Express Gene™ Hearing Impairment Genetic testing (Hearing) Panel

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The Hearing Impairment Genetic testing (Hearing) Panel is a genetic testing panel designed to identify variations in genes associated with hearing impairment. Both syndromic (linked with other tissue and organ problems), and non-syndromic (only problem with deafness), are in included in this comprehensive genetic testing panel. Deafness also classified as recessive, dominant and X-linked based on mode of inheritance mode. These various forms of deafness all included in the Hearing genetic testing panel. The Hearing Impairment Genetic testing (Hearing) Panel is a genetic testing panel specifically designed to identify mutations in genes associated with deafness.

What is deafness:

Hearing impairment refers to a condition in which an individual experiences a diminished ability to perceive sounds, ranging from mild to profound deafness. This reduction in hearing acuity can affect one or both ears and may manifest across various frequencies, impacting the individual's capacity to understand speech, engage in communication, and fully experience auditory stimuli.

Genetic factors play a significant role in hearing impairment, contributing to both congenital and adult-onset cases. Genetic mutations or variations in specific genes associated with the development and function of the auditory system can lead to disruptions in the intricate processes that facilitate hearing. These genetic factors may affect structures within the inner ear, the auditory nerve, or other components of the auditory pathway, influencing the overall integrity of the hearing mechanism.

In cases of genetic hearing impairment, the condition can be inherited from one or both parents, and the degree of hearing loss can vary widely. Genetic testing is a valuable tool in identifying specific genetic markers or mutations that may be associated with hearing impairment. Understanding the genetic basis of hearing loss not only aids in accurate diagnosis but also facilitates informed decision-making regarding treatment options, intervention strategies, and considerations for family planning.

Purpose of the hearing genetic test:

The Hearing Panel may be appropriate for anyone who has a personal or family history of deafness, particularly if those

conditions are affect more than one individual in the family.

This panel can help confirm a diagnosis and guide the course of treatment. Diagnosis through genetic testing can help with the development of a management plan.

The Hearing Panel would help physicians to establish or confirm the appropriate diagnosis. By confirming diagnosis, the Hearing Panel help to identify risks for additional related symptoms and help in providing prenatal diagnosis.

Clinical Utility:

The Hearing Panel genetic testing aims to identify germline genetic variations that may be contributing to or causing deafness. This information can be crucial for diagnosis, prognosis, and the development of targeted treatment plans. Early identification of these genetic variations can also be valuable for managing and preventing complications associated with deafness.

The Hearing Panel result in more personalized treatment and symptom management, inform family members about their own risk factors, connect patients to relevant resources and support, provide options for family planning.

Method:

The test looks for inherited genetic variations (germline mutations) associated with hearing impairment genes.

Genes are instructions, written in DNA, for building protein molecules. Different people can have different versions of the same gene. Each version has a slightly different DNA sequence. Some of these variants affect health, such as those gene variants linked to metabolic function. Testing whether someone carries a harmful (pathogenic) variant in one of these genes can confirm whether a condition is, indeed, the result of an inherited syndrome.

The Hearing Panel investigates a panel of genes (listed below) for the presence of genetic changes compared to human reference (variants) that are linked to developmental metabolic related conditions.

Express Gene™ Hearing Impairment Genetic testing (Hearing) Panel is a Laboratory Developed Tests (LDT) validated at Express Gene Molecular Diagnostics Laboratory, using Twist Exome 2.0 and Illumina NovaSeq6000 Next Generation Sequencing (NGS) Platform. This test has not been cleared or approved by the FDA.

What is the outcome of genetic test results:

A. Positive Result. A positive test result indicates a pathogenic variant linked to metabolic disorder has been identified. In some cases, deafness is dominant in which one copy of defective gene is sufficient to cause the disease.

Most other deafness are recessive disorders, meaning that both copies of defective genes must be present to cause the disease. **Having a heterozygous pathogenic variation means that the individual is a carrier of the disease and may not experience the disease condition**.

