

Facts about blood cancer

A guide for patients and healthcare professionals

What is blood cancer?

When a problem develops with white blood cells, blood cancers can occur.

The white blood cells will stop working properly and can multiply, stopping the normal function of blood, such as fighting infection, stopping bleeding or healing wounds. Malignant white cells may also multiply and cause swelling of the lymph glands, small swellings in the lymphatic system.

What causes blood cancer?

Blood cells are made in the bone marrow. Everyday millions of new blood cells are made to replace those that are old and worn out, and within each cell is DNA, a genetic code controlling how all our cells behave.

When a cell divides to make a new copy of itself the DNA replicates, but sometimes this process goes wrong resulting in mistakes in the DNA code. This is called a genetic mutation. When the DNA in any cell carries a mistake or mutation it may behave abnormally – for example, it may grow and divide uncontrollably, it may not die when it should, or it may fail to mature normally. Genetic mutations in the DNA of white blood cells can cause blood cancer.

These mutations usually occur spontaneously, but there are some circumstances where the mutations causing blood cancer may be more common, for example in people who have previously had chemotherapy or radiotherapy to treat other cancers.

As we age mutations become more common which is why blood cancers affect older people more than younger people. It is very rare for the mutation responsible for a blood cancer to be passed through the family. Unlike many other cancers, lifestyle habits such as diet, exercise, weight and smoking have little impact on the development of blood cancer.

Blood facts

- Blood is produced in the bone marrow found in the middle of some of our bones, such as the pelvis, long bones of the arms and legs, ribs, and vertebrae.
- There are three types of blood cells; red cells, platelet cells and white cells.

Red Cells	contain hemoglobin, a protein that carries oxygen around the body
Platelet cells	are tiny blood cells that help your body form clots to stop bleeding.
White cells	are part of the body's immune system – they help the body fight infection and other diseases.

- The lymphatic system is a network of tissues and organs that help rid the body of toxins. The mature cells we see in the blood and lymphatic system of the body, develop from immature stem cells that live in the bone marrow.
- Once matured, the early stem cells have the capacity to produce all types of blood cells and can multiply them. They are the everlasting 'seeds' of the bone marrow.
- The blood that is found in a new born baby's umbilical cord and placenta is very rich in stem cells.

Cancer facts

- Blood cancers develop from the mutations of different types of white blood cells found in our blood, bone marrow and lymphatic system.
- Blood cancer is the fifth most common type of cancer in the UK.
- There are over 100 types of blood cancer, many of which are extremely rare.
- There are more than 240,000 patients living with blood cancer in the UK, with over
- 40,000 new cases diagnosed every year



What are the symptoms?

Symptoms of blood cancer can vary according to the type of cancer. However, the most common symptoms include:

Fatigue	Fevers and
Easy bruising or bleeding	Weight loss
Frequent infections	Bone pain
Swollen lymph glands in	Itchy skin
the neck, armpit or groin	

sweats

It is important to note that not everyone will have the same symptoms, and many non-cancer related illnesses, such as viral infections, can produce similar symptoms.

How is it diagnosed?

Blood cancer is usually diagnosed with a combination of blood tests and biopsies of the bone marrow or lymph glands. Early signs of some blood cancers can be picked-up incidentally when blood tests are done for other reasons

Types of blood cancer

There are three main types of blood cancer.

Leukaemia – a cancer of the white blood cells that originates in the bone marrow. This form of cancer produces too many immature white blood cells which stop the body from producing the other types of cells which are essential for the immune system.

Lymphoma – a cancer of a specific type of white cell called a lymphocyte. Lymphocytes are part of the immune system and are found in your blood, bone marrow, lymph glands and spleen. This form of cancer is caused by lymphocytes not dying when they should or not dividing normally. **Myeloma** - a cancer of the plasma cells, a white blood cell, found in the bone marrow. This form of cancer is caused by plasma cells multiplying uncontrollably in the bone marrow, which interferes with the production of red blood cells, causing anaemia and bone damage.

Within these three main types of blood cancer, there are many different variations, all with slightly differing symptoms, treatments and prognoses.

Leukaemia

Leukaemia is a cancer characterised by the accumulation of cancerous white blood cells in the bone marrow which then spill out into the blood.

