LYMPHATIC SYSTEM

The lymphatic system consists of lymph, lymphatic vessels, lymphatic tissue, lymphatic nodules, lymph nodes, tonsils, the spleen, and the thymus. The lymphatic system consists of a fluid called lymph, vessels called lymphatic vessels that transport the lymph, a number of structures and organs containing lymphatic tissue, and red bone marrow, where stem cells develop into the various types of blood cells, including lymphocytes. It assists in circulating body fluids and helps defend the body against disease-causing agents. As you will see shortly, most components of blood plasma filter through blood capillary walls to form interstitial fluid. After interstitial fluid passes into lymphatic vessels, it is called lymph. The major difference between interstitial fluid and lymph is location: Interstitial fluid is found between cells, and lymph is located within lymphatic vessels and lymphatic tissue.

LYMPHATIC VESSELS, CAPILLARIES AND LYMPH FLOW

1. Lymphatic vessels carry lymph away from tissues.
2. Lymphatic capillaries lack a basement membrane and have loosely overlapping epithelial cells. Fluids and other substances easily enter the lymphatic capillary.
3. Lymphatic capillaries join to form lymphatic vessels.
   ▪ Lymphatic vessels have valves that ensure the one-way flow of lymph.
   ▪ Contraction of lymphatic vessel smooth muscle, skeletal muscle action, and thoracic pressure changes move the lymph.
4. Lymph from the right thorax, the upper-right limb, and the right side of the head and the neck enters the right subclavian vein (often through the right lymphatic duct).
5. Lymph from the lower limbs, pelvis, and abdomen; the left thorax; the upper-left limb; and the left side of the head and the neck, enters the left subclavian vein through the thoracic duct.

FUNCTIONS

1. Fluid balance.
   Approximately 30 L of fluid pass from the blood capillaries into the interstitial spaces each day, whereas only 27 L pass from the interstitial spaces back into the blood capillaries. If the extra 3 L of fluid were to remain in the interstitial spaces, edema would result, causing tissue damage and eventual death. Instead, the 3 L of fluid enters the lymphatic capillaries, where the fluid is called lymph (limf, clear spring water), and it passes through the lymphatic vessels back to the blood. In addition to water, lymph contains solutes derived from two sources: (1) Substances in plasma, such as ions, nutrients, gases, and some proteins, pass from blood capillaries into the interstitial fluid and become part of the lymph and (2) substances derived from cells, such as hormones, enzymes, and waste products, are also found in the lymph.
2. Fat absorption.
   The lymphatic system absorbs fats and other substances from the digestive tract. Lymphatic capillaries called lacteals are located in the lining of the small intestine. Fats enter the lacteals and pass through the lymphatic vessels to the venous circulation. The lymph passing through these lymphatic vessels, called chyle, has a milky appearance because of its fat content.
Pathogens are filtered from lymph by lymph nodes and from blood by the spleen. In addition, lymphocytes and other cells are capable of destroying pathogens.

**LYMPHATIC CAPILLARIES, LYMPHATIC VESSELS**

The lymphatic system, unlike the circulatory system, does not circulate fluid to and from tissues. Instead, the lymphatic system carries fluid in one direction, from tissues to the circulatory system. Fluid moves from blood capillaries into the interstitial spaces. Most of the fluid returns to the blood, but some of the fluid moves from the interstitial spaces into lymphatic capillaries to become lymph. The lymphatic capillaries are tiny, closed-ended vessels consisting of simple squamous epithelium. Lymphatic capillaries differ from blood capillaries in that they lack a basement membrane and the cells of the simple squamous epithelium slightly overlap and are attached loosely to one another. Two things occur as a result of this structure. First, the lymphatic capillaries are far more permeable than blood capillaries, and nothing in the interstitial fluid is excluded from the lymphatic capillaries. Second, the lymphatic capillary epithelium functions as a series of one-way valves that allow fluid to enter the capillary but prevent it from passing back into the interstitial spaces. The lymphatic capillaries join to form larger lymphatic vessels, which resemble small veins. Small lymphatic vessels have a beaded appearance because of one-way valves that are similar to the valves of veins. When a lymphatic vessel is compressed, the valves prevent the backward movement of lymph. Consequently, compression of lymphatic vessels causes lymph to move forward through them.

