

to enhance the cartilage regenerative potential. Strategies are being developed to deliver appropriate bioactive factors that may optimize this regenerative process. These involve either direct delivery of the factors or delivery of the transgene coding for the factors. Cartilage tissue engineering is another promising approach of regenerative medicine to tackle this problem.

4) Ligament and Tendon healing- they have a high incidence of injuries and usually lead to instability and loss of function. With surgical intervention, the grafts (eg. In ACL reconstruction) are gradually replaced by scar tissue which is of mechanical inferior quality. In case of tendon injuries, problem of healing as well as complication of adhesion development is also there. Regenerative medicine aims to potentiate the healing of natural ligaments and tendons with a more biologic plausible tissue and to prevent the above complications. Meniscus engineering⁵ is another field which is promising for treatment of meniscal injuries.

5) Spine- There are three main fields:

- o *Intervertebral disc degeneration-* It is characterized by progressive loss of matrix proteoglycans rendering disc more susceptible to injury and degeneration. Gene therapy has focused on up regulating the matrix synthesis utilizing BMPs, IGF-1, TGF- β etc.
- o *Spinal fusion-* spinal fusion is a commonly performed yet often unsuccessful procedure. Strategies to enhance spinal fusion include use of extracted and partially purified proteins including BMPs, recombinant BMP-2 & 7 and gene therapy i.e. delivery of gene or osteoinductive factor itself.
- o *Spinal cord injury-* Ability of stem cells to incorporate into the spinal cord, differentiate, and to improve locomotor recovery hold promise for a cure. Stem cells have the ability to remyelinate the demyelinated injured neurons. SCs have neurotrophic, ECM, and cell adhesion properties that are favorable to axonal regeneration in the peripheral nervous system^{9, 10}. Akiyama Y (2001)⁶ reported functionally significant extensive remyelination of the cord after neural stem cells were transplanted into the demyelinated adult rat spinal cord. Iwanami A et al (2005)⁷ showed that the bar grip power and the spontaneous motor activity of the stem cells transplanted animals were significantly higher than those of sham-operated control animals. Syková (2004)⁸ reported varying degrees of improvement in spinal cord injury patients after autologous MSCs were intravenously delivered to nine people who had sustained spinal cord injury.

6) Osteoarthritis⁴- The treatment of osteoarthritis includes a wide spectrum of approaches. At present, with the exception of surgery, all other treatments are palliative. That is to say that many of these treatments relieve pain and increase function. However, on the basis of medical evidence, these treatments do not change the course of the disease. Surgical interventions, including joint replacement and osteotomy, reverse the progress of osteoarthritis and provide long-term improved function and pain relief for specific joints. The goal of treating osteoarthritis is to arrest and reverse its progress regionally or globally through biologic methodology. Meaningful progress for biologic intervention accumulates annually. Pluripotent mesenchymal cells can be coaxed into chondrocytes or stem cells. Cytokines, growth factors, chemokines, protease inhibitors, kinases, apoptosis,

mechanics, and genetics are increasingly recognized to play key roles in the control of the articular cartilage behavior. Modulating IL-1 is a promising strategy to retard the progression of osteoarthritis. Gene replacement, gene control and gene addition are new areas of research for gene therapy for osteoarthritis.

7) Rheumatoid arthritis- Haematopoietic stem cell transplantation (HSCT) is now being investigated as a potential therapy. It is especially useful in severe refractory rheumatoid arthritis unresponsive to conventional therapies¹², including tumor necrosis factor-alpha blockade and is well tolerated in patients with rheumatoid arthritis. Level of disease activity and progression of joint destruction in rheumatoid arthritis closely parallels the IL-1 levels in plasma and joint fluid. IL-1 receptor antagonist (IL-1ra) is a potential therapeutic agent for use in treatment of rheumatoid arthritis which is the focus for gene therapy for rheumatoid arthritis.

8) Orthopaedic oncology- A significant opportunity exists to improve the cancer therapy beyond the capabilities of traditional cancer treatments such as chemotherapy and radiation. It focuses on the development of cancer vaccines and angiogenesis inhibitors. Regenerative medicine is shaping these new therapies through the integration of its genomics, gene and cell therapy, small molecule drug discovery, and protein therapeutic capabilities.

9) Other potential areas- Avascular necrosis, Cystic lesions of bone, revision arthroplasties, tumor reconstruction surgeries are being explored as potential areas of research for regenerative medicine. Although the prospect of growing entire new knees, hips and shoulders is still decades from becoming a clinical reality, regenerative medicine holds real potential to improve the quality of care currently available to patients suffering from various orthopaedic problems. Surgeons, scientists and engineers are using a variety of tools, including advanced materials, cells, and biomolecules and engineering design tools to develop and refine new treatments, making regenerative medicine a truly interdisciplinary area of research and development in orthopedics.

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