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(54) **COMPOSITIONS AND METHODS FOR CARTILAGE REPAIR**

ZUSAMMENSETZUNGEN UND VERFAHREN ZUR KNORPELREPARATUR

COMPOSITIONS ET PROCÉDÉS POUR LA RÉPARATION DE CARTILAGE

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Description

TECHNICAL FIELD

[0001] The invention generally relates to compositions and these compositions for use in facilitating cartilage repair in a patient in need thereof. More particularly, the invention relates to autologous compositions and these compositions for use in inducing chondrogenesis at sites in need of cartilage repair in patients in need thereof.

BACKGROUND

[0002] Mesenchymal stem cells are pluripotent blast or embryonic- like cells located in blood, bone marrow, dermis and perisosteum. In general, these cells are capable of renewing themselves over extended periods of time as well as, under various environmental conditions, differentiating into cartilage, bone and other connective tissue. Recently, various investigators have researched the potential for using these cells to repair or regenerate target tissues, e.g., bone, cartilage, etc. In this manner MSCs have been reported to have regenerative capabilities in a number of animal models. See Acosta et al. (2005) Neurosurg Focus 19 (3) : E4; Barry (2003) Novartis Found Symp. 249: 86- 102, 170- 4, 239- 41; Brisby et al. (2004) Orthop Clin. North Am. 35 (1) : 85- 89; Buckwalter and Mankin (1998) Instr Course Lect. 47: 487-504; Caplan (1991) J Orthop Res. 9 (5) : 641- 650.

[0003] Recently, Centeno et al. (US Patent Application 11/773, 774) described a method for expanding MSC's using a growth channel and autologous platelet lysate. Also described were methods for transplanting certain levels of growth factors (platelet lysate or platelets) with the expanded MSC's to the area in a patient in need of repair. The levels of these growth factors were based on a percentage of platelet lysate needed to optimally expand the cells ex- vivo.

[0004] MSC's can readily differentiate in culture depending on cytokine exposure, environmental conditions (pressure, attachment opportunities, passage treatment, etc...), or other chemical exposure. For example, exposure to varying levels of TGF-beta, FGF, and/or PDGF can all have impacts on the final cell phenotype produced in culture. In addition, leaving cells in culture longer also has impacts on differentiation potential. Cells can be cultured for a certain visual morphology, confluence, or density, all of which has an impact on the final cell product produced and its potential for certain types of tissue repair.

[0005] In replacing or repairing tissue with MSC's, one concern is the use of autologous or non-autologous cells. While MSC's have been traditionally considered immune privileged, recent investigations have demonstrated their activation of the natural killer cell system in a foreign host. (Spaggiari, Capobianco et al. 2006) This makes the use of non-autologous cells difficult, as it is anticipated that the host's immune system will attack these foreign cells and potentially decimate the population of transplanted MSCs, thus severely limiting their repair capabilities.

[0006] There is a need in the art for MSC expansion techniques that do not use drugs or growth factors which are not FDA approved and can be effectively used to replace tissue in a patient in need thereof. This is especially true where the tissue in the patient in need of repair is cartilage. Cartilage repair is a major issue in health care which will only continue to increase as the median age in the United States continues to increase.

[0007] There is a need for autologous techniques to yield MSC and non-MSC based cartilage repair techniques.

[0008] The present invention is directed toward overcoming one or more of the problems discussed above.

SUMMARY OF THE EMBODIMENTS

[0009] The present invention provides repair compositions for facilitating repair and/or replacement of cartilage in patients in need thereof. Repair compositions include an effective amount of a platelet-based material in combination with one or more chondrogenesis inducing agents. In some cases the platelet-based material and/or the chondrogenesis inducing agent(s) are autologous.

[0010] Aspects of the platelet-based material include one or more of the following solutions: platelet lysate, platelet rich plasma, platelet rich fibrin, and/or whole cell platelet concentrate.

[0011] Aspects of the chondrogenesis inducing agent include growth factors, cytokines, steroid hormones and nutrients for facilitating cartilage formation in patients in need thereof. One or more agents are combined with the platelet-based material. Chondrogenesis inducing agents can be autologous to the patient.

