

# CRANIOFACIAL ANOMALIES GENE PANEL DG 2.12 (147 genes)

Gene	Median	% covered > 10x	% covered > 20x	Associated Phenotype description and OMIM disease ID
ADAMTSL4	90.7	99	98	Ectopia lentis et pupillae, 225200 Ectopia lentis, isolated, autosomal recessive, 225100
ALX1	153.1	99	98	?Frontonasal dysplasia 3, 613456
ALX3	103	73	70	Frontonasal dysplasia 1, 136760
ALX4	132.7	98	92	Frontonasal dysplasia 2, 613451 Parietal foramina 2, 609597 {Craniosynostosis 5, susceptibility to}, 615529
AMELX	98.7	99	95	Amelogenesis imperfecta, type 1E, 301200
ANKRD11	96.4	97	94	KBG syndrome, 148050
ARHGAP29	136.4	98	94	No OMIM phenotype Cleft lip with or without cleft palate (Leslie (2015) Am J Hum Genet 96,397)
AXIN2	117.5	100	99	Colorectal cancer, somatic, 114500 Oligodontia-colorectal cancer syndrome, 608615
BCOR	111	99	96	Microphthalmia, syndromic 2, 300166
BMP2	173.7	100	99	Brachydactyly, type A2, 112600 {HFE hemochromatosis, modifier of}, 235200
BMP4	151.9	100	99	Microphthalmia, syndromic 6, 607932 Orofacial cleft 11, 600625
C4orf26	198.1	100	100	Amelogenesis imperfecta, type IIA4, 614832
CDC45	160.7	99	97	Meier-Gorlin syndrome 7, 617063
CDON	143.8	100	99	Holoprosencephaly 11, 614226
CDSN	19.9	16	16	Hypotrichosis 2, 146520 Peeling skin syndrome 1, 270300
CHD7	150.9	99	98	CHARGE syndrome, 214800 Hypogonadotropic hypogonadism 5 with or without anosmia, 612370
COL11A1	90.8	94	89	Fibrochondrogenesis 1, 228520 Marshall syndrome, 154780 Stickler syndrome, type II, 604841 {Lumbar disc herniation, susceptibility to}, 603932

COL11A2	13.2	14	14	Deafness, autosomal dominant 13, 601868 Deafness, autosomal recessive 53, 609706 Fibrochondrogenesis 2, 614524 Otospondylomegaepiphyseal dysplasia, 215150 Stickler syndrome, type III, 184840 Weissenbacher-Zweymuller syndrome, 277610
COL2A1	103.6	99	98	Achondrogenesis, type II or hypochondrogenesis, 200610 Avascular necrosis of the femoral head, 608805 Czech dysplasia, 609162 Epiphyseal dysplasia, multiple, with myopia and deafness, 132450 Kniest dysplasia, 156550 Legg-Calve-Perthes disease, 150600 Osteoarthritis with mild chondrodysplasia, 604864 Otospondylomegaepiphyseal dysplasia, 215150 Platyspondylic skeletal dysplasia, Torrance type, 151210 SED congenita, 183900 SMED Strudwick type, 184250 Spondyloepiphyseal dysplasia, Stanescu type, 616583 Spondyloperipheral dysplasia, 271700 Stickler syndrome, type I, nonsyndromic ocular, 609508 Stickler syndrome, type I, 108300 Vitreoretinopathy with phalangeal epiphyseal dysplasia
COL9A1	120.5	99	96	Stickler syndrome, type IV, 614134 /?Epiphyseal dysplasia, multiple, 6, 614135
COL9A2	65.1	98	88	Epiphyseal dysplasia, multiple, 2, 600204 ?Stickler syndrome, type V, 614284 {Intervertebral disc disease, susceptibility to}, 603932
COL9A3	65.4	95	86	Epiphyseal dysplasia, multiple, 3, with or without myopathy, 600969 {Intervertebral disc disease, susceptibility to}, 603932
CTSK	105.1	100	99	Pycnodysostosis, 265800
DHODH	92.3	100	99	Miller syndrome, 263750
DISP1	210.9	99	99	No OMIM phenotype Craniofacial and neuro-developmental abnormalities (Roessler (2009) Hum Genet 125,393) Diaphragmatic hernia, congenital (Kantarci (2010) Am J Med Genet A 152A,2493) Tetralogy of Fallot (Silversides (2012) PLoS Genet 8, e1002843)