There are many types of leukaemia, but the four most common types are:

- Acute myeloid leukaemia (AML)
- Chronic myeloid leukaemia (CML)
- Acute lymphoblastic leukaemia (ALL)
- Chronic lymphocytic leukaemia (CLL)



Acute Myeloid Leukaemia

AML is the most common form of acute leukaemia in adults over 60. However, it can affect people of all ages but is known to be rare in children. Symptoms include fatigue, bleeding and infection. There are many types of AML with differing underlying genetic mutations which have differing prognoses. It may occur out of the blue or after a pre-existing blood condition such as myelodysplasia or myeloproliferative disease.

AML may also be triggered by damage to the bone marrow as a result of radiation or chemotherapy exposure given to treat other diseases or cancers. If untreated, AML is rapidly fatal but with modern treatments many patients are cured.



Acute Lymphocytic Leukemia

ALL is the most common childhood leukaemia with 75% of cases occurring before the age of six. In adults it is less common than AML. ALL's symptoms are similar to those of bone marrow failure but include bone pain and swollen lymph glands. ALL may also affect the nervous system and present visual problems or testicular swelling in male patients. Treatment of ALL depends on the age and fitness of the patient. Supportive care medications will treat bleeding and infection, while blood transfusions are usually given to all patients. Those who are young and fit may be given high dose chemotherapy and donor stem cell transplants which offer a potential cure.

New targeted molecular drugs are now being commonly used to directly inhibit some of the DNA mutations found in AML and ALL.

Chronic Lymphocytic Leukaemia

CLL is a chronic slow-growing leukaemia affecting mature white blood cells called B lymphocytes. It is the most common type of leukaemia in adults but does not affect children. Around 1 in 200 people will develop CLL in their lifetime.

CLL presents no symptoms and is only diagnosed when patients have blood tests done for other reasons. However, if advanced it may present the signs and symptoms of bone marrow failure or swollen glands.

Many patients with CLL, particularly at an early stage, may not require treatment, although patients with a more aggressive disease will be treated with a combination of chemotherapy (commonly in tablet form) and immunotherapy.

Immunotherapy consists of antibodies, an immune protein made in a laboratory, being circulated into the body through an intravenous infusion, commonly known as an IV drip. The antibody treatment specifically targets the leukaemia cells



and, in combination with the chemotherapy, kills the leukaemia cells. There are also molecular targeted therapies directed at the underlying genetic makeup of CLL cells which are available for some patients. CLL is currently not considered to be curable but most patients will live many years with CLL.

Chronic Myeloid Leukaemia

CML accounts for approximately 15% of all leukaemia and can occur at any age, but most commonly between the ages of 40-60. In 50% of cases the diagnosis is made incidentally but symptoms can include fever, weight loss and an enlarged spleen. The spleen may be grossly enlarged in CML and cause abdominal pain, lack of appetite and a feeling of fullness.

The DNA in our cells is arranged into 46 chromosomes. Chromosomes are divided into sections called genes which control all of our body's functions. In CML chromosomes 9 and 22 become mixed up, producing a small chromosome called the Philadelphia chromosome.

The Philadelphia chromosome contains a new gene called BCR ABL which causes blood cells to divide faster and live longer than they should. It is not known why this occurs but it is not inherited and the chromosome does not pass on through generations. There are three phases of CML - chronic phase, accelerated phase and blast crisis.

Most patients are diagnosed in the chronic phase and are treated relatively easily with drugs called tyrosine kinases inhibitors, a substance that blocks the active and high levels of enzymes found in some types of cancer cells, and directly targets the BCR ABL gene. Blocking chemical messengers can stop bad cells from growing and dividing. With tyrosine kinase therapy most patients now live for many years with nearly a normal quality of life. It is thought that in some cases CML may be now curable in those patients who make a full response to the tyrosine kinases.

If CML is left untreated it may progress to a more aggressive form, known as the "accelerated phase" and from there to "blast crisis", which is the same as acute leukaemia. Patients with accelerated phase and blasts crisis require chemotherapy and stem cell transplants, as well as tyrosine kinases.

Lymphoma

Lymphoma is a cancer of the white blood cells that make up the immune system – the **lymphocytes**. This form of cancer is caused by lymphocytes (the white cells that normally fight infection), not dying when they should or not dividing normally. Lymphocytes are found in the blood, bone marrow, lymph glands and spleen. Symptoms of lymphoma include swollen lymph glands in the neck, armpit or groin.

