GLOSSARY

For use in Shwachman-Diamond Syndrome (SDS)

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GENERAL

Bacteria – microorganisms (single-celled); some can be healthy such as those that cohabitate and live in the intestine. They and others can cause serious infections upon access to other parts of our body (such as blood or kidneys).

Biogenesis – refers to the production of new living organisms, or of the components of living organisms.

Chronic illness – any long-standing loss or abnormality of bodily function (refers to unhealthy changes in an individual's body).

Differentiated cell – a cell that carries out functions within an organ and typically possesses some proliferative capacity to from cells only like itself.

Dysplastic cells – cells with unusual shape under the microscope that can indicate abnormal tissue; can be seen in pre-cancerous tissue.

Hematology – the study of blood, blood forming cells and the disorders associated with them.

Intravenous – administered directly into a vein (such as an injection).

Morphology – form and structure of organisms or their cells.

Pathogenesis – the processes of the origin and development of a disease, or morbid process.

Progenitor cell – a cell that typically arises from a stem cell with some capacity to proliferate and form a range of (often related) cell types.

Ribosome – a complex machine within cells that can interpret gene blue prints to synthesize protein products. A ribosome has two major parts, known as the '40S' and '60S' ribosomal components. A working ribosome reads the gene's blue print via RNA molecules that are copied from the DNA of the chromosomes using 'the genetic code'. The genetic code is common to all living organisms.

Stem cell – a cell that has capacity to proliferate and to form a wide range of 'mature' cell types.

Subcutaneous (Sub-q) – located or placed just below the skin.

GENETICS

Chromosome – a structure of nucleic acid and protein found in the nucleus of most living cells, carrying genetic information in the form of genes. Normal human cells contain 23 pairs of chromosomes. For each individual, one of each pair is inherited separately from the mother and father.

Clone – an aggregate of genetically identical cells produced from a single progenitor cell.

Cytogenetics – the study of structure and function of chromosomes.

Gene – heredity unit. A gene corresponds to the blue print for a basic working molecule in cells, such as a protein. Each human cell has 28,000 (plus) genes. About 12,000 genes are active in any given cell type.

Pathogenic gene variant – a blue print change in a gene that may lead to deleterious consequences resulting in inherited disease (is disease-causing); also known as a 'mutation'

Non-pathogenic gene variant – can reflect population variation (is non-disease causing) and is considered to be benign; can also be known as a 'polymorphism'.

Gene variant of unknown significance (VUS) – a blue print change in a gene whose consequences are unknown or cannot presently be interpreted.

Germ cells – egg or sperm cells that can lead to generation of offspring.

Somatic cells – any of the cells of tissues that make up an organism other than germ cells.

Inherited gene variants – specific gene changes that are passed from parent to offspring via germ cells.

Acquired gene variants – specific gene changes that are gained, usually within somatic cells of a single tissue (such as the bone marrow and in blood cells). Acquired gene changes can contribute to the development of cancer.

Acquired chromosomal changes – specific cytogenetic or chromosomal changes (can involve loss or gain), usually within a single tissue (such as the bone marrow and in blood cells). Acquired chromosomal changes can contribute to the development of cancer.

Heterogeneous genetic disease – the occurrence of identical or similar disorder by different genetic causes (including different genes). In some contexts, to say that a disease is 'heterogeneous' can also refer to disease presentation that is highly variable.

Phenotype – the observable manifestation of a specific genetic makeup.
Wild-type allele – a typical standard form of a gene, in contrast to a mutant form.

Recessive – a disease (or trait) phenotype is said to be recessive if an individual must receive two copies of disease causing variants, one from each parent, to develop an inherited disease. For recessive phenotypes, individuals with only one disease-causing variant (and one non-disease causing allele) will not have clinical symptoms; they are called 'carriers'.

GENES (with relevance to SDS)

SBDS – Shwachman-Bodian-Diamond syndrome associated; the gene that is at fault in most cases of SDS. The protein product from SBDS is thought to be involved in the biogenesis of ribosomes and their function to help with the manufacture of a cell's proteins.