DLX3	110.1	100	99	Amelogenesis imperfecta, type IV, 104510 Trichodontoosseous syndrome, 190320
DLX4	159.5	99	99	?Orofacial cleft 15, 616788
DSPP	155.9	99	99	Deafness, autosomal dominant 39, with dentinogenesis, 605594 Dentin dysplasia, type II, 125420 Dentinogenesis imperfecta, Shields type II, 125490 Dentinogenesis imperfecta, Shields type III, 125500
EDA	92.4	85	76	Ectodermal dysplasia 1, hypohidrotic, X-linked, 305100 Tooth agenesis, selective, X-linked 1, 313500
EDAR	138.8	100	99	Ectodermal dysplasia 10A, hypohidrotic/hair/nail type, autosomal dominant, 129490 Ectodermal dysplasia 10B, hypohidrotic/hair/tooth type, autosomal recessive, 224900 [Hair morphology 1, hair thickness], 612630
EDARADD	99.3	99	93	Ectodermal dysplasia 11A, hypohidrotic/hair/tooth type, autosomal dominant, 614940 Ectodermal dysplasia 11B, hypohidrotic/hair/tooth type, autosomal recessive, 614941
EDN1	145.4	100	100	Auriculocondylar syndrome 3, 615706 Question mark ears, isolated, 612798 {High density lipoprotein cholesterol level QTL 7}
EFNA4	106.7	100	100	No OMIM phenotype Craniosynostosis 1 (Merrill et al. (2006) Hum Molec Genet 15)
EFNB1	119.4	100	99	Craniofrontonasal dysplasia, 304110
EFTUD2	124.4	100	99	Mandibulofacial dysostosis, Guion-Almeida type, 610536
EIF4A3	106.8	100	99	Robin sequence with cleft mandible and limb abnormalities, 268305
ENAM	148.8	100	99	Amelogenesis imperfecta, type IB, 104500 Amelogenesis imperfecta, type IC, 204650
ERF	107.7	99	97	Chitayat syndrome, 617180 Craniosynostosis 4, 600775
EYA1	144.4	100	99	Anterior segment anomalies with or without cataract, 113650 Branchiootic syndrome 1, 602588 Branchiootorenal syndrome 1, with or without cataracts, 113650 ?Otofaciocervical syndrome, 166780
EZH2	139.1	99	97	Weaver syndrome, 277590
FAM83H	76.9	94	87	Amelogenesis imperfecta, type III, 130900
FGD1	86.4	92	86	Aarskog-Scott syndrome, 305400 Mental retardation, X-linked syndromic 16, 305400

FGF10	142.2	100	100	Aplasia of lacrimal and salivary glands, 180920 LADD syndrome, 149730
FGF3	74	91	75	Deafness, congenital with inner ear agenesis, microtia, and microdontia, 610706
FGF8	111.5	90	79	Hypogonadotropic hypogonadism 6 with or without anosmia, 612702
FGFR1	148.3	99	98	Encephalocraniocutaneous lipomatosis,613001 Hartsfield syndrome, 615465 Hypogonadotropic hypogonadism 2 with or without anosmia, 147950 Jackson-Weiss syndrome, 123150 Osteoglophonic dysplasia, 166250 Pfeiffer syndrome, 101600 Trigonocephaly 1, 190440
FGFR2	142.4	97	96	Antley-Bixler syndrome without genital anomalies or disordered steroidogenesis, 207410 Apert syndrome, 101200 Beare-Stevenson cutis gyrata syndrome, 123790 Bent bone dysplasia syndrome, 614592 Craniofacial-skeletal-dermatologic dysplasia, 101600 Craniosynostosis, nonspecific Crouzon syndrome, 123500 Gastric cancer, somatic, 613659 Jackson-Weiss syndrome, 123150 LADD syndrome, 149730 Pfeiffer syndrome, 101600 Saethre-Chotzen syndrome, 101400 Scaphocephaly and Axenfeld-Rieger anomaly Scaphocephaly, maxillary retrusion, and mental retardation, 609579