There are two main types of lymphoma; Hodgkin lymphoma and Non-Hodgkin lymphoma.

Hodgkin Lymphoma

Around 2,000 people in the UK are diagnosed with Hodgkin lymphoma each year, and it is most common in young adults below 40 years of age. Firm, non-tender enlarged lymph glands are a common symptom, and 60% of the time these are found in the neck. Patients with lymph node areas may also have fevers and suffer from weight loss, night sweats, itching or pain in the swollen glands when drinking alcohol.

A diagnosis for Hodgkin lymphoma is made by taking a biopsy for a lymph node, and is usually treated with a combination of chemotherapy, with or without radiotherapy. 85% of patients are cured.

Non-Hodgkin Lymphoma

There are many types of Non-Hodgkin lymphoma. Their presentation and prognosis vary more than Hodgkin lymphoma, and can involve many organs and mimic many diseases. The most common symptoms include swollen lymph glands and / or fevers, sweats and weight loss.

There are two types of lymphocytes; B cell and T cell, which can develop into Non-Hodgkin lymphoma.

B cell Non-Hodgkin lymphoma is a more common type of cancer and the treatment is usually a combination of chemotherapy and immunotherapy, using monoclonal antibodies against B cells.

Every year in the UK around 12,000 people are diagnosed with this form of cancer. Non-Hodgkin lymphoma can be further divided into low grade and high-grade cancer.

- Low grade is a slow growing, less aggressive disease, but it is considered to be incurable.
- High grade develops quickly and is often associated with fevers and sweats.
 It is considered curable in some cases.



Myeloma

Myeloma is a cancer of white cells called plasma cells. Plasma cells live in our bone marrow and are responsible for producing the antibodies that help us fight infection. When a plasma cell becomes malignant it reproduces itself many times and takes over the bone marrow.

The malignant plasma cells form clusters that affect the bones either side of the marrow causing holes called lytic lesions. These can be painful and eventually make the bone so weak it can break. Common places for fractures and bone pain in patients with myeloma include the vertebrae, ribs, breast bone, pelvis and arm and leg bones. In destroying bones in the body, plasma cells release large amounts of calcium into the blood. When the myeloma replaces enough of the good bone marrow, the production of blood reduces and anaemia can develop.

Malignant plasma cells still produce antibodies but in a defective way. When there are large amounts of plasma cells the antibody they produce, called a monoclonal protein or para protein, can be measured in the blood or urine.



In high enough quantities the monoclonal protein can damage the kidneys.

It is very common to have a small number of abnormal plasma cells producing a monoclonal protein as we get older. 3-4% of those over 50 and 10% of those over 85 will have a monoclonal protein. This is called monoclonal gammopathy of uncertain significance - MGUS.

Patients with MGUS have a small number of cancerous plasma cells and a small level of monoclonal protein with no damage. The diagnosis of myeloma is made when the cancerous plasma cells increase and begin to cause damage to the blood, bone or kidneys. This is much rarer than MGUS.

Patients with MGUS do not need treating but they do need monitoring to prevent myeloma.

When a patient is diagnosed with myeloma, they will need urgent treatment to protect the bones and kidneys from further damage. The treatment of myeloma varies depending on the age and fitness of the patient. There are many types of chemotherapy and immunotherapy used to treat myeloma. Myeloma cannot be cured but the outlook is significantly better than it was 15 years ago, with patients living in excess of 10 years from diagnosis.

Types of treatment

Blood cancer treatments vary depending on the type of cancer diagnosed. For many of the chronic blood cancers, especially those that are not causing symptoms, doctors adopt a 'watch and wait' strategy. This is because there is no evidence that treating early blood cancer, which shows no symptoms, is of benefit to the patient, and many patients go on to require no treatment at all.

If a patient has a more acute or serious form of blood cancer, or is developing symptoms, then treatment is given. Surgery is not used to treat blood cancer, as cancerous white cells are found throughout the body and cannot be physically removed. However, surgery such as a biopsy may be used to diagnose some types of blood cancer, by removing small pieces of tissue from the abnormal area to see if it contains cancer cells.