DNAJC21 – DnaJ Heat Shock Protein Family (Hsp40) Member C21; the gene has been found to be fault in some families with SDS or with bone marrow failure. The protein product provides instructions for making a protein that is involved in the early steps of ribosome biogenesis.

EFL1 – Elongation factor-like GTPase 1 (formerly known as EFTUD1); a gene found to be at fault in a few families with SDS-like disease. The protein product of EFL1 is thought to work with SBDS to help with the manufacture of a cell's proteins.

TP53 – Tumor suppressor protein 53, this gene provides instructions for a protein that acts as a tumor suppressor, that is involved in alerting the cell to pause in growing or dividing due to various stresses. Prolonged or elevated activation of p53 can also alert a cell to undergo 'a suicide process' known as apoptosis. Loss or change of TP53/p53 can be acquired in early stages of the development of cancer in a tissue, leading to the bypass of the safety controls offered by normal p53 action in that tissue.

ELANE – The 'Elastase, neutrophil expressed' gene provides instructions for a protein called neutrophil elastase. When the body starts an immune response to fight an infection, neutrophils release neutrophil elastase to help fight the infection.

BLOOD

Absolute neutrophil count (ANC) – determined by adding the percentage of neutrophils or polys in the blood with the percentage of bands in the blood, then multiplying that number by the white blood cell count and multiplying the product by 10. This number represents the number of neutrophils which are available for defending the body against infection.

Anemia – a decrease in blood cells which contain hemoglobin. Hemoglobin is necessary to carry oxygen to all of the body's cells.

B-cells – lymphocytes that produce antibodies which help to fight infection.

Bands – immature cells. They are usually counted as neutrophils when determining total neutrophils in the blood.

Bone marrow – soft tissue within the bones where the various blood cell types are manufactured.

Complete blood count (CBC) – number or percent of blood cells, which includes white cells, red cells and platelets.

Cyclic or intermittent neutropenia – when the neutrophil count fluctuates between a normal and a low count. The timing of cycles averages about every 21 days, and last from 3 to 6 days, but can vary.

Differential count – a measure of the percentage of each type of white blood cell in the blood.

Granulocytes (also called neutrophils) – white blood cells that fight bacterial infections.

Hematocrit (HCT) – ratio of red cells to plasma in the blood, the portion of the blood's total volume that is made up of red cells.

Hematopoiesis – the process by which blood cells are formed from stem cells in the bone marrow, including red blood cells, white blood cells and platelets.

Hematopoietic stem cells – cells in the bone marrow that grow and divide to make more stem cells as well as 'progenitor' blood cells that lead to the red cells, white cells and platelets.

Hemoglobin (HB or HGB) – the oxygen carrying pigment of the red cells; binds with oxygen in the lungs and is carried to the body's cells.

Hemorrhage – bleeding from any site in the body.

Leukopenia – low, total white blood cell count.

Lymphocytes (T-cell or B-cell) – cells of the immune system, critical for fighting disease and to help eliminate damaged cells.

Neutropenia – a low absolute neutrophil count (ANC), typically defined as below 1,500 per microliters of blood.

Neutrophil – (also known as Granulocyte) – a mature white blood cell that fights a bacterial infection.

Neutrophil chemotaxis (also known as neutrophil mobility) – movement of the neutrophils toward a bacterium or an area of tissue damage. Neutrophils must be able to migrate to the affected part of the body to fight off infections.

Pancytopenia – abnormally low number of all blood cells.

Petechiae – tiny red dots on the skin due to bleeding under the skin, usually caused by low platelet count.

Phagocytosis – engulfment and destruction of bacteria or damaged cells by some types of white blood cells, including neutrophils.

Plasma – yellowish fluid of the blood which contains cells, various proteins and other substances. Red cells, white cells and platelets are suspended in plasma.

