TISSUE ENGINEERING
Volume 11, Number 7/8, 2005

Review

Mesenchymal Stem Cells: Cell-Based Reconstructive Therapy in Orthopedics

ARNOLD I. CAPLAN, Ph.D.

ABSTRACT

Adult stem cells provide replacement and repair descendants for normal turnover or injured tissues. These cells have been isolated and expanded in culture, and their use for therapeutic strategies requires technologies not yet perfected. In the 1970s, the embryonic chick limb bud mesenchymal cell culture system provided data on the differentiation of cartilage, bone, and muscle. In the 1980s, we used this limb bud cell system as an assay for the purification of inductive factors in bone. In the 1990s, we used the expertise gained with embryonic mesenchymal progenitor cells in culture to develop the technology for isolating, expanding, and preserving the stem cell capacity of adult bone marrow-derived mesenchymal stem cells (MSCs). The 1990s brought us into the new field of tissue engineering, where we used MSCs with site-specific delivery vehicles to repair cartilage, bone, tendon, marrow stroma, muscle, and other connective tissues. In the beginning of the 21st century, we have made substantial advances: the most important is the development of a cell-coating technology, called painting, that allows us to introduce informational proteins to the outer surface of cells. These paints can serve as targeting addresses to specifically dock MSCs or other reparative cells to unique tissue addresses. The scientific and clinical challenge remains: to perfect cell-based tissue-engineering protocols to utilize the body's own rejuvenation capabilities by managing surgical implantations of scaffolds, bioactive factors, and reparative cells to regenerate damaged or diseased skeletal tissues.

INTRODUCTION

In adults, all the skeletal tissues constantly rejuvenate themselves. This process involves the death of end-stage differentiated cells such as osteoblasts, that is, bone-forming cells, and their replacement by newly differentiated osteoblasts. The new osteoblasts arise in a complex, multistep sequence, called a lineage, from multipotent progenitor cells called mesenchymal stem cells, MSCs, found in bone marrow and other sites.[1,2] The MSCs have the capacity to differentiate into other phenotypes including those that fabricate cartilage, muscle, marrow stroma, tendon/ligament, fat, and other connective tissues (Fig. 1). Thus, adult MSCs *in vivo* function to supply replacement units for the differentiated cells that naturally expire or succumb to injury or disease. This process of stem cell-generated replacement cells decreases with age after reaching its peak in the mid to late 20s in humans. Therefore, past the age of 30 years, supplementation and management of the innate cell-mediated rejuvenation ca-

Skeletal Research Center, Department of Biology, Case Western Reserve University, Cleveland, Ohio.

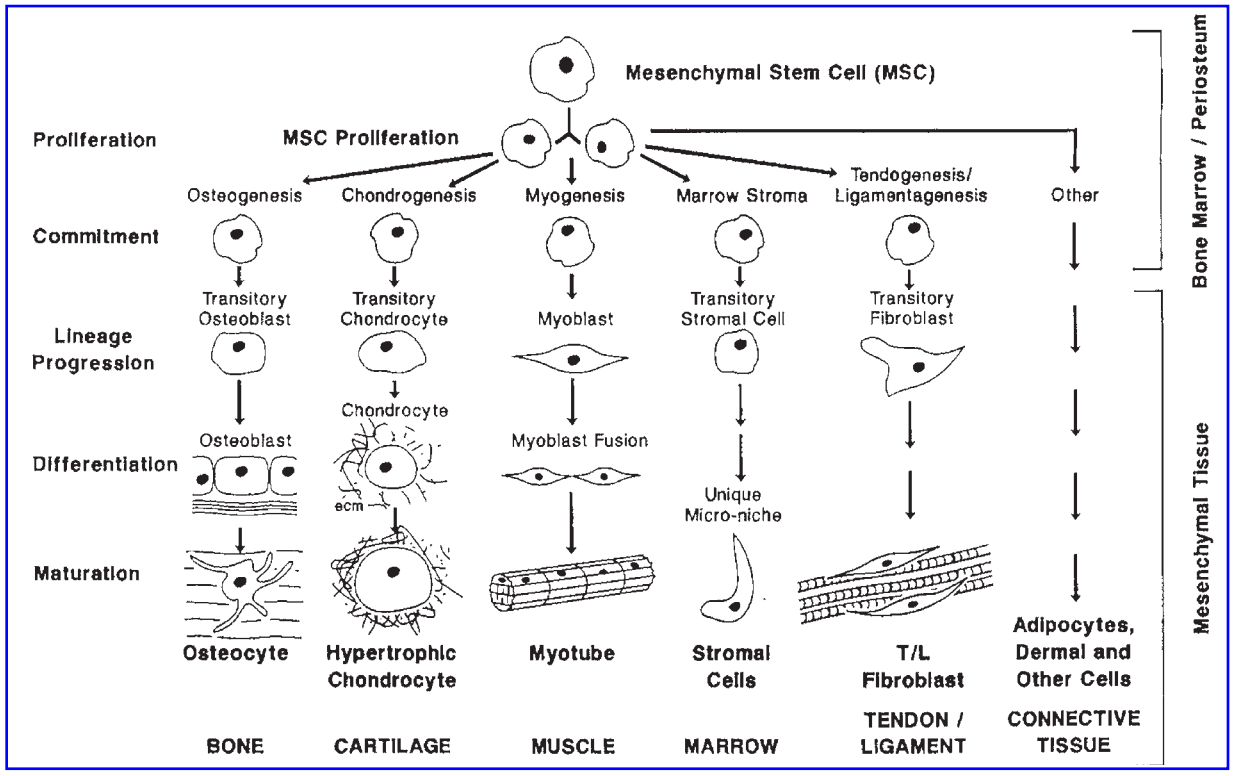

FIG. 1. The mesengenic process. Mesenchymal stem cells (MSCs) have the capacity to differentiate into bone, cartilage, muscle, marrow stroma, tendon/ligament, fat, and other connective tissues.[1,2] The sequence of this differentiation involves multistep lineages controlled by growth factors and cytokines. This figure is structured in a manner comparable to hematopoietic lineage progression and involves well-described lineages for osteogenic differentiation[38] with decreasing information available from left to right.

pacity will enhance skeletal tissue performance and repair.[3]

The cure for many genetic diseases that affect skeletal tissues could be "cell replacement therapy," whereby the host stem cells are replaced by donor cells that do not carry the genetic defect. For example, in the case of osteogenesis imperfecta (OI), host osteoblasts carry a gene lesion in type I collagen. When osteoblasts fabricate the matrix of bone, the type I collagen-rich osteoid is defective and the resulting mineral deposition is likewise defective. The end result is bone stock that is brittle and that fractures at a fraction of the maximum load tolerated by normal bone. If the host MSCs, the source of all osteoblasts, are replaced with genetically normal donor allogeneic MSCs, the newly formed donor-derived osteoblasts will make normal bone stock that naturally replaces the defective stock.[4] Indeed, successful short-term amelioration of OI has been reported by introducing allogeneic MSCs into young, growing OI patients.[5,6]

It follows that the control of MSC number, location, differentiation potential, and rate of differentiation can affect skeletal tissues, their growth and physical properties, and their maintenance and repair capacities. For example, the rate of fracture repair is directly controlled by the rate of fracture callus formation and differentiation; the callus is made up of MSCs and blood vessels. In mechanically unstable breaks, the lack of vasculature causes the bulk of the MSCs to develop into bridging cartilage that eventually spans the defect and then is further stabilized by a surrounding bony bridge.

I outline below how we have developed cell-based and tissue-engineering therapies for skeletal tissues by using MSCs. Because MSCs are present at concentrations of less than 1 in 100,000–500,000 nucleated cells in bone marrow aspirates from adults, the MSCs must be culture expanded to obtain sufficient numbers for clinical use.

The evolution of MSC technology at Case Western Reserve University (Cleveland, OH) and its development into clinical protocols is the focus of this review. The current deficits of this technology provide the goals for future technology. In this regard, perhaps the subtitle for this review should be *Yesterday, Today, and Tomorrow*.

YESTERDAY

In the 1970s, my laboratory reported our studies on the disassociation of embryonic stage 24 chick limb bud mes-

enchymal progenitor cells and their subsequent differentiation into bone, cartilage, muscle, and other mesenchymal tissues[7–9] (Fig. 2). In the early 1980s, we used these embryonic chick limb bud cells in culture as an assay to purify bioactive molecules from demineralized bone matrix.[10–14] Cultures were seeded at sufficiently low density that they did not differentiate into cartilage. Extracts of demineralized bone were exposed to these cultures and this exposure induced chondrogenic differentiation in a dose-dependent manner (Fig. 3A). Schemes to purify the crude extract of such demineralized bone established that the "chondrogenic stimulating activity" (CSA) was a 31-kDa protein on sodium dodecyl sulfate (SDS)–polyacrylamide gel electrophoresis displays (Fig. 3B) that we now know was a heterodimer of bone morphogenetic proteins (BMPs).

