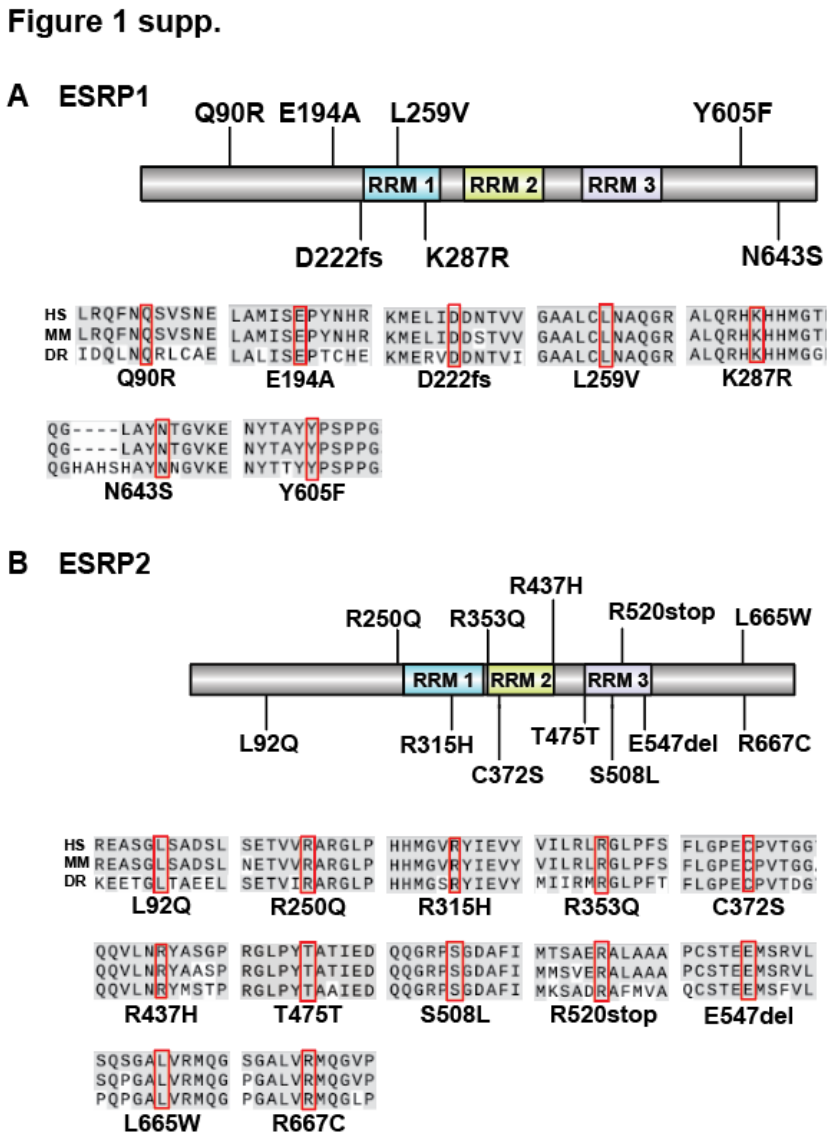
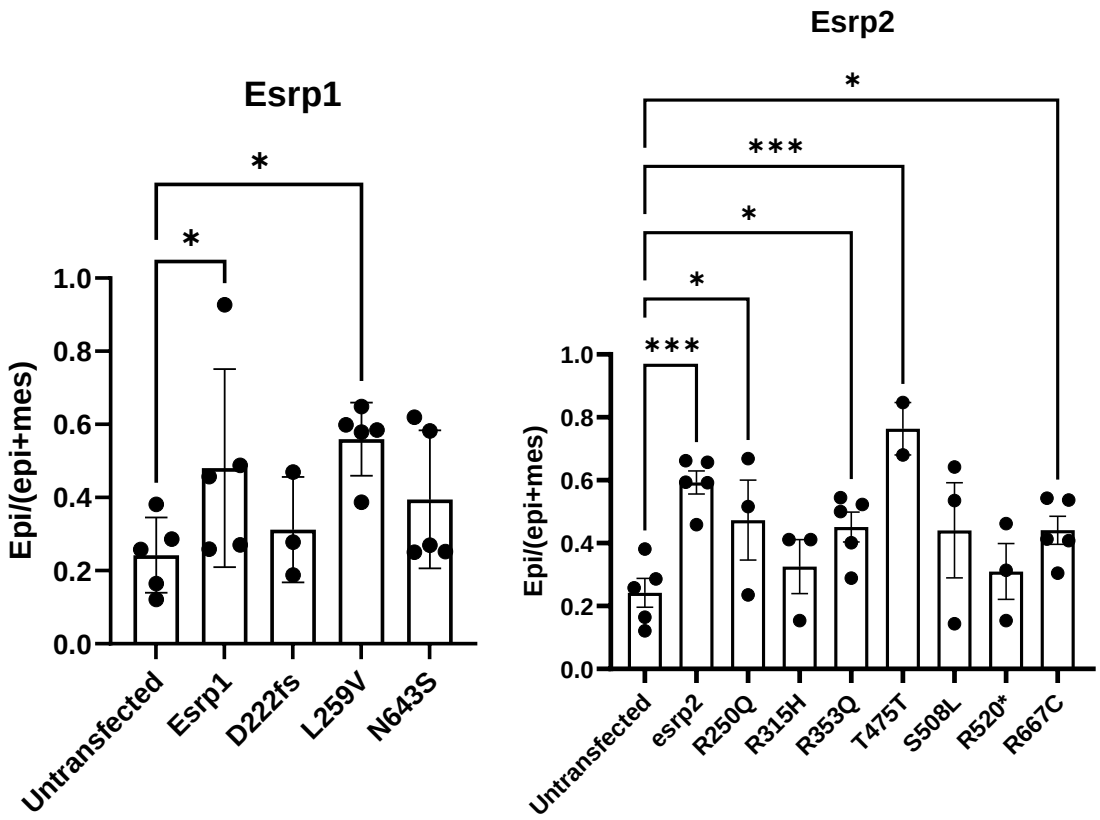
Supplemental Information