Platelets (also known as Thrombocytes) – blood cells that prevent bleeding and bruising. Normal counts range from 150,000 to 400,000 per microliter of blood. They help to form a blood clot.

Platelet aggregation – the sticking of platelets to each other to form a clot. This ability can be evaluated by laboratory testing. Abnormal results reflect an increased tendency to bleed (poor clotting), despite a normal platelet count.

Red Blood Cells (RBC) – small round cells in blood that contain hemoglobin and are necessary to carry oxygen throughout the body. Red blood cells account for almost half of the blood volume.

Sepsis – infection of the blood stream or body tissues. Sepsis can be very serious and should be treated immediately.

Severe chronic neutropenia – a condition with susceptibility to recurrent infections where the ANC (absolute neutrophil count) is less than 500 per microliter of blood.

Thrombocytopenia – a condition in which the number of platelets is less than 100,000 per microliter of blood. Thrombocytopenia may increase the risk of bleeding.

White blood cells (WBC) – blood cells that fight infections. The normal count is about 8,000 per microliter of blood. There are several types of white blood cells (leukocytes), including the two most common types – lymphocytes and neutrophils.

BONE MARROW

Aplastic Anemia – a rare, but serious condition that results from the unexplained failure of the bone marrow to produce blood cells.

Myelodysplastic syndrome (MDS) – any of a group of diverse disorders in which the bone marrow does not produce sufficient healthy blood cells. Some of the blood cells present may exhibit abnormality in shape and size.

Blast cells – immature cells found in bone marrow. These cells are not fully developed, and are thus not able to carry out their eventual blood or immune cell functions.

Blast cell count for MDS – a bone marrow blast count under 20%.

Blast cell count to indicate AML (see below) – a bone marrow blast count over 20%.

Bone marrow – soft tissue within the bones where the various blood cells are manufactured.

Bone marrow aspiration – a liquid sample of the bone marrow is removed by needle aspiration (suction). The liquid sample can be used for examination and evaluation of blood cell precursors and to carry out cytogenetic analysis.

Bone Marrow Biopsy (BMB) – a solid core of bone marrow is removed with a biopsy needle. The biopsy is helpful in determining the cellularity of the marrow and can be used to carry out pathology investigations.

Colony stimulating factor and other blood cell growth factors (also known as a hematopoietic growth factors or cytokines) – protein factors produced by the body that stimulate the production of specific blood cells. Some of these proteins can be manufactured and used as treatments, including granulocyte stimulating factor (G-CSF or Neupogen) and various interleukins.

Hypocellular bone marrow – refers to an abnormally low volume ratio of haematopoietic cells (cells that make blood cells) in the marrow.

Leukemia – cancer of white blood cells with uncontrolled increase in total white blood cell count. Acute myelogenous leukemia (AML) is a type of leukemia that can involve white blood progenitor (or blast) cells.

Myelodysplastic syndrome (MDS) – any of a group of diverse disorders in which the bone marrow does not produce sufficient healthy blood cells. Some of the blood cells present may exhibit abnormality in shape and size.

Stroma – the supporting tissue for the bone marrow.

PANCREAS

Pancreas – a large gland that lies behind the stomach. It is made up two parts, the endocrine and the exocrine components.

Amylase (can be measured in the blood) – digestive enzyme produced by the salivary gland and the pancreas that breaks down ingested starches.

Diabetes Mellitus (diabetes) – a chronic condition with high levels of sugar in the blood. Diabetes occurs when the endocrine pancreas does not produce enough insulin or when tissues no longer respond to insulin. Insulin is the hormone made by the endocrine pancreas that is responsible for controlling the blood levels of glucose and for the absorption of glucose by tissues. Glucose is needed for energy.

Endocrine – the component of the pancreas that produces and secretes insulin and other hormones, that are necessary to control blood sugar levels.

Exocrine – the component of the pancreas that produces several digestive enzymes.

Lipase (can be measured in the blood) – digestive enzyme produced by the pancreas that breaks down ingested fats.

