

Supplementary Table 1: Clinicopathologic, genetic, and mechanistic features of congenital neutropenia syndromes

Disorder OMIM Code	Genetics and Molecular Pathophysiology				Diagnostic Evaluation			
	Genetic Association (Locus) Critical References	Inheritance Pattern	Intracellular Localization	Typical Function	Clinical Manifestations	Peripheral Blood Findings	Bone Marrow Findings	Associated Risk for Malignancy
Benign Ethnic Neutropenia OMIM#: Not assigned	DARC (1q23.2) Reference: 234	Autosomal Dominant	Cellular membrane	Duffy antigen receptor, regulator of chemokine-mediated cell migration and inflammation	No increased risk of recurrent fevers, infection, oral ulcers, lymphadenopathy, splenomegaly, cytopenias	Isolated neutropenia (1000-1500 cells/uL)	Normal bone marrow cellularity and myeloid maturation	No associated risk
	CXCL2 (4q13.3) Reference: 9	Undetermined	Extra-cellular milieu, cellular membrane	Potent chemotactic agent				No associated risk
	CXCR2 (2q35) Reference: 10	Undetermined	Cellular membrane	G-protein coupled receptor, responsible for neutrophil chemotaxis to the site of infection/injury				No associated risk
	CDK6 (7q21.2) Reference: 10	Undetermined	Nucleus	Cyclin-dependent kinase, regulator of cell cycle transition from G0 to G1 to S phase				No associated risk
	PSMD3-CSF3 region (17q) References: 10, 11	Undetermined	---	Intergenic SNP associated with PSMD3 expression; PSMD3 is a non-ATPase subunit of the 19S regulator to 26S proteasome, involved in regulation of the cell cycle by ubiquitin-proteasome				No associated risk
	PLCB4 (20p12.3-p12.2) Reference: 11	Undetermined	Cellular membrane	Phospholipase downstream of CXCR2, involved in cleavage of PIP2 to IP3 and DAG intracellular signaling molecules				No associated risk
Cyclic Neutropenia OMIM#: 162800	ELANE (19q13.3) References: 36, 37	Autosomal Dominant	Myeloid primary/azurophilic granules, monocyte phagolysosomes	Serine protease, serves as cytotoxic element in innate immune response and in tissue remodeling	Generally less severe, diagnosed around two years old Recurrent fevers, malaise, stomatitis, gingivitis, bacterial infections are mostly self resolving but severe cases of pneumonia, mastoiditis, peritonitis can occur Usually without extra-hematopoietic manifestations	Intermittent neutropenia with regular, periodic oscillations in ANC from normal to <200cells/uL, reciprocal monocytosis, often cycling of other cells lines also seen (PLTs, reticulocytes) 14-35 days, mostly q21 with 7-10 days of profound neutropenia	Morphology correlates with ANC oscillations, ranging between normal bone marrow to mimicking SCN	No associated risk
Severe Congenital Neutropenia, Type 1 OMIM#: 202700	ELANE (19q13.3) References: 37	Autosomal Dominant	Neutrophil primary/azurophilic granules, monocyte phagolysosomes	Serine protease, serves as cytotoxic element in innate immune response and tissue remodeling	Recurrent fevers, oral ulcers, skin infections (omphalitis), deep tissue abscesses within first months of life Usually without extra-hematopoietic manifestations	Marked, chronic neutropenia with normal morphology, often with compensatory monocytosis or eosinophilia Anemia of chronic disease Hypergammaglobulinemia	Promyelocyte-to-myelocyte maturation arrest, reduced or absent mature granulocytes	Increased risk of myeloid neoplasia
Severe Congenital Neutropenia, Type 2 OMIM#: 613107	GFI1 (1p22) Reference: 55	Autosomal Dominant	Nucleus	Transcriptional repressor of ELANE	Usually without extra-hematopoietic manifestations	Chronic, mild to severe neutropenia, replacement of mature neutrophils with indistinct, immature myeloid cells Lymphopenia	Promyelocyte-to-myelocyte maturation arrest, reduced or absent mature granulocytes (+/-)	Increased risk of myeloid neoplasia