**THREE FACTORS CAUSING COMPRESSION OF THE LYMPHATIC VESSELS**

1. The periodic contraction of smooth muscle in the lymphatic vessel wall.
2. The contraction of surrounding skeletal muscle during activity.
3. Pressure changes in the thorax during respiration. The lymphatic vessels converge and eventually empty into the blood at two locations in the body. Lymphatic vessels from the right upper limb and the right half of the head, neck, and chest empty into the right subclavian vein. These lymphatic vessels often converge to form a short duct, 1 cm in length, called the right lymphatic duct, which connects to the subclavian vein. Lymphatic vessels from the rest of the body enter the thoracic duct which empties into the left subclavian vein. The thoracic duct is the largest lymphatic vessel. It is approximately 38–45 cm in length, extending from the twelfth thoracic vertebra to the base of the neck.

**FORMATION AND LYMPH FLOW**

Most components of blood plasma filter freely through the capillary walls to form interstitial fluid, but more fluid filters out of blood capillaries than returns to them by reabsorption. The excess filtered fluid—about 3 liters per day—drains into lymphatic vessels and becomes lymph. Because most plasma proteins are too large to leave blood vessels, interstitial fluid contains only a small amount of protein. Proteins that do leave blood plasma cannot return to the blood by diffusion because the concentration gradient (high level of proteins inside blood capillaries, low level outside)
opposes such movement. The proteins can, however, move readily through the more permeable lymphatic capillaries into lymph. Thus, an important function of lymphatic vessels is to return the lost plasma proteins to the bloodstream.

LYMPHATIC ORGANS AND TISSUES

TISSUES:

Lymphatic tissue is reticular connective tissue that contains lymphocytes and other cells.

2. Lymphatic tissue can be surrounded by a capsule (lymph nodes, spleen, thymus).

3. Lymphatic tissue can be nonencapsulated (diff use lymphatic tissue, lymphatic nodules, tonsils).

4. Diffuse lymphatic tissue consists of dispersed lymphocytes and has no clear boundaries.

5. Lymphatic nodules are small aggregates of lymphatic tissue (e.g., Peyer’s patches in the small intestines).

ORGANS:

1. The tonsils

   ▪ The tonsils are large groups of lymphatic nodules in the oral cavity and nasopharynx.

   ▪ The three groups of tonsils are the palatine, pharyngeal, and lingual tonsils.

2. Lymph nodes

   ▪ Lymphatic tissue in the node is organized into the cortex and the medulla. Lymphatic sinuses extend through the lymphatic tissue.

   ▪ Substances in lymph are removed by phagocytosis, or they stimulate lymphocytes (or both).

   ▪ Lymphocytes leave the lymph node and circulate to other tissues.

3. The spleen

   ▪ The spleen is in the left superior side of the abdomen.

   ▪ Foreign substances stimulate lymphocytes in the white pulp.

   ▪ Foreign substances and defective red blood cells are removed from the blood by phagocytes in the red pulp.

   ▪ The spleen is a limited reservoir for blood.

4. The thymus

   ▪ The thymus is a gland in the superior mediastinum and is divided into a cortex and a medulla.

   ▪ Lymphocytes in the cortex are separated from the blood by epithelial cells.

   ▪ Lymphocytes produced in the cortex migrate through the medulla, enter the blood, and travel to other lymphatic tissues, where they can proliferate.

