Introduction

Cartilage has an important biomechanical function in distributing load onto the underlying bone, and in providing a smooth low-friction surface for joint articulation. To achieve these functions, it has a highly specialised structure, and is an example of a tissue predominantly formed of extracellular matrix (ECM). As no vessels or nerves permeate it, cartilage is avascular and aneural, so it lacks some of the complexity of other tissues. The main component of the tissue is an expanded and highly specialised ECM, in which a single cell type, the chondrocyte, is embedded. These cells form only 1–2% of the tissue mass, but are very important for cartilage health — chondrocytes are responsible for producing and assembling the cartilage ECM, and continue to do so throughout an individual's life. The ECM is predominantly formed of a dense network of collagen fibres embedded in a high concentration of proteoglycan (1). The collagen, mainly type II, with lower amounts of types IX and XI, provides tensile strength. Proteoglycans, mostly aggrecan, endow the tissue with elasticity and compressive resilience. A major contribution to these properties comes from the biophysical properties of aggrecan, which forms supramolecular aggregates with hyaluronan and link-protein, and is thereby made largely immobile in the collagen fibre network (2–4). Aggrecan is a protein with ten times its weight of chondroitin sulphate and keratan sulphate, attached in 100 or more extended chains. It forms a 'bottle brush' structure with many highly charged sulphate and carboxylate groups. Its concentration in cartilage is about 50mg/ml, which for aggrecan is ~25μM, but the immobile anionic charged groups attached to it are ~200mM. This attracts mobile counterions, and creates a large Donnan osmotic pressure, which draws water into the cartilage matrix. The influx of water extends the collagen network until tension in the collagen balances the tissue swelling pressure. Cartilage is ~75% water and its compressive resilience and elasticity result from the combined functions of the fibrillar collagen, which is hydrated and extended by the polyanionic aggrecan (1). It is, therefore, important for the function of the articular cartilage that the integrity of the collagen network, and the high content of aggrecan that surrounds it in the tissue, are maintained throughout life. Equally, in any strategy to replace the tissue with a biological repair or with a temporary or permanent synthetic substitute, it is important that these properties are replicated.

As a result of this composite structure — i.e. sparse cells embedded in a large and well-organised ECM, coupled with an absence of vasculature to allow the interaction of systemic cells with the local environment — cartilage has a limited ability to repair once it is physically damaged. Thus, injuries to cartilage, which are common in sports activities, frequently lead to more serious joint pathology and osteoarthritis (OA). OA is an age-related degenerative disease of high prevalence, in which cartilage damage and loss of tissue frequently occur (5).