Severe Congenital Neutropenia, Type 3 (Kostmann Syndrome, infantile Genetic Agranulocytosis) OMIM#: 610738	HAX1 (1q21.3) Reference: 59	Autosomal Recessive	Mitochondria, endoplasmic reticulum, nucleus	Anti-apoptotic protein	Neurocognitive retardation/Seizure disorder	Profound neutropenia occurring in the 1st week of life	Promyelocyte-to-myelocyte maturation arrest, reduced or absent mature granulocytes	Increased risk of myeloid neoplasia
Severe Congenital Neutropenia, Type 4 (Dursun Syndrome) OMIM#: 612541	G6PC3 (17q21) References: 69, 73	Autosomal Recessive	Endoplasmic reticulum	Catalyzes hydrolysis of glucose-6-phosphate to glucose and phosphate in gluconeogenesis and glycogenolysis	Cardiac malformations and arrhythmias, prominent superficial veins, exocrine pancreatic insufficiency, chronic diarrhea/IBD, neurocognitive retardation, uroopathy, cryptorchidism	Thrombocytopenia	Promyelocyte-to-myelocyte maturation arrest, reduced or absent mature granulocytes (+/-)	Increased risk of myeloid neoplasia
Severe Congenital Neutropenia, Type 5 OMIM#: 615285	VPS45 (1q21.2) References: 74	Autosomal Recessive	Cellular trafficking vesicles	Orchestrates segregation of intracellular molecules into distinct organelles	Neurological abnormalities (developmental delay, vision and hearing loss, thin corpus callosum, EEG dysrhythmias), osseous abnormalities with osteoclerosis, poor weight gain, hepatosplenomegaly	Neutropenia Anemia Thrombocytopenia	Myelofibrosis Extramedullary hematopoiesis	Increased risk of myeloid neoplasia
Severe Congenital Neutropenia, Type 6 OMIM#: 616022	JAGN1 (3p25.3) Reference: 78	Autosomal Recessive	Endoplasmic reticulum, early secretory pathway	Glycosylase, anti-apoptotic factor	Exocrine pancreatic insufficiency	Hypogranular neutrophils	Promyelocyte-to-myelocyte maturation arrest, reduced or absent mature granulocytes (+/-)	Increased risk of myeloid neoplasia
Severe Congenital Neutropenia, Type 7 OMIM#: 617014	CSF3R (1p34.3) Reference: 80	Autosomal Recessive	Cellular membrane	Cytokine receptor with signal transduction mediated through STAT-3/5, Ras-MAPK, and PI3K-Akt pathways	Usually without extra-hematopoietic manifestations	Peripheral neutropenia	No myeloid maturation arrest Unresponsive to G-CSF	Increased risk of myeloid neoplasia
Severe Congenital Neutropenia, Type 8 OMIM#: 618752	SRP54 (14q13.2) Reference: 85	Autosomal Dominant	Cytosol	GTPase and regulatory subunit of the SRP complex, which targets nascent proteins to the ER	Usually without extra-hematopoietic manifestations	Peripheral neutropenia	Promyelocyte-to-myelocyte maturation arrest, reduced or absent mature granulocytes	Increased risk of myeloid neoplasia

Severe Congenital Neutropenia, Type 9 OMIM#: 619813	<i>CLPB</i> (11q13.4) References: 93-98	Autosomal Dominant and Autosomal Recessive	Mitochondria	Cooperates with Hsp70 in the disaggregation of protein aggregates	Congenital cataracts, neurocognitive retardation, epilepsy, psychomotor regression during febrile episodes, 3-methylglutaconic aciduria	Peripheral neutropenia Leukopenia Thrombocytopenia	Promyelocyte-to-myelocyte maturation arrest, reduced or absent mature granulocytes Abundant macrophages, hemophagocytosis, and atypical lymphocytes Vacuolar degeneration of monocytes and macrophages	Increased risk of myeloid neoplasia
X-Linked Severe Congenital Neutropenia OMIM#: 300299	<i>WAS</i> (Xp11.4-p11.21) Reference: 99	X-linked Recessive	Cytoskeleton	Regulates the actin cytoskeleton	Usually without extra-hematopoietic manifestations	Chronic severe neutropenia Monocytopenia	Promyelocyte-to-myelocyte maturation arrest, reduced or absent mature granulocytes	Increased risk of myeloid neoplasia
SEC61A1-associated Congenital Neutropenia OMIM#: Not assigned	<i>SEC61A1</i> (3q21.3) Reference: 212	Autosomal Dominant	Endoplasmic reticulum	Subunit of Sec61 complex, which regulates protein transport and passive calcium leakage in the ER	Usually without extra-hematopoietic manifestations	Peripheral neutrophils with nuclear hyposegmentation	No myeloid maturation arrest	Undetermined
