

Disease	Mutation	Inheritance	Function	Clinical Notes
Duchenne Muscular Dystrophy	translocation / deletion	X-linked recessive	loss	high CK, low dystrophin, X inactivation, disruption of reading frame, Gower's maneuver, test 65-70% sensitive and 100% specific
Becker Muscular Dystrophy	deletion: read frame OK	X-linked recessive	loss	high CK, mild Duchenne
Hyperkalemic Periodic Paralysis	missense	autosomal dominant	gain	no bananas (K ⁺), sodium channelopathy, muscle electrically silent, theta & LOD
Paramyotonia Congenita	missense	autosomal dominant	gain	cold associated, sodium channelopathy
Achondroplasia	missense	autosomal dominant	gain	growth inhibited by FGFR3, mutation v. SNP
Breast Cancer		autosomal dominant	loss*	BRCA1/2 mutation, tumor suppressor gene (v. oncogene), penetrance, gene test patent
(Connective Tissue Disease)		dominant-negative	loss	missense mutation worse than whole deletion
Neurofibromatosis		dominant	loss*	congenital mutation is 1st hit, somatic mutation is 2nd hit, variable expressivity
Familial Hypercholesterolemia		dominant - haploinsufficiency	loss	LDLR defect
Acute Intermittent Porphyria		dominant - haploinsufficiency	loss	block in heme biosynthesis pathway, vampire
Rett Syndrome		X-linked dominant (girls only)	gain	half cells make all protein, MeCP2, recurrent pregnancy loss (boys)
Angelman / Prader-Willi	deletion	autosomal dominant	gain	imprinting: dad --> Ang, mom --> P-W
Fragile X Syndrome	trinucleotide repeat	X-linked recessive	loss	CGG repeat, hypermethylation, genetic anticipation, often FraXA, X-inactivation, "rule out" genetic test sensitive and specific, developmental delay
Huntington's Disease	trinucleotide repeat	dominant - paternal	gain	polyglutamine --> precipitation (neuropathy)
Myotonic Dystrophy	trinucleotide repeat	dominant - maternal	gain	clinically variable, CTG repeat in 3' untranslated region, mRNA toxicity
Cystic Fibrosis		recessive	loss	CFTR, all cells make half protein

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DiGeorge Syndrome	22q11 deletion	dominant - haploinsufficiency	loss	dosage problem, many genes effected, somatic (v. gonadal) mosaicism, 6% of carriers asymptomatic, recurrence risk
Velocardiofacial Syndrome	22q11 deletion	dominant - haploinsufficiency	loss	
Charcot-Marie-Tooth	duplication	dominant	gain	duplication of myelin protein --> myelination imbalance, foot drop, haploinsufficiency would have same clinical manifestation
RET mutation		dominant	loss*	loss of tumor suppressor --> thyroid cancer, multiple endocrine neoplasia, childhood testing?
Hydatidiform Mole	uniparental disomy (nondisjunction)			trisomic rescue, all chromosomes paternal --> no fetal tissue + uncontrollably growing placenta, imprinting
Down Syndrome	nondisjunction			trisomy 21, frequency increases with maternal age, dosage/chromosomal imbalance
Turner Syndrome	nondisjunction			45 XO, somatic mosaicism, female phenotype
Klinefelter's Syndrome	nondisjunction			47 XXY, male phenotype, infertility (paternity?)
Robertsonian Translocation				acrocentric chromosomes 14 + 21; 45 XX der(14;21)(q10;q10)
	point mutations			frequency increases with paternal age
		maternal		via mitochondrial DNA
Single Nucleotide Polymorphism	non-pathological variation			AKT-1: muscle hypertrophy and atrophy, T2DM

loss* = loss at cell scale, gain at patient scale