IMMUNITY

• Ability to resist damage from pathogens and internal threats
• Prevents the entry of pathogens into the body and eliminates them
• Categorized as innate immunity and adaptive immunity

Innate Immunity

• Recognizes general types of microorganisms
• Rapid response (within hours to days)
• Intimately linked to adaptive immunity
• Provides a general, first line of defense against pathogens
• Initiates and helps regulate adaptive immune response

Adaptive Immunity

• Slow response (days to weeks)
• Takes many days to destroy a particular pathogen
• We develop immunological memory, ability of adaptive immunity to “remember” previous encounters with a particular pathogen. Upon second exposure to the same pathogen, adaptive response “remembers” the pathogen and responds rapidly and effectively
• Powerful second line of defense that uses many of the components of innate immunity to destroy pathogens

Immune cells
Communicates with each other and with other cell types by secreting cytokines, proteins or peptides that bind to receptors on neighboring cells, stimulating a response.

Cytokines
  - **Fx**: attracts other immune cells to sites of infections, promotes phagocytosis and inflammation, regulates the intensity and duration of innate and adaptive immune response.

Overview of Lymphatic System

B Cells and T Cells
  - Primary adaptive immunity cells
  - Lymphocytes with receptors that bind to antigens
  - Antigens bind to B-cells, the B cells divide and differentiate to form plasma cells which produce and secrete antibodies which are proteins that bind to the antigen that stimulated their production.
  - Antigens bind to T cells results in the formation of cytotoxic T cells, which kill other cells, and helper T cells, which secrete cytokines that regulate the activities of B cells, cytotoxic T cells, and other immune cells.

Innate Immunity Cells
  - **Pathogen-Associated Molecular Patterns**
    - Molecules common to groups of pathogens but are not found in humans
  - **Toll-like receptors**
    - Most important family of innate immunity receptors

Neutrophils
  - Small, motile, phagocytic white blood cells.
  - Contain a battery of destructive chemicals stored in an inactive form as granules.
  - Effective at ingesting and killing bacteria
  - First cells to leave the blood and enter infected tissues
Unable to replenish their granules and are programmed to die by *apoptosis* after phagocytosis

- *Pus*, accumulation of dead neutrophils, dead microorganisms, debris from dead tissue
- Secretes cytokines that recruit and activate other white blood cells and promote inflammation

**Monocytes**

- White blood cells that leave the blood, enter tissues, and enlarge to become macrophages
- *Macrophages*, large, motile, phagocytic cells that outlive neutrophils. They are responsible for most phagocytic activity in the late stages of infection
- Secretes cytokines that recruit and activate other white blood cells and promote inflammation

### Immune Cells and Their Primary Functions

<table>
<thead>
<tr>
<th>Cell</th>
<th>Primary Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Innate Immunity</td>
<td></td>
</tr>
<tr>
<td>Neutrophil</td>
<td>Phagocytosis and inflammation</td>
</tr>
<tr>
<td>Monocyte</td>
<td>Leaves the blood and enters tissues to become a macrophage</td>
</tr>
<tr>
<td>Macrophage</td>
<td>Phagocytosis and inflammation; located throughout the body to &quot;intercept&quot; foreign substances; processes antigens and is involved in the activation of B cells and T cells</td>
</tr>
<tr>
<td>Dendritic cell</td>
<td>Detects pathogens and recruits other immune cells to sites of infection; processes antigen and is involved in the activation of B cells and T cells</td>
</tr>
<tr>
<td>Natural killer cell</td>
<td>Kills virus-infected cells and tumor cells</td>
</tr>
<tr>
<td>Mast cell</td>
<td>Detects pathogens and recruits other immune cells to sites of infection; releases chemicals that promote inflammation</td>
</tr>
<tr>
<td>Basophil</td>
<td>Releases chemicals that promote inflammation</td>
</tr>
<tr>
<td>Adaptive Immunity</td>
<td></td>
</tr>
<tr>
<td>Eosinophil</td>
<td>Releases chemicals that promote inflammation and kills worm parasites</td>
</tr>
<tr>
<td>B cell</td>
<td>Divides and differentiates to become plasma cells or memory B cells</td>
</tr>
<tr>
<td>Plasma cell</td>
<td>Produces antibodies that are directly or indirectly responsible for destroying antigens</td>
</tr>
<tr>
<td>Memory B cell</td>
<td>Provides a quick and effective response to an antigen against which adaptive immunity has previously reacted</td>
</tr>
<tr>
<td>Cytotoxic T cell</td>
<td>Responsible for destroying cells by apoptosis or producing cytokines</td>
</tr>
<tr>
<td>Helper T cell</td>
<td>Regulates B cells and cytotoxic T cells</td>
</tr>
<tr>
<td>Memory T cell</td>
<td>Provides a quick and effective response to an antigen against which adaptive immunity has previously reacted</td>
</tr>
</tbody>
</table>