This knowledge provides the patient and health care provider an opportunity to understand and, in some cases, manage their treatment plans.

B. Variation of uncertain significance (VUS).

If genetic testing shows a change that has not been previously associated with deafness, the person's test result may report a VUS. This result may be interpreted as uncertain, which is to say that the information does not help to clarify contribution of VUS to disease condition and is typically not considered in making health care decisions.

Some gene variants may be reclassified as researchers learn more about variants. Variants that initially classified as variants of uncertain significance may reclassified as being benign (not clinically important) or may eventually be found to be associated with disease phenotype. Therefore, it is important for the person who is tested to keep in touch with the health care provider to ensure that they receive updates if any new information on the variant is learned.

C. Negative result.

A negative test result means that the laboratory did not find the specific disease linked variant on list of genes that the test was designed to detect. Therefore, patient does not have a genetic variation in the genes tested by the Hearing Panel genetic testing panel.

Limitations of Testing

This test is designed to detect individuals with a germline pathogenic variant. Repeat expansion disease, large deletion, duplication and copy number variations, are not detectable by next generation sequencing (NGS) and require different test methodologies. Mutations in the upstream and downstream regulatory regions and mutations outside exons of protein-coding genes are not investigated.

Certain types of variants, such as structural rearrangements, inversions, translocations, variants in regions with low complexity, regions with complex architecture, short tandem repeats, or segmental duplications cannot be detected by this method. Additionally, low level mosaicism, phasing, regions with matching pseudogenes causing mapping ambiguity cause incorrect or insufficient variant calling.

Express Gene™ Hearing Impairment Genetic testing (Hearing) Panel: Express Gene™ Hearing Impairment Genetic testing (Hearing) Panel examines genes associated with variety of deafness listed below.

Row	Gene	Condition	Inheritance
1	ABHD12	Polyneuropathy, hearing loss, ataxia, retinitis pigmentosa, cataract	AR
2	ACTB	Baraitser-Winter syn, hearing impairment	AD
3	ACTG1	Deafness, autosomal dominant	AD
4	ADCY1	Deafness, autosomal recessive	AR
5	ADGRV1	Usher syndrome, type 2C	AD, AR
6	AIFM1	Deafness, X-linked	XLR
7	ALMS1	Alstrom syn Hearing loss	AR
8	AMMECR1	Midface hypoplasia, hearing impairment, elliptocytosis	XLR
9	ANKH	Craniometaphyseal dysplasia, Mixed hearing loss	AD
10	ASAH1	Farber lipogranulomatosis, Spinal muscular atrophy	AR
11	ATP2B2	Deafness, autosomal dominant	AD, AR
12	ATP6V1B1	Deafness autosomal recessive	AR
13	BCS1L	Hearing loss , Bjornstad syn	AR
14	BDP1	Deafness, autosomal recessive	AR
15	BLOC1S6	Syndromic Hearing loss	AR
16	BRAF	Syndromic Hearing loss	AD
17	BSND	Deafness autosomal recessive	AR
18	BTD	Hearing loss, Biotinidase deficiency	AR
19	CABP2	Deafness autosomal recessive	AR
20	CACNA1D	Deafness autosomal recessive	AR
21	CCDC50	Deafness, autosomal dominant	AD
22	CD164	Deafness, autosomal dominant	AD
23	CDC14A	Deafness autosomal recessive	AR
24	CDC42	Hearing impairment, Takenouchi-Kosaki syn	AD
25	CDH23	Deafness autosomal recessive	AR
26	CEACAM16	Deafness, autosomal dominant	AD
27	CEP78	Cone-rod dystrophy and hearing loss	AR
28	CHD7	Deafness, CHARGE syn	AD
29	CHSY1	Deafness, Temtamy preaxial brachydactyly syn	AR
30	CIB2	Deafness autosomal recessive	AR
31	CISD2	Sensorineural hearing loss, Wolfram syn	AR
32	CLDN14	Deafness autosomal recessive	AR
33	CLIC5	Deafness autosomal recessive	AR
34	CLPP	Hearing loss, Perrault syn	AR
35	CLRN1	Retinitis pigmentosa, Usher syndrome, hearing impairment	AR