[0012] Repair compositions of the invention can further include cell-based materials, including: mesenchymal stem cells, chondrocytes, isolated bone marrow nucleated cells, chondrocyte progenitor cells, osteoblasts, or non-human embryonic stem cells of other lineages. Cells are typically autologous to the patient, being harvested from the patient prior to cartilage repair and expanded to sufficient numbers for optimal treatment.

[0013] Repair compositions of the invention can also include carrier materials, including: gels, hydrogels, absorbable polymers, and the like. Carriers act as scaffolding for cartilage formation within the site of cartilage repair. Carriers can be added to the site of repair contemporaneously with the repair compositions or be part of the repair composition.

[0014] The present invention provides pharmaceutical compositions for use in therapeutic applications. Pharmaceutical compositions herein are used to treat patients having a site in need of cartilage repair, in some cases the patient has osteoarthritis or other like degenerative disease.

[0015] The present invention provides kits having one or more of the following materials: one or more platelet

based material, one or more chondrogenesis inducing agent(s), one or more cell based material and one or more carrier. In some aspects the kit includes the materials necessary to harvest the target material from a patient rather than the material itself, for example the tools and supplies necessary to harvest and prepare a platelet lysate. Kits may include vials, tissue culture flasks, culture medium, and other like laboratory materials necessary for the harvest and isolation of materials necessary to practice the present invention.

[0016] Described herein are also methods for facilitating cartilage repair or replacement in a patient in need thereof. Methods include harvesting and preparing a platelet-based material, for example a 5% to 40% platelet lysate, from a patient having a cartilage repair site in need of treatment; optionally harvesting and preparing a chondrogenesis inducing agent from the same patient, e.g., isolating IGF-1 from the patient, and/or obtaining and administering a non-autologous chondrogenesis inducing agent (such as dexamethasone, ascorbic acid, etc...); optionally harvesting and preparing a cell-based therapy from the same patient, e.g., harvesting and isolating mesenchymal stem cells from the patient's bone marrow, and/or obtaining and administering a non-autologous cell based material; optionally obtaining a carrier material; administering to the repair site a repair composition of the invention; monitoring and re-administering repair compositions of the invention to patient's that require additional treatment for cartilage repair.

[0017] These and various features and advantages of the invention will be apparent from a reading of the following detailed description and a review of the appended claims.

DETAILED DESCRIPTION

Definitions

[0018] The following definitions are provided to facilitate understanding of certain terms used frequently herein.

[0019] "About" refers to a +/-10% variation from the nominal value. It is to be understood that such variation is always included in any given value provided herein, whether or not it is specifically identified.

[0020] "Chondrogenesis inducing agent" refers to any agent capable of inducing or facilitating cartilage formation above the levels of cartilage formation found in a normal and untreated subject. Chondrogenesis inducing agents include but are not limited to; growth factors, cytokines, hormones, and various essential nutrients. Illustrative growth factors include Transforming Growth Factor-beta (TGF-β), Fibroblast Growth Factors (FGFs), Insulin Like Growth Factors (IGFs), Bone Morphogenic Protiens (BMPs); illustrative cytokines including Cytokine-like 1 (Cytl1); illustrative hormones include Human Growth Hormone (HGH); and Testosterone and illustrative essential nutrients include Ascorbic Acid, pyruvate, and amino acids. A chondrogenesis inducing agent can include one or more of the materials as described above, for example a combination of TGF-β and pyruvate.

[0021] "Mesenchymal stem cells" or "MSCs" refers to multipotent stem cells capable of differentiating into osteoblasts, chondrocytes, myocytes, adipocytes, neuronal cells, pancreatic islet cells, and the like. Additionally, methods and compositions detailing MSCs are described in US Patent No. 5,486,359, 6,387,367 and 5,197,985. In more detail, mesenchymal stem cells are multipotent stem cells located in the bone marrow, peripheral blood, adipose tissue and other like sources. Source MSCs of the invention can be harvested from the iliac crest of the patient in need (or other source such as the IVD, periosteum, synovial fluid, or the vertebral body or pedicle) of the restorative/replacement therapy (or a suitable donor), such patient is referred to herein as a "patient in need or patient in need thereof (note that other sources, such as adipose tissue, synovial tissue, and connective tissue have recently been identified and are also considered as MSC sources within the scope of the present invention). In one embodiment, approximately 10-100 cc of bone marrow is harvested and "isolated" using methods described in US Patent Application 60/761,441 to Centeno or through adherence to plastic, as described in US Patent No. 5,486,359 to Caplan et al.