**Dendritic cells**

- Large, motile cells with long, cytoplasmic extension
- Highly concentrated in lymphatic tissues and skin

**Dendritic Cells**

- Large, motile cells with long, cytoplasmic extensions
- Highly concentrated in lymphatic tissues and skin
- Dendritic cells in the skin are often called *Langerhans cells*

**Natural Killer Cells**

- White blood cells, comprising 5%-20% of lymphocytes.
- Recognize and kill classes of host cells.

**Mast Cells**

- Nonmotile cells in connective tissue

**Basophils**

- White blood cells containing granules that are similar to mast cells.
- Promotes inflammation
- Activated through their innate immunity receptors and antibodies

**Eosinophils**

- White blood cells that can move from the blood into infected tissues in response to...
cytokines released by mast cells and other cells.

- Granules of eosinophils include cytotoxic and neurotoxin proteins that can be released to kill multicellular worm parasites, which are too large to be ingested and killed by phagocytosis.
- Release toxic and inflammatory mediators through an adaptive immune response.

**Innate Immunity**

- Epithelial barriers prevent the entry of pathogens or kill them.
- Extracellular pathogens are outside of host cells, whereas intracellular pathogens are inside.

### Chemical Mediators of Innate Immunity and Their Functions

<table>
<thead>
<tr>
<th>Chemical</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complement</td>
<td>Complement is a group of plasma proteins that increase vascular permeability, stimulate the release of histamine, activate kinins, lyse cells, promote phagocytosis, and attract neutrophils, monocytes, macrophages, and eosinophils.</td>
</tr>
<tr>
<td>Cytokines</td>
<td>Cytokines are proteins or peptides that function as mediators of immune and inflammatory responses; secreted mainly by macrophages and NK cells in innate immunity and by B cells and T cells in adaptive immunity (see table 19.1).</td>
</tr>
<tr>
<td>Defensins</td>
<td>Defensins are peptides produced by neutrophils and epithelial cells that disrupt microbial membranes.</td>
</tr>
<tr>
<td>Histamine</td>
<td>Histamine is an amine released from mast cells, basophils, and platelets; histamine causes vasodilation, increases vascular permeability, stimulates gland secretions (especially mucus and tear production), causes smooth muscle contraction of airway passages (bronchioles) in the lungs, and attracts eosinophils.</td>
</tr>
<tr>
<td>Interferons</td>
<td>Interferons are proteins, produced by most cells, that interfere with virus production and infection.</td>
</tr>
<tr>
<td>Kinins</td>
<td>Kinins are polypeptides derived from plasma proteins; kinins cause vasodilation, increase vascular permeability, stimulate pain receptors, and attract neutrophils.</td>
</tr>
<tr>
<td>Leukotrienes</td>
<td>Leukotrienes are a group of lipids, produced primarily by mast cells and basophils, that cause prolonged smooth muscle contraction (especially in the lung bronchioles), increase vascular permeability, and attract neutrophils and eosinophils.</td>
</tr>
<tr>
<td>Prostaglandins</td>
<td>Prostaglandins are a group of lipids (PGEs, PGFs, thromboxanes, and prostacyclins), some of which cause smooth muscle relaxation and vasodilation, increase vascular permeability, and stimulate pain receptors.</td>
</tr>
<tr>
<td>Pynogens</td>
<td>Pynogens are chemicals, released by neutrophils, monocytes, and other cells, that stimulate fever production.</td>
</tr>
<tr>
<td>Surface chemicals</td>
<td>Surface chemicals (Lysozymes in tears, saliva, nasal secretions, and sweat) lyse cells; defensins (antimicrobial peptides produced by all epithelia) and acid secretions (sebum in the skin and hydrochloric acid in the stomach) prevent microbial growth or kill pathogens; mucus on the mucous membranes traps pathogens until they can be destroyed.</td>
</tr>
</tbody>
</table>