36	COCH	Deafness, autosomal dominant	AD
37	COL11A1	Deafness, autosomal dominant	AD
38	COL11A2	Deafness, autosomal	AD, AR
39	COL17A1	Syndromic Hearing loss	AD, AR
40	COL1A1	Hearing loss, Osteogenesis imperfecta	AD
41	COL2A1	Deafness, autosomal dominant	AD
42	COL3A1	Syndromic Hearing loss	AD, AR
43	COL4A3	Deafness, Alport syn	AD
44	COL4A4	Deafness, Alport syn	AR
45	COL4A5	Deafness, Alport syn	XLD
46	COL4A6	Deafness, X-linked	XLR
47	COL5A1	Syndromic Hearing loss	AD
48	COL5A2	Syndromic Hearing loss	AD
49	COL9A1	Sensorineural hearing loss, Stickler syn	AR
50	COL9A2	Hearing loss, Stickler syn	AR
51	COL9A3	Sensorineural hearing loss, Stickler syn	AR
52	CRYM	Deafness, autosomal dominant	AD
53	CYBA	Syndromic Hearing loss	AR
54	DCDC2	Deafness autosomal recessive	AR
55	DIABLO	Deafness, autosomal dominant	AD
56	DIAPH1	Deafness, autosomal dominant	AD
57	DIAPH3	Auditory neuropathy	AD
58	DLX5	Split-hand malformation, sensorineural hearing loss	AR
59	DNMT1	Deafness, autosomal dominant	AD
60	DSPP	Deafness, autosomal dominant	AD
61	EDN3	Deafness, sensorineural, Waardenburg syn	AD, AR
62	EDNRB	Deafness, sensorineural, Waardenburg syn	AD, AR
63	ELMOD3	Deafness autosomal recessive	AR
64	EPS8	Deafness autosomal recessive	AR
65	ERCC2	Sensorineural deafness, Xeroderma pigmentosum	AR
66	ERCC3	Sensorineural deafness, Xeroderma pigmentosum	AR
67	ESPN	Deafness autosomal	AD, AR
68	ESRRB	Deafness autosomal recessive	AR
69	EYA1	Hearing loss, Otofaciocervical syn	AD
70	EYA4	Deafness, autosomal dominant	AD
71	FGF3	Deafness autosomal recessive	AR
72	FGFR1	Syndromic Hearing loss	AD

73	FGFR2	Conductive hearing loss	AD
74	FGFR3	Hearing loss, sensorineural, Hypochondroplasia, Muenke syn	AD
75	FOXI1	Deafness, autosomal recessive	AR
76	GATA3	Deafness, autosomal dominant	AD
77	GFER	Myopathy mitochondrial, congenital cataract, hearing loss	AR
78	GIPC3	Deafness autosomal recessive	AR
79	GJA1	Hearing loss, Craniometaphyseal dysplasia	AD, AR
80	GJB2	Deafness, autosomal dominant	AD
81	GJB3	Deafness, autosomal dominant	AD
82	GJB6	Deafness, autosomal dominant	AD
83	GLI3	Syndromic Hearing loss	AD
84	GPSM2	Hearing loss, Chudley-McCullough syn	AR
85	GRHL2	Deafness, autosomal dominant	AD
86	GRXCR1	Deafness autosomal recessive	AR
87	GRXCR2	Deafness autosomal recessive	AR
88	GSDME	Deafness, autosomal dominant	AD
89	HARS	Charcot-Marie-Tooth dis axona, Usher syn	AR
90	HARS2	Hearing loss, sensorineural, Perrault syn	AR
91	HGF	Deafness autosomal recessive	AR
92	HOMER2	Deafness, autosomal dominant	AD
93	HOXA1	Sensorineural deafness, Athabaskan brainstem dysgenesis syn	AR
94	HOXA2	Deafness autosomal	AD, AR
95	HOXB1	Hearing loss, Facial paresis hereditary	AR
96	HSD17B4	Hearing loss, sensorineural, Perrault syn	AR
97	IGF1	Deafness autosomal recessive	AR
98	ILDR1	Deafness autosomal recessive	AR
99	KARS	Deafness autosomal recessive	AR
100	KCNE1	Congenital sensorineural hearing loss	AR
101	KCNJ10	Deafness, autosomal recessive	AR
102	KCNQ1	Congenital sensorineural hearing loss, Jervell	AR
103	KCNQ4	Deafness, autosomal dominant	AD
104	KITLG	Deafness, autosomal dominant	AD
105	LARS2	Hearing loss , Perrault syn	AR
106	LHFPL5	Deafness autosomal recessive	AR
107	LHX3	Deafness, sensorineural, Pituitary hormone deficiency	AR
108	LOXHD1	Deafness autosomal recessive	AR
109	LRP2	Deafness, sensorineural, Donnai-Barrow syn	AR
110	LRTOMT	Deafness autosomal recessive	AR

