International Orthopaedics (SICOT) (2007) 31:719–720
DOI 10.1007/s00264-007-0425-7

EDITORIAL

Biological aspects of bone, cartilage and tendon regeneration

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Received: 15 June 2007 / Accepted: 15 June 2007 / Published online: 18 August 2007

Current orthopaedic procedures in supporting regeneration of bone, cartilage and tendon are dependant on our understanding of the molecular processes responsible for tissue repair. At present we know how to regenerate bone when physiological mechanisms of fracture repair fail [13]. Since the original description of the potential of demineralised bone matrix to induce bone at an ectopic site, it has taken more than 3 decades to bring bone morphogenetic proteins (BMPs) to clinical use. By the end of 2007 nearly 1 million patients worldwide will have been treated with BMPs for spinal fusions, non-unions, acute fractures and maxillofacial reconstruction. Use of animal models, genomics and proteomics has deciphered new mechanisms and candidate molecules for the regeneration of joint cartilage and tendons, opening new avenues in regenerative orthopaedics.

This special issue reviews novel strategies in the regeneration of bone, cartilage and tendon. Bishop and Einhorn [2] describe the clinical use of recombinant BMP-2 and BMP-7. They predict that current techniques in engineering bone for restoring defined skeletal defects represent a unique opportunity for BMPs in the future. McKay and colleagues [9] review the clinical applications of BMP-2 (INFUSE Bone Graft), while Vaccaro, McKee and colleagues [14] describe the clinical applications of BMP-7 (OP-1 implant or Osigraft). The authors suggest that recombinant human BMP-based devices, when properly applied, can eliminate the need to harvest autologous bone for grafting procedures, benefiting both the surgeon and patients. Grgurevic and collaborators [6] describe molecules discovered by proteomic analysis in the plasma of patients with an acute bone fracture. The characterisation and use of potential new biomarkers, like TGF-β-induced protein IG-H3, cartilage acidic protein 1, procollagen C proteinase enhancer protein and TGF-β receptor III, for bone and cartilage regeneration are discussed. Sendak and colleagues [11] review the newly discovered role of thyroid-stimulating hormone (TSH) and follicle-stimulating hormone (FSH) in bone remodelling. It has been recently found that low doses of TSH increase bone volume and improve bone microarchitecture and strength in aged osteoporotic rats, suggesting that TSH directly affects bone remodelling in vivo [10]. Grasser and collaborators [5], by using a genomic approach, decipher the potential mechanism of bone augmentation following systemic administration of BMP-6, suggesting that IGF-1 and EGF mediate, at least in part, the effects of BMP-6 on bone, which has been recently reported [12]. The role of prostaglandin E2 receptors and their analogs in bone formation is reviewed by Li and colleagues [8], demonstrating that the PGE2 receptor is essential for restoring bone defects in animal models. Cartilage regeneration and chronic back pain due to degenerative disc disease are among major obstacles in orthopaedics. Chubinskaya and colleagues [4] summarise the role of osteogenic protein-1 (BMP-7) in animal models of osteochondral and chondral defects, osteoarthritis and degeneration in intervertebral disc cartilage. They show that OP-1 exhibits unique pro-anabolic and prominent anti-catabolic properties having a potential for treating cartilage and disc lesions.

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Overuse tendon disorders are common and associated with a significant morbidity. Tendon and ligament function engineering and repair are discussed in articles by Aspenberg [1] and by Hoffman and Gross [7]. Aspenberg found that the repair of subcutaneous tendon ruptures can be stimulated by a single application of one of several growth factors, including PDGF, TGF-β, IGF-1, VEGF and GDF-5,-6,-7, or by a thrombocite concentrate. The response is dependent on the mechanical microenvironment, which is crucial for the repair process.

Hoffmann and Gross specifically discuss gene-therapeutic approaches using mesenchymal stem cells for a potential future application in tendon/ligament regeneration.

Borovecki and colleagues [3] discuss the potential of a genomic approach in analysing bone homeostasis and diseases. Gene expression profiling studies yielded novel insights into the complex interplay of osteoblast and osteoclast regulation, paracrine and endocrine control of bone and cartilage remodelling, as well as the pathophysiology of osteoporosis and bone tumours.

We believe that this issue will provide basic and clinical scientists with the state of the art knowledge in regenerative orthopaedics.

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