CRANIOFACIAL ANOMALIES GENE PANEL DG 2.9

Gene	*Median coverage*	*% covered > 10x*	*% covered > 20x*	*Associated Phenotype description and OMIM disease ID*
ADAMTSL4	108.6	99%	98%	Ectopia lentis et pupillae, 225200 Ectopia lentis, isolated, autosomal recessive, 225100
ALX1	174.7	99%	98%	?Frontonasal dysplasia 3, 613456
ALX3	123.3	81%	72%	Frontonasal dysplasia 1, 136760
ALX4	145.9	99%	94%	Frontonasal dysplasia 2, 613451 Parietal foramina 2, 609597 {Craniosynostosis 5, susceptibility to}, 615529
AMELX	104.2	99%	97%	Amelogenesis imperfecta, type 1E, 301200
ANKRD11	118.5	98%	95%	KBG syndrome, 148050
ARHGAP29	180.7	99%	97%	No OMIM phenotype Cleft lip with or without cleft palate (Leslie (2015) Am J Hum Genet 96,397)
AXIN2	132.5	100%	99%	Colorectal cancer, somatic, 114500 Oligodontia-colorectal cancer syndrome, 608615
BCOR	117.5	99%	97%	Microphthalmia, syndromic 2, 300166
BMP2	203.5	100%	100%	Brachydactyly, type A2, 112600 {HFE hemochromatosis, modifier of}, 235200
BMP4	164.2	100%	100%	Microphthalmia, syndromic 6, 607932 Orofacial cleft 11, 600625
C4orf26	260.2	100%	100%	Amelogenesis imperfecta, type IIA4, 614832
CDC45	183.8	99%	97%	Meier-Gorlin syndrome 7, 617063
CDON	147.2	100%	99%	Holoprosencephaly 11, 614226
CDSN	20.4	58%	40%	Hypotrichosis 2, 146520 Peeling skin syndrome 1, 270300
CHD7	168.4	100%	99%	CHARGE syndrome, 214800 Hypogonadotropic hypogonadism 5 with or without anosmia, 612370
COL11A1	112.4	96%	92%	Fibrochondrogenesis 1, 228520 Marshall syndrome, 154780 Stickler syndrome, type II, 604841

				{Lumbar disc herniation, susceptibility to}, 603932
COL11A2	14.6	59%	23%	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	119.3	99%	99%	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 sydrome, type I, nonsyndromic ocular, 609508 Stickler syndrome, type I, 108300 Vitreoretinopathy with phalangeal epiphyseal dysplasia
COL9A1	143.9	99%	97%	Stickler syndrome, type IV, 614134 /?Epiphyseal dysplasia, multiple, 6, 614135
COL9A2	77.1	99%	94%	Epiphyseal dysplasia, multiple, 2, 600204 ?Stickler syndrome, type V, 614284 {Intervertebral disc disease, susceptibility to}, 603932
COL9A3	78.3	97%	91%	Epiphyseal dysplasia, multiple, 3, with or without myopathy, 600969 {Intervertebral disc disease, susceptibility to}, 603932
CTSK	118.2	100%	99%	Pycnodysostosis, 265800
DHODH	102.8	100%	99%	Miller syndrome, 263750
DISP1	239.3	100%	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	128.9	99%	96%	Amelogenesis imperfecta, type IV, 104510 Trichodontoosseous syndrome, 190320
DLX4	184.3	99%	99%	?Orofacial cleft 15, 616788
DSPP	150.9	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	99.3	92%	82%	Ectodermal dysplasia 1, hypohidrotic, X-linked, 305100 Tooth agenesis, selective, X-linked 1, 313500
EDAR	151.6	99%	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	105.1	99%	96%	Ectodermal dysplasia 11A, hypohidrotic/hair/tooth type, autosomal dominant, 614940 Ectodermal dysplasia 11B, hypohidrotic/hair/tooth type, autosomal recessive, 614941
EDN1	166.6	100%	100%	Auriculocondylar syndrome 3, 615706 Question mark ears, isolated, 612798 {High density lipoprotein cholesterol level QTL 7}
EFNA4	116.7	100%	100%	No OMIM phenotype Craniosynostosis 1 (Merrill et al. (2006) Hum Molec Genet 15)
EFNB1	144.7	100%	99%	Craniofrontonasal dysplasia, 304110
EFTUD2	127.2	99%	99%	Mandibulofacial dysostosis, Guion-Almeida type, 610536
EIF4A3	115.1	100%	99%	Robin sequence with cleft mandible and limb abnormalities,268305
ENAM	154.1	100%	100%	Amelogenesis imperfecta, type IB, 104500 Amelogenesis imperfecta, type IC, 204650
ERF	127.9	99%	98%	Chitayat syndrome,617180 Craniosynostosis 4, 600775
EYA1	167.2	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	166.9	99%	98%	Weaver syndrome, 277590
FAM83H	93.9	96%	91%	Amelogenesis imperfecta, type III, 130900
FGD1	98.4	94%	88%	Aarskog-Scott syndrome, 305400 Mental retardation, X-linked syndromic 16, 305400

