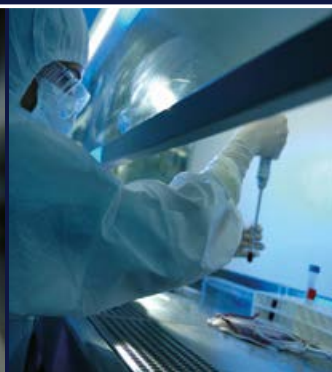
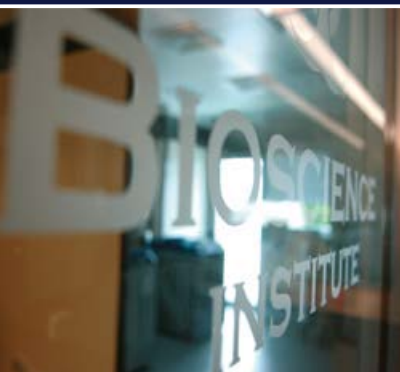




 **BIO SCIENCE**
I N S T I T U T E

DEDICATED UMBILICAL CORD CRYOPRESERVATION



CELL FACTORY

Bioscience Institute is a cell factory dedicated to biological cryopreservation, cellular culture and scientific research. The Bioscience Institute laboratories engage in the extraction, analysis, expansion and planned freezing of several types of cells. The cryopreservation room, on the other hand, is used to store the stem cells extracted from blood in the umbilical cord, fat tissue, peripheral blood, as well as mature cells such as fibroblasts. Bioscience Institute, in collaboration with prestigious Italian and foreign universities, conducts research aimed at expanding the possible chemical applications of stem cells in several areas of medicine: cardiology, surgery, neurology, gynaecology and dermatology.

In view of the high value of the stored cells, and in compliance with European Directives implemented in Italy, Bioscience Institute was awarded the GMP (Good Manufacturing Practice) certification, which confirms the top-quality standard adopted.

This level of excellence is there for everyone to see on the Bioscience Institute web site, which makes it possible to get a view of the laboratories from the internal video cameras and to appreciate the quality of the operational procedures followed by our staff. Moreover the laboratories include 220 m² of sterile environments (Clean Rooms) and are equipped with laser particle counters which constantly monitor the biological safety level.

Apart from the Operational Procedures, it is also possible to monitor the sterility level of the environments from the www.bioinst.com website, as confirmation of the high reliability and safety level of the laboratories. Having adopted, through the GMP certification, the highest quality standard acknowledged by the European Union is a way of safeguarding all those who intend to store their stem cells and are looking for excellence parameters in order to make a careful choice. Indeed, the guarantees received by Bioscience Institute clients include the highest operational and technological standards provided by a solid, reliable and transparent company.



STEM CELLS

The stem cells are “mother cells” (undifferentiated or immature) which have not yet undergone the transformation process into the specialised cells making up the various human tissues and organs.

The stem cells remain undifferentiated or immature until a stimulus occurs which induces their transformation into specialised cells for a specific function (becoming cells in organs or tissues).

Stem cells are either embryonic or adult:

- embryonic cells are found in the embryo from conception to the fourth day of gestation; they are totipotent, which means that they can produce any type of specialised cells
- adult stem cells, found in the blood in the umbilical cord, bone marrow, peripheral blood, amniotic liquid and fat tissue, are multipotent, that is to say they can turn into some types of specialised cells

STEM CELLS FROM THE UMBILICAL CORD

These are adult stem cells which have the potential of turning into various blood cell types, as well as into those of the nervous, cardiac, pancreatic and epithelial tissue. They are collected at childbirth, either natural or C-section, by extracting the blood in the placenta and in the umbilical cord which has just been cut.

The procedure is safe and painless, both for the mother and the baby, because it takes place after birth during the phase before disposal of the cord and of the placenta.