[0022] "Platelet lysate" refers to the combination of natural growth factors contained in platelets that have been released through lyses of the platelets. Lyses can be accomplished through chemical means (i.e., $CaCl_2$), osmotic means (use of distilled H_2O), or through freezing/thawing procedures. Platelet lysates of the invention can also be derived from whole blood and can be prepared as described in US Patent No. 5,198,357.

[0023] "Repair" refers to restoration of some or all of a surface's cartilage to an acceptable operating condition. In some instances this may entail a 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 100%, and 100+% increase over the untreated condition in the patient in need of cartilage repair.

[0024] "Whole cell platelet concentrate", "platelet rich plasma", and "platelet rich fibrin" are as generally known in the art. For example, platelet rich plasma or PRP can be obtained through methods as described in Landesberg et al., J Oral Maxillogac Surg 58:297, 2000.

Aspects of the Invention

[0025] Aspects of the present invention provide cartilage repair compositions for facilitating cartilage repair in a patient in need thereof as defined in the claims. Embodiments include a therapeutically effective amount of platelet lysate in conjunction with one or more chondrogenesis inducing agents. The platelet lysate is an autologous platelet lysate. In some cases the chondrogenesis inducing agent is an autologous chondrogenesis inducing agent.

[0026] In one embodiment, a repair composition includes a therapeutically effective amount of one or more of a platelet rich plasma, platelet rich fibrin, or a whole cell platelet concentrate in conjunction with one or more chondrogenesis inducing agents. The platelet rich plasma, platelet rich fibrin and/or whole cell platelet concentrate can be autologous. For purposes of the invention, any one or more of platelet lysate, platelet rich plasma, platelet rich fibrin and/or whole cell platelet concentrate will be referred to as a platelet-based material.

[0027] In another embodiment, the repair composition includes a therapeutically effective amount of a combination of a platelet lysate and two or more of platelet rich plasma, platelet rich fibrin or whole cell platelet concentrate in conjunction with one or more chondrogenesis inducing agent(s). As above, either or both of the platelet lysate and two or more of platelet rich plasma, platelet rich fibrin or whole cell platelet concentrate can be autologous. In some embodiments the chondrogenesis inducing agent(s) is also autologous.

[0028] In still another embodiment, a repair composition of the invention herein includes from about 10, 0000 to 10, 000, 000, 000 mesenchymal stem cells. In typical cases the mesenchymal stem cells are autologous and prepared per methods described in the definition section above or as described in US Patent Application No. 11, 773, 774 (and U.S. Provisional Patent Application No. 61/014, 987) . Alternatively, about from 10, 000 to 10, 000, 000, 000 chondrocytes can be combined with repair compositions of the invention, chondrocytes can be autologous. Autologous chondrocytes can be isolated and expanded using techniques as described herein for MSCs as well as through a review of the relevant art, e.g., Johnson et al., Tissue Engineering, 2004 10 (9- 10) 1308- 1318. In other embodiments the mesenchymal stem cells or chondrocytes are non- autologous and purchased from a vendor. In general, any combination of cells useful for inclusion in the repair compositions herein will be referred to as cell- based materials.

[0029] As such, repair compositions as described herein can include one or more of the following: autologous or non-autologous platelet-based material(s); autologous or non-autologous chondrogenesis inducing agent(s); and autologous or non-autologous cell-based materials(s).

[0030] Other aspects described herein provide methods for facilitating cartilage repair in a patient in need thereof.

[0031] Methods described herein include, administering a repair composition (e.g., platelet lysate and chondrogenesis inducing agent) of the invention to a site in a patient in need of such therapy. Methods described herein would include preparation of the repair composition as either a autologous composition or non autologous composition. Where any one component of the repair composition is from a non-autologous source (excluding excipients, solutions, e.g., sterile PBS, and other materials required to administer the repair composition) the entire composition is considered non-autologous.