FGF10	176	100%	100%	Aplasia of lacrimal and salivary glands, 180920 LADD syndrome, 149730
FGF3	86.6	96%	87%	Deafness, congenital with inner ear agenesis, microtia, and microdontia, 610706
FGF8	137.4	87%	80%	Hypogonadotropic hypogonadism 6 with or without anosmia, 612702
FGFR1	165.2	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	155.6	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	129.1	100%	99%	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
FOXC1	39.3	94%	79%	Axenfeld-Rieger syndrome, type 3, 602482 Iridogoniodysgenesis, type 1, 601631 Iris hypoplasia and glaucoma, 601631 Rieger or Axenfeld anomalies, 602482
FOXE1	37.4	81%	62%	Bamforth-Lazarus syndrome, 241850 {Thyroid cancer, nonmedullary, 4}, 616534
GDF3	137.7	100%	100%	Klippel-Feil syndrome 3, autosomal dominant, 613702 Microphthalmia with coloboma 6, 613703 Microphthalmia, isolated 7, 613704
GDF6	88.9	98%	92%	Klippel-Feil syndrome 1, autosomal dominant, 118100 Leber congenital amaurosis 17, 615360 Microphthalmia with coloboma 6, digenic, 613703 Microphthalmia, isolated 4, 613094
GJA1	238.2	100%	100%	Atrioventricular septal defect 3, 600309 Craniometaphyseal dysplasia, autosomal recessive, 218400 Erythrokeratodermia 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
GJB6	214	100%	100%	Deafness, autosomal dominant 3B, 612643 Deafness, autosomal recessive 1B, 612645 Deafness, digenic GJB2/GJB6, 220290 Ectodermal dysplasia 2, Clouston type, 129500
GLI2	148.1	99%	97%	Culler-Jones syndrome, 615849 Holoprosencephaly-9, 610829
GLI3	168.4	99%	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	132	99%	97%	Auriculocondylar syndrome 1, 602483
GRHL3	162.5	100%	100%	Van der Woude syndrome 2, 606713
HOXA2	86.9	99%	97%	?Microtia with or without hearing impairment (AD), 612290 ?Microtia, hearing impairment, and cleft palate (AR), 612290
HUWE1	107.1	99%	96%	Mental retardation, X-linked syndromic, Turner type, 300706
HYAL2	229.1	100%	100%	No OMIM phenotype Orofacial clefting (Muggenthaler (2017) PLoS Genet 13,e1006470) ?Hypertelorism and high myopia (Shaheen (2016) Genet Med 18,686)
IFT122	165.7	100%	99%	Cranioectodermal dysplasia 1, 218330
IFT43	128	100%	100%	Cranioectodermal dysplasia 3, 614099
IFT88	95.4	99%	95%	No OMIM phenotype
IKBKG	57.4	83%	72%	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	155.9	100%	99%	Craniosynostosis and dental anomalies, 614188
IRF6	134.4	99%	98%	Popliteal pterygium syndrome 1, 119500 van der Woude syndrome, 119300 {Orofacial cleft 6}, 608864
KAT6B	194.1	99%	99%	Genitopatellar syndrome, 606170 SBBYSS syndrome, 603736
KDM1A	166	99%	97%	Cleft palate, psychomotor retardation, and distinctive facial features, 616728
KDM6A	118	95%	89%	Kabuki syndrome 2, 300867
KLK4	210	99%	99%	Amelogenesis imperfecta, type IIA1, 204700
KMT2D	158.6	100%	99%	Kabuki syndrome 1, 147920
KREMEN1	175.1	95%	93%	Ectodermal dysplasia 13, hair/tooth type, 617392
LRP2	205.6	100%	99%	Donnai-Barrow syndrome, 222448
LRP6	178.9	100%	99%	Tooth agenesis, selective, 7, 616724 {Coronary artery disease, autosomal dominant, 2}, 610947
LTBP3	128.7	98%	97%	Dental anomalies and short stature, 601216
MASP1	160.1	99%	99%	3MC syndrome 1, 257920

