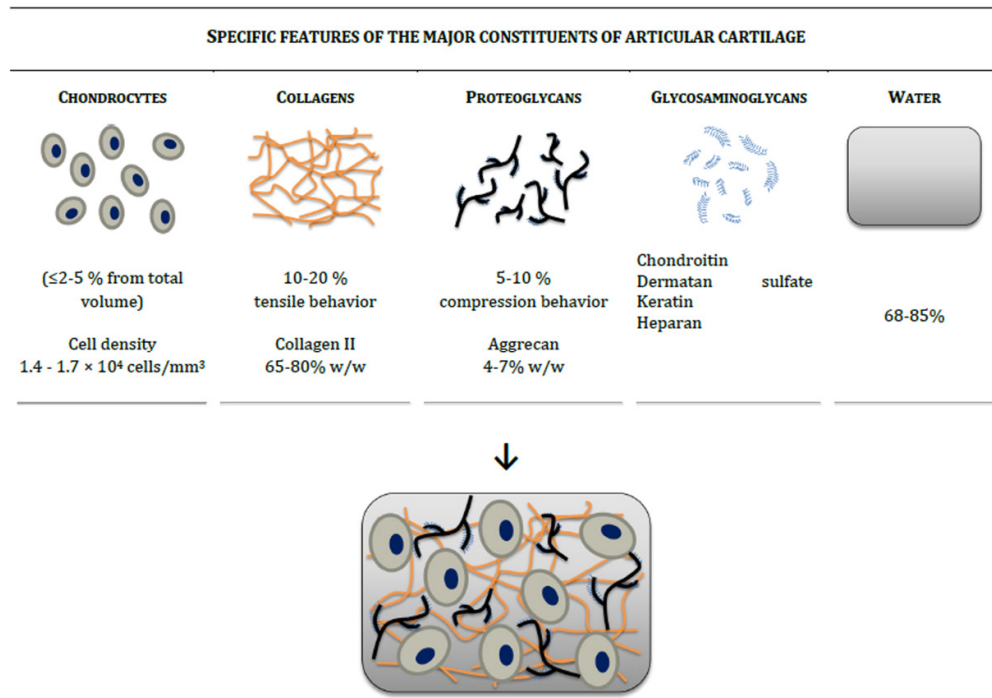


Supplementary Data

Supplementary Figure S2 Schematic representation showing the structured organization of native cartilage tissue, as well as specific features of its main constituents, adapted (Shortkroff and Spector 1998).



Supplementary Table S1 Summary of clinical strategies for articular cartilage replacement, based on (Beris et al. 2005; Haleem and Chu 2010).

ARTHROSCOPIC TECHNIQUES		CARTILAGE REPLACEMENT TECHNIQUES	CELL BASED THERAPIES	
NON REPARATIVE PROCEDURES	REPARATIVE PROCEDURES – BONE MARROW STIMULATION		AUTOLOGOUS CHONDROCYTE IMPLANTATION (ACI)	TISSUE ENGINEERING
debridement	Pridie drilling	mosaicplasty	First generation two stage procedure	Chondrocytes /MSCs
chondral shaving	microfracture technique		Second generation collagen matrix	scaffolds or hydrogels
knee joint lavage	abrasion chondroplasty	osteocondral/ chondral allografts	Third generation MACI	GF/ cytokines
			Fourth generation MSCs	

MACI - Matrix-induced autologous chondrocyte implantation, MSCs - mesenchymal stem cells, GF - growth factors.

Supplementary Table S2 List of supporting and opposing arguments in applying stem cells versus somatic, precommitted cells for cartilage tissue engineering.

CELL SOURCE	PRIMARY CULTURE	STEM CELL		REF.
	<i>CHONDROCYTES</i>	<i>BONE MARROW (BMSCs)</i>	<i>ADIPOSE TISSUE (ASCs)</i>	
Collection procedures	Cartilage biopsy	Marrow aspirate	Liposuction or reconstructive surgery	(Varma et al. 2007)
Isolation site influence	donor site morbidity & contamination or potential infection	more invasive, painful and not frequently result of another intervention	performed in parallel with another surgery, safe and easy to obtain	
Cell yield (number)	limited	limited numbers, quickly amplified in monolayer	high 400000 stem cells/ml adipose tissue	(Aust et al. 2004)
Mitotic potential	slow	medium	high	
Self renewal capacity	low	limited	high	
Plasticity	tendency to dedifferentiation	dedifferentiation is not an issue	dedifferentiation is not an issue	(Kino-Oka et al. 2005)
Isolated tissue origin	provoke immune rejection	supportive cells for haematopoiesis, exists 1 out of every 105 cells	not an issue	
Additional procedures	no need of GF or can use GF to not dedifferentiate (TGF- β 3)	TGF- β 1, TGF- β 3, BMPs	TGF- β 1, TGF- β 3, BMPs	(Erickson et al. 2002)

BMSCs – bone marrow mesenchymal stem cells; ASCs – adipose derived stem cells, Growth factors- GF; transforming growth factor β - (TGF- β); Bone Morphogenetic Proteins - (BMPs)

Supplementary Table S4 Main advantages and disadvantages of carbohydrate polysaccharide hydrogels from algae origin.

POLYMER NAME	ADVANTAGES	DISADVANTAGES	REF.
ALGINATE	<ul style="list-style-type: none"> <input checked="" type="checkbox"/> Low toxicity <input checked="" type="checkbox"/> Cheap <input checked="" type="checkbox"/> Easy to gel 	<ul style="list-style-type: none"> <input checked="" type="checkbox"/> Degrades through ionic exchange with surrounding media <input checked="" type="checkbox"/> Minimal cellular interaction <input checked="" type="checkbox"/> Protein not easily absorbed 	(Pawar and Edgar 2012; Therese Andersen et al. 2012)
AGAROSE	<ul style="list-style-type: none"> <input checked="" type="checkbox"/> Easy to control pore sizes <input checked="" type="checkbox"/> Easy to gel 	<ul style="list-style-type: none"> <input checked="" type="checkbox"/> Larger pores ideal for cellular growth introduce structural instability <input checked="" type="checkbox"/> Low mechanical properties 	(Laurienzo 2010; Schuh et al. 2011)
CARRAGEENAN	<ul style="list-style-type: none"> <input checked="" type="checkbox"/> Thermally reversible <input checked="" type="checkbox"/> Cheap <input checked="" type="checkbox"/> Easy to gel & manipulate <input checked="" type="checkbox"/> Display close similarity with mammalian glycosaminoglycans 	<ul style="list-style-type: none"> <input checked="" type="checkbox"/> Degrades through ionic exchange with surrounding media <input checked="" type="checkbox"/> Influenced by temperature, pH and cations concentration 	(Daniel-Da-Silva et al. 2007; Grenha et al. 2009; Mehrban N et al. 2009)
ULVAN	<ul style="list-style-type: none"> <input checked="" type="checkbox"/> Abundant and cheap source <input checked="" type="checkbox"/> Great chemical functionalities <input checked="" type="checkbox"/> Display close similarity with mammalian glycosaminoglycans 	<ul style="list-style-type: none"> <input checked="" type="checkbox"/> Contain proteins which need specific purification protocols <input checked="" type="checkbox"/> Formation of microaggregates when dissolved in water 	(Chiellini and Morelli 2011)