

WHAT IS CLAIMED IS:

1. An AAV vector comprising a nucleic acid molecule encoding an Anc80 capsid protein and one or more transgenes selected from the group consisting of TMC1, TMC2, MYO7A, USCH1C, CDH23, PCDH15, SANS, CIB2, USH2A, VLGR1, WHRN, CLRN1, PDZD7.

2. An AAV vector comprising a nucleic acid molecule encoding an Anc80 capsid protein and one or more transgenes selected from the group consisting of TMC1, TMC2, MYO7A, USCH1C, CDH23, PCDH15, SANS, CIB2, USH2A, VLGR1, WHRN, CLRN1, PDZD7, for use in therapy.

3. An AAV vector comprising a nucleic acid molecule encoding an Anc80 capsid protein and one or more transgenes selected from the group consisting of TMC1, TMC2, MYO7A, USCH1C, CDH23, PCDH15, SANS, CIB2, USH2A, VLGR1, WHRN, CLRN1, PDZD7, for use in the treatment of a hearing disorder, or for use in the prevention of hearing loss.

4. Use of an AAV vector comprising a nucleic acid molecule encoding an Anc80 capsid protein and one or more transgenes selected from the group consisting of TMC1, TMC2, MYO7A, USCH1C, CDH23, PCDH15, SANS, CIB2, USH2A, VLGR1, WHRN, CLRN1, PDZD7 in the manufacture of a pharmaceutical composition for the treatment of a hearing disorder, or for the prevention of hearing loss.

5. Use of an AAV vector comprising a nucleic acid molecule encoding an Anc80 capsid protein and a transgene in the manufacture of a pharmaceutical composition for the treatment of a hearing disorder, or for the prevention of hearing loss, wherein the AAV is to be administered to the inner ear in a subject, thereby delivering the transgene to one or more cells in the inner ear of the subject.

6. The use of claim 5, 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.

7. The use of claim 5, wherein the transgene is a TMC1 or TMC2 transgene.

8. The use of claim 5, wherein the transgene is an Usher transgene.

9. The use of claim 8, wherein the Usher transgene is selected from the group consisting of MYO7A, USH1C, CDH23, PCDH15, SANS, CIB2, USH2A, VLGR1, WHRN, CLRN1, PDZD7.

10. The use of any one of claims 5, 7 or 8, 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).

11. The use of claim 10, wherein the transgene is to be delivered to at least 80% of inner hair cells and at least 80% of outer hair cells.

12. The use of any one of claims 5, 7 or 8, wherein the one or more cells in the inner ear are selected from the group consisting of spiral ganglion neurons, vestibular hair cells, vestibular ganglion neurons, supporting cells and cells in the stria vascularis.

5 13. The use of any one of claims 5, 7 or 8, wherein the Anc80 capsid protein has the sequence shown in SEQ ID NO:1.

14. The use of any one of claims 5, 7 or 8, wherein the Anc80 capsid protein has the sequence shown in SEQ ID NO:2.

10 15. The use of any one of claims 5, 7 or 8, wherein the transgene is under control of a heterologous promoter sequence.

15 16. The use of claim 15, 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 prestin promoter, a KCNQ4 promoter, a Myo7a promoter, a Myo6 promoter, a Gfi1 promoter, a Vglut3 promoter, and an Atoh1 promoter.

20 17. The use of claim 5, wherein the transgene encodes a neurotrophic factor.

18. The use of claim 17, wherein the neurotrophic factor is selected from the group consisting of GDNF, BDNF, NT3, and HSP70.

25 19. The use of claim 5, wherein the transgene encodes an antibody or fragment thereof.

20. The use of claim 5, wherein the transgene encodes an immunomodulatory protein.

30 21. The use of claim 5, wherein the transgene encodes an anti-oncogenic transcript.

22. The use of claim 5, wherein the transgene encodes for an antisense, silencing, or long non-coding RNA species.

23. The use of claim 5, wherein the transgene encodes a genome editing system selected from the group consisting of a genetically-engineered zinc finger nuclease, TALEN, and CRISPR.

24. The use of any one of claims 5, 7 or 8, wherein the Anc AAV vector is to be administered via injection through the round window.

25. The use of any one of claims 5, 7 or 8, wherein the Anc AAV vector is to be administered during a cochleostomy or during a canalostomy.

26. The use of any one of claims 5, 7 or 8, wherein the Anc AAV vector is to be administered to the middle ear and/or the round window via one or more drug delivery vehicles.

27. The use of any one of claims 5, 7 or 8, 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 restoring hearing or vestibular function.

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

29. The article of manufacture of claim 28, 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,
 5 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, TECTA, TIMM8A, TJP2, TNC, TMC1, TMC2, TMIE, TMEM132E,
 10 TMPRSS3, TRPN, TRIOBP, TSPEAR, USH1C, USH1G, USH2A, USH2D,
 VLGR1,WFS1, WHRN, and XIAP.