TCIRG1-associated Congenital neutropenia OMIM#: Not assigned	<i>TCIRG1</i> (11q13.2) Reference: 213	Autosomal Dominant	Intracellular compartments	Regulates pH of intracellular compartments and organelles	Skin angiomatosis	Undetermined	No myeloid maturation arrest	Undetermined
Defects in Other Signal Recognition Particle (SRP) Components OMIM#: Not assigned	<i>SRP68</i> (17q25.1) Reference: 214	Autosomal Recessive	Cytosol	Recognizes the signal peptide of nascent proteins for ribosome association prior to ER targeting	No reported extra-hematopoietic manifestations	Severe neutropenia (ANC 200/uL), elevated monocyte count (AMC 1,700/uL), anemia (Hgb 7.5 g/dL), iron deficiency, moderate thrombocytopenia (1,490/uL)	Promyelocyte-to-myelocyte maturation arrest, reduced or absent mature granulocytes, promyelocytes and rare neutrophils with numerous condensed granulations, abnormal nuclei, clumped chromatin	Undetermined
	<i>SRP19</i> (5q22.2) Reference: 215	Undetermined	Cytosol	Binds free SRP RNA within the nucleolus, allowing docking of SRP54 and other SRP subunits	Pancreatic insufficiency, congenital neutropenia, growth failure, bronchiectasis	Electron microscopy studies of neutrophil granulocytes showed a significant reduction of electron-dense granules	Promyelocyte-to-myelocyte maturation arrest, paucity of electron-dense granules	Undetermined
	<i>SRPRA</i> (11q24.2) Reference: 215	Undetermined	Endoplasmic reticulum	Interacts with SRP-ribosome-nascent RNA complex to initiate translocation of nascent RNA across ER				Undetermined
WHIM Syndrome 1 OMIM#: 193670	<i>CXCR4</i> (2q21) References: 129, 130	Autosomal Dominant	Cellular membrane	Chemokine receptor to CXCL12, important in stem cell bone marrow retention and regulating quiescence	Cardiac malformations/Tetralogy of Fallot, HPV-associated lesions, <i>Mycobacteria</i> infections	Monocytopenia Chronic ANC <500cells/uL from infancy or childhood caused by exaggerated response of CXCL12-CXCR4 binding resulting in failed downregulation/internalization of CXCR4 and myelokathexis with BM retention of neutrophils and leukocytes in the BM (PMID: 15536153, 21178277) Monocytopenia, severe lymphopenia Defective granulocyte and lymphocyte trafficking	No myeloid maturation arrest Myelokathexis, hypercellular marrow with increased centrally-located reserve compartment (neutrophils, metamyelocytes) and increased myeloid to erythroid ratio, increased bands and mature neutrophils, with apoptotic appearance (vacuolization, hypersegmented pyknotic nuclei), long interlobular filaments) (PMID: 16487166) Macrophages may contain ingested neutrophils	No associated risk increase reported
WHIM Syndrome 2/CXCR2 Deficiency OMIM#: 619407	<i>CXCR2</i> (2q35) Reference: 131	Autosomal Recessive	Cellular membrane	G-protein-coupled receptor for IL-8, mediating neutrophil chemotaxis and bone marrow release	Usually without extra-hematopoietic manifestations	Transient episodes of lymphopenia	No major granulocyte maturation defect, +/-myelokathexis	No associated risk increase reported
Shwachman Diamond Syndrome 1 OMIM#: 260400	<i>SBD5</i> (7q11.22) References: 132, 137	Autosomal Recessive	Nucleus, concentrated within nucleolus, cytosol	Stabilization of mitotic spindle Processing of rRNA Removal of eukaryotic initiation factor 6 from the 60S ribosomal subunit as necessary for formation of the 80S ribosome	Exocrine pancreatic insufficiency, cardiac malformations and cardiomyopathy, xerosis eczema, metaphyseal dysplasia, neurocognitive retardation, myopathy, palatal cleft	Neutropenia is intermittent (more common) to persistent. ANC ranges mild (more common) to severe. Neutrophil chemotaxis defects Low B cell count with suboptimal immunoglobulin production, abnormal T cell proliferation Thrombocytopenia or anemia are each present in ~ 50% of cases 10-65% of SDS patients present with or develop pancytopenia. Bone marrow failure is believed to be the underlying condition that drives the expansion of the paroxysmal nocturnal hemoglobinuria	Variable but often hypocellular, left-shifted/hypoplasial myelopoiesis with dysgranulopoiesis Dysmegakaryopoiesis	Increased risk