MED12	111.4	98%	94%	Lujan-Fryns syndrome, 309520 Ohdo syndrome, X-linked, 300895 Opitz-Kaveggia syndrome, 305450
MEGF8	142.7	99%	98%	Carpenter syndrome 2, 614976
MEOX1	110.2	98%	95%	Klippel-Feil syndrome 2, 214300
MID1	177.2	99%	98%	Opitz GBBB syndrome, type I, 300000
MITF	173.3	100%	100%	Tietz albinism-deafness syndrome, 103500 Waardenburg syndrome, type 2A, 193510 Waardenburg syndrome/ocular albinism, digenic, 103470 {Melanoma, cutaneous malignant, susceptibility to, 8}, 614456
MMP20	112.5	99%	98%	Amelogenesis imperfecta, type IIA2, 612529
MSX1	93.5	98%	94%	Ectodermal dysplasia 3, Witkop type, 189500 Orofacial cleft 5, 608874 Tooth agenesis, selective, 1, with or without orofacial cleft, 106600
MSX2	116.3	99%	96%	Craniosynostosis, type 2, 604757 Parietal foramina 1, 168500 Parietal foramina with cleidocranial dysplasia, 168550
NAA10	109.4	99%	96%	Ogden syndrome, 300855 ?Microphthalmia, syndromic 1, 309800
NFKBIA	126	98%	93%	Ectodermal dysplasia, anhidrotic, with T-cell immunodeficiency, 612132
NIPBL	142.5	97%	95%	Cornelia de Lange syndrome 1, 122470
NOG	219.2	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	181.1	100%	100%	Beckwith-Wiedemann syndrome, 130650 Leukemia, acute myeloid, 601626 Sotos syndrome 1, 117550
OFD1	59.2	87%	75%	Joubert syndrome 10, 300804 Orofaciodigital syndrome I, 311200 Simpson-Golabi-Behmel syndrome, type 2, 300209 ?Retinitis pigmentosa 23, 300424
OTX2	140.5	100%	99%	Microphthalmia, syndromic 5, 610125 Pituitary hormone deficiency, combined, 6, 613986

				Retinal dystrophy, early-onset, with or without pituitary dysfunction, 610125
PAX3	128.2	100%	99%	Craniofacial-deafness-hand syndrome, 122880 Rhabdomyosarcoma 2, alveolar, 268220 Waardenburg syndrome, type 1, 193500 Waardenburg syndrome, type 3, 148820
PAX6	135.8	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	124.9	100%	100%	Rhabdomyosarcoma 2, alveolar, 268220
PAX9	266	99%	99%	Tooth agenesis, selective, 3, 604625
PITX2	146.1	99%	98%	Axenfeld-Rieger syndrome, type 1, 180500 Iridogoniodysgenesis, type 2, 137600 Peters anomaly, 604229 Ring dermoid of cornea, 180550
PLCB4	139.4	99%	97%	Auriculocondylar syndrome 2, 614669
POLR1C	117.5	99%	95%	Leukodystrophy, hypomyelinating, 11, 616494 Treacher Collins syndrome 3, 248390
POLR1D	193.8	100%	100%	Treacher Collins syndrome 2, 613717
PORCN	142.4	100%	99%	Focal dermal hypoplasia, 305600
PTCH1	127.7	98%	96%	Basal cell carcinoma, somatic, 605462 Basal cell nevus syndrome, 109400 Holoprosencephaly-7, 610828
PTH1R	118.4	99%	98%	Chondrodysplasia, Blomstrand type, 215045 Eiken syndrome, 600002 Failure of tooth eruption, primary, 125350 Metaphyseal chondrodysplasia, Murk Jansen type, 156400
PVRL1	166.5	100%	99%	Cleft lip/palate-ectodermal dysplasia syndrome, 225060 Orofacial cleft 7, 225060
RAB23	141.3	100%	100%	Carpenter syndrome, 201000

