

**Supplementary Table S1:** List of Zebrafish ages, tissues used, and the amount of each one shown in parentheses.

<u>Samples for RNA extraction</u>		
<u>Technique</u>	<u>Specimen age</u>	<u>Tissue and quantity used</u>
<u>in situ Hybridization</u>	<u>5 dpf</u>	<u>pool of 80 larvae</u>
	<u>1 year</u>	<u>whole organism (1)</u>
<u>RT-qPCR</u>	<u>4 months</u>	<u>IE (2)</u>
		<u>IE (1)</u>
		<u>pool of Utricule (7) + Lagena (5)</u>
	<u>2-3 years</u>	<u>Heart (2)</u>
		<u>Swimming bladder (2)</u>

**Supplementary Table S2:** List of primers used for real-time quantitative PCR analyses.

Gene	Sequence	Size	Reason of selection	Reference
<i>Ppp3r1a</i>	F: GCTGTTCAATTCCGAGGGG R: TGCGAGCACATTCCAGGG	84bp	candidate to DFNA58	Lezirovitz et al. 2020
<i>Ppp3r1b</i>	F: GTCAGATTCTGCACAAGGCG R: TGTGAGCACATCTCCAAGGG	84bp	candidate to DFNA58	Lezirovitz et al. 2020
<i>Plek</i>	F: AGGTGCGATAGTCAAACAGGG R: GCCCAGAGGATCATCTTCACC	142bp	candidate to DFNA58	Lezirovitz et al. 2020
<i>Cnrip1b</i>	F: CAGCCTGTTTCAGGTCAGCATACA R: ATGCTGTGAAGCTGTTCCCC	109bp	candidate to DFNA58	Lezirovitz et al. 2020
<i>Cnrip1a</i>	F: CAACTACGACACTGAGGGCG R: AGACGGTTTCGAACATCCCG	101bp	candidate to DFNA58	Lezirovitz et al. 2020
<i>Elavl4</i>	F: CAGAAGGAGCTGGAACAACCTCT R: GCGAGCCACCTGTGGGG	94bp	Important expression in the IE/ SAG neuronal marker	Schwarzer et al., 2020; Li et al., 2020
<i>Gab1</i>	F: TCGACTTGGACCCTGGGAAATCAA R: TGCTGATCCACCAGCACATAGTCT	106bp	Important expression in the inner ear- IE marker / Associated with DFNB26	Yousaf et al., 2018
<i>Mettl13</i>	F: AGACATGCAGGCTGTCCAATCAGA R: AAGCACTGAGCCCTCTTCCAATCA	146bp	Important expression in the IE/ Associated with DFNM1	Yousaf et al., 2018
<i>Gsdmea</i>	F: ACTCCGTTTCTCCATCTTGGTC R: AGCTTCGTCAGTCTCAGG	103bp	Important expression in the spiral ganglion/ Associated with DFNA5	Hosoya et al., 2016
<i>Gsdmeb</i>	F: TCTACAGTCAAACAACCACGAGA R: AGGCACAACACTGGGATCAG	141bp	Important expression in the spiral ganglion/ Associated with DFNA5	Hosoya et al., 2016
<i>Eya4</i>	F: CCCACTGCCCAAGTATGAA R: GGACTGAATCCACTGCTGCT	131bp	Important expression in the spiral ganglion/ Associated with DFNA10	Matsuzaki et al., 2018
<i>Pou4f1</i>	F: GGACTCGTCAACAACGGACT R: CACCCCGAGTTTGATCTCC	108bp	Important expression in the spiral ganglion/ Sensory neuron marker in zebrafish	Lie t al., 2020
<i>Slc1a3a</i>	F: TGTCGTATCGGGAGGTGAAG R: ACTGTCCAGAGTGCCATTC	122bp	Important expression in the inner ear of Zebrafish and low in the surrounding tissues. Mice that are null for this gene have vestibular phenotype of late-onset circling behavior at 7 months of age.	Schraven et al., 2012;; Thisse et al., 2004
<i>Rpl13</i>	F: AGCTGCGTATTCCAAGAAGA R: ACTGCGATCTTGCTCTCAACG	79bp	Endogenous Gene/Housekeeping/Reference	Rassier et al., 2020
<i>Eef1a1</i>	F: CTGGAGGCCAGCTCAAACAT R: ATCAAGAAGAGTAGTACCGTAGCATTAC	176bp	Endogenous Gene/Housekeeping/Reference	Rassier et al., 2020
<i>Rps18</i>	F: GGGAAATACAGCCAGGTCCTT R: CACGGTGAGCCCTGATCTTC	88bp	Endogenous Gene/Housekeeping/Reference	Rassier et al., 2020
<i>Actb2</i>	F: CGTGCTGTCTTCCCATCCA R: TCACCAACGTAGCTGTCTTTCTG	86bp	Endogenous Gene/Housekeeping/Reference	Rassier et al., 2020
<i>Sep15</i>	F: CCTGTGAGCTTCTGGGTCAG R: TCAAGGATGGCTCTGGGTA	115bp	Endogenous Gene/Housekeeping/Reference	Xu et al., 2016
<i>Metap1</i>	F: CCATGGCCCGGTACAGATA R: CTCCGACATCCCCAAAGGATGA	123bp	Endogenous Gene/Housekeeping/Reference	Xu et al., 2016
<i>Gapdh</i>	F: AATTCTGGGATACACGGAGCACCA R: TCAGGTCACATACACGGTTGCTGT	167bp	Endogenous Gene/Housekeeping/Reference	Yousaf et al., 2018; Rassier et al., 2020