**Adaptive Immunity**

- B cells are responsible for antibody-mediated immunity, which protects against extracellular pathogens.
- T cells are responsible for cell-mediated immunity, which protects against intracellular pathogens.
- Origin and maturation of lymphocytes:
  - B cells and T cells originate in red marrow. B cells in red bone marrow and T cells mature in Thymus.
  - Blood-thymus barrier prevents the entry of foreign antigens into the thymus.
- Naive Lymphocytes:
  - Mature helper T cell, cytotoxic T cell, or B cell that has not been exposed to the antigen for which it is specific.
  - Dendrite cells and macrophages present antigens to naïve lymphocytes.

**Immunological Tolerance**

- Is suppression of the immune response to an antigen.

**Immunotherapy**

- Stimulates or inhibits the immune response to treat diseases.
Acquired Immunity

- **Active Natural Immunity**
  - Results from natural exposure to an antigen
- **Active Artificial Immunity**
  - Results from deliberate exposure to an antigen
- **Passive Natural Immunity**
  - Results from the transfer of antibodies from a mother to her fetus or baby
- **Passive Artificial Immunity**
  - Results from the transfer of antibodies (or cells) from an immune animal to a nonimmune animal

Common diseases and disorders in LYMPHATIC SYSTEM

Since the lymphatic system is responsible for draining excess fluid from tissues and organs, the most common symptom of diseases and disorders of the lymphatic system is swelling. For example, a disease known as elephantiasis, which is caused by a filarial worm infestation, involves the blockage of the lymphatics. When the lymphatics are blocked, fluid cannot be drained and swelling occurs in the affected areas. Administering ethyl-carbamazine drugs, elevating the area and wearing a compression stocking can treat elephantiasis.

Tonsillitis is another disease of the lymphatic system. Tonsillitis usually involves a bacterial or viral infection located within the tonsils. The tonsils are swollen, and the patient experiences a fever, sore throat, and difficulty swallowing. This can be treated by the use of antibiotics or through a surgical procedure called a tonsillectomy.

A condition common among individuals following surgery for breast cancer or prostate cancer is lymphedema. It is caused by blockage of lymph vessels or lymph nodes located near the surgical site and can result in swollen arms or legs. If microorganisms cause the swelling, then antibiotics are used as treatment. If microorganisms are not the cause, then compression garments and message therapy are used as treatment.

There are also cancers called lymphosarcomas and cancers of the lymph nodes that can affect the lymphatic system. The causes of these cancers are not known and there is not a consensus on what preventative measures can be taken to reduce the risk of developing these cancers. Symptoms of cancers affecting the lymphatic system include loss of appetite, energy, and weight, as well as swelling of the glands. As with many cancers, treatment includes surgical removal followed by adjuvant radiation and chemotherapy.

**SOURCE: BOOKS**


**DISEASES OF IMMUNE SYSTEM**

- **Asthma**

Asthma affects more than 5% of the population of the US, including children. It is a chronic inflammatory disorder of the airways characterized by coughing, shortness of breath, and chest tightness. A variety of "triggers" may initiate or worsen an
Asthma attack, including viral respiratory infections, exercise, and exposure to irritants such as tobacco smoke. The physiological symptoms of asthma are a narrowing of the airways caused by edema (fluid in the intracellular tissue space) and the influx of inflammatory cells into the walls of the airways.