The BMPs were cloned in the late 1980s[15] and because of our studies and assays for CSA, I suspected that stem cells comparable to the embryonic chick limb bud mesenchymal cells must reside in adult tissues. This view was principally based on the many studies by Marshall Urist showing that when demineralized bone or extracts from it were implanted into subcutaneous or intramuscular sites, they caused cartilage and bone formation.[16–19]

Furthermore, two important additional facts were known in the mid-1980s. First, orthopedic surgeons routinely used freshly isolated bone marrow to provide rapid and extensive repair of large bone defects or for spinal fusions.[20] This implied that marrow contained reparative or osteogenic cells that contributed to these mesenchymal repair sites. Second, the work of Friedenstein[21,22] and, in particular, of Owen[23,24] indicated that cells isolated and adhered to petri dishes from marrow had osteogenic and adipogenic potential. On the basis of these experiences and facts, Stephen Haynesworth and I developed the technology for isolating and culture expanding adult marrow-derived MSCs.[25–30]

MSC Technology

In standardizing the embryonic chick limb bud mesenchymal progenitor cell culture system, we routinely screened many separate batches of fetal bovine serum (FBS) for its ability to enhance cell attachment and proliferation and to support density-dependent differentiation of cartilage, bone, and muscle.[31] This screening was started in the 1970s when large differences could be seen between individual batches of FBS. In fact, by merely lining up the ten to fifteen 100-mL bottles of different batches of FBS, we could eliminate half of them because we knew that those that had a green hue (hemolysis) would not be suitable for the limb bud cells. Today, unfortunately, large batches of FBS are blended together and greater care is taken in their production that they all look the same.

Thus, when Stephen Haynesworth and I set forth to purify and culture expand human (h) MSCs from fresh bone marrow, we had prescreened batches of FBS that were suitable for embryonic mesenchymal progenitor cells. As this technology evolved, we eventually gained enough experience with hMSCs to develop assays specific to these progenitor cells and, thus, stopped using the

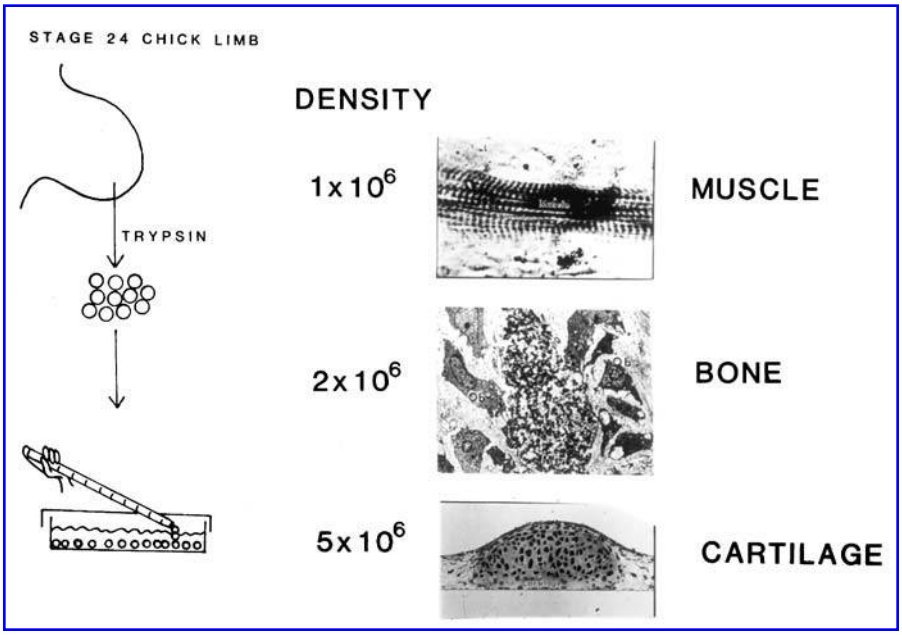

FIG. 2. Stage 24 chick limb bud mesenchymal cell cultures exhibit muscle, bone, and cartilage phenotypes depending on the original plating density in 60-mm petri dishes. The chick limb bud cells are liberated in a trypsin disassociation step after their dissection from the embryos. The cells are plated, and a sequence of differentiation into these phenotypes has been described.[1,7–9]

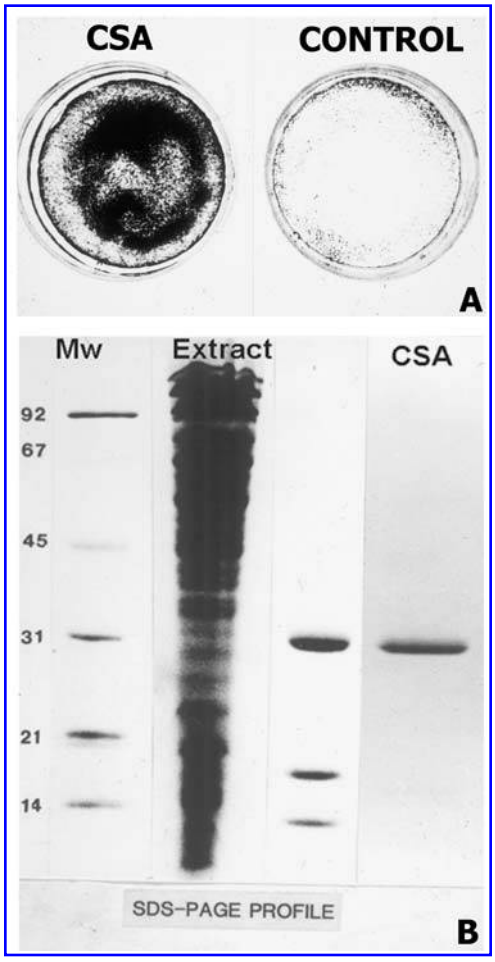

FIG. 3. Chondrogenic stimulating activity (CSA) has been purified by using the embryonic chick limb bud mesenchymal cell culture assay.[12,13] Pictured are petri dishes that have been plated at 2 million cells per 60-mm dish; little chondrogenesis could be expected except at the edges of the control plate as seen in (**A**) on the right. Cultures treated with CSA extracts show a dramatic upregulation of chondrogenesis in these toluidine blue-stained dishes. Pictured in (**B**) is an SDS–polyacrylamide gel molecular weight standards, total extract profile, partially pure preparation, and purified CSA preparation at 31,000 Da, respectively, from left to right.

embryonic chick cells in our serum screen. The current technology selects suitable batches of serum on the basis of hMSC colony counts, cell proliferation (numbers of cells at each passage), and *in vitro* and *in vivo* assays for osteogenesis and chondrogenesis.[31]

The historic and current "gold standard" assay for all MSC preparations is to place the cells onto the pore walls of fibronectin-coated porous calcium phosphate ceramics and, after a brief *in vitro* incubation at 37°C to allow the cells to attach, the cell–ceramic composite is placed in a subcutaneous pocket of immunocompromised rodent or autologous host[32–34] (Fig. 4). These implantation sites are highly vascular and the quantitative estimation of bone (Fig. 5) and/or cartilage in the pores is taken as an indication of the quality of the MSC preparation. By testing 10 to 15 different batches of serum with MSCs from the same donor, the effects of these different serums can be directly compared. Again, currently 1 in 20 or 30 batches of FBS is suitable for hMSCs. It must be firmly stated that the batch of serum suitable for hMSCs is not suitable for rat, rabbit, or mouse marrow-derived MSCs. Because we use a variety of experimental animal preclinical models, we must screen serum batches for the MSCs of each animal, for suitability to support selective attachment to culture dishes and for proliferation with the maintenance of the stem cell properties. More troublesome, with each newly purchased batch of FBS for one species-specific MSC preparation, we expect slight differences in the ability of the MSCs to divide or differentiate. On top of this serum species specificity, every donor or MSC preparation varies even from inbred species. For hMSCs, we have published that the constitutive secretion into the medium of cytokines and growth factors is quantitatively different although the percent increase due to growth factor stimulation is relatively uniform from donor to donor.[35]

Because both whole marrow and purified and expanded MSCs make bone in the calcium phosphate porous ceramics in these *in vivo* incubation sites,[36] these cell delivery vehicle composites have been used in rodent and canine preclinical models for massive bone repair.[37–43] The choice of these calcium phosphate ceramic vehicles is based on their osteoconductive properties, but in addition, these materials support the induction of osteogenesis of MSCs; whether this is due to direct interaction of MSCs with the calcium phosphate surfaces or the binding of specific growth factors to the surface has not been determined. In addition, the MSCs bound to ceramic vehicles can be superinduced *in vitro* to enter the osteogenic lineage before implantation.[36] Thus, MSC-mediated osteogenesis can be jump-started in culture before clinically relevant implantation. MSCs produce bone in the pores of the ceramic faster than is seen with whole marrow, and the jump-started MSCs produce bone faster than uninduced MSCs. These features may be important in bone repair or implant fixation protocols in older patients, whose MSC titers are much lower than in young individuals.[3]

It is important to stress that we have developed *in vitro* assays for MSCs to differentiate into osteoblasts,[44] chondrocytes,[45,46] adipocytes, hematopoietic support[47,48] (both hematopoietic stem cells and monocyte-macrophage development into osteoclasts), and myoblasts.[49] These *in vitro* assays serve as vehicles for studying the control of the pathways of differentiation from MSCs, but they also serve as the starting point for the tissue-engineering strategies of today.

