SUMMARY

Musculoskeletal disorders are among the most common medical disorders that result in substantial reduction in health and quality of life, and are the most common causes of severe long-term pain and physical disability, affecting hundreds of millions of people around the world.

Those disorders have improved over the past 10 to 20 years, through sophisticated rehabilitation programs, and novel operative techniques. Despite this considerable progress, no optimal therapy has been found.

In recent years, tissue engineering has gained increasing support, as a method to treat musculoskeletal disorders than traditional methods.

The combination of tissue engineering and gene therapy techniques is another field of reach was explored.

Tissue engineering is a new knowledge involving the use of scaffolds, natural tissues, cells and growth factors, with the goal of enhancing the natural healing process or replacing damaged or deficient tissue by natural tissues.

Scaffolds are biodegradable materials that provide a framework for cell proliferation, differentiation and communications. They include ceramics, synthetic and natural materials.

The common synthetic polymers used include: the polyglycolic acid, polylactic acid, polycarpolactone, polyethylene glycol, silicone and

polyphosphazenes. Natural polymers, such as collagen, hyaluronic acid, fibrin, laminin and fibronectin.

The advantage of biodegradable implants is that they degrade, after they have fulfilled their function. Therefore, a second operation for removing metal implants is not necessary. Additionally, the healing process may be stimulated by the successive loss of the mechanical properties of the implant during degradation.

Cells, over the past few years, researches on animal and human stem cells are almost daily loudly revealed to the public on the front-page of newspapers.

Several strategies are being investigated and include stem cells, bone marrow mesenchymal stem cells, cord blood stem cells, as well as cells of the same tissues and organs, and from genetically modified tissues.

Expansion of the cell population in vitro is a vital step in the process of building a construct containing cellular elements, in which the cells undergo proliferation, differentiation and communication with scaffolds. All of these are called tissue culture. If the cell culture is done in the Biobox system, the result will be better than other systems.

An important area for future study is the field of neural regeneration toward end-organ tissues, such as skeletal or smooth muscle. The neuronal cells have a high metabolic requirement. As such, it is difficult to isolate a large number of viable cells. An alternative approach may be the use of less mature progenitor cells or stem cells.

Growth factors initiate cell differentiation and cell growth. The growth factors bind to cell surface receptor that activates multiple cascades. The cascades include: mitogen activated protein kinase (MAP kinase), phosphinositide kinase (PI-3 kinase) and inositol-lipid (IP_3). The net result of these pathways is stimulation of stable cells to enter the growth cycle.

The use of growth factors or cell transplants to treat osteochondral defects or cartilage degeneration requires some method of delivering and possibly stabilizing the growth factors or cells within the defect. Methods of delivery include: single or multiple intra-articular injections, implantable osomtic pump, various forms of artificial matrices and genetically engineered cells.

Growth factors include: Bone Morphogenetic Proteins (BMPs), Transforming Growth Factors (TGF-Bs), Platelet Derived Growth Factors (PDG-Fs) Insulin like Growth Factors (IGFs), Fibrobalst Growth Factors (FGFs), Hepatocyte Growth Factors (HGFs) and Epidermal Growth Factor (EGF).

Gene therapy is a technique in which a therapeutic gene is transferred to target cells for a therapeutic effect.

There are two main strategies for transferring genes to sites in the body. **Direct (in vivo) gene delivery**, the new genetic material is introduced directly into the patient. **Indirect (ex vivo) gene delivery**, cells are removed genetically manipulated outside the body, and then returned to the body.

Gene delivery is facilitated by the use of vectors which include: non viral vectors i.e., Plasmids, Liposomes and Particle Mediated Gene Transfer and viral vector include adenovirus.

Applications

Bone tissue engineering

There are several drawbacks to autogenous bone graft, that have fueled the interest in orthopedic tissue engineering of cells and matrices, that can exceed osseous repair.