Types of treatment include:

- **Chemotherapy** drugs given by mouth or administered by intravenous therapy (IV) that directly kills cancer cells by interrupting the cancer cells growing.
- **Immunotherapy** drugs called monoclonal antibodies are used to directly target cancer cells and help the immune system to fight cancer.
- **Radiation therapy** ionising radiation is used to kill rapidly growing cells.
- **Targeted molecular therapies** drugs designed to directly target the genetic mutations and disordered DNA responsible for causing blood cancers. It is hoped that targeted therapy will replace chemotherapy and radiotherapy with a personalised approach targeting an individual's own cancer.

Stem cell transplants - prior to a stem cell transplant, high doses of chemotherapy and/or radiotherapy are used to try and kill all the cancerous blood cells in the body. The body's normal blood and bone marrow stem cells are also destroyed in the process due to high radiation doses. The patient is often unable to make new blood cells themselves and a stem cells transplant is given to encourage the production of new blood.

Stem cell transplants

There are a number of options to sourcing stem cells for a transplant, including:

- The patient's own stem cells stored prior to the high dose chemotherapy and given back after the treatment.
- A donor's stem cells either a family member or an unrelated donor who is a tissue type match.
- Umbilical cord blood stem cells.

Patient or donor marrow stem cells are usually harvested from the peripheral blood, which is the flowing, circulating blood of the body.

The collection of stem cells

Stem cells are mobilised from the marrow into the blood once a special growth hormone has been given, which allows the stem cells to be easily collected from the blood by a specialist machine. This process is called peripheral blood stem cell harvesting.

Stem cells can also be directly removed by a needle from the pelvis during an operation – this method is called a bone marrow harvest. Bone marrow harvest is less frequently used as it requires a general anaesthetic so it can often be more difficult to process the cells, and challenging for the donor. Peripheral blood stem cell harvesting is an easier process of collecting stem cells.

Umbilical cord blood stem cell collection

Umbilical cord blood stem cells can be collected at the time of a baby's delivery and the stem cells can be stored for a potential future use, either for the baby or their blood relatives in a private bank such as Leukaemia & Myeloma Research UK's own Model Cell Biobank, or donated to a public bank. The

stem cells can

be kept frozen for many years awaiting potential use.

Umbilical cord blood and cord tissue contain Mesenchymal Stem Cells (MSC). MSC are the building blocks for tissues such as fat, bone, muscle, and cartilage.

Using MSCs in regenerative medicine, such as the replacement and repair of damaged tissues, is a rapidly developing field.



For more information about the Model Cell Biobank visit www.modelcellbiobank.org



Advantages of umbilical cord blood stem cells

- The stem cells are easily available, having already been harvested and stored.
- A new born baby has been exposed to fewer viruses and infections and so the stem cells are less likely to transmit infection and react with the patient.
- The stem cells do not need to be an exact tissue match to the patient.

Disadvantages of umbilical cord blood stem cells

- The stem cell dosage is often small and not suitable for large adults, although this can be overcome by using more than one stored cord harvest.
- The stem cells are a one-off product, and once used cannot be transferred back.
- When the stem cells are stored in a public bank, doctors are unable to contact the original donor for more cells in the future.

Case study

Jonathan was 16 years old when he was diagnosed with leukaemia in 2011. Umbilical cord blood stem cells saved his life.

"Jonathan hadn't been very well – he was very tired and losing weight, and it got to the stage where he didn't have the energy to walk", said his mother, Jacqui Albans.

"The next day he couldn't get out of bed. I went to check on him and found him unresponsive, which was terrifying. I also noticed bruises on his chest so I called an ambulance and they sent a first responder to come and assist. The emergency teams were great, and in hindsight I think they saved his life in the back of the ambulance.

"At the hospital Jonathan was given a blood transfusion while a nurse explained to me that they were doing tests to see if he had leukaemia. The results confirmed the worst and he was transferred to Sheffield's Royal Hallamshire Hospital almost immediately to begin treatment.

"Jonathan underwent a lot of different treatments. He didn't respond to chemotherapy so they began radiotherapy. We looked into the possibility of a stem cell transplant from a donor in America, but it didn't work out.



"We had a meeting with our Consultant, Professor Snowdon, who suggested another treatment we could try which used the stem cells from a baby's umbilical cord. It was Jonathan's last chance so we gave it a shot.

"The transplant team used radiotherapy to kill the cancer cells, then attached a bag of cord blood. His blood cells were very slow in responding, but we were thrilled to find out it had worked.

