GENE	DISEASE OR MUTATION	CHARACTERISTICS OF DISEASE OR MUTANT	REFS.
AP2 (*TFAP2A*) (human)	Branchiooculofacial syndrome (BOFS)	Low birth weight, retarded postnatal growth, bilateral branchial cleft sinuses, congenital strabismus, obstructed nasolacrimal ducts, broad nasal bridge, protruding upper lip, and carp mouth. Occasionally seen are coloboma, microphthalmia, auricular pits, lip pits, highly arched palate, dental anomalies, and subcutaneous cysts of the scalp	(1–4)
Ap2 (mouse)	*Ap2*$^{-/-}$ Ap2 alpha -/-	Die perinatally with cranioabdominoschisis and severe dysmorphogenesis of the face, skull, sensory organs and cranial ganglia Neural tube defects followed by craniofacial and body wall abnormalities	(5) (6)
FLI1 (human)	Paris-Trousseau type Thrombocytopenia (TCPT): Homozygous deletion of *FLI1*	Mental retardation, facial dysmorphism, clinodactyly, pyloric stenosis and thrombocytopenia	(7)
FOXD3 (human)		Autosomal dominant vitiligo regulator of melanoblast differentiation	(8)
FoxD3 (mouse)		Embryonic lethality at E6.5, required for maintenance of epiblast cells and expansion of extraembryonic ectoderm and endoderm.	(9)
FoxD3 (zebrafish)	*mother superior* mutation	Depletion of crest derivatives, leading to a protruding lower jaw, loss of cartilage in hyoid and posterior branchial arches, pigmentation defects particularly in the trunk iridophores and reduced number of neural precursors resulting in defective peripheral nervous system.	(10)
PAX3 (human)	Waardenburg Syndrome type I and III Tumours	Hearing loss and changes in skin and hair pigmentation Rhabdomyosarcoma and tumours ofneural crest origin, including melanoma and neuroblastoma	(11)
Pax3 (mouse)	Splotch mutant	Defects in neural crest derivatives such as, pigment cells, sympathetic ganglia and cardiac neural crest-derived structures.	(11)
ZEB2 (*SIP1, ZFHX1B, SMADIP1*) (human)	Mowat-Wilson syndrome	Hirschprung associated with microcephaly, mental retardation, hypertelorism, submucous cleft palate, short stature	(12–15)
Zeb2 (*Sip1, ZFHX1B, SMADIP1*) (mouse)		Early arrest in cranial neural crest migration	(16)
Snail1/*Snail2* (mouse)	Double knockout resembles Pierre Robin Sequence	Micrognathia, fused mandible, enlarged parietal foramen in skull vault	(17)
Snail2 (human)	Waardenburg-Shah syndrome 2 Piebaldism (non-Kit related)	Defects in melanocytes, also seen with Mitf mutation Heterozygous deletion of SNAI2 gene	(18–20) (21)
Snail2 (chicken and frog)	Inhibition of function	Defective EMT and migration of neural crest and mesoderm	(22–24)
Sox8 (mouse)		No effect as a single mutation but increases the severity of *Sox10* heterozygote; may be jointly required with *Sox10* for maintenance of vagal neural crest cells	(25)
SOX9 (human)	Campomelic dysplasia	Congenital skeletal malformation syndrome, includes cleft palate, low set ears, loss of the 12th pair of ribs, abnormal pelvic bones, small chest and hip dislocations. May include absence of olfactory bulbs, renal and/or cardiac defects and XY sex reversal with genital malformations. Frequently associated with conductive and sensorineural hearing loss	(26, 27)
Sox9 conditional (mouse)	*Sox9*$^{flox/flox}$;*Foxg1*^{Cre} Cre activity driven in the prospective otic ectoderm	Sox9 controls adhesive properties of placode cells; otic placodes are normally specified but invagination is impaired.	(28)
Sox9a (zebrafish)	*Jellyfish* mutation	Lack cartilage elements of the neocranium, branchial arches and pectoral girdle; cartilage morphogenesis also disrupted	(29)

SOX10 haploinsufficinecy (human)	Hirschprungs disease (HSCR) Waardenburg-Shah syndrome type 4	Failure of enteric ganglia to populate the distal colon Deafness/pigmentation defect in addition to HSCR; also seen in EDN3 and EDNRB mutants	(30–32) (31)
Sox10$^{-/-}$ (mouse, *Xenopus*, zebrafish)	Colorless (*D. rerio*)	Loss of melanocytes, autonomic and enteric neurons and peripheral glia. Crest cells fail to differentiate and die, can result in embryonic lethality	(33–37)
TBX1 (human)	Di George syndrome	Cardiac outflow tract anomalies,absence or hypoplasia of thymus and parathyroid glands, nasal voice (often associated with cleft palate or submucosal cleft palate) and facial dysmorphism. Known as conotruncal anomaly face	(38)
TGFBR1 (human)	Loeys-Dietz syndrome (LDS1A and 2A) Non-FBN1 related Marfan syndrome	LDS1 and 2 are clinically indistinguishable. Autosomal dominant aortic aneurysm syndromes characterized by the triad of arterial tortuosity and aneurysms, hypertelorism, and bifid uvula or cleft palate; Type 1 category presents cleft palate, craniosynostosis, or hypertelorism. Some patients assigned to the type 2 category had a bifid uvula.	(39, 40)
TGFBR2 (human)	LDS 1B and 2B Non-FBN1 related Marfan syndrome	Marfan syndrome shows striking pleiotropism and clinical variability. The cardinal features occur in 3 systems: skeletal, ocular, and cardiovascular; a highly arched palate with crowding of the teeth are frequent skeletal features	(41–43)
Tgfrb2 (mouse)	*Tgbfr2*$^{fl/fl}$; Wnt1-cre	Severe skull defects, missing frontal and severely retarded parietal bone, cleft palate, reduced mandible and maxilla; skull size is 25% smaller than littermates	(39, 44)
Treacle (human)	Treacher-Collins syndrome	Antimongoloid slant of the eyes, coloboma of the lid, micrognathia, microtia and other ear deformities, hypoplastic zygomatic arches and macrostomia. Conductive hearing loss and cleft palate	(45)
Treacle (mouse)	*Tcof*$^{+/-}$ haploinsufficient embryos generated	Reduced head size, frontonasal dysplasia, failure of palatal shelves to fuse resulting in cleft palate, poorly formed nasal passages, die within 24h of birth from respiratory arrest due to cranioskeletal malformations. Required for ribosome biogenesis necessary for crest cell proliferation.	(46)
Treacle (Macaca mulatta)	Resus Tcof1 homolog is 93.8% identical in terms of protein	Infant macaque discovered displaying Treacher-Collins phenotype. No mutation found in TCOF1 coding or splice sites, but 87% reduction of spleen TCOF1 mRNA	(47)
Treacle (dog)		Genetic analysis showed mapping to this region of mutation leading to brachycephaly in domestic dog breeds	(48)
Twist (human)	Saethre-Chotzen syndrome	Craniosyntosis, limb deformities and dysmorphic facial features including facial asymmetry.	(49, 50)
Twist (mouse)	*Twist1*$^{-/-}$ Twist conditional mutant	Embryonic lethal at E11.5, open cranial neural tube, retarded forelimb bud development and branchial arch malformations. Heterozygotes have craniofacial defects and polydactyly	(51) (52)

Supplementary Fig. 1. Disorders related to defects in neural crest genes/EMT

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