

## What's the Future of Osteoarthritis Treatment?

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Thanks to a global collaboration in the orthopaedic field, a multitude of novel therapeutic strategies have been developed to conquer previously incurable conditions. However, some diseases remain without suitable treatments. In particular, osteoarthritis (OA) continues to lack remedies that halt disease progression or cure the condition.

OA is the most common form of arthritis and leads to functional decline and loss in quality of life by causing stiffness, pain, and impaired joint movement. In fact, OA has been recognized as one of the leading causes of disability for decades. Due to increasing life expectancy and a growing population with related disorders, such as obesity, the prevalence and incidence of OA are expected to rise sharply. Unfortunately, considering that there is no current simple and efficient cure for OA, it appears that OA will continue to be one of the most prevalent incurable chronic diseases. It is, and will continue to be, a heavy financial burden for the world economy.

According to a recent white paper published by the Osteoarthritis Research Society International (OARSI), neither diagnosis nor treatment of OA meets the expectations of the society. For rheumatoid arthritis (RA), C-reactive protein (CRP) is recognized as a clinically acceptable biomarker that is accompanied by a diverse panel of potential indicators, including heat shock protein family A member 6 (HSPA6), matrix metalloproteinase 1 (MMP1), MMP13, and tumor necrosis factor superfamily member 10 (TNFSF10). On the contrary, there are no accepted specific diagnostic biomarkers for OA. Thus, OA is currently diagnosed by physical examination and, when necessary, X-ray, magnetic resonance imaging (MRI), and arthroscopy imaging techniques. However, these diagnostic tools have low sensitivity and specificity, and as a result, can lead to uncertain diagnoses for patients seeking treatment for their symptoms.

Meanwhile, since OA has long been classified as a prototypical non-inflammatory arthritis, which has a primary symptom of pain in the affected joint(s), the current guidelines for OA treatment are predominantly limited to palliation for pain relief until a joint replacement is indicated. Aside from analgesia and non-steroidal anti-inflammatory drugs (NSAIDs), there is a wide range of palliative strategies practiced in clinical settings, such as viscosupplementation with intra-articular hyaluronate injections, intra-articular corticosteroid injections, and autologous chondrocyte implantation into the damaged areas. However, there are no approved pharmaceutical products that can halt or reverse the onset of OA, making osteoarthritic progression inevitable for OA patients.

With the substantial progress in molecular biology during the last two decades, OA has now been recognized as an inflammatory disease, and a diversity of proinflammatory factors have been discovered to play vital roles in OA initiation and progression. With these new and essential findings, multiple attempts have been made to adapt RA treatment methods to OA. Sadly, the efficacy of functional chemical or biological disease-modifying antirheumatic drugs (DMARDs) has not been replicated in OA conditions.

Further, despite articular cartilage destruction being the primary concern of OA progression, none of these currently available medications actively promote chondrocyte bioactivities that battle against the degeneration of cartilage tissue. Thus, the investigation for new OA therapeutics has shifted from synthetic chemicals to biological molecules, including several transcription factors such as nuclear factor of activated T cells 1 (NFATC1), NFATC2, and runt related transcription factor 1 (RUNX1), and growth factors such as transforming growth factor  $\beta$ s (TGF $\beta$ s), bone morphogenetic proteins (BMPs), and insulin like growth factors (IGFs). Neverthe-

less, all of these potential treatments are still in their respective infancies with published pre-clinical results that require further verification.

In our opinion, there is an enormous and urgent need to identify novel technologies that sensitively and effectively diagnose OA, establish a comprehensive and practical prevention strategy to decrease the incidence of OA, and develop safe and efficient therapies that can reduce, and even reverse, the progression of OA.

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