## Supplemental Data 1. Pathogenicity grades

| | Pathogenic | UV4 | UV3 | UV2 | UV1 | Neutral |
|---|---|---|---|---|---|---|
| **Frequency in ethnically matching controls (N=876 chromosomes) ≤ 0.236%** | yes | yes | yes | yes* | unknown | no |
| ***In trans* with a 'Pathogenic' or 'UV4' mutation** | yes | yes | unknown | unknown | unknown | no |
| **Segregates with disease in >2 NCUS families or previously published as 'Pathogenic' or 'UV4'** | yes | no | no | no | no | no |
| **Novel, segregates with disaese in only one NCUS family** | Not applicable | yes | yes | yes | no | no |
| **Indentified in proband with one or two other mutations with a higher pathogenicity grade** | no | no | no | no | yes or unknown | yes or unknown |

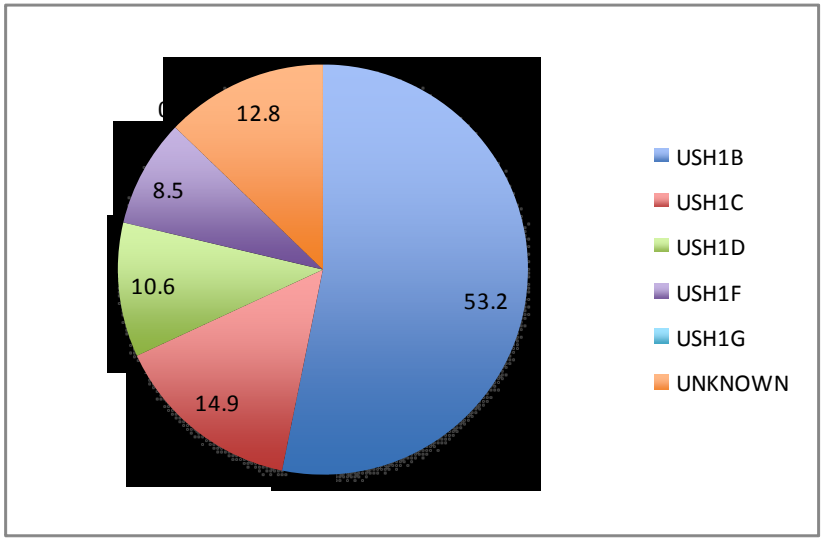
*Genotyped in 96 CEPH control chromosomes

**Supplemental Data 2. USH1C:c.496+1G>A assay**

The following primers were used: forward 5'-TAGGGGACGAGATCGTCCGGATCA-3' and reverse (introduced mutation is underlined): 5'-TGGAGTACTGCCCTGCTCTGGCCTCACACA-3'. The reverse primer was designed in order to create an artificial restriction site in c.496+1G>A mutant sequence, but not the wild type, using the web-based program dCAPS Finder v2.[21] For each PCR reaction 1ng/µl genomic DNA was amplified with 0.5pmol/µl of each primer, 1M betaine (Sigma-Aldrich), 0.25mM dNTPs (Microzone Ltd), 1x buffer, 1.5mM $MgCl_2$ and 0.5% BIOTAQ$^{TM}$ DNA polymerase (all Bioline). The PCR program consisted of a denaturation step of 10 min at 95°C, followed by 37 cycles of 30 sec at 95°C, 30 sec at 61°C, 40 sec at 72°C and a final extension at 72°C for 10 min. Restriction digests were prepared using *PciI* (New England Biolabs) according to manufacturer's instructions. The digested product was run on 4% agarose gel.

Supplemental Data 3.

a) Relative proportions of molecular subtypes in Usher Type 1




b) Relative proportions of molecular subtypes in Usher Type 2