FGFR3	110.5	99	97	<p>Achondroplasia, 100800  Bladder cancer, somatic, 109800  CATSHL syndrome, 610474  Cervical cancer, somatic, 603956  Colorectal cancer, somatic, 114500  Crouzon syndrome with acanthosis nigricans, 612247  Hypochondroplasia, 146000  LADD syndrome, 149730  Muenke syndrome, 602849  Nevus, epidermal, somatic, 162900  SADDAN, 616482  Spermatocytic seminoma, somatic, 273300  Thanatophoric dysplasia, type I, 187600  Thanatophoric dysplasia, type II, 187601</p>
FOXC1	32.8	86	68	<p>Axenfeld-Rieger syndrome, type 3, 602482  Iridogoniodysgenesis, type 1, 601631  Iris hypoplasia and glaucoma, 601631  Rieger or Axenfeld anomalies, 602482</p>
FOXE1	29.2	72	56	<p>Bamforth-Lazarus syndrome, 241850  {Thyroid cancer, nonmedullary, 4}, 616534</p>
GDF3	135.1	100	100	<p>Klippel-Feil syndrome 3, autosomal dominant, 613702  Microphthalmia with coloboma 6, 613703  Microphthalmia, isolated 7, 613704</p>
GDF6	75	98	89	<p>Klippel-Feil syndrome 1, autosomal dominant, 118100  Leber congenital amaurosis 17, 615360  Microphthalmia with coloboma 6, digenic, 613703  Microphthalmia, isolated 4, 613094</p>
GJA1	246.5	100	100	<p>Atrioventricular septal defect 3, 600309  Craniometaphyseal dysplasia, autosomal recessive, 218400  Erythrokeratoderma variabilis et progressiva, 133200  Hypoplastic left heart syndrome 1, 241550  Oculodentodigital dysplasia, 164200  Oculodentodigital dysplasia, autosomal recessive, 257850  Palmoplantar keratoderma with congenital alopecia, 104100  Syndactyly, type III, 186100</p>

GJB6	185.4	100	100	Deafness, autosomal dominant 3B, 612643 Deafness, autosomal recessive 1B, 612645 Deafness, digenic GJB2/GJB6, 220290 Ectodermal dysplasia 2, Clouston type, 129500
GLI2	138.7	99	97	Culler-Jones syndrome, 615849 Holoprosencephaly-9, 610829
GLI3	154.4	100	99	Greig cephalopolysyndactyly syndrome, 175700 Pallister-Hall syndrome, 146510 Polydactyly, postaxial, types A1 and B, 174200 Polydactyly, preaxial, type IV, 174700 {Hypothalamic hamartomas, somatic}, 241800
GNAI3	110.6	99	92	Auriculocondylar syndrome 1, 602483
GRHL3	140.8	100	99	Van der Woude syndrome 2, 606713
HOXA2	74.4	99	95	?Microtia with or without hearing impairment (AD), 612290 ?Microtia, hearing impairment, and cleft palate (AR), 612290
HUWE1	99.1	99	97	Mental retardation, X-linked syndromic, Turner type, 300706
HYAL2	223.3	100	100	No OMIM phenotype Orofacial clefting (Muggenthaler (2017) PLoS Genet 13,e1006470) ?Hypertelorism and high myopia (Shaheen (2016) Genet Med 18,686)
IFT122	152.3	100	99	Cranioectodermal dysplasia 1, 218330
IFT43	114.8	100	100	Cranioectodermal dysplasia 3, 614099
IFT88	76.4	98	90	No OMIM phenotype
IKBKG	52.9	84	73	Ectodermal dysplasia, hypohidrotic, with immune deficiency, 300291 Ectodermal, dysplasia, anhidrotic, lymphedema and immunodeficiency, 300301 Immunodeficiency 33, 300636 Immunodeficiency, isolated, 300584 Incontinentia pigmenti, 308300 Invasive pneumococcal disease, recurrent isolated, 2, 300640
IL11RA	140.1	100	99	Craniosynostosis and dental anomalies, 614188
IRF6	113.7	99	98	Popliteal pterygium syndrome 1, 119500 van der Woude syndrome, 119300 {Orofacial cleft 6}, 608864
KAT6B	192.3	99	98	Genitopatellar syndrome, 606170 SBBYSS syndrome, 603736
KDM1A	129.5	96	93	Cleft palate, psychomotor retardation, and distinctive facial features, 616728