Shwachman Diamond Syndrome 2/EFL1-related Neutropenia OMIM#: 617941	<i>EFL1</i> (15q25.2) Reference: 216	Autosomal Dominant	Cytosol	Serves to catalyze GTP-dependent removal of the assembly factor EIF6 in conjunction with SBD5 gene	Exocrine pancreas deficiency, metaphyseal dysplasia, mental retardation	Dyserythropoiesis Mild neutropenia	Low cellularity with normal trilineage hematopoiesis; Neutrophil segmentation defects, reduced megakaryocytes, and an increase in iron storage reported	Single case reported (PMID: 27346687)

Bone Marrow Failure Syndrome 3/ DNAJC21-related Neutropenia OMIM: 617052	<i>DNAJC21</i> (5p13.2) Reference: 217	Autosomal Recessive	Nucleus, cytosol	In conjunction with HSP70 chaperones, serves in translation, translocation, protein folding/refolding, and degradation	Pancreatic insufficiency, dyskeratosis congenita, retinal dysplasia, variable and nonspecific abnormalities: poor growth, microcephaly, short stature, joint/skeletal anomalies	Pancytopenia in early childhood	Hypocellular	Single case reported
Pearson Syndrome OMIM#: 557000	Mitochondrial DNA: m.8470_13446del4977 Reference: 218	Complex Inheritance	Mitochondria	Deletion in mitochondrial DNA	Exocrine pancreatic insufficiency	Anemia Thrombocytopenia	Vacuolization of BM precursors, Perls staining reveals ring sideroblasts	No associated risk increase reported
Wolcott-Rallison Syndrome OMIM#: 226980	<i>EIF2AK3</i> (2p11.2) Reference: 219	Autosomal Recessive	Endoplasmic reticulum	PKR-like endoplasmic reticulum kinase serves as a chaperone mediating unfolded protein response	Exocrine pancreatic insufficiency/Insulin-dependent neonatal diabetes	Isolated neutropenia	Promyelocyte-to-myelocyte maturation arrest, reduced or absent mature granulocytes	No associated risk increase reported
Specific Granule Deficiency 1 OMIM: 245480	<i>CEBPE</i> (14q11.2) Reference: 220	Autosomal Dominant and Recessive Forms	Nucleus	Transcription factor	Recurrent bacterial infections in infancy or early childhood, especially <i>Staphylococcus</i> skin abscesses that progress to invasive infection	Neutrophils with atypical hyposegmented or bilobed nuclei, decreased to absent granules Low eosinophil counts	Myeloid hypoplasia with predominance of promyelocytes, myelocytes, and low neutrophils	No associated risk increase reported
Specific Granule Deficiency 2 OMIM#: 617475	<i>SMARCD2</i> (17q23.3) Reference: 221	Autosomal Recessive	Nucleus	Hypothesized transcription factor	Delayed umbilical cord separation, recurrent bacterial infections in infancy or early childhood, facial dysmorphism, developmental delay, distal bone abnormalities, chronic diarrhea/IBD	Decreased mature neutrophils with bilobed pseudo Pelger-Huet anomaly and hypogranulation	Hypercellular bone marrow with promyelocyte-to-myelocyte maturation arrest, reduced or absent mature granulocytes, and dysplastic megakaryocytes; excess blasts and myelofibrosis	No associated risk increase reported
Immunodeficiency 21/ GATA2 Deficiency OMIM#: 614172	<i>GATA2</i> (3q21.3) References: 114-119	Autosomal Dominant	Nucleus	Transcription factor	Uropathy, lymphedema, inner ear defects, HPV-associated lesions, <i>Mycobacteria</i> infections	Mild neutropenia Macrocytosis Monocytopenia Thrombocytopenia B, NK, and CD4 lymphocytopenia CD4:CD8 ratio <1	Hypoplastic bone marrow mimicking aplastic anemia; no myeloid maturation arrest, atypical megakaryocytes; small mononuclear and dysplastic forms with separated nuclear lobes	MDS and leukemia are a common manifestation of disease.
