Supplemental Text 1: Genetic Results

Eleven subjects had at least one novel mutation on screening, and a total of fourteen novel mutations were found. All novel mutations were analyzed using the public domain tools SIFT v. 1.03 (cutoff score = 0.05), PROVEAN v. 1.1.3 (cutoff score = -2.5), and PolyPhen-2 v. 2.2.2 (cutoff = 0.900 for “possibly damaging” and 0.950 for “probably damaging”), which attempt to predict pathogenicity resulting from mutations which cause amino acid changes.

In three of fourteen novel cases (RPGR c.1374_1375insT; p.Val459Cys fs*4, EYS c.9286_9295del10; p.Val3096Leu fs*28, and CIB2 c.300_309del10; p.Glu100Asp fs*28, no predictions were generated as splice variants and frameshifts cannot be analyzed using the listed tools. In nine out of fourteen novel cases, all available methods of prediction agreed. One such case, USH2A c.8016G>A; p.Leu2672Leu, was predicted to be non-pathogenic. This was a novel mutation found in subject DH_10161 (simplex RP), in whom both a novel predicted-pathogenic and a previously reported pathogenic mutation were found. In another seven cases in which predictions agreed, RPIL1 c.190C>T; p.Leu64Phe, LCA5 c.2006G>T; p.Arg669Met, CEP290 c.3853A>G; p.Lys1285Glu, IFT140 c.2323G>A; p.Ala775Thr, TRPM1 c.587C>T; p.Ser196Phe, MYO7A c.5967C>A; p.Tyr1989X, and GPR98 c.17996T>C; p.Leu5999Pro were predicted to be pathogenic. These were novel mutations found in subjects KS_10070 (simplex RP – both RPIL1 and LCA5 mutations), KS_10510 (ADRP – CEP290, IFT140, and TRPM1 mutations), MP_10137 (Usher I – MYO7A mutation), and both JC_1088 and KS_1077 (two siblings with Usher III – GPR98 mutations), respectively. In KS_10070, JC_1088, and KS_1077, the aforementioned novel mutations were the only mutations found likely to be pathogenic. In the case of KS_10510, one previously published mutation was found; in MP_10137, two other
mutations were found, including a previously-published splice variation\textsuperscript{1} and another mutation which has been reported on ClinVar (Variation ID 43305) to be associated with Usher type I.\textsuperscript{2}

In the remaining three of fourteen novel mutations, there were discrepancies in predictions as follows (prediction scores for each test in parentheses): in DH\_10161, a subject with ARRP, the mutation $BBS12$ c.1237C>G; p.Leu413Val was predicted to be damaging by SIFT (0.007) and probably damaging by PolyPhen-2 (0.992), but neutral by PROVEAN (-1.30). This subject was also found to harbor two other mutations, including one previously published in conjunction with Usher syndrome.\textsuperscript{3} In KS\_10084, a subject with Usher Type II, $USH2A$ c.15017C>T; p.Thr5006Met was predicted to be damaging by SIFT (0.007) and probably damaging by PolyPhen-2 (1.000), but Neutral by PROVEAN (-2.46). It should be noted that a PROVEAN score of -2.46 is very close to the cutoff of -2.50, and this discrepancy is possibly within a margin of error. Additionally, this individual carried two additional mutations, the previously published $USH2A$ c.9842G>T; p.Cys3281Phe\textsuperscript{4} and $USH2A$ c.15017C>T; p.Thr5006Met, which has previously been reported in association with Usher syndrome.\textsuperscript{2} Finally, in both JC\_1088 and KS\_1077 (siblings with Usher III), $GPR98$ c.17761T>C; p.Cys5921Arg was predicted to be damaging by SIFT (0.011), but benign by PolyPhen-2 (0.241) and neutral by PROVEAN (-1.24). Both individuals with this mutation also carried a second, novel mutation mentioned above, which was predicted to be pathogenic by all three methods.
Supplemental References

1. Schorderet DF, Escher P. NR2E3 mutations in enhanced S-cone sensitivity syndrome (ESCS),
   Goldmann-Favre syndrome (GFS), clumped pigmentary retinal degeneration (CPRD), and


3. McGee TL, Seyedahmadi BJ, Sweeney MO, Dryja TP, Berson EL. Novel mutations in the
   long isoform of the USH2A gene in patients with Usher syndrome type II or non-syndromic

   Usher syndrome genes in the UK National Collaborative Usher Study. *J Med Genet*