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Opinion
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Tissue Engineering and Regenerative Medicine: The Challenges to Fully Restore Cartilage Functionality

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Opinion

Osteoarthritis (OA) is a chronic joint condition affecting over 250 million people worldwide [1]. Along with a significant impact on health-care and society, the Global Burden of Disease Study from the World Health Organization reported that knee OA is the 11th leading cause of disability, and shows a growing trend [2] Although it may damage any joint in the human body, the most common disorders affect joints in the hips, knees, hands and spine. Thus, with a society facing a demographic transformation, with an epidemic increase of obesity, integrated interventions to weaken the problem are mandatory. Each year, more than 50 million people visit doctors because of joint pain; half of them with a damage of the articular cartilage.

Apart from not being possible to reverse the underlying process, in its early stages OA symptoms can usually be effectively managed. In fact, adopting a healthy lifestyle may slow the disease progression, and help improve joint function and reduce pain [3]. On the other hand, in the following stages, surgery may be required. Thus, significant efforts are being developed worldwide in the fields of tissue engineering and regenerative medicine, but full cartilage restoration remains a paramount challenge [4]. Tissue engineering is a multidisciplinary scientific field, which applies a wide variety of methodologies. Therefore, multidisciplinary research teams can provide suitable inputs for its development [5]. One of the major goals is to produce biological substitutes to restore, maintain or improve tissue function, using biocompatible and biodegradable support structures, i.e. scaffolds, in conjunction with human cells [6].

Gathering tissue engineering and regenerative medicine, researchers have been interested on developing alternative approaches for restoring joint functionality. For instance, the creation of constructs with a structure and composition resembling native cartilage and yielding similar mechanical behavior [7]. To do so, one of the most promising methodologies involves the use of additive manufacturing (AM) processes. AM technologies allow the production of complex 3D structures with a high level of control, predefined geometry, size and interconnected pores, in a reproducible way. This controlled organization enhances the vascularization and, thus, transport of oxygen and nutrients throughout the whole structure, providing an adequate biomechanical environment for tissue regeneration [8]. However, adapting the adequate technology with enhanced biomaterials, to obtain customized implants that mimic the native tissue, remains an utmost challenge to be solved.

Cartilage is a tissue with a huge complexity, which is present in the human body in three types: hyaline cartilage, fibrocartilage and elastic cartilage. Apart to some resemblances, these types are quite different and play unlike roles for human functionality. For instance, the hyaline cartilage, also known as articular cartilage, has a major role in providing joints with a surface that combines low friction with high lubrication. A deeper knowledge on cartilage characterization, bridging the gap between anatomy and physiology, may lead the way for better implants aiming cartilage repair and regeneration [9]. This is of even more interest as cartilage is an a vascular tissue of the human body, hence with an extremely low capability for tissue regeneration. Regardless of the low metabolic activity and relatively poor ability to heal of chondrocytes, hyaline cartilage is a dynamic and responsive tissue, where the contribution of cell produced extracellular matrix components play a major role [10]. It is well documented in the literature that hyaline cartilage has remarkable mechanical properties (elastic modulus of ~123MPa; mechanical tensile strength of 17 MPa; compressive modulus varying between 0.53 and 1.82 MPa; and compressive stress between 14-59 MPa) [11] and lasting durability, despite its few millimeters of thickness. The referred complexity and properties, demonstrate the challenges faced by research groups aiming to fully restore cartilage functionality [12-14].

Concluding, in the last years, the world has assisted an increase in the number of debilitating conditions and severe pain caused by cartilage defects, being the scientific and clinical community aware of the major problem that our society is facing. Regarding treatment, tissue science and regenerative medicine have emerged as promising disciplines concerning tissue and/or organ repair and regeneration. In fact, choosing the right approach for tissue regeneration is a major concern for every researcher in this field. However, although there has been a huge amount of work aiming to regenerate cartilage, a tailored construct has not been achieved yet.

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