[0032] In another embodiment, described herein the components that make up a repair composition can be administered sequentially, for example, the platelet lysate (and/or platelet rich plasma, platelet rich fibrin and/or whole cell platelet concentrate) and chondrogenesis inducing agent can be administered in a non-contemporaneous manner, for example within one minute of each other, within ten minutes of each other, within one hour of each other, within one day of each other or within one week of each other. Methods described herein include any administration procedure that results in the components of the repair composition being administered to the site in need of repair, as long as the administration is directed at repair of the same site in need of repair in the patient in need of repair.

[0033] Methods described herein can include preparing platelet lysate solutions, platelet rich plasma, platelet rich fibrin and/or whole cell platelet concentrates from the patient in need of treatment. These platelet based materials are then autologous to the patient in need of therapy. Methods for isolating and preparing these materials are described in US Patent Application Nos. 11/773,774 and US Provisional Patent No. 61/014,987.

[0034] As noted above, in some embodiments described herein, mensenchymal stem cells are administered in a therapeutic amount to the site in need of cartilage repair either contemporaneously or non-contemporaneously with the repair compositions of the invention.

Cartilage Repair Compositions

[0035] In more detail, composition embodiments of the invention include cartilage repair compositions having an enhanced capacity for cartilage repair in a patient in need thereof. Cartilage repair composition embodiments in accordance with the invention include various combinations of: platelet lysate solution, platelet rich fibrin, platelet rich plasma, and whole cell platelet concentrate with one or more chonodrogenesis inducing agent(s). Chondrogenesis inducing agents include various growth factors, cytokines, hormones and nutrients that have been shown to induce or facilitate cartilage growth in the *in vivo* or *in vitro* setting.

[0036] In some embodiments, the platelet lysate solution, platelet rich fibrin, platelet rich plasma and/or whole cell platelet concentrate are autologous to the patient receiving the repair composition. In other embodiments, the chondorgenesis inducing agent(s) is also autologous to the patient receiving the repair composition.

[0037] Autologous platelet-based materials are harvested and prepared as described in US Patent Application 11/773,774. Autologous chondrogenesis inducing agents are obtained per the target agent, for example, growth factors like BMP-7 and BMP-2 can be purchased from Stryker, Inc and Medtronic , cytokines like entanercept (TNF-alpha inhibitor) can be purchased from Am-

gen/Wyeth, Inc, and the like.

[0038] In typical embodiments the repair compositions include stem cell or cartilage cell growth enhancing compositions of autologous platelet lysate solution. The platelet lysate solution of the invention is typically from about 5% to about 40% plaelet lysate, and more typically between about 5% and 20% platelet lysate. Optimal levels of platelet lysate for any given patient can be determined based on bioavailability and concentrations of growth factors in the patients lysate. Optimal levels can be determined by reference to US Patent Application No. 11/773,774.

[0039] Typical chondrogenesis inducing agents herein include growth factors that induce or facilitate cartilage growth. Growth factors include: fibroblast growth factor, insulinlike growth factor-1, transforming growth factor-beta, bone morphogenetic protein-2, human growth hormone, PDGF-BB, and the like. (see for example: Cassiede et al., J Bone Miner Res., 1996. 11(9): p. 1264-73; Miyata et al., J Cell Physiol., 2005. 204(3): p. 948-55; Kawamura et al., Exp Hematol., 2005. 33(8): p. 865-72; Zhang et al., J Huazhong Univ Sci Technolog Med Sci., 2004. 24(3): p. 275-8; Toh et al., Growth Factors, 2005. 23(4): p. 313-21; Chrisman, O.D., Clin Orthop Relat Res., 1975 (107): p. 232-8; Denko et al., Semin Arthritis Rheum, 2005. 35(1): p. 24-34). Illustrative amounts of chondrogenesis inducing agents include: 1-100 ng/ml (1-500 nM) dose of corticosteroid, 1-500 ng/ml of TGF-beta, 1-500 nM Ascobic Acid (1-500 mg/ml), FGF-2 of 1-100 ng/mL, 10-500 ng/mL of IGF-I.