**Supplementary Table S3:** Cycle Threshold (Ct) values of the different genes among the different zebrafish tissues under analysis.

<i>Gene</i>	<b>Mean of C<sub>t</sub> ± DP values among the different tissues</b>					
	<b>LG+UT</b>	<b>BRN</b>	<b>HRT</b>	<b>SWB</b>	<b>IE</b>	<b>SD</b>
<i>Ppp3r1a</i>	28.19±0.81	21.76±0.00	26.70±0.10	17.84±0.32	19.84±0.04	
<i>Ppp3r1b</i>	28.60±0.04	21.65±0.05	23.83±0.09	21.85±0.14	25.29±0.07	
<i>Cnrip1b</i>	33.44±0.68	26.38±0.06	34.02±0.24	28.18±0.32	33.97±0.30	
<i>Cnrip1a</i>	28.87±0.27	23.05±0.12	28.18±0.10	28.09±0.24	28.15±0.31	
<i>Plek</i>	29.95±0.25	26.83±0.19	26.53±0.12	27.34±0.08	26.42±0.10	
<i>Slc1a3a</i>	25.21±0.11	24.51±0.02	25.44±0.05	23.66±0.06	24.59±0.09	
<i>Eya4</i>	29.94±0.53	32.78±0.12	30.83±0.46	32.10±0.40	29.42±0.34	
<i>Elavl4</i>	27.88±0.12	21.45±0.16	29.30±0.18	28.37±0.17	26.35±0.12	
<i>GsmdeB/dfna5b</i>	30.28±0.16	28.92±0.37	28.32±0.32	26.19±0.19	27.03±0.06	
<i>GsmdeA/dfna5a</i>	30.42±0.12	28.27±0.02	27.29±0.13	26.61±0.24	27.20±0.03	
<i>Pou4f1</i>	24.72±0.26	24.70±0.19	undet.	26.33±0.11	26.97±0.15	
<i>Gab1</i>	30.13±0.31	27.14±0.05	26.28±0.03	23.05±0.12	27.31±0.15	
<i>Mettl13</i>	29.21±0.16	27.78±0.34	29.04±0.5	22.95±0.08	29.38±0.16	
<i>Gapdh</i>	26.42±0.30	21.87±0.07	14.97±0.12	16.09±0.24	18.58±0.04	4.50
<i>Actb2</i>	21.08±0.30	17.28±0.04	17.49±0.12	15.67±0.22	17.17±0.03	1.94
<i>Rpl13</i>	22.84±0.09	19.82±0.30	18.65±0.15	17.84±0.32	19.84±0.04	1.83

LG+UT=Lagera+Utricle. BRN=Brain. HRT=Heart. SWB=swim bladder. IE=inner ear

SD=standard deviation

**Supplementary Table S4:** List of primers used to perform the amplification of the cDNA that was used as a template for the transcription of the sense and antisense RNA probes in the in situ hybridization experiments, and the size in bp of the expected PCR fragments, as well as where each primer anneals. The bold lowercase letters in the forward and reverse primers correspond to the T7 promoter sequence. All primers anneal in the untranslated regions (UTR), 5' and 3'.