WHY STORE STEM CELLS FROM THE UMBILICAL CORD

- Childbirth is the only opportunity in the course of an individual's life to extract stem cells in a non-invasive way and to cryopreserve them for future use to the advantage of the newborn or next of kin
- The blood contained in the umbilical cord is rich in stem cells; it may be collected with a simple and risk-free procedure, before the cord is disposed of as hospital “special waste”
- Storing one's own stem cells before the possible outbreak of serious diseases makes it possible, if necessary, to avoid both the search for a donor and the risk of rejection or infection after the transplant
- The more than 20,000 stem cells transplants worldwide, used to cure many pathologies, confirm the importance and scientific validity of their preservation
- Most of the investment allocated to research, which in the past was destined to the pharmaceutical sector, is now used to study stem cells, thus paving the way for further clinical applications

TREATED DISEASES

LEUKEMIAS

Acute Leukemia

- Acute Lymphoblastic Leukemia (ALL)
- Acute Myelogenous Leukemia (AML)
- Acute Biphenotypic Leukemia
- Acute Undifferentiated Leukemia

Chronic Leukemia

- Chronic Myelogenous Leukemia (CML)
- Chronic Lymphocytic Leukemia (CLL)
- Juvenile Chronic Myelogenous Leukemia (JCML)
- Juvenile Myelomonocytic Leukemia (JMML)

MELODYPLASTIC SYNDROMES

- Refractory Anemia (RA)
- Refractory Anemia with Ringed Sideroblasts (RARS)
- Refractory Anemia with Excess Blasts (RAEB)
- Refractory Anemia with Excess Blasts in Transformation (RAEB-T)
- Chronic Myelomonocytic Leukemia (CMML)

LYMPHOMAS

- Hodgkin's Lymphoma
- Non-Hodgkin's Lymphoma Burkitt's Lymphoma

INHERITED RED CELL (ERYTHROCYTE)

ABNORMALITIES

(Red cells contain hemoglobin and carry oxygen to the body)

- Beta Thalassemia Major (also known as Cooley's Anemia)
- Blackfan-Diamond Anemia
- Pure Red Cell Aplasia
- Sickle Cell Disease

OTHER DISORDERS OF BLOOD CELL PROLIFERATION

Anemias

- severe Aplastic Anemia
- Congenital Dyserythropoietic Anemia
- Fanconi Anemia (Note: the first cord blood transplant in 1988 was for this disease)
- Paroxysmal Nocturnal Hemoglobinuria (PNH)
- Pure Red Cell Aplasia

Inherited Platelet Abnormalities

- Amegakaryocytosis / Congenital Thrombocytopenia
- Glanzmann Thrombasthenia

Myeloproliferative Disorders

- Acute Myelofibrosis
- Agnogenic Myeloid Metaplasia (Myelofibrosis)
- Polycythemia Vera
- Essential Thrombocythemia

Inherited Immune System Disorders -

- Severe Combined Immunodeficiency (SCID)
- SCID with Adenosine Deaminase Deficiency (ADA-SCID)
- SCID which is X-linked
- SCID with absence of T & B Cells
- SCID with absence of T Cells, Normal B Cells
- Omenn Syndrome

Inherited Immune System Disorders - Neutropenias

- Kostmann Syndrome
- Myelokathexis

Inherited Immune System Disorders - Other

- Ataxia-Telangiectasia
- Bare Lymphocyte Syndrome
- Common Variable Immunodeficiency
- DiGeorge Syndrome
- Leukocyte Adhesion Deficiency
- Lymphoproliferative Disorders (LPD)
- Lymphoproliferative Disorder, X-linked (also known as Epstein-Barr Virus Susceptibility)
- Wiskott-Aldrich Syndrome

Phagocyte Disorders

- Chediak-Higashi Syndrome
- Chronic Granulomatous Disease
- Neutrophil Actin Deficiency
- Reticular Dysgenesis

CANCERS IN THE BONE MARROW

(PLASMA CELL DISORDERS)

- Multiple Myeloma
- Plasma Cell Leukemia
- Waldenstrom's Macroglobulinemia

OTHER CANCERS

(NOT ORIGINATING IN THE BLOOD SYSTEM)

- Neuroblastoma
- Retinoblastoma

TRANSPLANTS FOR INHERITED DISORDERS

EFFECTING THE IMMUNE SYSTEM & OTHER ORGANS

- Cartilage-Hair Hypoplasia
- Gunther's Disease (Erythropoietic Porphyria)
- Hermansky-Pudlak Syndrome
- Pearson's Syndrome
- Shwachman-Diamond Syndrome
- Systemic Mastocytosis

