#	Gene	Transcript	c.DNA	Rules activated by ClinGen HL-EP	Rules activated by VIP-HL	Explanations for discordant rules
1	*MYO6*	NM_004999.3	c.2836C>T	BA1	BS1	The popmax filtering allele frequency is 0.00075 in Other in gnomAD.
2	*USH2A*	NM_206933.2	c.11241C>A	PVS1, PM2_P	PVS1, PM2	The popmax filtering allele frequency is 0.000054 in African-American in gnomAD.
3	*USH2A*	NM_206933.2	c.14419G>A	PM2P	PM2	The popmax filtering allele frequency is 0.000064 in South Asian in gnomAD.
4	*GJB2*	NM_004004.5	c.101T>C	PM5	PM5, PM1, PP3, BS2	PM1 is applied because this variant locates in a mutational hotspot region: 8 pathogenic missense variants and 0 benign missense variant in chr13:20763603-20763633. PP3 is activated because REVEL score is 0.702, greater than the threshold (0.7) that ClinGen Hearing Loss Expert Panel recommends for PP3. BS2 was activated because 16 homozygotes are reported in the gnomAD control dataset.
5	*GJB2*	NM_004004.5	c.109G>A	PM5	PM5, PM1, BS2	PM1 is applied because this variant locates in a mutational hotspot region: 8 pathogenic missense variants and 0 benign missense variant in chr13:20763603-20763633. BS2 was activated because 50 homozygotes are reported in the gnomAD control dataset.
6	*GJB2*	NM_004004.5	c.-22-2A>C	BS1	BS1, PVS1	GT-AG 1,2 splice sites -> Exon skipping or use of a cryptic splice site disrupts reading frame and is predicted to undergo NMD -> Exon is present in biologically relevant transcript(s) -> PVS1
7	*KCNQ4*	NM_004700.3	c.720C>G	BP4, BP7	BP4, BP7, PM2	PM2 is applied because this variant does not exist in gnomAD.
8	*KCNQ4*	NM_004700.3	c.853G>A	PM2, PM5, PM1	PM2, PM5, PM1, PP3	PP3 is activated because REVEL score is 0.793, greater than the threshold (0.7) that ClinGen Hearing Loss Expert Panel recommends for PP3.

Table 1 Analysis of rules activated by VIP-HL and ClinGen Hearing Loss Expert Panel (HL-EP). Four variants (#1-#3) have discrepant rules between ClinGen HL-EP and VIP-HL, spanning BA1 and PM2_P. Five variants (#4-#8) have rules that were not activated by ClinGen HL-EP, but activated by VIP-HL.

ClinVar	VIP-HL (semi-automated interpretation)			All
	Pathogenic or Likely pathogenic	Uncertain Significance	Benign/Likely benign	
Pathogenic or Likely pathogenic	376	280	2	658
Uncertain Significance	4	894	97	995
Benign/Likely benign	1	211	3083	3295
All	381	1385	3182	4948

Table 2. Illustration of automated interpretation of variants submitted in ClinVar