RAD21	109	99%	97%	Cornelia de Lange syndrome 4, 614701
RECQL4	152.3	99%	98%	Baller-Gerold syndrome, 218600 RAPADILINO syndrome, 266280 Rothmund-Thomson syndrome, 268400
RUNX2	111.8	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	144	99%	98%	Townes-Brocks branchiootorenal-like syndrome, 107480 Townes-Brocks syndrome, 107480
SALL4	161.4	98%	96%	Duane-radial ray syndrome, 607323 IVIC syndrome, 147750
SATB2	122.4	99%	94%	Glass syndrome, 612313
SEMA3E	179.1	100%	99%	?CHARGE syndrome, 214800
SF3B4	85.7	99%	93%	Acrofacial dysostosis 1, Nager type, 154400
SH3BP2	126.1	91%	91%	Cherubism, 118400
SHH	114.4	99%	95%	Holoprosencephaly-3, 142945 Microphthalmia with coloboma 5, 611638 Schizencephaly, 269160 Single median maxillary central incisor, 147250
SIX1	125.4	99%	96%	Brachiootic syndrome 3, 608389 Deafness, autosomal dominant 23, 605192
SIX3	172.7	99%	98%	Holoprosencephaly-2, 157170 Schizencephaly, 269160
SKI	96.2	98%	96%	Shprintzen-Goldberg syndrome, 182212
SMAD6	111	91%	83%	Aortic valve disease 2, 614823
SMC1A	114.2	100%	98%	Cornelia de Lange syndrome 2,300590
SMC3	96.1	94%	88%	Cornelia de Lange syndrome 3, 610759
SMOC2	135	97%	93%	Dentin dysplasia, type I, with microdontia and misshapen teeth, 125400
SNAI2	128.7	100%	99%	Piebaldism, 172800 Waardenburg syndrome, type 2D, 608890
SOX10	74.6	98%	95%	PCWH syndrome, 609136 Waardenburg syndrome, type 2E, with or without neurologic involvement, 611584 Waardenburg syndrome, type 4C, 613266
SOX6	116.6	99%	98%	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	164.4	100%	99%	Opitz GBBB syndrome, type II, 145410 ?Facial clefting, oblique, 1, 600251
SUMO1	22.3	63%	45%	Orofacial cleft 10, 613705
TBX22	139.9	99%	96%	Cleft palate with ankyloglossia, 303400 ?Abruzzo-Erickson syndrome, 302905
TCF12	173.7	100%	100%	Craniosynostosis 3, 615314
TCOF1	110.5	99%	97%	Treacher Collins syndrome 1, 154500
TFAP2A	126.8	100%	99%	Branchiooculofacial syndrome, 113620
TGFBR1	204.7	94%	93%	Loeys-Dietz syndrome 1, 609192 {Multiple self-healing squamous epithelioma, susceptibility to}, 132800
TGFBR2	212.4	100%	100%	Colorectal cancer, hereditary nonpolyposis, type 6, 614331 Esophageal cancer, somatic, 133239 Loeys-Dietz syndrome 2, 610168
TGIF1	151.7	100%	99%	Holoprosencephaly-4, 142946
TP63	226.8	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	109.2	97%	89%	No OMIM phenotype Ectodermal dysplasia, hypohidrotic (Wisniewski (2012) Br J Dermatol 166,1353)
TSHZ1	178.2	98%	98%	Aural atresia, congenital, 607842
TWIST1	135.7	94%	85%	Craniosynostosis, type 1, 123100 Robinow-Sorauf syndrome, 180750 Saethre-Chotzen syndrome with eyelid anomalies, 101400 Saethre-Chotzen syndrome, 101400
UBB	64.6	100%	99%	Cleft palate, isolated, 119540
VAX1	68.4	90%	83%	?Microphthalmia, syndromic 11, 614402
WDR19	170	100%	99%	Nephronophthisis 13, 614377 Senior-Loken syndrome 8, 616307

				?Cranioectodermal dysplasia 4, 614378 ?Short-rib thoracic dysplasia 5 with or without polydactyly, 614376
WDR35	186.3	99%	98%	Cranioectodermal dysplasia 2, 613610 Short-rib thoracic dysplasia 7 with or without polydactyly, 614091
WDR72	161.3	99%	98%	Amelogenesis imperfecta, type IIA3, 613211
WNT10A	135.1	99%	99%	Odontoonychodermal dysplasia, 257980 Schopf-Schulz-Passarge syndrome, 224750 Tooth agenesis, selective, 4, 150400
ZEB2	195.1	100%	99%	Mowat-Wilson syndrome, 235730
ZIC1	213	100%	100%	Craniosynostosis 6, 616602
ZIC2	116.8	92%	84%	Holoprosencephaly-5, 609637

Gene symbols used follow HGCN 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 versions DG 2.9

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