[0040] Other typical chondrogenesis inducing agents herein can include cytokines that induce or facilitate cartilage growth. Illustrative cytokines include: interleukin-1 (IL-1) and Cytokine-like 1 (Cytl1). Typical chondrogenesis inducing agents herein can also include steroid hormones like corticosteroid, human growth hormone, testosterone.

[0041] Note also that typical chondrogenesis inducing agents herein can include various cartilage inducing nutrients, for example: glucosamine, hyaluronic acid, (Zhu et al., Stem Cell 2005), collagen, glycoaminoglycans, amino acid mixtures, sodium pyruvate, ascorbic acid, carbohydrates, and the like.(Cassiede et al.; Miyata et al.; Kawamura et al.; Zhang et al.; Toh et al.; Bosnakovski et al., Biotechnol Bioeng., 2006. 93(6): p. 1152-63; Derfoul et al., Osteoarthritis Cartilage, 2007. 15(6): p. 646-55; Song et al., Cytotherapy, 2004. 6(6): p. 596-601). In some embodiments, combinations of one or more types of chondrogenesis inducing agents are combined with the platelet-based solutions of the invention, for example: a growth factor in combination with a cytokine, a growth factor in combination with a nutrient, or other like combinations.

[0042] In one embodiment, an about 5% to 40% platelet lysate solution is combined with one or more chondrogeneis inducing agents. Illustrative chondorgenesis inducing agent combinations include IGF-1 and corticosteroid with or without collagen. Platelet lysate with 50ng/ml of dexamethasone, platelet lysate with ascorbic acid, dexamethasone, and pyrate, and the like.

[0043] In other repair compositions described herein, mesenchymal stem cells are combined with the platelet-based solutions and chondrogenesis inducing agents of the invention. Mesenchymal stem cells are typically autologous and can be harvested and expanded from the patient in need thereof by the methods described above. In alterative embodiments, chondrocytes are combined with the platelet-based solutions and chondrogenesis inducing agents of the invention. Chondrocytes are typically autologous and can be harvested and expanded from the patient in need thereof. In some embodiments a mix of mesenchymal stem cells and various differentiated forms of mesenchymal stem cells (up to and including chondrocytes) are combined with the platelet-based solutions and chondrogenesis inducing agents. Regardless of the nature of the cells, they can be expanded prior to implantation into the patient in need thereof in accordance with aspects of the present invention.

[0044] In still other repair compositions, a carrier material is added to modify the capacity of the embodiments to remain at the site of injury or the timing of release of the composition into the site of injury. Illustrative carriers include: gels, hydrogels, foams, or like materials. These carriers can be combined with the platelet-based materials and chondrogenesis inducing agents with or without cell additives, e.g., mesenchymal stem cells, chondrocytes, etc of the invention. In some aspects the carriers are incorporated as a scaffolding for cell additives or for endogenous cells (generally mesenchymal stem cells or chondrocytes) at or close to the site of injury.

[0045] As noted previously, repair compositions can be administered to a site in need of repair as a single composition or sequentially, where each component of the composition is added at an appropriate time to maximize repair.

Methods Of Inducing Or Facilitating Cartilage Repair In A Patient In Need Thereof

[0046] Described herein are also therapeutic methods for restoring cartilage at a site in need of repair in a patient in need thereof. A site in need of repair is any site in a mammal, e.g., human, horse, dog, etc., in need of cartilage repair or replacement. An illustrative site is a knee joint in a patient having osteoarthritis.

[0047] An initial determination is made as to what type and how much repair composition would be effective in treating the site in need of repair. This determination is based on site of repair, age of patient, autologous or non-autologous platelet-based lysate, type and amount of chondrogenesis inducing agent, etc. A determination is also made as to the timing of delivery of the different aspects of the repair composition. For example, chondrogenesis inducing agents can be selected for their capacity for degranulation of platelets at an optimal time after administration to the patient. The correct timing in

such case must be determined, especially where the platelet-based composition is administered at a time zero and the chondrogenesis inducing agent, e.g., cytokine, is administered at a time X, X representing the optimal time at which to have administered platelet materials degranulate. Various aspects of this initial determination are described in PCT application PCT/US2008/087452, Compositions and methods to promote implantation and engraftment of stem cells.