Asthma is a what is known as a "complex" heritable disease. This means that there are a number of genes that contribute toward a person's susceptibility to a disease, and in the case of asthma, chromosomes 5, 6, 11, 14, and 12 have all been implicated. The relative roles of these genes in asthma predisposition are not clear, but one of the most promising sites for investigation is on chromosome 5. Although a gene for asthma from this site has not yet been specifically identified, it is known that this region is rich in genes coding for key molecules in the inflammatory response seen in asthma, including cytokines, growth factors, and growth factor receptors.

The search for specific asthma genes is ongoing. Assisting in this international human effort are model organisms such as mice, which have similar chromosomal architecture to our chromosome 5 site on their chromosomes 11, 13, and 18. Further study of the genes in these areas (and others) of the human genome will implicate specific genes involved in asthma and perhaps also suggest related biological pathways that play a role in the pathogenesis of asthma.

- Immunodeficiency with hyper-IgM

Immunodeficiency with hyper-IgM (HIM) is a rare primary immunodeficiency characterized by the production of normal to increased amounts of IgM antibody of questionable quality and an inability to produce sufficient quantities of IgG and IgA. Individuals with HIM are susceptible to recurrent bacterial infections and are at an increased risk of autoimmune disorders and cancer at an early age.

In a normal immune response to a new antigen, B cells first produce IgM antibody. Later, the B cells switch to produce IgG, IgA and IgE, antibodies that protect tissues and mucosal surfaces more effectively. In the most common form of HIM there is a defect in the gene TNFSF5, found on chromosome X at q26. This gene normally produces a CD40 antigen ligand (CD154), a protein on T cells which binds to the CD40 receptor on B and other immune cells. Without CD154, B cells are unable to receive signals from T cells, and thus fail to switch antibody production to IgA and IgG. The absence of CD 40 signals between other immune cells makes individuals with HIM susceptible to infections by opportunistic organisms such as Pneumocystis and Cryptosporidium species.

- Diabetes

Diabetes is a chronic metabolic disorder that adversely affects the body's ability to manufacture and use insulin, a hormone necessary for the conversion of food into energy. The disease greatly increases the risk of blindness, heart disease, kidney failure, neurological disease, and other conditions for the approximately 16 million Americans who are affected by it. Type 1, or juvenile onset diabetes, is the more severe form of the illness.

Type 1 diabetes is what is known as a 'complex trait', which means that mutations in several genes likely contribute to the disease. For example, it is now known that the insulin-dependent diabetes mellitus (IDDM1) locus on chromosome 6 may harbor at least one susceptibility gene for Type 1 diabetes. Exactly how a mutation at this locus adds to patient risk is not clear, although a gene maps to the region of chromosome 6 that also has genes for antigens (the molecules that normally tell the immune system not to attack itself). In Type 1 diabetes, the body's immune system mounts an immunological assault on its own insulin and the pancreatic cells that manufacture it. However, the mechanism of how this happens is not yet understood.

About 10 loci in the human genome have now been found that seem to confer susceptibility to Type 1 diabetes. Among these are 1) a gene at the locus IDDM2 on chromosome 11 and 2) the gene for glucokinase (GCK), an enzyme that is key to glucose metabolism which helps modulate insulin secretion, on chromosome 7. Conscientious patient care and daily insulin dosages can keep patients comparatively healthy. But in order to prevent the immunoresponses that often cause diabetes, we will need to experiment further with mouse models of the disease and advance our understanding of how genes on other chromosomes might add to a patient's risk of diabetes.
- DiGeorge syndrome is a rare congenital (i.e. present at birth) disease whose symptoms vary greatly between individuals but commonly include a history of recurrent infection, heart defects, and characteristic facial features.

DiGeorge syndrome is caused by a large deletion from chromosome 22, produced by an error in recombination at meiosis (the process that creates germ cells and ensures genetic variation in the offspring). This deletion means that several genes from this region are not present in DiGeorge syndrome patients. It appears that the variation in the symptoms of the disease is related to the amount of genetic material lost in the chromosomal deletion.

