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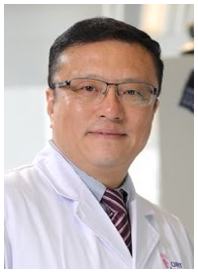
Editorial

Basic research is the foundation and driving force for clinical translation



In this issue, the osteoarthritis (OA) biology and treatment are still the main theme. Chondrocytes maintain cartilage morphology and are mechanically sensitive. Mechanical loading within the physiological range preserves chondrocyte homeostasis. Abnormal loading caused by obesity, joint instability, overuse, or trauma can lead to cartilage degeneration and OA. Zhu et al. found that ribosomal protein L35 (RPL35) regulated chondrocyte catabolic metabolism activities and is responsible for cartilage homeostasis [1]. It has been long known that inflammation factors in the joint play crucial roles in OA development and progression, among these contributing factors M1 macrophage activation which is regulated by transcriptional activity of SMARCC1 gene, and this could be a new therapeutic target for OA [2]. Jiang et al. discussed the use of a new imaging technique Radiomics for precise detection of early OA, its progression tracking, and prediction of treatment efficacy [3]. For OA management, Xia et al. reported a simple movement, active knee swing in a randomised, single-blind clinical trial significantly improved symptoms of knee OA patients through reducing intra-articular pressure [4]. Mao et al. reported the use of quercetin-3-O-β-D-glucuronide (Q3GA) for OA treatment, Q3GA reduced the cartilage degradation and the expression of inflammatory related proteins and genes in OA rats and promoted cartilage repair [5]. Zheng et al. reported the use of costal chondrocyte-derived chondrocytes to engineer cartilage-like tissues for articular cartilage regeneration, and ascorbic acid treatment enhances outcomes by promoting cartilage matrices production [6]. Extracellular vesicles (EVs) present advantages to cell-based treatments, Forteza-Genestra MA et al. compared the regenerative potential of MSC-derived EVs (cEVs) and platelet-derived EVs (pEVs) in rat OA model and found that pEVs-treated knee had better subchondral bone integrity and a greater inhibition of OA progression in female rats [7].

Soft tissues repair such as ligament, tendon, interverbal disc and muscle remain to be challenging. Prevention of adhesion formation following flexor tendon repair is essential for restoration of normal finger function. Shi et al. reported that the use of Pentamidine with gelatin has good dynamic release, biocompatibility, and degradation, significantly reduced tendon adhesions and improved tendon gliding function without interfering with tendon healing [8]. Tissue engineering approach for anterior cruciate ligament (ACL) reconstruction using acellular bone, fibrocartilage, and tendon scaffolds with multiple recombinant growth factors BMP-2, TGF-β3, or/and GDF-7 was studied and showed enhanced ACL repair as well as enthesis regeneration in animal model [9]. The accumulation of senescent cells and the continuous release of senescence-associated secretory phenotype perpetually impede disc homeostasis and hinder tissue regeneration. Intervertebral disc degeneration, and this impairment should be taken into consideration for clinical implementation of intervertebral disc repair [10]. Wan et al. comprehensively explored exosome's diverse biological functions and translational potential in the context of skeletal muscle diseases and underscored their promising future as a therapeutic target in skeletal muscle repair and regeneration [11]. Zhang et al. studied the patterns of low back pain (LBP) and its risk factors in China from 1990 to 2019 and provided strong evidence that there were diverse changing patterns for different risk factors. The rates for LBP increased dramatically with age for high BMI population, peaked at 40–60 years for manual workers, 65–80 years for smokers [12].