[0048] Once the above determinations have been made, methods described herein require administration of repair compositions of the invention to the patient in need thereof. Administration to the site in need of repair can be accomplished through a surgical incision, arthroscopically, or percutaneously.

[0049] Administration may be performed one or more times in order to maximize cartilage repair or replacement. Injury site analysis can be performed to ensure that acceptable results have been achieved.

Therapeutic Applications

[0050] Repair compositions of the invention provide optimal cartilage repair and/or replacement conditions/environment to repair a site in a patient in need thereof.

[0051] Repair compositions herein can be formulated as pharmaceutical compositions and administered to a patient in need thereof, typically a mammalian, including a human patient. Repair compositions can be formulated in a variety of forms adapted for the chosen route of administration.

[0052] For administration of the compositions of the invention as an injectable solution (whether it be through a surgical incision or arthroscopically), compositions can be formulated according to techniques well-known in the art, using suitable dispersing or wetting agents, such as sterile oils, including synthetic mono- or di-glycerides and fatty acids, including oleic acid.

[0053] Solutions or suspensions of the repair compositions can be prepared in water, isotonic saline (PBS), and optimally mixed with an nontoxic surfactant. Dispersions may also be prepared in glycerol, liquid polyethylene, glycols, vegetable oils, triacetin and mixtures thereof. Under customary use and storage conditions, the repair compositions herein may contain one or more preservatives to prevent growth of microorganisms.

[0054] "Therapeutic applications" herein refers to use of the methods described herein or the compositions of the invention for use in treating a patient having a site in need of cartilage repair or replacement. Described and/or claimed herein are also therapeutic applications in patients having disease states that limit the inherent ability of the patient to repair or re-grow cells at the repair site. For example, patient's that have osteoarthritis.

[0055] The description of the present invention has been presented for purposes of illustration and description, but is not intended to be exhaustive or limiting of the invention to the form disclosed. The scope of the present invention is limited only by the scope of the following claims. Many modifications and variations will be apparent to those of ordinary skill in the art. The embodiment described and shown in the figures was chosen and described in order to best explain the principles of the invention, the practical application, and to enable others of ordinary skill in the art to understand the invention for various embodiments with various modifications as are suited to the particular use contemplated.

[0056] While the invention has been particularly shown and described with reference to a number of embodiments, it would be understood by those skilled in the art that changes in the form and details may be made to the various embodiments disclosed herein and that the various embodiments disclosed herein are not intended to act as limitations on the scope of the claims.

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Claims

1. A composition for use in facilitating cartilage repair in a patient in need thereof comprising a therapeutically effective amount of an autologous platelet lysate, autologous mesenchymal stem cells (MSCs) and one or more chondrogenesis inducing agent(s), wherein the chondrogenesis inducing agent or one of the chondrogenesis inducing agents is corticosteroid.

2. The composition for use of claim 1 wherein the platelet lysate is from about 5% to about 40% platelet lysate solution.

3. The composition for use of claim 1 further comprising platelet rich plasma, platelet rich fibrin, whole cell platelets or a mixture thereof.

4. The composition for use of claim 1 further comprising a gel, hydrogel, foam, or other carrier material.

5. A 5% to 40% platelet lysate solution for use in facilitating cartilage repair, wherein said platelet lysate solution is prepared from platelets obtained from a patient in need of cartilage repair, and wherein said platelet lysate solution, autologous mesenchymal stem cells (MSCs) and one or more chondrogenesis inducing agent(s) are administered to a site in the patient in need of cartilage repair, wherein the chondrogenesis inducing agent or one of the chondrogenesis inducing agents is corticosteroid.

6. The platelet lysate solution for use of claim 5, wherein a platelet rich plasma, platelet rich fibrin, whole cell platelet or a mixture or mixtures thereof is/are administered to the patient in need thereof, and wherein the administration is at the site in the patient in need of repair.