Genes	Probes	Primer name	Sequence (5'-3')	Anneal to	Fragment Size
<i>Cnr1p1a</i>	anti-sense	CNRIP1a-ZF-antisense-F	AAACAGCTTCCTGGGAGCATC	Exon 1	679 bp
		CNRIP1a-ZF-antisense-R	taattacgactcactataggagATACCCTGACGGATCGCTTG	Exon 3	
	sense (control)	CNRIP1a-ZF-sense-F	taattacgactcactataggagAAACAGCTTCCTGGGAGCATC	Exon 1	679 bp
		CNRIP1a-ZF-sense-R	ATACCCTGACGGATCGCTTG	Exon 3	

**Supplementary Table S5:** Relative quantification of each gene in the different tissues analyzed in zebrafish. In the last column, genes differentially expressed between hair cells and their surrounding cells, among those studied by us, are highlighted studied in zebrafish.

	Zebrafish adult (11-13 months)		Zebrafish adult (3 months)	Zebrafish adult (~36 months)	Zebrafish adult (11-13 months)
Ref	Barta et al.. 2018		Oosterhof et al.. 2017	Baumgart et al.. 2016	Barta et al.. 2018
Gene	Cell/tissue				Fold difference (Log2)
	HC	ncSC	Microglial	Liver	CC/ncSC
<i>Plek</i>	2.65±2.96	1.4±0.43	96.19±19.13	0.94±0.67	-----
<i>Ppp3r1a</i>	6.99±0.99	3.75±0.51	8.93±4.60	2.19±0.26	-----
<i>Ppp3r1b</i>	10.63±0.77	12.80±0.14	20.96±1.06	6.85±0.44	-----
<b><i>Cnrip1a</i></b>	<b>52.01±1.17</b>	<b>0.92±0.27</b>	<b>0.32±0.32</b>	<b>0.07±0.04</b>	<b>5.83</b>
<i>Cnrip1b</i>	0	0	0.00	0.02±0.03	-----
<i>Slc1a3a</i>	<b>62.12±2.58</b>	<b>5.17±0.5</b>	40.56±3.32	32.43±3.02	<b>3.59</b>
<i>Eya4</i>	<b>140.07±3.29</b>	<b>2.38±0.27</b>	0.10±0.17	0.33±0.11	<b>5.88</b>
<i>Elavl4</i>	4.00±0.18	2.29±0.6	1.14±0.17	0.02±0.01	-----
<i>Gsmdea</i>	0	0.2±0.03	2.55±1.01	4.79±1.47	0.20
<i>Gsmdeb</i>	5.5±0.2	4.85±0.56	0.24±0.26	0.00	-----
<i>Pou4f1</i>	<b>35.65±2.45</b>	<b>0.11±0.02</b>	0.09±0.1	0	<b>8.30</b>
<i>Gab1</i>	6.98±0.13	8.94±1.24	8.57±3.03	2.87±0.61	-----
<i>Mettl13</i>	0.37±0.07	0.98±0.03	1.38±0.89	0.42±0.1	<b>1.39</b>

Supplementary Table S6: RPKM values of the Li et al. (2018) study performed with mice.

Mouse (P28-P35)						
Ref	Li et al.. 2018					
<i>Gene</i>	IHC	OHC	DEG (IHC/OHC)	Deiters	Pilar	DEG (Deiters/Pilar)
<i>Plek</i>	0.00	0.15±0.06	---	1.32±0.14	1.97±0.13	---
<i>Ppp3r1</i>	17.34±1.55	9.95±0.87	0.80	29.84±2.05	14.63±1.25	1.03
<i>Cnrip1</i>	0.11±0.06	0.23±0.04	-1.06	0.85±0.19	0.61±0.13	0.48
<i>Slc1a3</i>	<b>131.02±1.47</b>	<b>7.67±0.25</b>	<b>2.02</b>	<b>5.53±0.34</b>	<b>213.19±1.22</b>	<b>-5.27</b>
<i>Eya4</i>	7.24±0.13	12.32±0.82	-0.77	5.63±0.44	9.25±0.42	-0.72
<i>Elavl4</i>	0.61±0.07	0.8±0.09	-0.39	1.88±0.1	0.82±0.18	1.20
<i>Gsmde/Dfna5</i>	0.62±0.1	0.27±0.05	1.20	0.65±0.09	0.95±0.15	-0.55
<i>Pou4f1</i>	0.00	0.00	---	0.02±0.03	0.15±0.05	---
<i>Gab1</i>	12.36±0.5	9.18±0.65	0.43	41.04±1.15	28.14±0.90	0.54
<i>Mettl13</i>	0.79±0.02	1.78±0.21	-1.17	2.36±0.28	2.15±0.20	0.13