Bone biology is the foundation for bone pathology and the in-depth understanding of bone biology leads to potential novel treatment. Lin et al. studied the role of Pip5k1c in bone, which plays essential functions in regulating cytoskeleton, biomembrane and Ca2+ release of cells. Loss of Pip5k1c in osteocytes led to a low bone mass and impaired biomechanical properties [13]. The search for natural compounds as drugs for musculoskeletal disorders is on. Nitrate is a key component of saliva and having widely physiological functions, Li et al. reported nitrate deficiency exacerbated osteoporosis, while nitrate supplementation prevented bone loss in OVX mice, suggesting saliva nitrate as a candidate for maintenance of bone homeostasis [14]. Hong et al. reported that Pinocembrin, a predominant flavonoid found in damiana, honey and fingerroot, has potent inhibitory effects on osteoclastogenesis and bone resorption, suggesting a promising candidate for managing osteolytic bone diseases [15]. Wang et al. reported a natural compound Cycloastragenol, an osteoclast inhibitor with protective effect on bone loss, could be used to treat glucocorticoid-induced osteonecrosis of the femoral head in patients [16]. The pursue for new biomaterials for bone regeneration continues. Wei et al. developed a customized porous CaSiO3 (nCSi) scaffold and demonstrated that the personalized nCSi bioceramic scaffold had good biocompatibility and osteogenic capability *in vivo* and might be developed as next-generation of oral implant [17]. Recently, the osteogenic potential of Adiponectin-labelled audiogenic lineage progenitors (Adipoq-lineage progenitors) in bone marrow has been identified as important cell population for bone homeostasis

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and repair. Single-cell sequencing demonstrated that Adipo-lineage progenitors express higher levels of Shn3 comparing to other mesenchymal cell populations in mice and human, depletion of Shn3 in Adipoq-lineage progenitors resulted in a significant increase in trabecular bone mass and bone formation *in vivo*, and knocking down Shn3 in Adipoq lineage progenitors enhanced bone fracture healing, suggesting Shn3 was a negative regulator for bone formation and might be a new drug target [18]. It has been known for long that angiogenesis and neurogenesis are essential elements for bone formation. Recently, the role of lymphogenesis in tissue repair has driven more interests. Zheng et al. reported inhibition of lymphatic drainage significantly delayed fracture healing, and increasing lymphatic drainage might be a new therapeutic target for tissue repair [19].

Management of bone infection is still a clinical challenge. Beagan et al. reviewed the use of sheep as preclinical models for bone infection research, and they found that majority of sheep developed osteomyelitis and tolerated the infection well [20]. Li et al. reviewed that antibacterial coating strategies for reducing bacterial infections in animal models. Future studies of implant coatings should focus on optimal biocompatibility, antibacterial effects against multi-drug resistant bacteria and polymicrobial infections, and osseointegration and osteogenesis promotion especially in osteoporotic bone [21]. Shock waves treatment was reported to be able to enhance Vancomycin into *S.aureus* infected osteoblasts through activating P2X7 receptor on osteoblasts, and demonstrated efficacy and safety of shock-wave assisted antibiotics in the treatment of chronic osteomyelitis in rat [22]. Diabetic foot ulcers are major complications of diabetes with severe soft tissue destruction and infections. The tibial cortex transverse transport (TTT) method has been invented and used for management of severe diabetic ulcers. Kong et al. used rat TTT model and carried protein profile analysis and found a key differentially expressed protein, osteopontin, which significantly promoted migration and proliferation of vascular endothelial cells and might be part of the mechanisms why TTT surgery could promote diabetic ulcers healing [23].

Robotic surgery is a new development in recent years. Xu et al. reported a randomized, multicenter, parallel-controlled clinical study that demonstrated that the LANCET robotic system was superior to conventional total hip replacement surgery in terms of accuracy of acetabular cup placement and has no difference in postoperative hip functional recovery and complications [24]. Hallux valgus is a common progressive complex deformity of the first metatarsophalangeal joint, generally accompanied by pain or a bunion on the medial head of the first metatarsal bone. The corrective surgery for hallus valgus is a standard treatment, but it has many different surgical methods. The Foot and Ankle Committee of Orthopaedic Branch, Chinese Medical Doctor Association published a new clinical guideline in this issue on the third generation minimally invasive surgery for hallux valgus as recommendations for indications, contraindications, operative planning and techniques, post-operative managements [25].

In summary, this issue consists a variety of articles that cover all the hot topics of orthopaedic surgery and research. From basic bone and cartilage biology to new treatment strategies of OA, cartilage defect, ACL and tendon repair, osteoporosis, bone fracture healing, bone infection as well as robotic surgery and new clinical guideline for minimally invasive Hallus valgus surgery. All these studies are rotted from basic research and focused on translational potentials, which fit well with the purpose of our journal, that is to drive basic research into clinical translation.

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