111	MANBA	Deafness, Mannosidosis beta	AR
112	MARVELD2	Deafness autosomal recessive	AR
113	MET	Deafness autosomal recessive	AR
114	MIR96	Deafness, autosomal dominant	AD
115	MITF	Deafness, autosomal dominant	AD
116	MPZL2	Deafness autosomal recessive	AR
117	MSRB3	Deafness autosomal recessive	AR
118	MT-ATP8	mitochondrial hearing loss	MT
119	MT-CO1	mitochondrial hearing loss	MT
120	MT-CO2	mitochondrial hearing loss	MT
121	MT-CYB	mitochondrial hearing loss	MT
122	MT-ND1	mitochondrial hearing loss	MT
123	MT-ND4	mitochondrial hearing loss	MT
124	MT-ND6	mitochondrial hearing loss	MT
125	MT-RNR1	mitochondrial hearing loss	MT
126	MT-TC	mitochondrial hearing loss	MT
127	MT-TE	mitochondrial hearing loss	MT
128	MT-TF	mitochondrial hearing loss	MT
129	MT-TH	mitochondrial hearing loss	MT
130	MT-TK	mitochondrial hearing loss	MT
131	MT-TL1	mitochondrial hearing loss	MT
132	MT-TS1	mitochondrial hearing loss	MT
133	MT-TS2	mitochondrial hearing loss	MT
134	MT-TV	mitochondrial hearing loss	MT
135	MT-TW	mitochondrial hearing loss	MT
136	MYH14	Deafness, autosomal dominant	AD
137	MYH9	Deafness, autosomal dominant	AD
138	MYO15A	Deafness autosomal recessive	AR
139	MYO1A	Deafness, autosomal dominant	AD
140	MYO3A	Deafness autosomal recessive	AR
141	MYO6	Deafness, autosomal dominant	AD
142	MYO7A	Deafness, autosomal dominant	AD
143	NARS2	Deafness, autosomal recessive Combined oxidative phosphorylation	AR
144	NDP	Sensorineural deafness, Exudative vitreoretinopathy	XLR
145	NF2	Hearing loss, Schwannomatosis	AD
146	NLRP3	Deafness, autosomal dominant, Muckle-Wells syn	AD
147	OPA1	ensorineural deafness , Mitochondrial DNA deple syn	AD, AR
148	OSBPL2	Deafness, autosomal dominant	AD

