Development of body friendly biomedical implants or grafts using stem cells

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- Stem cells (SC) are undifferentiated cells capable of self renewal and developing into various tissues and organs.
- Multiple sources of human stem cells, embryonic and nonembryonic (bone marrow, adipose tissue and umbilical cord blood), have been characterized and studied in preclinical scenarios.
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- Each has its own particular advantageous and disadvantageous properties.
- Umbilical cord blood contains various populations of stem cells and progenitors including hematopoietic stem cells (HSC), mesenchymal stem cells (MSC), endothelial colony forming cells (ECFC) and more primitive unrestricted somatic stem cells (USCC).
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- Given its more naïve state and "younger" environmental exposure
- UCB retains great pluripotentiality,
- less immunogenicity, and
- fewer mutations.
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- Umbilical-cord blood is increasingly used as a source of stem cells to repopulate the bone marrow in the treatment of life-threatening diseases in children and adults.
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- Although exact statistics are not available, 5000 to 6000 cord-blood transplantations have now been performed worldwide.
- Primarily in the United States, Western Europe, Japan, and Australia. One of the richest sources of stem cell is cord blood.
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- The principle of cell transplantation in bionic or implantable devices as a replacement of diseased or lost tissue function has many potential fields of application.
- The hypoantigenic foetal tissue has the potentiality to make a perfect non-irritant, i.e., bio-friendly interface in case of different synthetic / metallic implants including stents in medicine and surgery.
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For example, any graft or implant, can be made much more bio-friendly using a foetal endothelial cell lining or mesenchymal stem cell cell lining and this can also lead to a minimization of progressive platelet and other cellular interaction vis-à-vis degradation and it can help extend the life expectancy of these stents.
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- In case of orthopaedic surgery, e.g., hip, knee or elbow replacement prostheses, if they are covered with foetal progenitor cells or stem cell, the life of the implant can be extended by the bio-friendly interface formation which can minimize the degradation of the implant, and prevent TH2 cellular responses by fibroblast proliferation and other tissue specific de-granulation / degradation attempts by the host tissue.
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- Fortunately, technology today has enabled the storage and preservation of foetal tissue for a significant period of time and supply and demand can thus coincide.

- Foetal cells and tissue are the richest sources of tissue specific and non-specific stem cells, whose enormous regeneration capacity and possible role in the reversal of Hayflicks limit of replicative senescence has not been evaluated adequately so far in Medicine and Biology. Work is continuing vigorously in this emerging area of research.
Recently, in the third generation of biomedical implants, the developed knowledge base of other allied fields, e.g., tissue engineering, nanoscience and technology, is amalgamated to design more efficient implants/devices/new tissues/organs.