T-cell Immunodeficiency, Recurrent Infections, and Autoimmunity with or without Cardiac Malformations/STK4 Deficiency OMIM#: 614868	<i>STK4</i> (20q13.12) Reference: 222	Autosomal Recessive	Cytoplasm	Serine/threonine protein kinase, upstream of the stress-induced mitogen-activated protein kinase (MAPK) cascade	Susceptibility to bacterial, viral infections and mucocutaneous candidiasis, cardiac malformations, HPV-associated lesions	Continuous or intermittent neutropenia Lymphopenia Monocytopenia	No myeloid maturation arrest	EBV-induced lymphoproliferative disorder has been reported PMID: 30386345
Charcot-Marie-Tooth disease, axonal type 2M and Charcot-Marie-Tooth disease, dominant intermediate B OMIM#: 606482	<i>DNM2</i> (19p13.2) Reference: 223	Autosomal Dominant	Cytoskeleton	Dynamin GTPase associated with endocytosis, motility, and in alteration of cell membrane	Congenital cataracts, muscle weakness, no significant increase in risk for recurrent infection	Generally isolated neutropenia	No myeloid maturation arrest	No associated risk increase reported
Immunodeficiency 102 OMIM#: 301082	<i>SASH3</i> (Xq26.1) Reference: 224	X-linked Recessive	Cytoplasm	Adaptor scaffolding protein involved in immune cell signaling	Autoimmunity, viral infections	Hemolytic anemia, thrombocytopenia, lymphopenia, and decreased NK cells	Not described	Single large granular lymphocytic leukemia reported on flow cytometry PMID: 33876203
Transcobalamin II Deficiency OMIM#: 275350	<i>TGN2</i> (22q12.2) Reference: 225	Autosomal Recessive	Cellular membrane	Plasma globulin that acts as the primary transport protein for vitamin B12, secretory protein induced receptor-mediated endocytosis	Failure to thrive in early life with vomiting and diarrhea, methylmalonic aciduria, recurrent infections, mental retardation and neurologic abnormalities requiring cobalamin treatment	Megaloblastic anemia Neutropenia, pancytopenia Peripheral blood smear revealed anisocytic erythrocytes with frequent macroovalocytes	Megaloblastic bone marrow failure; hypercellular marrow with frequent megaloblasts and few micromegakaryocytes, dysplastic erythroblasts, including nuclear-cytoplasmic asynchrony, nuclear lobation or irregular shapes, and frequent giant bands, neutrophils with abnormal nuclear lobation	No associated risk increase reported
Immunodeficiency 23 Immunodeficiency with Hyper IgE and Cognitive Impairment Immunodeficiency-Vasculitis-Myoclonus Syndrome OMIM: 615816	<i>PGM3</i> (6q14.1) Reference: 226	Autosomal Recessive	Endoplasmic reticulum, cytoplasm	Glycosylase responsible for Glc-Nac-6-P conversion to Glc-Nac-1-P in the pathway for forming UDP-GlcNac	Neonatal onset of recurrent bacterial and viral infections, inflammatory skin diseases, atopic dermatitis and atopic diatheses, and marked serum IgE elevation. Early neurologic impairment is evident including developmental delay, intellectual disability, ataxia, dysarthria, sensorineural hearing loss, myoclonus and seizures.	Neutropenia T-cell lymphopenia, particularly of CD8(+) T cells, and reduced memory B cell numbers Polycythemia	Not described	No associated risk increase reported
Cohen Syndrome OMIM#: 216550	<i>VPS13B</i> (8q22-q23) References: 190, 191	Autosomal Recessive	Golgi apparatus	Sorting and transporting proteins in ER and post-Golgi vesicles	Facial dysmorphism ("moon face")/Palatal cleft/Microcephaly Progressive retinochoroidal dystrophy/Myopia Neurocognitive retardation Psychomotor retardation/Hypotonia/Joint laxity Cryptorchidism	Neutropenia in 90% of cases associated with chronic gingivostomatitis	No myeloid maturation arrest Normo- to hypercellular marrow, left-shifted granulopoiesis	No associated risk increase reported