149	OTOA	Deafness autosomal recessive	AR
150	OTOF	Deafness autosomal recessive	AR
151	OTOG	Deafness autosomal recessive	AR
152	OTOGL	Deafness autosomal recessive	AR
153	P2RX2	Deafness, autosomal dominant	AD
154	PAX2	Sensorineural hearing loss, Papillorenal syn	AD
155	PAX3	Deafness, autosomal dominant	AD
156	PCDH15	Deafness autosomal recessive	AR
157	PDSS1	Hearing impairment, Coenzyme Q deficiency	AR
158	PDZD7	Deafness, autosomal recessive, Retinal dis, Usher syn	AR
159	PEX1	Sensorineural hearing loss, Heimler syn	AR
160	PEX6	Sensorineural hearing loss , Heimler syn	AR
161	PHEX	Hearing loss , Hypophosphatemic rickets	XLD
162	PJVK	Deafness autosomal recessive	AR
163	PNPT1	Deafness autosomal recessive	AR
164	POLR1C	Hearing loss, Treacher Collins syn	AR
165	POLR1D	Hearing loss, Treacher Collins syn	AD, AR
166	POU3F4	Deafness, X-linked	XLR
167	POU4F3	Deafness, autosomal dominant	AD
168	PRPS1	Deafness, X-linked	XLR
169	PRRX1	Hearing loss, Agnathia-otocephaly	AD, AR
170	PTPRQ	Deafness autosomal recessive	AR
171	RDX	Deafness autosomal recessive	AR
172	RIPOR2	Deafness autosomal recessive	AR
173	ROR1	Deafness autosomal recessive	AR
174	S1PR2	Deafness autosomal recessive	AR
175	SEMA3E	Syndromic Hearing loss	Un
176	SERAC1	Deafness autosomal recessive	AR
177	SERPINB6	Deafness autosomal recessive	AR
178	SIX1	Deafness, autosomal dominant	AD
179	SIX5	Branchiootorenal syndrome 2	AD
180	SLC17A8	Deafness, autosomal dominant	AD
181	SLC19A2	Sensorineural deafness, Thiamine-responsive anemia	AR
182	SLC26A4	Deafness autosomal recessive	AR
183	SLC26A5	Deafness autosomal recessive	AR
184	SLC4A11	Deafness autosomal recessive	AR
185	SLC52A2	Hearing loss, Brown-Vialetto-Van Laere syn	AR
186	SLC52A3	Sensorineural hearing loss, Brown-Vialetto-Van Laere syn	AR

187	SLITRK6	Deafness autosomal recessive	AR
188	SMAD4	Deafness, Polyposis juvenile intestinal	AD
189	SMPX	Deafness, X-linked	XLD
190	SNAI2	Syndromic Hearing loss	Un
191	SOBP	Mild cochlear hearing loss, maxillary protrusion and strabismus	AR
192	SOX10	Deafness, sensorineural, Waardenburg syn	AD
193	SOX9	Hearing loss, Campomelic dysplasia	AD
194	STRC	Deafness autosomal recessive	AR
195	SYNE4	Deafness autosomal recessive	AR
196	TBC1D24	Deafness, autosomal	AD, AR
197	TBL1X	Hearing loss, Hypothyroidism congenital	XLD, XLR
198	TCOF1	Hearing loss, Treacher Collins syn	AD
199	TECTA	Deafness, autosomal	AD, AR
200	TIMM8A	Sensorineural deafness, Mohr-Tranebjaerg syn	XLR
201	TJP2	Syndromic Hearing loss	AR
202	TMC1	Deafness, autosomal	AD, AR
203	TMEM132E	Deafness, autosomal	AD, AR
204	TMIE	Deafness autosomal recessive	AR
205	TMPRSS3	Deafness autosomal recessive	AR
206	TNC	Deafness, autosomal dominant	AD
207	TNFRSF11B	Hearing loss, sensorineural, Paget dis	AR
208	TPRN	Deafness autosomal recessive	AR
209	TRIOBP	Deafness autosomal recessive	AR
210	TSPEAR	Deafness autosomal recessive	AR
211	TWNK	Sensorineural hearing loss, Perrault syndrome	AR
212	USH1C	Deafness autosomal recessive	AR
213	USH1G	Hearing loss, Usher syn	AR
214	USH2A	Retinitis pigmentosa, Usher syn	AR
215	WFS1	Deafness, autosomal dominant	AD
216	WHRN	Deafness autosomal recessive	AR