Two populations of osteogenic precursor cell are present: determined osteogenic precursor cells (DOPCs) and inducible osteogenic precursor cells (IOPCs). Determined osteogenic precursor cells (DOPCs) are a committed stem cell, which can proliferate but has committed to differentiate toward an osteoblast phenotype. The IOPC represents a progenitor cell, that is capable of differentiation into one or more of a variety of connective tissue phenotypes when given appropriate stimulation.

If large numbers of osteoblastic progenitors are needed, the use of in vitro culture and expansion of osteoblastic progenitors harvested from bone marrow is an available option.

The scaffolds include: Ceramics (Porous Tricalcium Phosphate (TCP), Hydroxyapatite and Injectable Ceramic), Collagen, Polylactic Acid and Polyglycolic Acids.

Osseous repair involves a complex interaction of numerous local and systemic regulatory factors.

The scaffolds and growth factors must be implanted with osteoblastic progenitor cells to accomplish a reliable and optimal bone healing response**.**

Meniscal Tissue Engineering

Injuries to the knee menisci cause significant discomfort and can lead to cartilage injury on the articular surfaces of femur and tibia, leading to the later development of osteoarthritis.

The incidence of major complications in patients with open total meniscectomy is 14.6%, while patients with open partial meniscectomy suffered only 2.6% of major complications.

With recognition of the importance of the meniscus to proper knee function and prevention of accelerated degenerative changes, therapy attempted to preserve, repair, or reconstruct this tissue.

Several studies described the generation of new meniscal tissue in the laboratory using a nude mice model.

Cruciate ligament tissue engineering

The incidence of trauma to the anterior cruciate ligament (ACL) continues to rise, perhaps resulting from the increasing activity level of all age groups of the population. If left untreated, patients with ACL injuries can suffer from pain. Instability in the knee joint, articular cartilage damage and meniscal tear.

Artificial structures had limitations due to their chronic foreign body inflammation, particulate induced synovitis, some particle shedding into lymph nodes and complete graft rupture.

Investigators have recognized some of the limitations of permanent nondegradable synthetic prostheses, and have moved further on the spectrum of ligament replacements to more biologically based scaffolds.

Ligament cells treated with growth factors, such as [epidermal growth factor (EGF), platelet derived growth factor (PDGF) and fibroblast growth factor (FGF)] proliferated eight times more than untreated cells in one study.

Intervertebral disk tissue Engineering

Backache is one of the second leading causes of chronic disability in many industrial and agricultural economies, causing sick leave for workers. The majority of cases of backache are associated with some abnormality of the intervertebral disc.

In the 1970, there has been significant work in the development of prosthetic IVD replacement devices to solve the complications of the operative treatment of the IVD degeneration.

Recently, application of tissue engineering in IVD degeneration originates as result from the complications of artificial devices, and the operative solution not optimal.

Possible applications of tissue engineering lie in IVD degeneration mainly in its potential for induction of cellular differentiation and growth, with regeneration of proteoglycan in the nucleus pulposus and collagen in the anulus fibrosus.

Peripheral Nerve Tissue Engineering

Original attempts at nerve repair date back to 1608, but it was long after this time in the 19th century, those physicians began to focus on nerve restoration.

Current research is focused on creating the ideal scaffold, that can serve as a nerve guidance channel between the proximal and distal nerve ends, plus neuronal growth factors and cells alternative to Schwann cells.

Nerve guidance channels are either synthetic or natural tubular conduits, that are used to bridge the gap between injured nerve stumps. Synthetic material, as silicone, polylactic acid and polyphosphazenes, while natural material, as laminin, fibronectin, collagen and vein.

Guidance channel properties include: channel dimensions, surface texture, channel wall porosity, electrical properties, in corporation of insoluble proteins.

Neuronal growth factors can be incorporated directly into nerve guidance channels to further stimulate nerve regeneration.

The inclusion of neuronal support cells into guidance channels is another active area of research. Support cells (e.g., Schwann cells) can serve as a living source of various neuronal growth factors for the regenerating nerve.