Vasculitis, Autoinflammation, and Immunodeficiency, and Hematologic Defects Syndrome/Deficiency of ADA2 OMIM#: 615688	ADA2 (22q11.1) Reference: 227	Autosomal Recessive	Cytoplasm, cellular membrane	Deaminase involved in adenosine metabolism to inosine for ultimate conversion to hypoxanthine for excretion	Facial dysmorphism, truncal obesity, microcephaly, intellectual developmental delays, progressive retinopathy	Chronic and intermittent, mild and severe neutropenia Fluctuating thrombocytopenia	Early: hypocellular and mimicking aplastic anemia or hypercellular with orderly trilineage hematopoiesis Later: Myeloid hypoplasia, promyelocyte-to-myelocyte maturation arrest, reduced or absent mature granulocytes	No associated risk increase reported
Glycogen Storage Disease Type 1b OMIM#: 232220	SLC37A4 (11q23.3) Reference: 228	Autosomal Recessive	Endoplasmic reticulum	Glucose 6-phosphatase complex trans ER transporter	Chronic diarrhea/IBD, hypoglycemia, fasting hyperlactacidemia, glycogen overload of the liver	Pure red cell aplasia, immune-mediated neutropenia, and pancytopenia	No myeloid maturation arrest	No associated risk increase reported
Immunodeficiency with Hyper IgM, Type 1 OMIM#: 308230	CD40LG (Xq26.3) Reference: 229	X-linked Recessive	Cellular membrane	CD40L-CD40 interactions drive regulation of B cell affinity maturation, class switching, and memory B cell development. These interactions also activate dendritic cells and macrophages.	Recurrent respiratory and gastrointestinal bacterial infections, oral and rectal ulcers, hepatosplenomegaly, lymphadenopathy	autoimmune' hematologic disorders: neutropenia, hemolytic anemia, thrombocytopenia (especially due to ITP) Eosinophilia	Not described	No associated risk increase reported
Barth Syndrome OMIM#: 302060	TAZ (Xq28) Reference: 200-206	X-linked Recessive	Nucleus, cytoplasm, mitochondria, and cellular membrane	Cardiolipin transacylase in the inner mitochondrial membrane, transcriptional co-activator released from the cytosol for nuclear translocation by actin-angiotensin complex. Responsible for regulation of genes involved in various cellular processes such as cell proliferation, differentiation, and apoptosis.	Dilated cardiomyopathy and endocardial fibroelastosis, proximal skeletal myopathy, growth retardation, 3-methylglutaconic aciduria	Intermittent, variable neutropenia	No myeloid maturation arrest	No associated risk increase reported
Reticular Dysgenesis OMIM#: 267500	AK2 (1p35.1) Reference: 230	Autosomal Recessive	Mitochondria	Catalyzes the transfer of a phosphate from ATP to AMP, producing two ADP	Sensorineural hearing loss	Leukopenia	Hypocellular, with greatly reduced myeloid and lymphoid elements Promyelocyte maturation arrest in the myeloid and lymphoid lineages, leading to early onset, recurrent, and overwhelming infections	No associated risk increase reported
Immunodeficiency 67/ IRAK 4 Deficiency OMIM#: 607676	IRAK4 (12q12) Reference: 231	Autosomal Recessive	Cytoplasm	Serine/threonine kinase activated TLRs or IL-1Rs to phosphorylate downstream signaling molecules, leading to the activation of NF- κ B and production of pro-inflammatory cytokines/chemokines. Also plays a role in the activation of mitogen-activated protein kinases (MAPKs), regulating of cellular proliferation, differentiation, and apoptosis.	Recurrent early childhood bacterial infections but not viral, fungal, and parasitic infections, poor inflammatory responses to infection	Mild neutropenia without risk for severe infection	No myeloid maturation arrest	No associated risk increase reported