**Supplementary Table S7:** Gene expression of literature data regarding genes and tissues studied in zebrafish.

Gene expression								
Gene	Age studied	Organ/Tissue						Ref.
			Brain	IE	Eye	Heart	Swim bladder	
<i>Cnrip1a</i> ENSDARG00000037337	10 hpf	whole larval body						Fin et al., 2017
	?	Heart	X					BGEE database
	?	Swim bladder					X	BGEE database
	?	Inner Ear	X					BGEE database
	?	Brain	X					BGEE database
	24-60 hpf	Telencephalon	X					Fin et al., 2017
	24-60 hpf	anterior and postoptic commissure. pineal gland	X					Fin et al., 2017
	24-60 hpf	hindbrain	X					Fin et al., 2017
	24-60 hpf	spinal cord						Fin et al., 2017
	24-60 hpf	retinal ganglion cells. other ganglia of the head	X					Fin et al., 2017
	?	Inner Ear	X					BGEE database
	24-60 hpf	cnrip1a regions of postmitotic neurons						Fin et al., 2017
	24-60 hpf	olfactory receptors						Fin et al., 2017
<i>Cnrip1b</i> ENSDARG00000037337	10 hpf	whole larval body						Fin et al., 2017
	?	Heart	X					BGEE database
	?	Swim bladder					X	BGEE database
	?	Eye	X					BGEE database
	?	Brain	X					BGEE database
		diffuse spinal cord	X		X	Fin et al., 2017		[51]
	24-48 hpf	somites and pectoral fins	X		X			Fin et al., 2017
<i>Ppp3r1a</i> ENSDARG00000092659	?	Heart	X					BGEE database
	?	Swim bladder					X	BGEE database
	?	Eye	X					BGEE database
	?	Brain	X					BGEE database
	72-96 hpf	Epiphase and olfactory bulb	X					Hammond & Udvadia, 2010
<i>Ppp3r1b</i> ENSDARG00000069360	?	Heart	X					BGEE database
	?	Swim bladder					X	BGEE database
	?	Eye	X					BGEE database
	72-96 hpf	Brain	X					BGEE database
		Liver	Hammond & Udvadia, 2010				[78]	