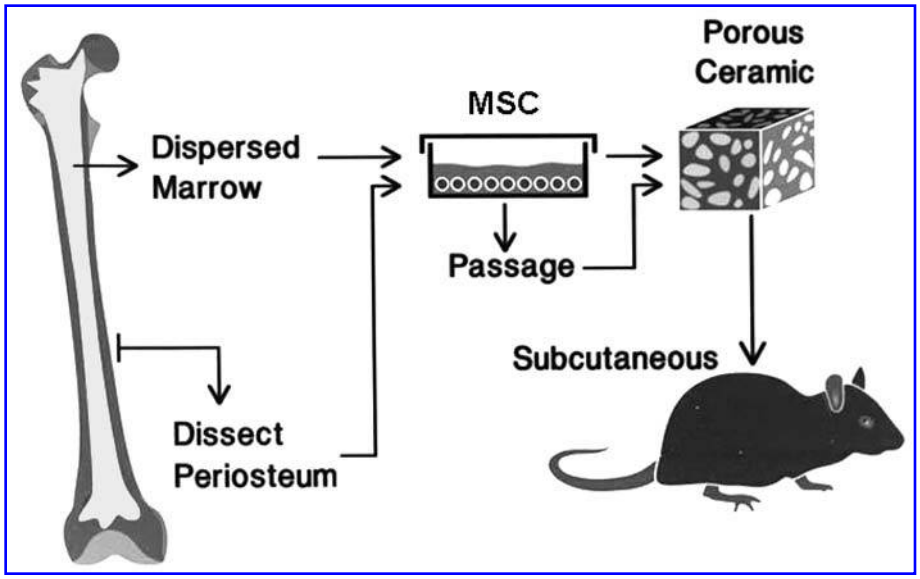

FIG. 4. Whole marrow or dissected periosteum can provide progenitor cells or MSCs. When passaged, the liberated cells can be loaded into fibronectin-coated porous calcium phosphate ceramic 3-mm cubes and implanted subcutaneously in immunounreactive or syngeneic animals.[31,33,34,36]

TODAY

Cell-based clinical therapies using MSCs involve at least three different approaches: First, tissue-engineering strategies in which MSCs are incorporated into three-dimensional (3-D) scaffolds for the replacement of 3-D pieces of *in vivo* tissues; second, cell replacement therapy, in which genetic defects can be cured by replacing the mutant host cells with normal allogeneic donor cells; and third, where MSCs act as cytokine/growth factor pumps to stimulate reparative events or to inhibit degenerative events.

Tissue engineering

We have published studies on the tissue-engineered repair/regeneration of cartilage,[50–57] bone,[39–43] and ten-

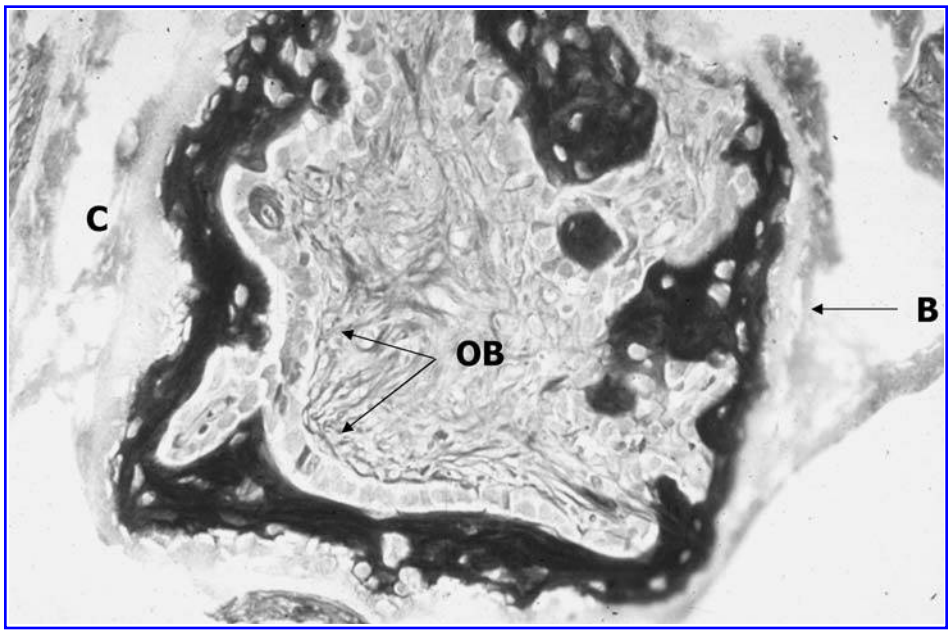

FIG. 5. Calcium phosphate porous ceramic cubes that are implanted in syngeneic or immunounreactive rodents are harvested at 3 or 6 weeks and yield specimens that exhibit bone and cartilage when examined in paraffin sections.[33,34] Shown in a decalcified cube section in which the dark-staining, newly formed bone (B) is being laid down by a layer of osteoblasts (OB) with vasculature at their backs. C, decalcified ceramic residue.

don.[37,58] Each site requires a different 3-D scaffold and a different logic. I emphasize cartilage here because the cell delivery vehicle itself provides cueing both on the initial exposure of the cells and also during the process of tissue filling.[59] The breakdown of the delivery vehicle triggers the final phases of tissue change and the breakdown products add value to the molecular and cellular events related to successful repair.

The important common tissue-engineering issues for all mesenchymally derived tissues with regard to the delivery of MSCs and their appropriate and sequential changes are as follows: the scaffold must

1. Allow for and encourage cell attachment
2. Be porous so the differentiated cells can make abundant and specialized extracellular matrix
3. Allow bioactive molecules to have access to the cells
4. Perfectly integrate into the neotissue or silently disappear
5. Provide some cellular cueing
6. Be mechanically sensitive to the site

Cartilage repair. For cartilage repair, we used a fibronectin-coated sponge formed from hyaluronan (HA) (Fig. 6). With embryonic chick limb bud mesenchymal cells, we showed that high molecular weight HA bonded to the petri dish was chondroinductive.[60,61] Moreover, high molecular weight HA is antiangiogenic. In addition, in porous calcium phosphate ceramic vehicles in subcutaneous sites, MSCs in vascular-excluded pores form cartilage. Thus, MSCs in porous HA sponges provide an avascular and chondroinductive microenvironment. In deep, critical-sized osteochondral defects made in the medial femoral condyle of adult rabbits (Fig. 6), sponges of HA filled with MSCs (Fig. 7) uniformly differentiate into chondrocytes. When the HA of the scaffold is degraded into oligomers, the oligomers trigger the entrance of vasculature into the hypertrophic cartilage at the base of the defect that is followed by replacement by vascularized bone. The cartilage at the top of the defect not only does not undergo replacement, but, more striking, integrates the neocartilage with the host cartilage. We suggest that the HA oligomers facilitate this tissue integration.[50–57] Thus, the 3-D HA delivery vehicle meets all the criteria listed above for a successful tissue-engineering scaffold.

