## Autosomal recessive human diseases:

Phenylketonuria (phenylalanine hydroxylase ch 12) missense mutation (transversion from a G to a C at codon 413)
-Albinism (tyrosinase)
-Tay-sachs disease (hexosaminidase(HEX)A ch 15 )
Sandhoff disease(hexosaminidase B)
-Cystic fibrosis (chloride transporter ch7) pleiotropy
Deletion of three base pairs
-Lesch-Nyah's syndrome (hypoxanthine guanine phosphoribosal transferase)
-Thalassemia (ch 16&11)
-Sickle-cell anemia (ch 11)

Overdominace : -Sickle cell anemia prevents malaria -Cystic fibrosis prevents cholera -Ray-Sachs prevents TB

Incomplete penetrance & expressivity : polydactyly, neurofibromatosis , retinoblastoma

Reduced penetrance : ectrodactyly (SHFM)

Autosomal dominant: -Familial hypercholesterolemia -Myotonic dystrophy -Huntington disease -Neurofibromatosis, Variable expressivity -Polycystic kidney disease, dominant or recessive -Achondroplasia, dominant (Aa)

X-linked recessive inheritance:-Hemophilia A-Duchenne muscular dystrophy-Color blindness

Dominant-Negative Variant: Marfan syndrome due to mutations in the FBN1(fibrillin-1 gene)

Haplo-insufficiency:polydactyly, GLI3 gene

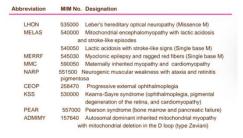
hypermorphic(gain of function): achondroplasia due to mutation in FGFR3 gene.

Myeloproliferative neoplasms(MPNs) due to mutation in JAK2 gene Neomorphic (BCR-ABL In chronic myeloid leukemia,IDH1,2 in gliomas)

Inter locus heterogeneity(one disease-several genes): deafness, hypertrophic cardiomyopathy, retinitis pigmentosa

-Allelic heterogeneity: cystic fibrosis Class 1: defect in the synthesis of CFTR (nosense,framshift mutations) Class2:defect in CFTR protein processing and trafficking (missence,amino acid deletion) Class3: defect in CFTR channel gating and regulation (missence,amino acid deletion) Class4: defect in CFTR channel conductance (missence,amino acid deletion) Class5: reduced synthesis of CFTR proteins (Splicing defect,missence) Class6: reduction in the stability of CFTR proteins (missence,amino acid deletion)

Mitochondrial diseases: -Type II Diabetes Mellitus, -Parkinson Disease, -Atherosclerotic Heart Disease, Stroke, -Alzheimer Dementia, and -Cancer.



-Diseases associated with trinucleotide repeat expansions: FragileXMentalRetardationsyndrome.(CGG,5'UTR,X-linked(Xq27.3),female) Huntington disease.(CAG, coding sequence,autosomal dominant, male) myotonic dystrophy.(CTG, 3'UTR, autosomal dominant,female) spinocerebellar ataxia. Kennedy disease. Joseph-disease. Friedreich ataxia.

Diseases associated with genomic imprinting:

Paternally-expressed genes (IGF2) enhance growth and proliferation. Hypomethylation of these genes can cause Beckwith-Wiedemann Syndrome (BWS) and cancer.

Maternally-expressed genes (CDKN1C) act as tumor suppressors, Hypermethylation can silence these genes leading to BWS

Prader-Willi Syndrome (PWS): Caused by the absence of paternal alleles on chromosome 15(15q11-13), leading to symptoms like obesity and mental retardation. Angelman Syndrome (AS): Caused by the absence of maternal alleles on 15q11-13, leading to symptoms like uncontrollable laughter and motor issues. Rett syndrome.