TRANSPLANTS FOR INHERITED METABOLIC

DISORDERS

- Mucopolysaccharidoses (MPS) Storage Disease
- Mucopolysaccharidoses (MPS)
- Hurler's Syndrome (MPS-IH)
- Scheie Syndrome (MPS-IS)
- Hunter's Syndrome (MPS-II)
- Sanfilippo Syndrome (MPS-III)
- Morquio Syndrome (MPS-IV)
- Maroteaux-Lamy Syndrome (MPS-VI)
- Sly Syndrome, Beta-Glucuronidase Deficiency (MPS-VII)
- Mucopolipidosis II (I-cell Disease)

Leukodystrophy Disorders

- Adrenoleukodystrophy (ALD)/Adrenomyeloneuropathy (AMN)
- Krabbe Disease
- (Globoid Cell Leukodystrophy)
- Metachromatic Leukodystrophy
- Pelizaeus-Merzbacher Disease

Lysosomal Storage Diseases

- Gaucher Disease
- Niemann-Pick Disease
- Sandhoff Disease
- Tay-Sachs Disease
- Wolman Disease (MPS-VII)
- Mucopolipidosis II (I-cell Disease)

Inherited Disorders - Other

- Lesch-Nyhan Syndrome
- Osteopetrosis

source: <http://parentsguidecordblood.org/>

STEM CELLS IN THE TREATMENT OF DISEASES

The discovery of stem cells and of their properties led to the establishment of a new area in modern medicine: regenerative medicine. The possibility of using stem cells to treat a large variety of pathologies is the main goal on which most medical-scientific research worldwide is focused. At the moment stem cells allow for effective action to counteract serious pathologies of haematology, immunological, genetic, metabolic and oncology origin.

To date more than 20,000 stem cell transplants have been conducted worldwide.

Due to the growing success rate in clinical applications, an increase in the use of stem cell-based treatments is expected.

Scientific research, moreover, is working on new therapies which use stem cells for the treatment of degenerative diseases such as Alzheimer, Parkinson's, stroke, type-1 diabetes, muscular dystrophy, cardiovascular pathologies and many other diseases for which there is currently no alternative cure.



PRESERVATION

DEDICATED AUTOLOGUS

Preservation is known as Dedicated when the stem cells contained in the blood in the umbilical cord are preserved for the benefit of the donor him/herself (the newborn) or of his/her compatible next of kin.

Dedicated cryopreservation may be conducted free of charge by accredited public hospitals in the event that, at the time of birth or earlier, it is discovered that the newborn or next of kin are suffering from a pathologies, or in the case of families at risk of having children affected by genetic disease. On the other hand, for prevention purposes, Dedicated preservation may be used to the advantage of the newborn or next of kin, by private structures abroad such as Bioscience Institute.

ALLOGENEIC

Preservation is known as Allogeneic when it comes from a donation of the mother who makes the stem cells from the umbilical cord available for use by others. In this case, the cells are stored in a public Bank and given to patients whose compatibility have been ascertained and who may need them for a transplant.

THE IMPORTANCE OF DEDICATED AUTOLOGOUS PRESERVATION

The units of cord blood stored for allogeneic use, to date, have never exceed the very low rate of 0.5% in respect of the total number of births per year.

This means that allogeneic preservation alone cannot prevent 99.5% of the umbilical cords available from being destroyed.

The limited number of cord blood units stored in public banks is certainly not attributable to the existence of autologous banks, where about 3-10 % of them is stored, but rather to organisational and structural shortcomings which prevent the National health Service from effectively making use of the rest.

It seems clear that, in order to avoid the useless destruction of such valuable biological material, the private structures which engage in autologous stem cell cryopreservation can integrate and strengthen the action of allogeneic cord banks, provided that they are able to provide excellent quality standards.





HOW TO JOIN

Bioscience Institute deals with the administrative, logistic and health aspects, assisting its customers with the necessary procedures to export the stem cells and to withdraw the blood sample from the hospital where the baby is born. Bioscience Institute also includes a scientific committee which provides medical information as to the therapeutic use of stem cells and the most recent developments in scientific research.

In order to request the Bioscience Institute collection Kit, it is sufficient to contact the company's free-phone service or fill in and send the on-line subscription form available at www.bioinst.com.

By requesting the Kit, the customer also applies for the assistance services offers by Bioscience Institute.