Tendon repair. For tendon repair, the same cells, MSCs, that form cartilage or bone were formatted into a type I collagen gel that formed in a trough around a resorbable suture, the ends of which were fastened to a spring that keep the suture under constant load (Fig. 8). The MSCs contracted the gel and because the suture was loaded, cells oriented with regard to the suture.[37,58] The partially contracted cell–gel–suture composite was sutured into and aligned with the load axis within an Achilles tendon defect in adult rabbits. At 3 months, the neotissue formed was well-integrated tendon tissue. Again, the tissue and site required a specific delivery vehicle to take advantage of the mechanical and chemical microenvironment necessary for the MSCs to develop into functional tenocytes.[37,58]

Cell Replacement Therapy

The bone marrow is a highly differentiated and complex, multicomponent tissue. The major component is the marrow stroma, which is a multicompartment connective

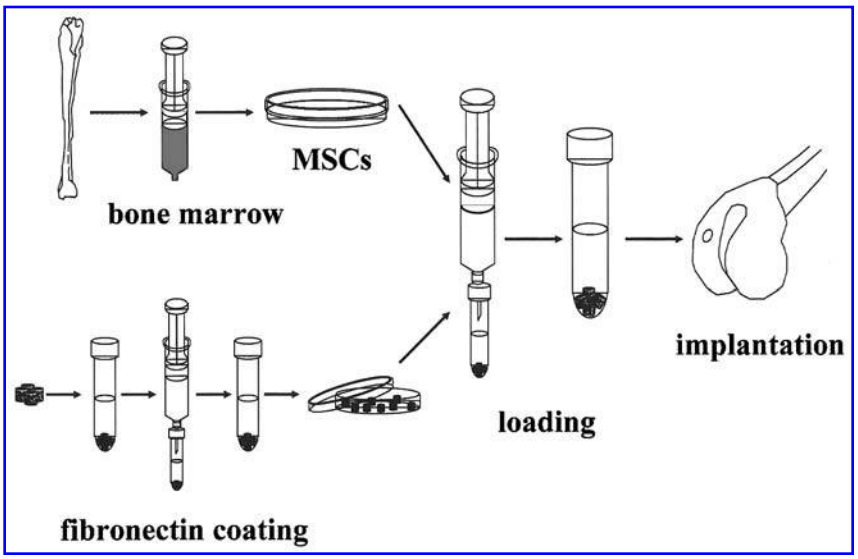

FIG. 6. Cartilage repair protocol in which sponges are coated with fibronectin and left to dry overnight. These sponges are filled with either freshly isolated whole bone marrow, liberated culture-expanded MSCs, or left empty as they are placed into full thickness defects in adult rabbit condyles.[50–52,54–56]

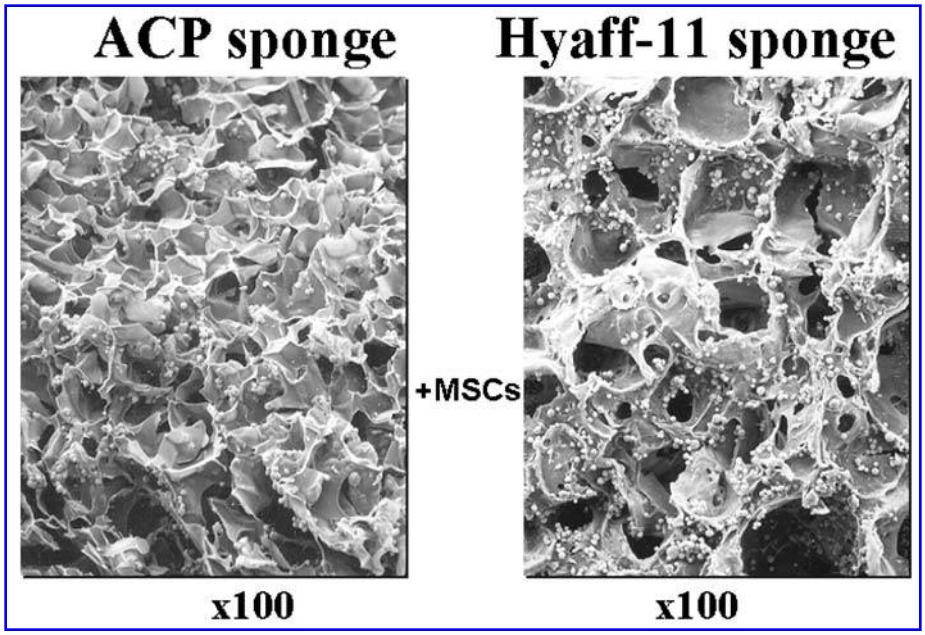

FIG. 7. ACP (auto-cross-linked polysaccharide) and Hyaff-11 sponges are pictured in scanning electron micrographs after coating the pores of these sponges with mesenchymal stem cell preparations from rabbit.[54,55] Original magnification: ×100.

tissue that houses and supports hematopoiesis. This support involves establishing niches that physically house specific arms of the multilineage hematopoietic pathway; both "floor space" and a specific microenvironment of cytokines are provided by the marrow stroma and its stromal cells. Thus, after chemotherapy or radiation, which destroys the hematopoietic progenitors and these pathways, these niches must be reestablished to facilitate hematopoietic engraftment and the production of various blood cells. The other major components of marrow are blood vessels, osteoprogenitor cells, and MSCs. Thus, we developed clinical protocols to establish that autologous

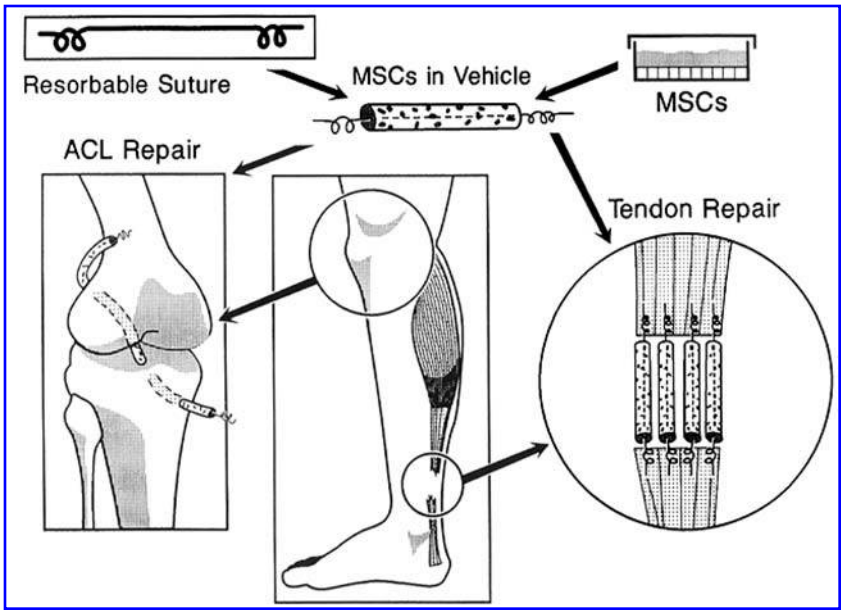

FIG. 8. Ligament/tendon repair is organized by taking a resorbable suture, which is held by a spring under fixed load in a trough that serves to house a collagen gel in which MSCs have been placed. This gel forms in the trough around the resorbable suture and the MSCs contract the gel around this loaded suture. This composite gel–cell–suture is then sutured into place into achilles tendon defects created in adult rabbits.[37,58]

MSCs could be safely and efficaciously delivered back to patients to reestablish this delicate marrow microenvironment.[62,63]

Cell replacement therapy involves eliminating cells with specific genetic defects or mutations and replacing them with allogeneic normal cells or gene therapy-transfected cells[64] (Fig. 9). For the genetic disease osteogenesis imperfecta (OI), there is usually a point mutation in the type I collagen gene. The type I collagen produced by osteoblasts is defective and, thus, the osteoid and subsequent mineral deposition are likewise defective. The resulting bone stock is brittle and multiple fractures occur because these bones cannot withstand normal loads. To cure OI, it would be theoretically possible to use allogeneic MSCs from an immunomatched donor[4] and to destroy some (or preferably all) of the host MSCs and replace them with donor (nonmutant) MSCs (Fig. 9). Indeed, this has been tried with children with OI in a two-step procedure.[5,6] The first step was to do a classic allotransplantation in which whole bone marrow from immunomatched donors was provided after mild chemotherapy. The result was to provide some allotolerance by engraftment of allohematopoietic stem cells and some allo-MSCs. Subsequently, after 18 to 32 months, the children were intravenously given isolated, culture-expanded allo-MSCs matching their original allograft.[5] Most of the children experienced rather substantial increases in skeletal growth. In my view, these therapies were not totally curative because I suspect, on the basis of labeling and imaging studies,[65] that the engraftment of allo-MSCs was low. As addressed below, we must find ways to improve MSC engraftment efficiency to ensure that these cell replacement therapies can provide cures.

Experimentally, we have also tried to cure muscular dystrophy in mice by providing MSCs that do not have the disease-causing mutation.[49,66] A mouse strain called *mdx* has a point mutation in the muscle-specific protein dystrophin (Fig. 10). Using an antibody against dystrophin, we can show that muscle sections are negative for dystrophin.[66] In muscles injected with congenic, normal MSCs, dystrophin-positive myotubes can be seen. The injected MSCs differentiate into myoblasts[66] and fuse with the mutant myotubes and the incorporated nuclei produce normal dystrophin. Control fibroblasts do not show this effect. Again, the limiting factor involves getting enough normal MSCs to the muscles of the *mdx* mouse to effect a cure; injecting every muscle in the body is neither feasible nor prudent.