Hermansky-Pudlak Syndrome, Type 2 OMIM#: 608233	AP3B1 (5q14.1) Reference: 147	Autosomal Recessive	Cytoplasm, endosomes, and lysosomes	Intraluminal trafficking of proteins from the Golgi to the lysosome, notable for documented ELANE interactions	Partial to complete oculocutaneous albinism, platelet defects, neutropenia and immunodeficiency, pulmonary fibrosis, conductive hearing loss, dysplastic hips	Pale platelets (with diagnostic absence of dense granules on EM) in abundant platelet clusters Normal leukocyte distribution and red cell morphology	No myeloid maturation arrest	Risk for hemophagocytic lymphohistiocytosis (HLH)
Chediak-Higashi Syndrome OMIM#: 214500	LYST (1q42.3) Reference: 153	Autosomal Recessive	Cytoplasm	Formation, maturation, transport, and fusion of lysosomes with other cellular compartments	Partial to complete albinism, photophobia, nystagmus	Giant intracellular azurophilic granules in neutrophils and immature myeloid precursors	Giant intracellular azurophilic, peroxidase-positive granules in neutrophils and immature myeloid precursors with intramedullary destruction	~85% of patients develop HLH or the 'accelerated phase' of CHS (massive lymphohistiocytic infiltration of major organs with profound immunodeficiency, especially due to EBV infection)
Griscelli Syndrome, Type 2 OMIM#: 607624	RAB27A (15q21.3) References: 172	Autosomal Recessive	Cytoplasm	Rab GTP-ase involved in vesicular trafficking and fusion	Partial to complete albinism, immunologic abnormalities with frequent pyogenic infections, neurologic impairment	Neutropenia (morphologically normal) with frequent thrombocytopenia Adequate T and B lymphocyte reserve with hypogammaglobulinemia and deficiency in antibody production	Normal bone marrow examination	Can have the accelerated phase of lymphohistiocytosis
Immunodeficiency due to Defect in MAPBP-interacting protein OMIM#: 610798	LAMTOR2 (p14)/ (1q22) Reference: 187	Autosomal Recessive	Lysosome	Forms multi-subunit complex called the Ragulator, which scaffolds assembly of the Rag GTPase heterodimer, to recruit and activate mTORC1 phosphorylation of downstream substrates involved in cell growth, metabolism, and autophagy	Partial to complete albinism, short stature, coarse facial features, and recurrent bronchopulmonary infections, especially from <i>S. pneumoniae</i>	Low peripheral neutrophil counts, with absolute neutrophil counts less than 500 per microliter	Normal bone marrow examination	No associated risk increase reported

Cartilage-Hair Hypoplasia OMIM: 250250	<i>RMRP</i> (9p13.3) Reference: 232	Autosomal Recessive	Nucleolus	Structural/catalytic component of mitochondrial RNA-processing endoribonuclease (RNase MRP). Involved in processing and maturation of mitochondrial RNA	Fine, sparse, light colored hair, metaphyseal dysplasia, dwarfism, aganglionic megacolon	Lymphopenia Hypoplastic anemia	No myeloid maturation arrest	No associated risk
Clericuzio-type Poikiloderma OMIM: 604173	<i>USB1</i> (16q13) Reference: 233	Autosomal Recessive	Nucleus	Involved in processing and maturation of U6 snRNA to generate a functional spliceosome component	Poikiloderma, hyperkeratotic nails, generalized hyperkeratosis on palms and soles, noncyclic neutropenia with recurrent pulmonary infections, short stature	Neutropenia with mild dysgranulopoiesis	No myeloid maturation arrest, minor dysgranulopoietic features	No associated risk increase reported