The collection kit is an isothermal airtight case made of plastic resin, with pressurisation valve and expanded polyurethane lining, containing:

- sterile bag for the collection of placenta blood
- safety lock with combination
- conformity certification of the Kit and contract
- double airtight isothermal casing





THE CORD BLOOD COLLECTION

On the day of hospitalisation, the Kit has to be handed over to the obstetric staff in charge of the childbirth, who need to be previously informed. After the placenta blood has been collected, the parents contact Bioscience Institute which will withdraw it from the childbirth point.

The bag travels at room temperature in a double isothermal container and does not require refrigerated vehicles. As soon as the Kit arrives the Bioscience Institute staff conducts the necessary procedures to separate the stem cells contained in the placenta blood for subsequent freezing and cryopreservation in a double bag.

Cryopreservation itself lasts at least 20 years; its duration is tacitly extended after proving cell survival for a longer period. Immediately after childbirth, the umbilical cord is cut and the needle from the collection bag is inserted into the part which is still connected to the placenta. The placenta blood flows by gravity into the bag; once the latter is full it is placed into the isothermal contained and in the airtight case for transport. The case is then closed with the lock provided as standard; its shipment can then be arranged by contacting Bioscience Institute, which directly withdraws the Kit from the childbirth point.



GUARANTEES

Bioscience Institute is a joint stock company and its articles of association stipulate that its annual financial statements are certified by the auditing company PricewaterhouseCoopers. Bioscience Institute is the exclusive owner of the laboratories where its research is conducted.



THE IMPORTANCE OF GUARANTEES

The parents who intend to store their child's stem cells for at least twenty years need to entrust them to a company which is solid, reliable and transparent.

The value of stem cells is such that is essential to carefully assess the guarantees and responsibility limitations of the company offering the service.

The sole guarantees a company can offer its customers consist in the resources that are deployed to conduct its work, through which it responds in a concrete and direct way (investment, stock capital, shareholders).

Bioscience Institute has a direct relationship with its customers; it does not outsource its services and does not avail itself of commercial companies which would not be able to offer the same guarantees.

Bioscience Institute is officially committed to maintaining its rigorously certified quality standard throughout the term of the contract.



CONTRACT

The autologous cryopreservation contract is entered with Bioscience Institute Spa, the company owning the laboratories and biological cryopreservation services, which is directly responsible for its operation, with the undertaking of never granting to third parties any rights deriving from the contract. Bioscience Institute is contractually bound to keep its quality level unchanged, by certifying the procedures adopted and the facilities in which it operates, as the only possibility to ensure reliability over time for its customers.

WHY CHOOSE BIOSCIENCE INSTITUTE

Our laboratories are the most advanced in Europe, both in terms of technological equipment and quality standards; this means that the stored stem cells can be used by any transplant centre in the world.

- There is a direct relationship with our customers, a guarantee which commercial companies would be unable to offer.
- The laboratories are located in the centre of Italy which means that transport is not at risk of potentially harmful delays.
- We carry out important research work concerning the use of stem cells, in collaboration with prestigious Italian and foreign universities.
- It is the only institute which allows for direct viewing of the site where the cells will be cryopreserved.
- We provide a neonatal screening service for early diagnosis of more than 50 rare genetic diseases.



LABORATORIES

- 220 m² Class B Laboratories
- 920 m² total surface
- 150 m² N/C laboratories
- 180 m² technical rooms
- 150 m² administration/training office
- 120 m² cryopreservation room
- 100 m² logistics