MSCs as Cytokine/Growth Factor Pumps

In two very different, but in some ways similar, animal models, MSCs have been introduced into infarct (ischemia) lesions in the heart[67–70] and brain[71,72] (stroke model). The MSCs do not act by differentiating into cardiac myocytes or neural elements, respectively, as shown by cell-marking experiments, but rather secrete molecules that increase angiogenesis and decrease scarring or fibrosis. There is no doubt that in the cardiac infarct model (rats and pigs) there is substantial cell death of muscle tissue. However, the contractility and flexibility of the tissue are not compromised and, thus, the heart output is not grossly affected.[67–70] In the case of brain, endogenous neural progenitors respond, migrating and functionally repairing neurological damage so that in functional tests, the animals clearly function.[71,72] In both

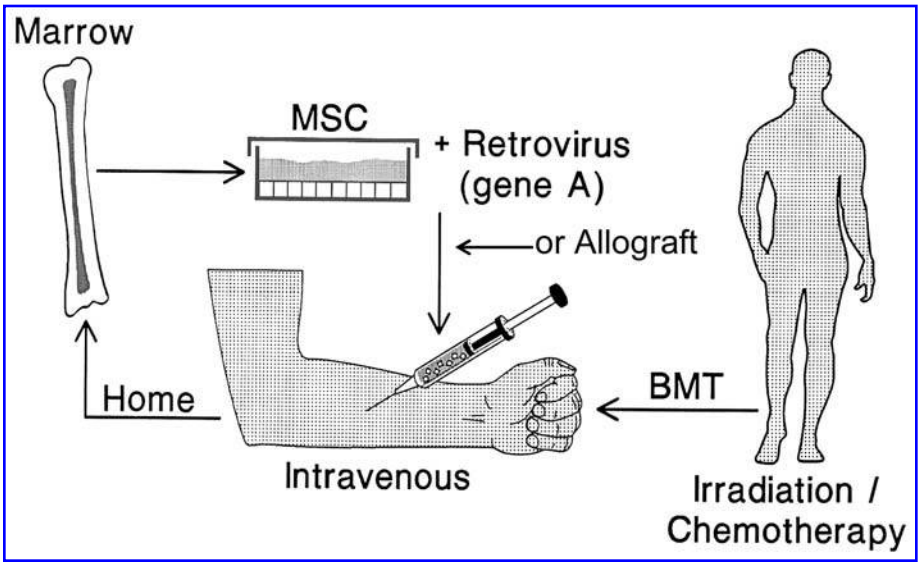

FIG. 9. Allo- or autologous gene therapy. Mesenchymal stem cells can be transfected with retrovirus to house normal genes or allograft preparations can be presented to patients undergoing bone marrow transplantation. Mesenchymal stem cells introduced in this way will home to bone marrow and have the potential to correct gene defects.[4,62,63]

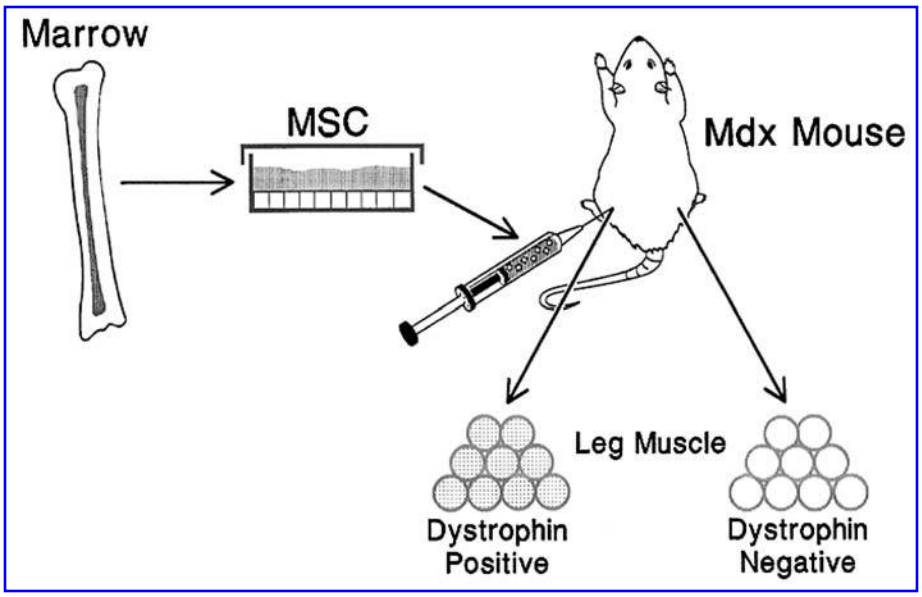

FIG. 10. Congenic bone marrow has been harvested and the MSCs purified. These MSCs have been injected into a specific muscle of the *mdx* mouse on the left side of the animal; on the right side, saline controls were injected. After 8 weeks, individual muscles were harvested, sectioned, and exposed to antibodies for dystrophin. MSC-injected muscles exhibited dystrophin-positive myotubes, which indicated that the injected MSCs differentiated into myoblasts that fused with the host myotubes. The newly fused nuclei, which are normal, produced dystrophin in the myotube and cured the genetic defect in these mice.[66]

of these ischemia models for heart and brain, the predominant mechanism for the improved functional outcomes are the MSC-caused inhibition of fibrosis or scar formation and the increase in vascular elements (angiogenesis). We have reported that human MSCs, as they enter the osteogenic versus stromal lineage, secrete a distinct set of cytokines constitutively.[35] Thus, I imagine that MSCs could exert therapeutic effects by this cytokine secretory activity alone, just as they provide such cytokine support of hematopoiesis in bone marrow.

TOMORROW

Luis Solchaga and others in our group have made unusual and significant gains in learning how to supplement

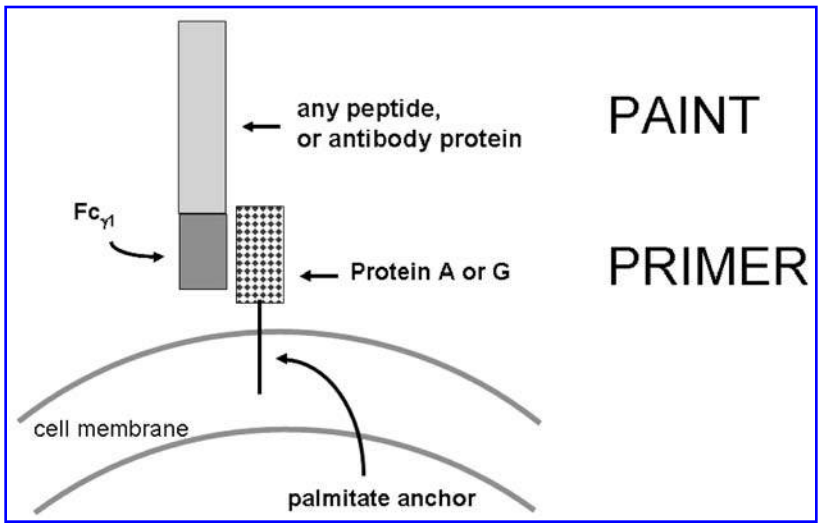

FIG. 11. By using fusion proteins (paints) that have the Fc region of antibodies at one end of the molecule, tight complexes can be assembled on protein A or protein G (primer) molecules, which are noncovalently anchored to cell membranes by palmitic acid. This primer-painting technology forms the basis for cell-targeting strategies that are now being experimentally used.[74]

MSC growth medium (with selected batches of FBS) with extra amounts of specific growth factors to enhance their mitogenic activity and to enhance MSC differentiation potency into specific phenotypes (our unpublished observations). It is premature to fully discuss this new approach here, but it is a "tomorrow" technology that will profoundly affect MSC therapies by structuring their culture expansion to provide maximally efficient and specific differentiation.