"Jonathan is now 24 years old. Every year he has to have a big blood test to make sure the leukaemia hasn't returned, but thankfully he is still in the all clear.

"I want as many people as possible to learn about this amazing treatment – it saved my son's life. Our team of specialists were talking to experts from around the world to get the best care for Jonathan and I can't thank them enough".

Profession John Snowden, Consultant Haematologist

"Some types of leukaemia have such a poor prognosis that they require a bone marrow stem cell transplant to offer any chance of a cure, but there is not always a suitable donor available. This is where the umbilical cord blood stem cell transplants, taken at the time of birth, can be of great value.

"The umbilical cord blood stem cells can be transplanted in a similar way to bone marrow stem cells, and provide a potential cure when there is no other donor available. In most cases we need more than one umbilical cord blood to provide sufficient cells.

"After a transplant there are many months and years of ongoing monitoring and treatment before we can confidently say that it has been successful and patients are cured, but we are optimistic".

Information for healthcare professionals

Presentation of Blood cancers

Haematologic cancer includes leukaemia, lymphoma and multiple myeloma. The symptoms of haematologically malignancy are unfortunately frequently nonspecific and vague.

Blood cancers are rare but many of the everyday conditions that share their presenting signs and symptoms, for example a viral infection or mechanical back pain, are extremely common making early diagnosis reliant on a high index of suspicion. Likewise, the duration of symptoms may vary enormously dependent on the speed of onset for the particular type of blood cancer. Common signs and symptoms include:

- Anaemia
- Thrombocytopaenia (unexplained bleeding and bruising)
- Leucopaenia (infections)

Lymphoid malignancies may be associated with lymphadenopathy, a disease of the lymph nodes in which they are abnormal in size or consistency, as well as constitutional symptoms ('B' symptoms) such as fever, drenching night sweats, and weight loss.

Less commonly, haematology malignancies can include abdominal symptoms due to hepatosplenomegaly, a disorder where both the liver and the spleen swell beyond their normal size. Other signs may include tissue infiltration with malignant cells, for example gum hypertrophy, an overgrowth of gum tissue around the teeth also known as gingival hyperplasia, in acute monocytic leukaemia, or subcutaneous lymphoma deposits, a rare form of cancer that affects the deepest layers of the skin, amongst others.

Investigation of blood cancer in a Primary Care setting

Blood tests

To diagnose blood cancer, a full blood count and blood film are usually used to make an immediate diagnosis. Whilst a full blood count makes a diagnosis of leukaemia unlikely, lymphoma or myeloma can be diagnosed in the setting of a normal blood count.

The investigation of suspected myeloma requires a serum electrophoresis, which is used to find abnormal substances in the blood, and a serum-free light chain profile to detect, diagnose and monitor plasma cell disorders. A full blood count and calcium measurement is usually implemented. If a patient has symptoms including night sweats, further tests are carried out including a hormone profile in perimenopausal women, and an examination of the thyroid function. Lactate dehydrogenase is an enzyme required during the process of turning sugar into energy for cells in the body. This may be raised in haematological malignancies; however, it is not a screening or diagnostic test.

Lactate dehydrogenase contributes to the scoring systems for the prognosis of many haematology malignancies once diagnosed. A normal lactate dehydrogenase does not exclude haematological cancer, and can be very nonspecific.



Imaging

Ultrasound scanning of a suspected enlarged lymph node may reveal reactive or malignant appearances and also provide the means for an ultrasound scan guided biopsy to be done at the same time. In practice, most imaging for suspected lymphoma is done in secondary care following an urgent referral.

Plain film x-rays on areas of bone pain, or an MRI of the spine done for back pain may reveal lytic bone lesions suspicious of the deconstruction of an area of bone, for the diagnosis of myeloma. However, patients with myeloma may have normal imaging. In practice, the definitive imaging of patients with suspected myeloma done with whole body MRI is usually done from secondary care.



When to refer a patient with suspected blood cancer

Leukaemia

Patients with leukaemia are usually identified by the secondary care following an abnormal full blood count and blood film. Patients identified to have acute leukaemia or chronic myeloid leukaemia will generally be seen on the same day as emergencies by the hospital haematology on call teams.