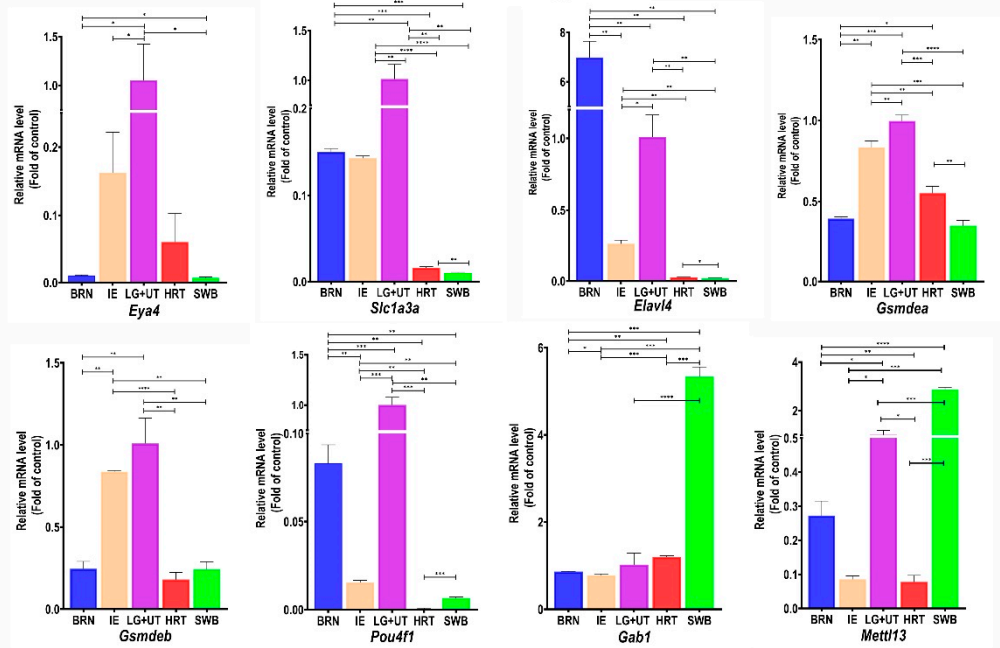
		optic tectum	X	Hammond & Udvadia, 2010				[78]
	72-96 hpf	olfactory bulb	X					Hammond & Udvadia, 2010
<i>Plek</i> ENSDARG00000104325	?	Heart	X					BGEE database
	?	Swim bladder	X					BGEE database
	?	Eye	X					BGEE database
	?	Brain	X					BGEE database
Gene expression								
Gene	Age studied	Organ/Tissue						Ref.
			Cérebro	IE	Eye	Heart	Swim bladder	
<i>Elavl4</i> ENSDARG00000045639 Marcador pan-neuronal	30-42 hpf	Heart	X					BGEE database
	?	Swim bladder	X					BGEE database
	?	Eye	X					BGEE database
	all	statoacoustic ganglion	X	X				Schwarzer et al., 2020
	24-60 hpf	Brain	X					Hao et al., 2017
<i>Gsdmeb (Dfna5)</i> ENSDARG00000040485	22-24 hpf	Neural crest. olfactory placode	X					Busch-Nentwich et al., 2003
	?	Eye	X					BGEE database
	?	Brain	X					BGEE database
	?	Swim bladder	X					BGEE database
	30-42 hpf	Heart	X					Thisse & Thisse, 2004
	48-60 hpf	Otic vesicle and semicircular canal	X					Blasiole et al., 2006
	48-90 hpf	Semicircular canal	X					Blasiole et al., 2006
<i>Gsdmea (Dfna5)</i> ENSDARG00000086762	?	Swim bladder	X					BGEE database
	?	Brain	X					BGEE database
	?	Heart	X				X	BGEE database
	5-6 dpf	Neuromasts						Jian et al., 2014
<i>Eya4</i> ENSDARG00000012397	Adult > 90 dpf	Heart	X					Schonberger et al.. 2005
	24-96 hpf / Adult > 60 dpf	Anterior and posterior macula	X					Wang et al.. 2008
	72-96 hpf / Adult > 60 dpf	Lateral crista	X					Wang et al.. 2008
	24-96	Neuromast						Schonberger et al.. 2005
	14-19 hpf	Otic placode						Wang et al.. 2008
	48-60 hpf / Adult > 60 dpf	Otic vesicle	X					Wang et al.. 2008
	24-42 hpf / Adult > 60 dpf	SAG	SAG					Wang et al.. 2008



	?	Swim bladder	X	BGEE database
<i>Gab1</i> <i>ENSDARG00000037018</i>	?	Swim bladder	X	BGEE database
	?	Heart	X	BGEE database
	12-48 hpf	Brain and otic vesicle	X X	Yousaf et al., 2018
<i>Mettl13</i>	?	Swim bladder	X	BGEE database
	12-48 hpf	Brain and otic vesicle	X X	Yousaf et al., 2018
<i>Slc1a3a</i>	72-96	Brain	X	Breuer et al., 2019
	72-96	Glial cell	SNC	Gesemann et al., 2010
	5-6 dpf	Lateral line		Thisse & Thisse, 2004
	5-6 dpf	Glial cells	SNC	Gesemann et al., 2010
	19-60	Otic vesicle	X	Thisse & Thisse, 2004
	19-60	Spinal cord	SNC	Thisse & Thisse, 2004
	Adult > 90 dpf	Cerebellum	X	Rico et al., 2010
	Adult > 90 dpf	Liver		Cheng et al., 2006
	Adult > 90 dpf	Brain	X	Rico et al., 2010
<i>Pou4f1</i>	16 hpf - Adult > 90 dpf	Brain	X	Sato et al., 2007
	32-72	Eye	X	Sato et al., 2007
	52hpf-77hpf	Otic Vesicle	X	Sato et al., 2007
	24-72	Heart	X	Maskell et al., 2017

## qPCR analysis - Zebrafish

### Controls genes



Supplementary Figure S1: Expression analysis (RT-qPCR) of the reference/control genes in the adult zebrafish tissues.

## ADDITIONAL REFERENCES

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