Patentansprüche

1. Zusammensetzung für die Verwendung zur Förderung der Knorpelreparatur bei einem Patienten, der diese benötigt, die eine therapeutisch wirksame Menge eines autologen Plättchenlysats, autologer mesenchymaler Stammzellen (MSCs) und eine oder mehrere Chondrogenese induzierende Substanzen umfasst, wobei die Chondrogenese induzierende Substanz oder eine von den Chondrogenese induzierenden Substanzen ein Corticosteroid ist.

2. Zusammensetzung für die Verwendung gemäß Anspruch 1, wobei das Plättchenlysat eine ungefähr 5%ige bis ungefähr 40%ige Plättchenlysat-Lösung ist.

3. Zusammensetzung für die Verwendung gemäß Anspruch 1, die ferner plättchenreiches Plasma, plättchenreiches Fibrin, ganze Plättchenzellen oder eine Mischung daraus umfasst.

4. Zusammensetzung für die Verwendung gemäß Anspruch 1, die ferner ein Gel, ein Hydrogel, einen Schaum oder ein anderes Trägermaterial umfasst.

5. 5%ige bis 40%ige Plättchenlysat-Lösung für die Verwendung zur Förderung der Knorpelreparatur, wobei die Plättchenlysat-Lösung aus Plättchen hergestellt ist, die von einem Patienten erhalten wurden, der eine Knorpelreparatur benötigt, und wobei die Plättchenlysat-Lösung, autologe mesenchymale Stammzellen (MSCs) und eine oder mehrere Chondrogenese induzierende Substanzen an einer Stelle im Patienten verabreicht werden, welche die Knorpelreparatur benötigt, wobei die Chondrogenese induzierende Substanz oder eine der die Chondrogenese induzierenden Substanzen ein Corticosteroid ist.

6. Plättchenlysat-Lösung für die Verwendung gemäß Anspruch 5, wobei ein plättchenreiches Plasma, plättchenreiches Fibrin, ganze Plättchenzellen oder eine Mischung oder Mischungen daraus dem Patienten, der diese benötigt, verabreicht wird/werden und wobei die Verabreichung an der Stelle von dem Patienten stattfindet, welche die Reparatur benötigt.

Revendications

1. Composition destinée à être utilisée pour faciliter la réparation de cartilage chez un patient le nécessitant comprenant une quantité thérapeutiquement efficace d'un lysat de plaquettes autologues, de cellules souches mésenchymateuses autologues (CSM) et d'un ou de plusieurs agents inducteurs de chondrogenèse, dans laquelle l'agent inducteur de chondrogenèse ou l'un des agents inducteurs de chondrogenèse est un corticoïde.

2. Composition destinée à être utilisée selon la revendication 1, dans laquelle le lysat de plaquettes est une solution de lysat de plaquettes à environ 5% à environ 40%.

3. Composition destinée à être utilisée selon la reven-

dication 1, comprenant en outre du plasma riche en plaquettes, de la fibrine riche en plaquettes, des plaquettes de cellules entières ou un mélange de ceux-ci.

4. Composition destinée à être utilisée selon la revendication 1, comprenant en outre un gel, un hydrogel, une mousse ou autre matériau vecteur.

5. Solution de lysat de plaquettes à 5% à 40% destinée à être utilisée pour faciliter la réparation de cartilage, dans laquelle ladite solution de lysat de plaquettes est préparée à partir de plaquettes obtenues d'un patient nécessitant une réparation du cartilage, et dans laquelle ladite solution de lysat de plaquettes, des cellules souches mésenchymateuses autologues (CSM) et un ou plusireurs agents inducteurs de chondrogenèse sont administrés à un site où la réparation de cartilage est nécessaire chez le patient, dans laquelle l'agent inducteur de chondrogenèse ou l'un des agents inducteurs de chondrogenèse est un corticoïde.

6. Solution de lysat de plaquettes destinée à être utilisée selon la revendication 5, dans laquelle un plasma riche en plaquettes, de la fibrine riche en plaquettes, des plaquettes de cellules entières ou un ou plusieurs mélanges de ceux-ci est/sont administrés au patient le nécessitant, et dans laquelle l'administration est réalisée au niveau du site où la réparation est nécessaire chez le patient.

REFERENCES CITED IN THE DESCRIPTION

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