Malabsorption – when the body does not absorb adequate levels of nutrients, vitamins and minerals. Chronic malabsorption can impair normal growth and development. Failure of the exocrine pancreas (or exocrine pancreatic insufficiency) may cause malabsorption.

Medium chain triglycerides – fats which are most easily absorbed by the body. These can be found in palm oil and coconut oil, for example.

Pancreatic dysfunction or exocrine pancreatic dysfunction – failure of loss of digestive

enzyme production by the pancreas.

Pancreatic elastase (also known as elastase 1 or serine elastase; can be measured in the stool) – a digestive enzyme produced by the pancreas that helps to break-down ingested proteins

Pancreatic insufficiency – the state where the pancreas does not produce sufficient enzymes to digest food.

Pancreatic sufficiency – the state where the pancreas has some, but low function – that is sufficient for digestion (without the continuous need for pancreatic enzymes with meals).

Polyunsaturated fats – fats that are liquid at room temperature.

Steatorrhea – presence of excessive fat in the stool.

Trypsinogen (Trypsin; can be measured in the blood) – an important digestive enzyme produced by the pancreas that breaks down ingested proteins.

SKELETON

Coxa Vara – a deformity of the hip in which the angle between the neck and the head of the femur, and the shaft of the femur is reduced causing shortening of the leg and a limp.

Femur – the thigh bone.

DEXA (dual energy x-ray absorptiometry) scan – a type of bone scan that measures bone mineral density.

Genu varus – bowing outward of the legs at the knee joint.

Genu valgum – 'knock-knees' deformity. (The opposite, of genu varus).

Growth plate – the hyaline cartilage plate in the metaphysis at each end of a long bone. The plate is found in children and adolescents. In adults, who have stopped growing, the plate is replaced by an epiphyseal line.

Metaphysis – growth plates at the end of the long bones.

Metaphyseal chondrodysplasia – X-ray abnormalities of the growth plates.

Syndactyly – deformity in which two or more fingers or toes are joined together.

Thoracic dysplasia – an abnormality of growth, abnormal size or shape of the thorax. In SDS, this can include a narrow chest and short rib bones, as well as other skeletal anomalies.

Thorax – chest.

Tibia – bone of the lower leg, also called the shin.

GROWTH AND NUTRITION

Failure to thrive – growth failure in an infant or young child; can be due to inadequate food intake or excessive nutrient losses due to malabsorption.

Fat (or oil) soluble vitamins – Vitamins A, D, E and K; the vitamins that depend on normal digestion to be absorbed properly.

Growth velocity – the rate at which a child grows.

Short stature – below average height for age, *i.e.* short, but not necessarily malnourished.

Malnutrition – poor nutritional state due to inadequate food intake; can occur with a chronic disease or with malabsorption. It can also be associated with being underweight.

TERMS REFERRING TO OTHER ORGANS

Alanine aminotransferases (ALT) – enzymes predominantly produced by the liver with some from the kidney. ALTs can be found in the blood when the liver is stressed or damaged.

Cirrhosis of the liver – extensive scar tissue that forms as the result of damage to the liver; may lead to decreased liver function.

Endocardial fibrosis – damage to the lining of the heart and valves.

Hepatitis – an inflammation of the liver tissue. The most common causes are viruses leading to hepatitis types A, B, C, D and E. Drug or alcohol use can also contribute.

Hepatomegaly – enlarged liver, not necessarily reflecting impaired function.

Hypotonia – presence of poor muscle tone.

Ichthyosis – a condition in which the skin is dry, rough or scaly.

Immunodeficiency – reduced ability of the body's immune system to fight infections.

Non-alcoholic steatohepatitis (NASH) – inflammation that occurs with markedly elevated liver fat, *i.e.* a fatty liver.

Renal tubular dysfunction – a malfunction of the fine tubular part of the kidney, through

which water and certain substances are typically reabsorbed back into the blood.

Xerophthalmia – eye disorder caused by vitamin A deficiency; prolonged deficiency can result in severe damage to the cornea.