti-oncogenic
transcript.

12. The method of claim 2, wherein the transgene encodes for an antisense,
25 silencing, or long non-coding RNA species.

13. The method of claim 2, wherein the transgene encodes a genome editing
system selected from the group consisting of a genetically-engineered zinc finger
nuclease, TALEN, and CRISPR.
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14. The method of claim 2, wherein the Anc80 capsid protein has the sequence
shown in SEQ ID NO:1.

15. The method of claim 2, wherein the Anc80 capsid protein has the sequence shown in SEQ ID NO:2.

16. The method of claim 3, wherein the transgene is under control of a
5 heterologous promoter sequence.

17. The method of claim 16, wherein the heterologous promoter sequence is selected from the group consisting of a CMV promoter, a CBA promoter, a CASI promoter, a PGK promoter, a EF-1 promoter, an alpha9 nicotinic receptor promoter, a
10 prestin promoter, a KCNQ4 promoter, a Myo7a promoter, a Myo6 promoter, a Gfi1 promoter, a Vglut3 promoter, and an Atoh1 promoter.

18. The method of claim 2, wherein the administering step comprises injecting the Anc AAV through the round window.
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19. The method of claim 2, wherein the Anc AAV is administered via injection through the round window.

20. The method of claim 2, wherein the Anc AAV is administered during a
20 cochleostomy or during a canalostomy.

21. The method of claim 2, wherein the Anc AAV is administered to the middle ear and/or the round window via one or more drug delivery vehicles.

22. The method of claim 2, wherein expression of the transgene results in
25 regeneration of inner hair cells (IHCs), outer hair cells (OHCs), spiral ganglion neurons, stria vascularis, vestibular hair cells, and/or vestibular ganglion neurons, thereby restoring hearing or vestibular function.

23. An article of manufacture comprising an AAV vector and a
30 pharmaceutical composition, wherein the AAV vector comprises an Anc80 capsid protein and a transgene operably linked to a promoter.

24. The article of manufacture of claim 23, wherein the transgene is selected from the group consisting of ACTG1, ADCY1, ATOH1, ATP6V1B1, BDNF, BDP1, BSND, DATSPER2, CABP2, CD164, CDC14A, CDH23, CEACAM16, CHD7, CCDC50, CIB2, CLDN14, CLIC5, CLPP, CLRN1, COCH, COL2A1, COL4A3, COL4A4, COL4A5, COL9A1, COL9A2, COL11A1, COL11A2, CRYM, DCDC2, DFNA5, DFNB31, DFNB59, DIAPH1, EDN3, EDNRB, ELMOD3, EMOD3, EPS8, EPS8L2, ESPN, ESRRB, EYA1, EYA4, FAM65B, FOXI1, GIPC3, GJB2, GJB3, GJB6, GPR98, GRHL2, GPSM2, GRXCR1, GRXCR2, HARS2, HGF, HOMER2, HSD17B4, ILDR1, KARS, KCNE1, KCNJ10, KCNQ1, KCNQ4, KITLG, LARS2, LHFPL5, LOXHD1, LRTOMT, MARVELD2, MCM2, MET, MIR183, MIRN96, MITF, MSRB3, MT-RNR1, MT-TS1, MYH14, MYH9, MYO15A, MYO1A, MYO3A, MYO6, MYO7A, NARS2, NDP, NF2, NT3, OSBPL2, OTOA, OTOF, OTOG, OTOGL, P2RX2, PAX3, PCDH15, PDZD7, PJKV, PNPT1, POLR1D, POLR1C, POU3F4, POU4F3, PRPS1, PTPRQ, RDX, S1PR2, SANS, SEMA3E, SERPINB6, SLC17A8, SLC22A4, SLC26A4, SLC26A5, SIX1, SIX5, SMAC/DIABLO, SNAI2, SOX10, STRC, SYNE4, TBC1D24, TCOF1, TECTA, TIMM8A, TJP2, TNC, TMC1, TMC2, TMIE, TMEM132E, TMPRSS3, TRPN, TRIOBP, TSPEAR, USH1C, USH1G, USH2A, USH2D, VLGR1, WFS1, WHRN, and XIAP.
25. A method of delivering a TMC1 or TMC2 transgene to one or more cells in the inner ear in a subject, the method comprising:
administering an adeno-associated virus (AAV) to the inner ear in a subject, wherein the AAV comprises an Anc80 capsid protein and a transgene.
26. A method of delivering an Usher transgene to one or more cells in the inner ear in a subject, the method comprising:
administering an adeno-associated virus (AAV) to the inner ear in a subject, wherein the AAV comprises an Anc80 capsid protein and a transgene.
27. The method of claim 25 or 26, wherein the Usher transgene is selected from the group consisting of MYO7A, USH1C, CDH23, PCDH15, SANS, CIB2, USH2A, VLGR1, WHRN, CLRN1, PDZD7.

28. The method of claim 25 or 26, wherein the one or more cells in the inner ear are selected from the group consisting of inner hair cells (IHCs) and outer hair cells (OHCs).
- 5 29. The method of claim 28, wherein the transgene is delivered to at least 80% of inner hair cells and at least 80% of outer hair cells.
30. The method of claim 25 or 26, wherein the one or more cells in the inner ear are selected from the group consisting of spiral ganglion neurons, vestibular hair cells, 10 vestibular ganglion neurons, supporting cells and cells in the stria vascularis.
31. The method of claim 25 or 26, wherein the Anc80 capsid protein has the sequence shown in SEQ ID NO:1.
- 15 32. The method of claim 25 or 26, wherein the Anc80 capsid protein has the sequence shown in SEQ ID NO:2.
33. The method of claim 25 or 26, wherein the transgene is under control of a heterologous promoter sequence. 20
34. The method of claim 33, wherein the heterologous promoter sequence is selected from the group consisting of a CMV promoter, a CBA promoter, a CASH promoter, a PGK promoter, a EF-1 promoter, an alpha9 nicotinic receptor promoter, a prestin promoter, a KCNQ4 promoter, a Myo7a promoter, a Myo6 promoter, a Gfi1 25 promoter, a Vglut3 promoter, and an Atoh1 promoter.
35. The method of claim 25 or 26, wherein the administering step comprises injecting the Anc AAV through the round window.
- 30 36. The method of claim 25 or 26, wherein the Anc AAV is administered via injection through the round window.

37. The method of claim 25 or 26, wherein the Anc AAV is administered during a cochleostomy or during a canalostomy.

5 38. The method of claim 25 or 26, wherein the Anc AAV is administered to the middle ear and/or the round window via one or more drug delivery vehicles.

39. The method of claim 25 or 26, wherein expression of the transgene results in regeneration of inner hair cells (IHCs), outer hair cells (OHCs), spiral ganglion neurons, stria vascularis, vestibular hair cells, and/or vestibular ganglion neurons, thereby
10 restoring hearing or vestibular function.