Patients with more indolent leukaemias, such as chronic lymphocytic leukaemia, will be seen in outpatient clinics at a time frame relevant to the degree of abnormality in the blood count. In many cases, elderly patients with early indolent chronic lymphocytic leukaemia may not need referral to a hospital and can be monitored with regular blood counts from Primary Care with input from a haematologist as necessary.

Lymphoma

The suspicious features of lymphadenopathy warranting referral include:

- The lymph nodes size is greater than 1cm, and is rapidly growing
- The lymph nodes have been present for more than 6 weeks
- The lymph nodes are not tender
- They are present in more than one area
- B symptoms or generalised pruritus (itchy skin) with no other cause are presented
- Pain in the lymph node on drinking alcohol - this is a very rare but pathognomonic symptom of Hodgkin lymphoma.

It is important to note that depending on the local referral pathways, cervical lymphadenopathy may be referred directly through surgical head and neck pathways, particularly if oral, throat or nasopharyngeal (a rare type of head and neck cancer) symptoms are also present.

When to refer a patient with suspected blood cancer continued

Myeloma

If paraprotein in urine is present in people over the age of 50, they should be referred with suspected blood cancer. This is extremely common in 3-4% of people over 50 years of age.

Criteria for referral will vary with local practices. However, consider referring anyone with a paraprotein and otherwise unexplained anaemia, abnormal renal function, hypercalcaemia or bone pain.

Low level paraproteins (< 10 g/l serum, kappa serum free light chain ratio less than 100. Lambda serum free light chain ratio greater than 0.01, urine Bence Jones protein less than 100 mg/l) with no immune paresis, i.e. otherwise normal levels of immunoglobulins may not require secondary care referral but must be monitored on a frequent basis every 4-6 months. If in doubt seek guidance from a haematologist.

We would like to give a special thanks to Consultant Haematologist, Dr Hannah Hunter for producing the contents of Leukaemia & Myeloma Research UK's blood cancer brochure.



Brief explanation of terms

ABO Rhesus	Blood type
Adult stem cells	Building blocks of the blood immune system
Allogeneic transplant	Collected stem cells, used to treat someone outside the family
Biobank	Storage for human cells and tissues for use by your family
Biovault	Chosen partner of <i>Leukaemia</i> & <i>Myeloma Research UK</i> to process and store cord stem cells
Bone marrow transplant	The most widely used stem cell therapy, in which stem cells taken from the bone marrow are transplanted into a recipient
CD34+	Stem cells
CMV	Cytomegalovirus
Cord blood banks	Cord blood stem cell storage: private cord blood banks store stem cells for that child or another member of the family; public cord blood banks store stem cells for anyone around the world to use

Cryoprotectant	Type of anti-freeze to protect the cells from any damage during the freezing process
HIV	Human immunodeficiency virus
Hodgkin lymphoma	A type of less common lymphoma
HTLV	Human T-cell lymphotrophic virus
Leukaemia	Cancer that affects the white blood cells and starts in the bone marrow
Leukocyte cells	White cells
Lymphocytes	White cells that reproduce themselves to fight infection
Lymphoma	Cancer that affects part of the immune system known as the lymphatic system
Maternal blood sample	Blood sample taken from the mother after the baby is delivered
Model Cell Biobank	Stem cell storage service offered by <i>Leukaemia &</i> Myeloma Research UK

Myeloma	One type of white cells start to multiply uncontrollably in the bone marrow
Non-Hodgkin ymphoma	The most common type of lymphoma
Peripheral blood	Circulating blood
Phlebotomist	Professional who collects blood samples
Platelets	Help the blood to clot
Red blood cells	Carry oxygen around the body
Stem cell herapy	Use of stem cells to treat a disease or condition
Total nucleated cells count	Measure of the cell count after cord blood processing
Volume reduction	Routine process to remove unwanted parts of the cord blood before storage
White blood cells	Routine process to remove unwanted parts of the cord blood before storage

Do you need more information or want to get in touch?



If you have any questions about Leukaemia & Myeloma Research UK please contact our head office:

Telephone: 0800 368 7309 Email: cs@leukaemiamyelomaresearchuk.org

- leukaemiamyelomaresearchuk.org
- 2 @LMRUK_org



For more information about collecting and storing cord blood stem cells, please contact a member of our customer service team:

Telephone: **0800 368 9540** Email: **cs@modelcellbiobank.org**