Although researchers now know that the DGS gene is required for the normal development of the thymus and related glands, counteracting the loss of DGS is difficult. Some effects, for example the cardiac problems and some of the speech impairments, can be treated either surgically or therapeutically, but the loss of immune system T-cells (produced by the thymus) is more challenging and requires further research on recombination and immune function.

- Burkitt lymphoma is a rare form of cancer predominantly affecting young children in Central Africa, but the disease has also been reported in other areas. The form seen in Africa seems to be associated with infection by the Epstein-Barr virus, although the pathogenic mechanism is unclear. Burkitt lymphoma results from chromosome translocations that involve the Myc gene. A chromosome translocation means that a chromosome is broken, which allows it to associate with parts of other chromosomes. The classic chromosome translocation in Burkitt lymphoma involves chromosome 8, the site of the Myc gene. This changes the pattern of Myc's expression, thereby disrupting its usual function in controlling cell growth and proliferation. We are still not sure what causes chromosome translocation. However, research in model organisms such as mice is leading us toward a better understanding of how translocations occur and, hopefully, how this process contributes to Burkitt lymphoma and other cancers such as leukemia.

- Severe combined immunodeficiency (SCID) represents a group of rare, sometimes fatal, congenital disorders characterized by little or no immune response. The defining feature of SCID, commonly known as "bubble boy" disease, is a defect in the specialized white blood cells (B- and T-lymphocytes) that defend us from infection by viruses, bacteria and fungi. Without a functional immune system, SCID patients are susceptible to recurrent infections such as pneumonia, meningitis and chicken pox, and can die before the first year of life. Though invasive, new treatments such as bone marrow and stem-cell transplantation save as many as 80% of SCID patients.

All forms of SCID are inherited, with as many as half of SCID cases linked to the X chromosome, passed on by the mother. X-linked SCID results from a mutation in the interleukin 2 receptor gamma (IL2RG) gene which produces the common gamma chain subunit, a component of several IL receptors. IL2RG activates an important signalling molecule, JAK3. A mutation in JAK3, located on chromosome 19, can also result in SCID. Defective IL receptors and IL receptor pathways prevent the proper development of T-lymphocytes that play a key role in identifying invading agents as well as activating and regulating other cells of the immune system.

In another form of SCID, there is a lack of the enzyme adenosine deaminase (ADA), coded for by a gene on chromosome 20. This means that the substrates for this enzyme accumulate in cells. Immature lymphoid cells of the immune system are particularly sensitive to the toxic effects of these unused substrates, so fail to reach maturity. As a result, the immune system of the afflicted individual is severely compromised or completely lacking.

Some of the most promising developments in the search for new therapies for SCID center on 'SCID mice', which can be bred deficient in various genes including ADA, JAK3, and IL2RG. It is now possible to reconstitute the impaired mouse immune system by using human components, so these animals provide a very useful model for studying both normal and pathological immune systems in biomedical research.

- Familial Mediterranean fever (FMF) occurs most commonly in people of non-Ashkenazi Jewish, Armenian, Arab, and Turkish background. As many as 1 in 200 people in these populations have the disease, with as many as 1 in 5 acting
as a disease carrier. FMF is an inherited disorder usually characterized by recurrent episodes of fever and peritonitis (inflammation of the abdominal membrane).

In 1997, researchers identified the gene for FMF and found several different gene mutations that cause this inherited rheumatic disease. The gene, found on chromosome 16, codes for a protein that is found almost exclusively in granulocytes—white blood cells important in the immune response. The protein is likely to normally assist in keeping inflammation under control by deactivating the immune response—without this "brake," an inappropriate full-blown inflammatory reaction occurs: an attack of FMF.

Discovery of the gene mutations will allow the development of a simple diagnostic blood test for FMF. With identification of the mutant protein, it may be easier to recognize environmental triggers that lead to attacks and may lead to new treatments for not only FMF but also other inflammatory diseases.