KDM6A	109.6	93	84	Kabuki syndrome 2, 300867
KLK4	185.5	100	98	Amelogenesis imperfecta, type IIA1, 204700
KMT2D	142.2	99	99	Kabuki syndrome 1, 147920
KREMEN1	149.1	94	93	Ectodermal dysplasia 13, hair/tooth type, 617392
LRP2	176.4	100	99	Donnai-Barrow syndrome, 222448
LRP6	169.5	100	99	Tooth agenesis, selective, 7, 616724 {Coronary artery disease, autosomal dominant, 2}, 610947
LTBP3	113.8	98	94	Dental anomalies and short stature, 601216
MASP1	148.9	100	99	3MC syndrome 1, 257920
MED12	106.5	98	94	Lujan-Fryns syndrome, 309520 Ohdo syndrome, X-linked, 300895 Opitz-Kaveggia syndrome, 305450
MEGF8	127.9	99	98	Carpenter syndrome 2, 614976
MEOX1	76.8	96	91	Klippel-Feil syndrome 2, 214300
MID1	176.5	99	98	Opitz GBBB syndrome, type I, 300000
MITF	155.2	100	99	Tietz albinism-deafness syndrome, 103500 Waardenburg syndrome, type 2A, 193510 Waardenburg syndrome/ocular albinism, digenic, 103470 {Melanoma, cutaneous malignant, susceptibility to, 8}, 614456
MMP20	100.5	100	98	Amelogenesis imperfecta, type IIA2, 612529
MSX1	75.1	95	87	Ectodermal dysplasia 3, Witkop type, 189500 Orofacial cleft 5, 608874 Tooth agenesis, selective, 1, with or without orofacial cleft, 106600
MSX2	94.5	98	85	Craniosynostosis, type 2, 604757 Parietal foramina 1, 168500 Parietal foramina with cleidocranial dysplasia, 168550
NAA10	103.3	98	96	Ogden syndrome, 300855 ?Microphthalmia, syndromic 1, 309800
NFKBIA	116.5	98	93	Ectodermal dysplasia, anhidrotic, with T-cell immunodeficiency, 612132
NIPBL	116	96	94	Cornelia de Lange syndrome 1, 122470
NOG	192.4	100	100	Brachydactyly, type B2, 611377 Multiple synostoses syndrome 1, 186500 Stapes ankylosis with broad thumb and toes, 184460 Symphalangism, proximal, 1A, 185800

				Tarsal-carpal coalition syndrome, 186570
NSD1	155.4	100	100	Beckwith-Wiedemann syndrome, 130650 Leukemia, acute myeloid, 601626 Sotos syndrome 1, 117550
OFD1	53	84	68	Joubert syndrome 10, 300804 Orofaciodigital syndrome I, 311200 Simpson-Golabi-Behmel syndrome, type 2, 300209 ?Retinitis pigmentosa 23, 300424
OTX2	155.1	100	99	Microphthalmia, syndromic 5, 610125 Pituitary hormone deficiency, combined, 6, 613986 Retinal dystrophy, early-onset, with or without pituitary dysfunction, 610125
PAX3	118.5	100	99	Craniofacial-deafness-hand syndrome, 122880 Rhabdomyosarcoma 2, alveolar, 268220 Waardenburg syndrome, type 1, 193500 Waardenburg syndrome, type 3, 148820
PAX6	121.9	100	100	Aniridia, 106210 Cataract with late-onset corneal dystrophy, 106210 Coloboma of optic nerve, 120430 Coloboma, ocular, 120200 Foveal hypoplasia 1, 136520 Keratitis, 148190 Optic nerve hypoplasia, 165550 Peters anomaly, 604229 ?Morning glory disc anomaly, 120430
PAX7	117.9	100	100	Rhabdomyosarcoma 2, alveolar, 268220
PAX9	239	99	99	Tooth agenesis, selective, 3, 604625
PITX2	147.9	99	97	Axenfeld-Rieger syndrome, type 1, 180500 Iridogoniodysgenesis, type 2, 137600 Peters anomaly, 604229 Ring dermoid of cornea, 180550
PLCB4	126.1	99	95	Auriculocondylar syndrome 2, 614669