QUALITY STANDARDS

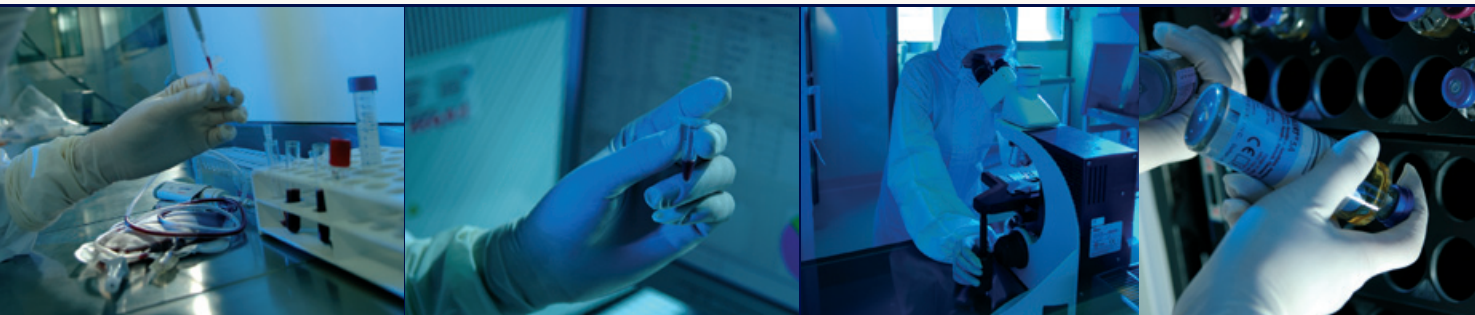
The GMP certification is the highest quality standard awarded to laboratories which, like Bioscience Institute, conduct research work and cryopreserve stem cells.

The minimum requirements stipulated by EU norms concerning the cryopreservation of stem cells, usually adopted by banks engaging in this activity, do not meet the maximum biological safety levels.

As a matter of fact, these can only be guaranteed if the laboratories are certified through the much more stringent standards required by GMP (Good Manufacturing Practice) procedures.

These requirements concern not only the design and construction of buildings and installations, but also the operational procedures which can only be applied if the laboratory has been built, equipped and furnished according to this rigorous standard.

Bioscience Institute has been awarded the GMP certification, the only one recognised both by the European Union and by the FDA (Food and Drug Administration), in order to make sure that its cells can be accepted and used by any Transplant Centre in the world.

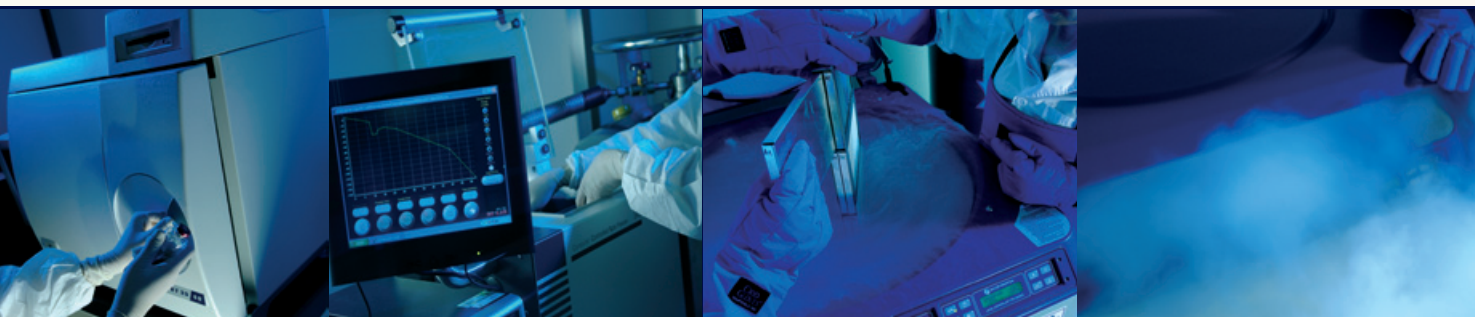




WHY ARE CERTIFICATIONS ESSENTIAL

Transplanting stem cells is an extremely risky and delicate operation to be conducted in specialised centres. A transplant with stem cells which have not been preserved correctly could put the patient's life at risk. For this reason there are international certifications which are issued only to laboratories after they have passed the audit inspections for sterility of the rooms and correctness of the cell handling procedures, especially if the latter are used for human beings.

In Europe, before a transplant, the Centres in charge run a check on the origin of the biological material to be transplanted. If the laboratory it comes from does not have an internationally-acknowledged certification, it will not be possible to transplant the stem cells because they do not offer the necessary biological safety and traceability guarantees. It is important to make a distinction between a GMP-certified laboratory and one which states that it meets the required standard but has not been issued the relevant certification. In other words, mere compliance is not the same as having been awarded a certification which is obtained only after stringent audits have been conducted by the cross-border entities in charge of its issuing.



www.bioinst.com

| AZIENDA CERTIFICATA |
| UNI EN ISO 9001:2015 |



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