Synthetic biomaterials and stem cells are two important tools that tissue engineering utilizes as building blocks for new tissues that incorporate living cells.
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- More precisely, it is the application of principles and methods of engineering and life sciences toward fundamental understanding of structure-function relationships in normal and pathological mammalian tissues and development of biological substitutes (for replacements as opposed to the use of inert implants) to restore, maintain, or improve tissue function. The modern-day ‘tissue engineering’ aims to manufacture complete tissues outside the body ready for future transplant of skin, cartilage, regeneration of bone, and other connective structural substitutes.
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- These replacements
- may consist of cells in suspension, cells implanted on a scaffold such as collagen, and replacements that entirely consist of cells and their extracellular products.
- The three general strategies identified for the creation of new tissues involve
- the use of (1) isolated cells or cell substitutes, (2) tissue-inducing substances, or
- (3) cells placed on or within matrices.
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- In this case, the product consists of individuals’ own cells; therefore, transplantation
- of engineered tissues or organs resides in the immunological acceptance,
- and it is not expected to evoke rejection. On the other hand, differentiated donor
- cells from another individual would likely have one or more surface markers that
- would be incompatible to the host. Since the availability of individual’s own cells
- at the time of need is unlikely, cost-effective universal donor cell lines that are nonimmunogenic
- are needed.
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- A multitude of applications for engineered tissues and organs exist in human health arena. Examples include whole organ replacements in life-threatening situations associated with liver, pancreas, heart, or kidney failure and replacement of lost skin-covering due to massive burns or chronic ulcers.
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- Other applications include
- repair of defective or missing supportive structures, such as long bones, cartilage, connective tissue, and intervertebral discs;
- replacement of worn out and poorly functioning
- tissues as exemplified by aged muscle or cornea; replacement of damaged
- blood vessels; and restoration of cells to produce necessary enzymes, hormones, and
- other metabolites.
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- In addition, tissue-engineered composites will be useful to establish safety and efficacy of potential new drugs, and may contribute to the development of understanding of genetic or environmental factors that may be responsible for the onset of diseases.
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- For bone tissue engineering, there is a direct link from the research on porous hydroxyapatite, which could provide a suitable matrix delivery system for osteoblasts.
- Or precursor stem cells. In the former case, such an approach would provide an autograft equivalent to bone grafting, without the need for a second operation.
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- An exciting prospect in the latter case is the production of both bone and cartilage through cell differentiation locally directed by scaffolds and scaffold chemistries, so as to produce a mini-implant of cartilage already in place on bone, e.g., a replacement acetabulum of bone complete with its cartilage lining, which would eliminate the considerable difficulty of fixing cartilage to bone in vivo. A complementary approach is to stimulate osteoblast recruitment, e.g., by local delivery of parathyroid receptor agonists through prior transfection of the PTH gene into local fibroblasts.
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- During the last decade, considerable attention has been directed toward the use of implants with bioactive fixation. This is defined as interfacial bonding of an implant to tissue by means of formation of a biologically active hydroxyapatite layer on the implant surface.
- Hence, the bioactive bond formed at the implant-bone interface has strength equal to or greater than that of bone. The level of bioactivity of a specific material can be related to the time taken for more than 50% of the interface to bond to bone ($t_{0.5bb}$):
  - Bioactivity index, $IB = 100/t_{0.5bb}$
  - In this, materials that exhibit an $IB = 100/t_{0.5bb}$ will bond to both soft and hard tissues, whereas materials that have $IB$ value less than 8 but greater than 0, e.g., synthetic hydroxyapatite, will bond only to hard tissue.
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- Also, a bioactive glass undergoes surface dissolution in a physical environment
- in order to form a hydroxycarbonate apatite (HCA) layer. The larger the solubility of the bioactive glass, the more pronounced the effect on the bone-tissue growth
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- Three-dimensional porous scaffolds promote new tissue formation by providing a
- surface and void volume that promotes the attachment, migration, proliferation, and
- desired differentiation of connective tissue progenitors throughout the region where
- new tissue is needed. Critical variables in scaffold design and function include the
- bulk material or materials from which it is made, the
- three-dimensional architecture,
- the surface chemistry, the mechanical properties, the
- initial environment in the area
- of the scaffold, and the late scaffold environment, which
- is often determined by
- degradation characteristics.
Development of body friendly biomedical implants or grafts using stem cells: use of stem cells

- The stem cells, the immature/undifferentiated cells capable of producing an identical daughter cell that may perpetuate over many generations resulting in considerable amplification of their numbers (when subjected to the right biochemical signal), are the key elements to conceive the idea of developing a complete implant consisting of bone and cartilages.
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- Depending on their respective decrease in potency, stem cells can be totipotent (e.g., the fertilized egg or zygote), pluripotent [e.g., embryonic (ES) and germ (EG) cells], or multipotent (bone marrow, stromal or mesenchymal stem cells). The characteristics that make stem cells an attractive proposition for tissue repair and regeneration have been outlined and there are specified mechanisms that activate stem cells or progenitor cells to replace the damaged cells:
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- (1) Generation of adequate number of cells and tissues to fill the defect or complete the repair,
- (2) Differentiation of the cells toward the correct phenotype and maintenance of this
- (3) Ensuring that the cells of tissues adopt the appropriate three-dimensional organization and produce the extracellular matrix.
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- This may require provision of structural support in the shape of resorbable scaffold
- (4) production of cells or tissues that are structurally and mechanically compliant with the normal demands of the native tissue
- (5) achievement of full integration with the local tissue with vascularization, if required
- (6) overcoming the risk of immunological rejection
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- The three major components of the acellular structure of bone are collagen, which is flexible but very tough; hydroxycarbonate apatite, which is the reinforcing phase of the composite; and bone matrix or the ground substance, which performs various cellular support functions.

- All are organized into a three-dimensional system that has maximum strength and toughness along the lines of applied stress. Two of the various types of bones that are of most concern in bioceramics are the cancellous bone and the cortical bone.

- The cancellous bone that occurs across the end of the long bones has lower modulus of elasticity and higher strain to failure than that of the cortical bone.

- The difference in elastic moduli between various types of soft connective tissues, e.g., tendons and ligaments, renders a smooth gradient in mechanical stress across a bone, between bones, and between muscles and bones.
Development of body friendly biomedical implants or grafts using Human mesenchymal cells: To improve visibility, the three cellular proteins have been stained: blue, core; green, F-Actin; red, Vinculin.
Development of body friendly biomedical implants or grafts using: Human mesenchymal cells on structured surfaces: left, unstructured; right, hemispheres.
Development of body friendly biomedical implants or grafts using stem cells bone is coated with the patient’s own stem cells with a hope that this bone will incorporate into the patient’s own tissue much faster than the artificial bone – and that will help build new bone marrow tissue.
Development of body friendly biomedical implants or grafts using stem cells: SEM displaying the cross-section of a composite disk, which had been seeded with cultured bone marrow stromal cells.
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