POLR1C	117.2	99	96	Leukodystrophy, hypomyelinating, 11, 616494 Treacher Collins syndrome 3, 248390
POLR1D	192	100	100	Treacher Collins syndrome 2, 613717
PORCN	118.7	100	99	Focal dermal hypoplasia, 305600
PTCH1	114.8	98	95	Basal cell carcinoma, somatic, 605462 Basal cell nevus syndrome, 109400 Holoprosencephaly-7, 610828
PTH1R	108.6	99	98	Chondrodysplasia, Blomstrand type, 215045 Eiken syndrome, 600002 Failure of tooth eruption, primary, 125350 Metaphyseal chondrodysplasia, Murk Jansen type, 156400
PVRL1	145.6	100	100	Cleft lip/palate-ectodermal dysplasia syndrome, 225060 Orofacial cleft 7, 225060
RAB23	110.4	99	97	Carpenter syndrome, 201000
RAD21	78.4	98	94	Cornelia de Lange syndrome 4, 614701
RECQL4	149.8	99	96	Baller-Gerold syndrome, 218600 RAPADILINO syndrome, 266280 Rothmund-Thomson syndrome, 268400
RUNX2	107.1	74	74	Cleidocranial dysplasia, 119600 Cleidocranial dysplasia, forme fruste, dental anomalies only, 119600 Cleidocranial dysplasia, forme fruste, with brachydactyly, 119600 Metaphyseal dysplasia with maxillary hypoplasia with or without brachydactyly, 156510
SALL1	138.8	99	98	Townes-Brocks branchiootorenal-like syndrome, 107480 Townes-Brocks syndrome, 107480
SALL4	147.6	97	96	Duane-radial ray syndrome, 607323 IVIC syndrome, 147750
SATB2	110.6	98	93	Glass syndrome, 612313
SEMA3E	142.5	99	98	?CHARGE syndrome, 214800
SF3B4	89.6	99	97	Acrofacial dysostosis 1, Nager type, 154400
SH3BP2	108.8	91	91	Cherubism, 118400
SHH	117.6	99	94	Holoprosencephaly-3, 142945 Microphthalmia with coloboma 5, 611638 Schizencephaly, 269160 Single median maxillary central incisor, 147250