In addition, we have been systematically trying to improve MSC engraftment and tissue-targeting efficiency.[65] We have adapted a cell-coating technology initially described by Mark Tykocinski and colleagues originally at our university,[73] but now at the University of Pennsylvania (Philadelphia, PA). This technology, which we have called cell painting,[74] involves attaching a coat of "primer," palmityl fatty acid to which we covalently link the antibody-binding protein, protein G (Fig. 11). The fatty acid quantitatively inserts into the plasma membrane of the cell with the protein G facing out. Protein G binds tightly to the Fc region of antibodies. Thus, we apply a coat of primer and then attach the paint (any antibody or antibody mixture or fusion protein containing the cassette for the Fc region of an antibody). We have shown that the primer and paint do not affect the viability, mitotic activity, or differentiation potential of MSCs or other cells. In an *in vitro* test of the targeting ability of antibody-painted human cells, we created a cartilage defect in an osteochondral plug from a rabbit knee (Fig. 12). The antibodies were against epitopes in deep cartilage matrix and did not bind to the top of cartilage. Not only did the cells specifically bind to the deep cartilage layer of the defect, but after a 2-week incubation in culture, the painted human chondrocytes made human cartilage matrix that started filling the rabbit defect[74] (Fig. 12). Thus, the challenge for us is to develop this targeting technology so that painted reparative cells can be injected directly into the joint space, where they will dock onto

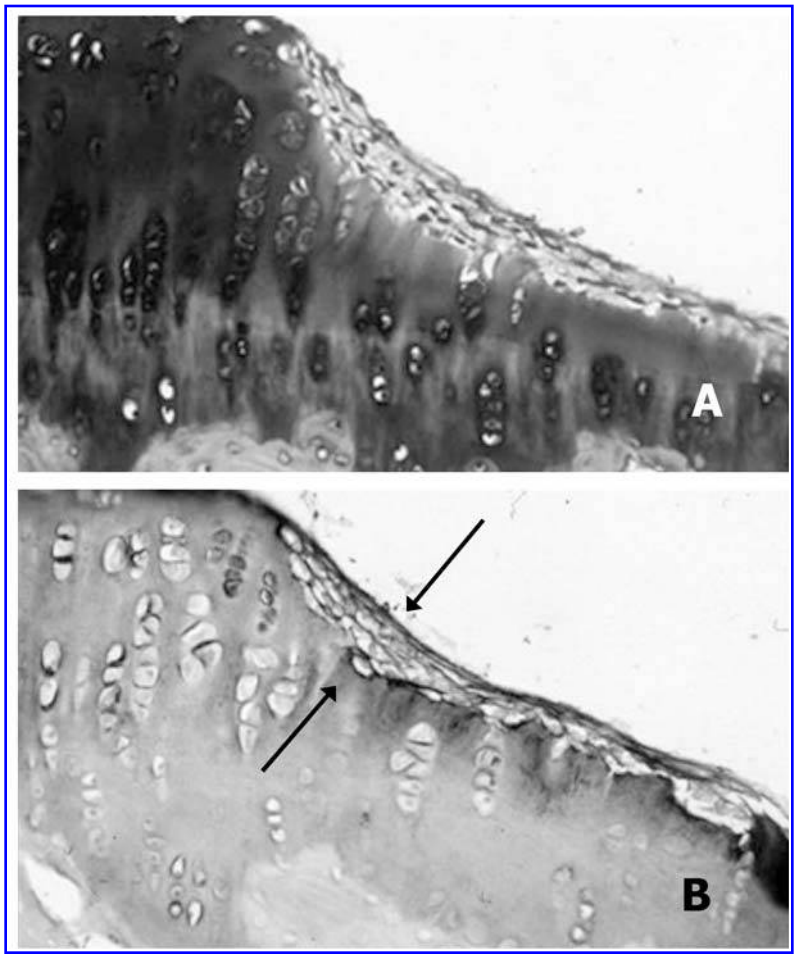

FIG. 12. Human chondrocytes that have been painted with antibodies to type II collagen and glycosaminoglycan epitopes and delivered *in vitro* to a defect in rabbit cartilage. The arrows in (**B**) indicate the human type II collagen-positive cartilage matrix that is being laid down after 2 weeks of *in vitro* incubation. (**A**) Toluidine blue-stained section; and (**B**) human type II collagen immunostaining.[74]

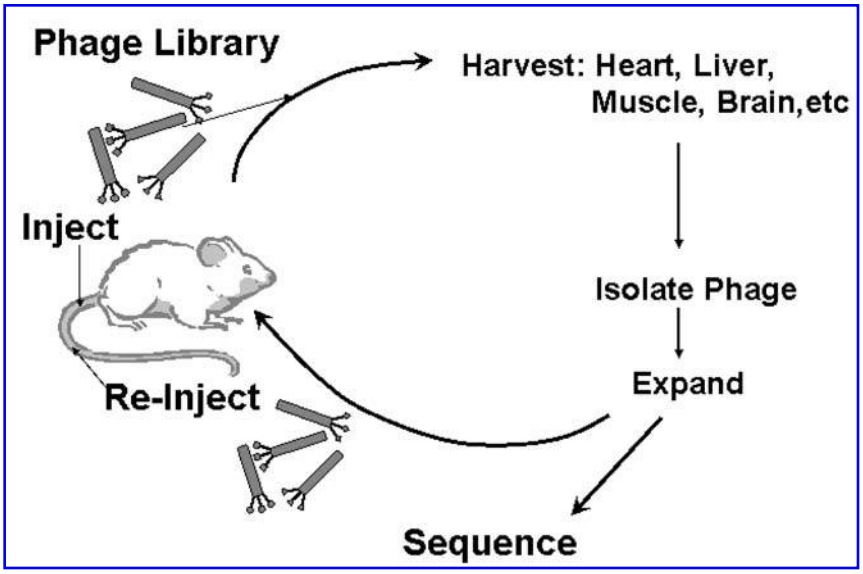

FIG. 13. Phage display library was injected intravenously into mice and individual organs were isolated. From these isolated organs, the associated phage were grown and injected in two more rounds, and the same tissue was isolated. After the third round of exposure the tissue-anchored phage were cloned and the DNA inserts were sequenced.[75,76]

damaged cartilage tissue and start to repair it. Because cartilage is avascular and is in the closed synovial space, it does not have access to reparative cells. By using a targeting strategy, it may be possible to deliver repair cells to the site of damage without opening the joint space: a tomorrow technology.

Likewise, how can we enhance engraftment of MSCs to bone marrow or to muscle to cure genetic diseases? Again, the painting technology can be adapted. On the basis of experiments of Ruoslahti and colleagues[75,76] (Fig. 13), the identity of peptides (Fig. 14) from a phage display library that bind specifically to certain tissues via the vascular tree are known. These vascular and tissue-specific peptide addresses have been shown also to be present in humans[77] (Fig. 14). Thus, a fusion protein of tissue-specific (e.g., muscle or bone marrow) peptide hooked to an Fc cassette will allow us to paint tissue-specific targeting molecules onto MSCs. The peptide region of the paint will bind with its docking site in the specific tissue. By using noninvasive imaging techniques, we intend to perfect this tomorrow technology in the near future.

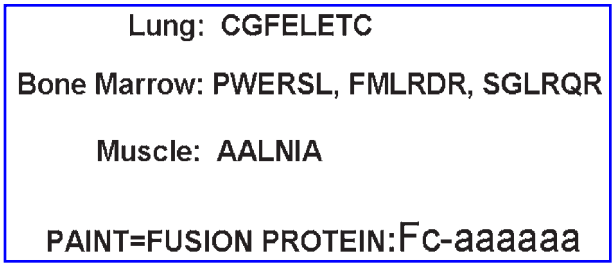

FIG. 14. From the experiments pictured in Fig. 13, targeting addresses for the phage peptide inserts for lung, bone marrow, and muscle have been obtained by sequencing phage clones associated with these tissues.[75,76]

PROSPECTUS

My colleagues and I have followed a basic science pathway that has led us from understanding the formative events in mesenchymal tissue development in the limb to establishing basic science principles of tissue engineering.[78] Orthopedic surgeons have been engineering complex tissue repair and replacement strategies for centuries. In this regard, the dominant principles were mechanical and the implant materials were primary metals. A new era of biologic orthopedics and orthobiologics encompasses new principles of cell and molecular therapies. This new era requires complicated new procedures, new materials, and new talents. The current cell-based, tissue-engineering strategies will set the foundation for learning how to manage the body's intrinsic capacity to repair and rejuvenate skeletal tissues. Ultimately, the expansion of cells outside the body must be replaced by pharmaceutical strategies to bring the reparative cells to the injury site, expand them and differentiate these cells to fill the defect, and induce the neotissue to functionally integrate into the host tissue. It is anticipated that the orthopedic surgeon will be required to transform from a hardware expert into a "mesenchemist" to ensure that the proper bioactive factor is placed in the proper location at the correct time and in the optimal amount to facilitate the body's self-repair by controlling its intrinsic repair-

regeneration capacity. In this regard, new industries must evolve to provide new implant materials that provide morphological boundaries, multiagent release characteristics, and dynamic structural changes to facilitate the proper mechanical and structural properties of the new tissue. Just as power tools have changed orthopedists from carpenters to cabinet makers, so will biologics transform them into conductors of cellular symphonies.