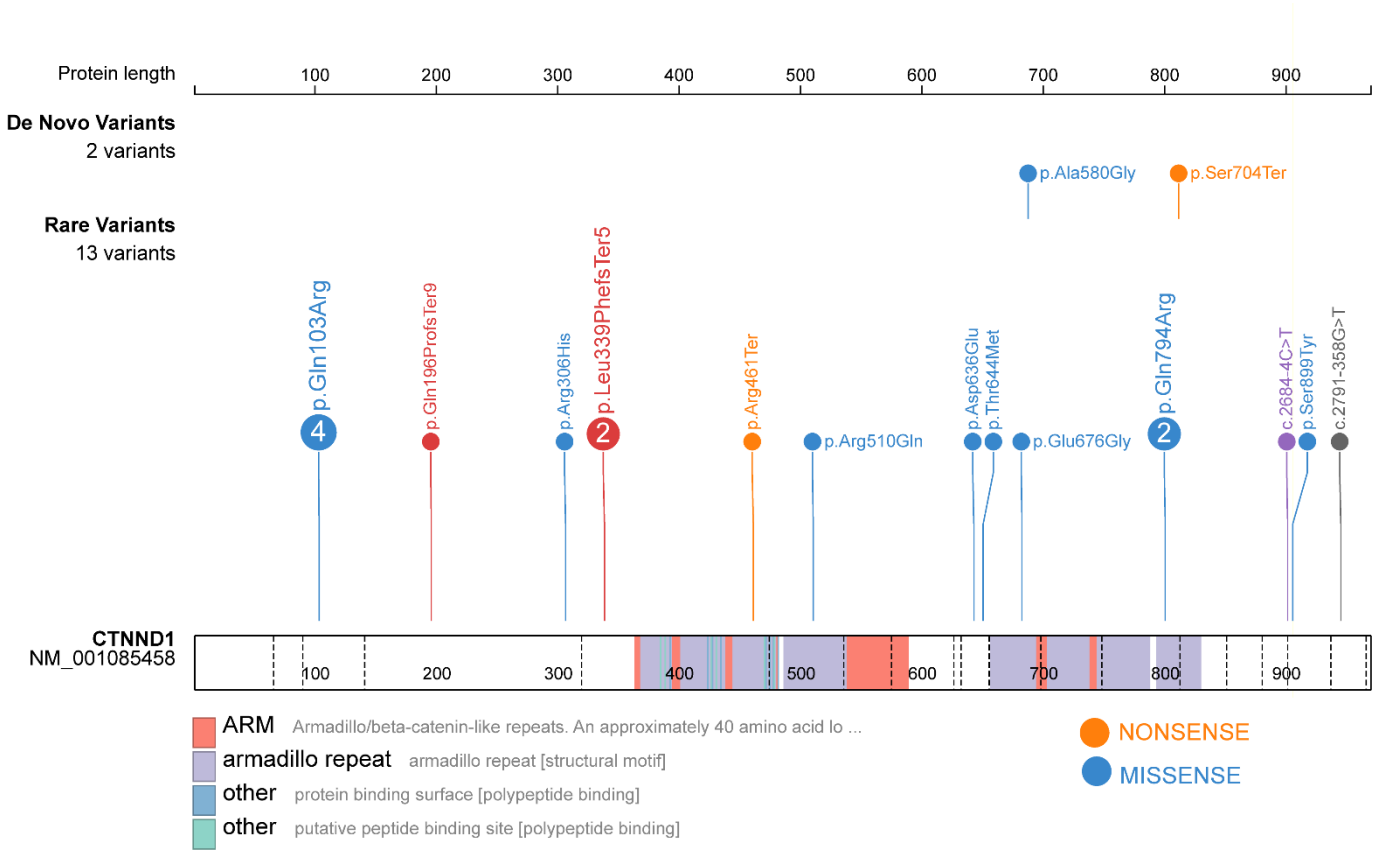
Supplementary Figure 1. Selection of evolutionarily conserved *ESRP1* and *ESRP2* gene variants. *ESRP1* and *ESRP2* gene variants were identified from OFC cases in the GMFK Children's dataset and ClinVar variants associated with cleft lip and/or palate or autosomal recessive deafness. Gene variants disrupting amino acid residues that are fully conserved between humans, mice, and zebrafish were selected: 7 in *ESRP1*, 12 in *ESRP2*. **(A)** Schematic of the ESRP1 protein labeled with 7 identified gene variants, including two variants in RRM1. Truncated alignments surrounding the gene variants are provided below the diagram. **(B)** Schematic of the ESRP2 protein labeled with 12 identified gene variants, including two variants in each of RRM1 and RRM2, three variants are in RRM3. A silent variant *ESRP2* T475T was used as a negative control. Truncated alignments surrounding the gene variants are provided below the diagram. Fully conserved residues between human, zebrafish, and mouse amino acid sequences surrounding the gene variants are highlighted in grey.