SIX1	117.3	99	97	Brachiootic syndrome 3, 608389 Deafness, autosomal dominant 23, 605192
SIX3	145.6	100	98	Holoprosencephaly-2, 157170 Schizencephaly, 269160
SKI	85.5	96	90	Shprintzen-Goldberg syndrome, 182212
SMAD6	100.5	81	73	Aortic valve disease 2, 614823
SMC1A	101.3	99	98	Cornelia de Lange syndrome 2,300590
SMC3	81.3	93	87	Cornelia de Lange syndrome 3, 610759
SMOC2	119	97	94	Dentin dysplasia, type I, with microdontia and misshapen teeth, 125400
SNAI2	130.1	100	99	Piebaldism, 172800 Waardenburg syndrome, type 2D, 608890
SOX10	65.8	98	91	PCWH syndrome, 609136 Waardenburg syndrome, type 2E, with or without neurologic involvement, 611584 Waardenburg syndrome, type 4C, 613266
SOX6	102.8	99	97	No OMIM phenotype Developmental delay and spinal syrinx (Scott (2014) J Child Neurol 29, NP164) Dystonia, dopa-responsive (Ebrahimi-Fakhari (2015) Pediatr Neurol 52,115) ?Craniosynostosis (Tagariello (2006) J Med Genet 43,534)
SPECC1L	157.9	100	100	Opitz GBBB syndrome, type II, 145410 ?Facial clefting, oblique, 1, 600251
SUMO1	17.7	58	37	Orofacial cleft 10, 613705
TBX22	122.5	99	96	Cleft palate with ankyloglossia, 303400 ?Abruzzo-Erickson syndrome, 302905
TCF12	147.9	100	99	Craniosynostosis 3, 615314
TCOF1	98.6	99	97	Treacher Collins syndrome 1, 154500
TFAP2A	109.5	100	99	Branchiooculofacial syndrome, 113620
TGFBR1	173.5	93	93	Loeys-Dietz syndrome 1, 609192 {Multiple self-healing squamous epithelioma, susceptibility to}, 132800
TGFBR2	193.8	100	99	Colorectal cancer, hereditary nonpolyposis, type 6, 614331 Esophageal cancer, somatic, 133239 Loeys-Dietz syndrome 2, 610168
TGIF1	138.4	100	100	Holoprosencephaly-4, 142946

TP63	206.5	100	100	ADULT syndrome, 103285 Ectrodactyly, ectodermal dysplasia, and cleft lip/palate syndrome 3, 604292 Hay-Wells syndrome, 106260 Limb-mammary syndrome, 603543 Orofacial cleft 8, 129400 Rapp-Hodgkin syndrome, 129400 Split-hand/foot malformation 4, 605289
TRAF6	107	96	87	No OMIM phenotype Ectodermal dysplasia, hypohidrotic (Wisniewski (2012) Br J Dermatol 166,1353)
TSHZ1	167	98	98	Aural atresia, congenital, 607842
TWIST1	134.5	96	87	Craniosynostosis, type 1, 123100 Robinow-Sorauf syndrome, 180750 Saethre-Chotzen syndrome with eyelid anomalies, 101400 Saethre-Chotzen syndrome, 101400
UBB	62.1	100	99	Cleft palate, isolated, 119540
VAX1	52.3	88	78	?Microphthalmia, syndromic 11, 614402
WDR19	132	99	98	Nephronophthisis 13, 614377 Senior-Loken syndrome 8, 616307 ?Cranioectodermal dysplasia 4, 614378 ?Short-rib thoracic dysplasia 5 with or without polydactyly, 614376
WDR35	145.1	99	97	Cranioectodermal dysplasia 2, 613610 Short-rib thoracic dysplasia 7 with or without polydactyly, 614091
WDR72	136.2	99	98	Amelogenesis imperfecta, type IIA3, 613211
WNT10A	114.2	100	99	Odontoonychodermal dysplasia, 257980 Schopf-Schulz-Passarge syndrome, 224750 Tooth agenesis, selective, 4, 150400
ZEB2	163.4	100	99	Mowat-Wilson syndrome, 235730
ZIC1	231.4	100	100	Craniosynostosis 6, 616602
ZIC2	122.8	90	78	Holoprosencephaly-5, 609637

Gene symbols used follow HGNC guidelines: Gray KA, Yates B, Seal RL, Wright MW, Bruford EA. Nucleic Acids Res. 2015 Jan;43(Database issue):D1079-85.

Median Coverage describes the average number of reads seen across 50 exomes.

% Covered 10x describes the percentage of a gene's coding sequence that is covered at least 10x.

% Covered 20x describes the percentage of a gene's coding sequence that is covered at least 20x.

Genes with Median Coverage and % Covered 10x/20x denoting NC are non-coding genes for which coverage statistics could not be generated.

*OMIM release used for OMIM disease identifiers and descriptions : April 14th, 2017.*

*This list is accurate for panel version DG 2.12*

*Ad 1. "No OMIM phenotype" signifies a gene without a current OMIM association Ad 2. OMIM phenotype descriptions between {} signify risk factors*

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