ACKNOWLEDGMENTS

It is with a deep sense of gratitude that I recognize and thank my collaborators and colleagues at Case Western Reserve University for their scholarly contributions to the work reviewed here. I am also grateful to the NIH and numerous corporations for their financial support. This manuscript is dedicated to Professors Edgar Zwilling and Marshall Urist, who showed that deep scholarship and persistence are eventually rewarded by scientific discovery proving that their insightful interpretations were correct.

REFERENCES

1. Caplan, A.I. Mesenchymal stem cells. J. Orthop. Res. **9,** 641, 1991.
2. Caplan, A.I. The mesengenic process. Clin. Plast. Surg. **21,** 429, 1994.
3. Haynesworth, S.E., Goldberg, V.M., and Caplan, A.I. Diminution of the number of mesenchymal stem cells as a cause for skeletal aging. In: Buckwalter, J.A., Goldberg, V.M., Woo, S.L.-Y., eds. Musculoskeletal Soft-Tissue Aging: Impact on Mobility. Rosemont, IL: American Academy of Orthopaedic Surgeons, 1994, pp. 79–87.
4. Caplan A.I. Osteogenesis imperfecta: Rehabilitation medicine and fundamental research. Connect. Tissue Res. **31,** S9, 1995.
5. Horwitz, E.M., Gordon, P.L., and Winston, K.K., *et al*. Isolated allogeneic bone marrow derived mesenchymal cells engraft and stimulate growth in children with osteogenesis imperfecta: Implications for cell therapy of bone. Proc. Natl. Acad. Sci. U.S.A. **99,** 8932, 2002.
6. Horwitz, E.M., Prockop, D.J., and Fitzpatrick, L.A., *et al*. Transplantability and therapeutic effects of bone marrow-derived mesenchymal cells in children with osteogenesis imperfecta. Nat. Med. **5,** 309, 1999.
7. Caplan, A.I. Effects of the nicotinamide-sensitive teratogen 3-acetylpyridine on chick limb cells in culture. Exp. Cell Res. **62,** 341, 1970.
8. Caplan, A.I. The molecular control of muscle and cartilage development. In: Subtelney S, Abbott U, and Liss AR, eds. 39th Annual Symposium of the Society for Developmental Biology. New York: Alan R. Liss, 1981, pp. 37–68.
9. Caplan, A.I., and Koutroupas, S. The control of muscle and cartilage development in the chick limb: The role of differential vascularization. J. Embryol. Exp. Morphol. **29,** 571, 1973.
10. Lucas, P.A., Syftestad, G.T., and Caplan, A.I. Partial isolation and characterization of a chemotactic factor from adult bone for mesenchymal cells. Bone **7,** 365, 1986.
11. Lucas, P.A., Syftestad, G.T., and Caplan, A.I. A water-soluble fraction from adult bone stimulates the differentiation of cartilage in explants of embryonic muscle. Differentiation **37,** 47, 1988.
12. Syftestad, G.T., and Caplan, A.I. A fraction from extracts from demineralized bone stimulates the conversion of mesenchymal cells into chondrocytes. Dev. Biol. **104,** 348, 1984.
13. Syftestad, G.T., and Caplan, A.I. Effects of osteoinductive bone matrix extracts on the transition of mesenchymal cells into chondrocytes. Calcif. Tissue Int. **36,** 625, 1984.
14. Syftestad, G.T., Lucas, P.A., and Caplan, A.I. The *in vitro* chondrogenic response of limb bud mesenchyme to a water-soluble fraction prepared from demineralized bone matrix. Differentiation **29,** 230, 1985.
15. Wozney, J.M., Rosen, V., Celeste, A.J., *et al*. Novel regulators of bone formation: Molecular clones and activities. Science **242,** 1528, 1988.
16. Caplan, A.I. Bioactive factors in bone: Marshall R. Urist, M.D. May 1988, Kerrville, Texas. Connect. Tissue Res. **23,** 103, 1989.
17. Caplan, A.I. Cartilage begets bone vs. endochondral myelopoiesis. Clin. Orthop. Relat. Res. **261,** 257, 1990.
18. Urist, M.R. Bone: Formation by autoinduction. Science **150,** 893, 1965.
19. Urist, M.R., DeLange, R.J., and Finerman, G.A.M. Bone cell differentiation and growth factors. Science **220,** 680, 1984.
20. Connolly, J.F., Guse, R., Tiedeman, J., and Dehne, R. Autologous marrow injection as a substitute for operative grafting of tibial nonunions. Clin. Orthop. Relat. Res. **266,** 259, 1989.
21. Friedenstein, A.J. Precursor cells of mechanocytes. Int. Rev. Cytol. **47,** 327, 1976.
22. Freidensten, A.J., Chailakhyan, R.K., Latsinik, N.V., Panasyuk, A.F., and Keiliss-Borok, I.V. Stromal cells responsible for transferring the microenvironment of the hemopoietic tissues: Cloning *in vitro* and retransplantation *in vivo*. Transplantation **17,** 331, 1974.
23. Owen, M. Lineage of osteogenic cells and their relationship to the stromal system. In: Peck, W.A., ed. Bone and Mineral. Amsterdam,: Elsevier, 1985, pp. 1–25.
24. Owen, J., and Friedenstein, A.J. Stromal stem cells: Marrow-derived osteogenic precursors. Ciba Found. Symp. **136,** 42, 1988.
25. Caplan, A.I., and Haynesworth, S.E. Method for enhancing the implantation and differentiation of marrow-derived mesenchymal cells. Patent no. 5,197,985, March 30, 1993.
26. Caplan, A.I., and Haynesworth, S.E. Method for treating connective tissue disorders. Patent no. 5,226,914, July 13, 1993.
27. Caplan, A.I., and Haynesworth, S.E. Human mesenchymal stem cells. Patent no. 5,486,359, January 23, 1996.
28. Caplan, A.I., and Haynesworth, S.E. Monoclonal antibodies for human osteogenic cell surface antigens. Patent no. 5,643,736, July 1, 1997.
29. Haynesworth, S.E., Baber, M.A., and Caplan, A.I. Cell sur-