Figure 2 supp.



Supplementary Figure 2. Py2T rescue assay statistical analysis. *ESRP1* and *ESRP2* specific variants were analyzed using ordinary one-way ANOVA to confirm rescue statistical significance in comparison with untransfected cells. Data mean ± SEM, *p<0.05, ***p<0.001.

Figure 3 supp.



Supplementary Figure 3. CTNND1 variants from OFC cohorts. 15 variants were identified in 759 OFC trios. 2 Variants were de novo, and 13 were considered rare variants.

47 Supplemental Table 1

ESRP1								
variant	**CHR:BP (hg38)**	**Ref Allele**	**Alt Allele**	**rs id**	**Transcript Change**	**AA Change**	**Source**	**Associated disease**
Q90R	8:94643310	A	G	rs778878601	NM_017697.4:c.269A>G	NP_060167.2:p.Gln90Arg	GMKF	-
E194A	8:94662362	A	C	rs1302067900	NM_017697.4:c.581A>C	NP_060167.2:p.Glu194Ala	GMKF	-
D222fs	8:94664716-94664734 -19bp deletion bp 665-683	-	-	-	NM_017697.4:c.665_683del	NP_060167.2:p.Asp222fs	ClinVar	Hearing loss, autosomal recessive 109
L259V	8:94664946	C	G	rs1554577402	NM_017697.4:c.775C>G	NP_060167.2:p.Leu259Val	ClinVar	Hearing loss, autosomal recessive 109
K287R	8:94665031	A	G	rs747729420	NM_017697.4:c.860A>G	NP_060167.2:p.Lys287Arg	GMKF	-
Y605F	8:94678365	A	T	rs1228296571	NM_017697.4:c.1814A>T	NP_060167.2:p.Tyr605Phe	GMKF	-
N643S	8:94692784	A	G	rs767362823	NM_017697.4:c.1928A>G	NP_060167.2:p.Asn643Ser	GMKF	-

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ESRP2								
variant	**CHR:BP (hg38)**	**Ref Allele**	**Alt Allele**	**rs id**	**Transcript Change**	**AA Change**	**Source**	**Associated disease**
L92Q	16:68235686	A	T	rs1567566981	NM_024939.3:c.275T>A	NP_079215.2:p.Leu92Gln	GMKF	-
R250Q	16:68232649	C	T	rs755729355	NM_024939.3:c.749G>A	NP_079215.2:p.Arg250Gln	ClinVar	Cleft lip with or without cleft palate
R315H	16:68232381	G	A	rs751873605	NM_024939.3:c.944G>A	NP_079215.2:p.Arg315His	ClinVar	Cleft lip with or without cleft palate
R353Q	16:68232043	C	T	rs201908706	NM_024939.3:c.1058G>A	NP_079215.2:p.Arg353Gln	GMKF	-
C372S	16:68231987	A	T	rs149234558	NM_024939.3:c.1114T>A	NP_079215.2:p.Cys372Ser	GMKF	-
R437H	16:68231684	C	T	rs750375203	NM_024939.3:c.1310G>A	NP_079215.2:p.Arg437His	GMKF	-
T475T	16:68231569	G	A	rs56323755	NM_024939.3:c.1425G>A	NP_079215.2:p.Thr475=	GMKF	-
S508L	16:68231366	C	T	rs143677348	NM_024939.3:c.1523C>T	NP_079215.2:p.Ser508Leu	ClinVar	Cleft lip with or without cleft palate
R520stop	16:68231331	C	T	rs142168544	NM_024939.3:c.1558C>T	NP_079215.2:p.Arg520Ter	ClinVar	Cleft lip with or without cleft palate
E547del	16: 68231248-68231250	GAG	-	-	NM_024939.3:c.1636GAG	NP_079215.2:p.Glu547del	ClinVar	Cleft lip with or without cleft palate
L665W	16:68230459	A	C	rs373594090	NM_024939.3:c.1994T>G	NP_079215.2:p.Leu665Trp	GMKF	-
R667C	16:68230454	G	A	rs575114143	NM_024939.3:c.1999C>T	NP_079215.2:p.Arg667Cys	GMKF	-

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