face antigens on human marrow-derived mesenchymal cells are detected by monoclonal antibodies. Bone **13,** 69, 1992.
30. Haynesworth, S.E., Goshima, J., Goldberg, V.M., and Caplan, A.I. Characterization of cells with osteogenic potential from human marrow. Bone **13,** 81, 1992.
31. Lennon, D.P., Haynesworth, S.E., Bruder, S.P., Jaiswall, N., and Caplan, A.I. Human and animal mesenchymal progenitor cells from bone marrow: Identification of serum for optimal selection and proliferation. In Vitro Cell Dev. Biol. **32,** 602, 1996.
32. Dennis, J.E., and Caplan, A.I. Porous ceramic vehicles for rat-marrow-derived (*Rattus norvegicus*) osteogenic cell delivery: Effects of pre-treatment with fibronectin or laminin. J. Oral Implant. **19,** 106, 1993.
33. Dennis, J.E., Haynesworth, S.E., Young, R.G., and Caplan, A.I. Osteogenesis in marrow-derived mesenchymal cell porous ceramic composites transplanted subcutaneously: Effect of fibronectin and laminin on cell retention and rate of osteogenic expression. Cell Transplant. **1,** 23, 1992.
34. Dennis, J.E., Konstantakos, E.K., Arm, D., and Caplan, A.I. *In vivo* osteogenesis assay: A rapid method for quantitative analysis. Biomaterials **19,** 1323, 1998.
35. Haynesworth, S.E., Baber, M.A., and Caplan, A.I. Cytokine expression by human marrow-derived mesenchymal progenitor cells *in vitro*: Effects of dexamethasone and IL-1α. J. Cell. Physiol. **166,** 585, 1996.
36. Ohgushi, H., and Caplan, A.I. Stem cell technology and bioceramics: From cell to gene engineering. J. BioMed. Mater. Res. **48,** 913, 1999.
37. Awad, H., Huibregste, B., and Caplan, A.I., *et al*. Autologous mesenchymal stem cell-mediated repair of tendon. Tissue Eng. **5,** 267, 1999.
38. Bruder, S.P., and Caplan, A.I. Discrete stages within the osteogenic lineage are revealed by alterations in the cell surface architecture of embryonic bone cells. In: Glimcher, M.J., and Lian, J.B., eds. The Chemistry and Biology of Mineralized Tissue. New York: Gordon and Breach, 1989, pp. 73–79.
39. Bruder, S.P., Fink, D.J., and Caplan, A.I. Mesenchymal stem cells in bone development, bone repair, and skeletal regeneration. J. Cell Biochem. **56,** 283, 1994.
40. Bruder, S.P., Kraus, K.H., Goldberg, V.M., and Kadiyala, S. The effect of implants loaded with autologous mesenchymal stem cells on the healing of canine segmental bone defects. J. Bone Joint Surg. Am. **80A,** 985, 1998.
41. Caplan, A.I., and Bruder, S.P. Cell and molecular engineering of bone regeneration. In: Lanza, R.P., Chick, W.L., and Langer, R., eds. Principles of Tissue Engineering. Austin, TX: R.G. Landes, 1996, pp. 599–618.
42. Caplan, A.I., and Bruder, S.P. Mesenchymal stem cells: Building blocks for molecular medicine in the 21st century. Trends Mol. Med. **6,** 259, 2001.
43. Liebergall, M., Young, R.G., Ozawa, N., Caplan, A.I., *et al*. The effects of cellular manipulation and TGF-β in a composite graft. In: Brighton, C.T., Friedlaender, G.E., and Lane, J.M., eds. Bone Formation and Repair. Tampa, FL: American Academy of Orthopaedic Surgeons Symposium, 1994, pp. 367–378.
44. Jaiswal, N., Haynesworth, S.E., Caplan, A.I., and Bruder, S.P. Osteogenic differentiation of purified, culture-expanded human mesenchymal stem cells *in vitro*. J. Cell Biochem. **64,** 295, 1997.
45. Johnstone, B., Hering, T.M., Goldberg, V.M., Yoo, J.U., and Caplan, A.I. *In vitro* chondrogenesis of bone marrow-derived mesenchymal progenitor cells. Exp. Cell Res. **238,** 265, 1998.
46. Yoo, J.U., Solchaga, L.A., and Caplan, A.I., *et al*. The chondrogenic potential of human bone-marrow-derived mesenchymal progenitor cells. J. Bone JoInt. Surg. **80,** 1745, 1998.
47. Dennis, J.E., Awadallah, A., and Caplan, A.I. A quadripotential mesenchymal progenitor cell isolated from the marrow of an adult mouse. J. Bone Miner. Res. **14,** 1, 1999.
48. Dennis, J.E., and Caplan, A.I. Differentiation potential of conditionally immortalized mesenchymal progenitor cells from adult marrow of a H-2K^b-tsA58 transgenic mouse. J. Cell. Physiol. **167,** 523, 1996.
49. Wakitani, S., Saito, T., and Caplan, A.I. Myogenic cells derived from rat bone marrow mesenchymal stem cells exposed to 5-azacytidine. Muscle Nerve **18,** 1417, 1995.
50. Caplan, A.I., Elyaderani, M., Mochizuki, Y., Wakitani, S., and Goldberg, V.M. The principles of cartilage repair/regeneration. Clin. Orthop. Relat. Res. **342,** 254, 1997.
51. Goldberg, V.M., and Caplan, A.I. Biological Resurfacing: An Alternative to Total JoInt. Arthroplasty. Orthopedics **17,** 819, 1994.
52. Goldberg, V.M., Solchaga, L.A., Yoo, J., Johnstone, B., and Caplan, A.I. Chondroprogenitor cell repair of full thickness defects of articular cartilage. J. Sports Traumatol. **20,** 81, 1999.
53. Pei, M., Solchaga, L.A., and Caplan, A.I., *et al*. Bioreactors mediate the effectiveness of tissue engineering scaffolds. FASEB J. **16,** 1691, 2002.
54. Solchaga, L.A., Dennis, J.E., Goldberg, V.M., and Caplan, A.I. Hyaluronic acid-based polymers as cell carriers for tissue engineered repair of bone and cartilage. J. Orthop. Res. **17,** 205, 1999.
55. Solchaga, L.A., Dennis, J.E., and Caplan, A.I., *et al*. Hyaluronic acid-based polymers in the treatment of osteochondral defects. J. Orthop. Res. **18,** 773, 2000.
56. Solchaga, L.A., Goldberg, V.M., and Caplan, A.I. Cartilage regeneration using principles of tissue engineering. Clin. Orthop. Suppl. **391,** S161, 2001.
57. Wakitani, S., Goto, T., and Caplan, A.I., *et al*. Mesenchymal cell-based repair of large full-thickness defects of articular cartilage and underlying bone. J. Bone JoInt. Surg **76,** 579, 1994.
58. Young, R.G., Fink, D.J., and Caplan, A.I., *et al.* The use of mesenchymal stem cells in achilles tendon repair. J. Orthop. Res. **16,** 406, 1998.
59. Caplan, A.I. Tissue engineering designs for the future: New logics, old molecules. Tissue Eng. **6,** 1, 2000.
60. Kujawa, M.J., and Caplan, A.I. Hyaluronic acid bonded to cell culture surfaces stimulates chondrogenesis in stage 24 limb mesenchyme cell cultures. Dev. Biol. **114,** 504, 1986.
61. Kujawa, M.J., Carrino, D.A., and Caplan, A.I. Substrate-bonded hyaluronic acid exhibits a size-dependent stimula-

tion of chondrogenic differentiation of stage 24 limb mesenchymal cells in culture. Dev. Biol. **114,** 519, 1986.
62. Koc, O.N., Gerson, S.L., and Caplan, A.I., *et al.* Rapid hematopoietic recovery after coinfusion of autologous blood stem cells and culture expanded marrow mesenchymal stem cells in advanced breast cancer patients receiving high dose chemotherapy. J. Clin. Oncol. **18,** 307, 2000.
63. Lazarus, H.M., Haynesworth, S.E., Gerson, S.L., Rosenthal, N., and Caplan, A.I. *Ex vivo* expansion and subsequent infusion of human bone marrow-derived stromal progenitor cells (mesenchymal progenitor cells) [MPCs]: Implications for therapeutic use. Bone Marrow Transplant. **16,** 557, 1995.
64. Allay, J.A., Dennis, J.E., and Caplan, A.I., *et al*. LacZ and IL-3 expression *in vivo* after retroviral transduction of marrow-derived human osteogenic mesenchymal progenitors. Hum. Gene Ther. **8,** 1417, 1997.
65. Gao, J, Dennis, J.E., Muzic, R.F., Lundberg, M., and Caplan, A.I. The dynamic *in vivo* distribution of bone marrow-derived mesenchymal stem cells after infusion. Cells Tissues Organs **169,** 12, 2001.
66. Saito, T., Dennis, J.E., Lennon, D.P., Young, R.G., and Caplan, A.I. Myogenic expression of mesenchymal stem cells within myotubes of *mdx* mice *in vitro* and *in vivo*. Tissue Eng. **1,** 327, 1996.
67. Askari, A.T., and Penn, M.S. Cell therapy for the treatment of ischemic heart disease: Approaching a new frontier. In: Topal, E.J., ed. Textbook of Interventional Cardiology. Philadelphia, PA: W.B. Saunders, 2003, pp. 1053–1061.
68. Askari, A.T., Unzek, S., and Penn, M.S., *et al.* Effect of stromal-cell-derived factor-1 on stem cell homing and tissue regeneration in ischaemic cardiomyopathy. Lancet **362,** 697, 2003.
69. Shake, J.G., Gruber, P.J., Pittenger, M.F., *et al. In vivo* mesenchymal stem cell grafting in a swine myocardial infarct model: Molecular and physiologic consequences. Ann. Thoracic Surg. **73,** 1919, 2002.
70. Toma, C., Pittenger, M.J., Cahill, K.S., Byrne, B.J., and Kessler, P.D. Human mesenchymal stem cells differentiate to a cardiomyocyte phenotype in the adult murine heart. Circulation **105,** 93, 2002.
71. Chen, J., Zhang, Z.G., and Chopp, M., *et al.* Intravenous administration of human bone marrow stromal cells induces angiogenesis in the ischemic boundary zone after stroke in rats. Circ. Res. **92,** 692, 2003.
72. Mahmood, A., Lu, D., Lu, M., and Chopp, M. Treatment of traumatic brain injury in adult rats with intravenous administration of human bone marrow stromal cells. Neurosurgery **53,** 697, 2003.
73. Tykocinski, M.L., Kaplan, D.R., and Medof, M.E. Antigen-presenting cell engineering: The molecular toolbox. Am. J. Pathol. **148,** 1, 1996.
74. Dennis, J.E., Cohen, N., Caplan, A.I., and Goldberg, V.M. Targeted delivery of progenitor cells for cartilage repair. J. Orthop. Res. **22,** 735, 2004.
75. Pasqualini, R., and Ruoslahti, E. Organ targeting *in vivo* using phage display peptide libraries. Nature **380,** 364, 1999.
76. Rajotte, D., Arap, W., and Ruoslahti, E., *et al.* Molecular heterogeneity of the vascular endothelium revealed by *in vivo*. phage display. J. Clin. Invest. **102**, 430, 1998.
77. Arap, W., Kolonin, M.G., and Trepel, M., *et al.* Steps toward mapping the human vasculature by phage display. Nat. Med. **2,** 121, 2002.
78. Caplan, A.I. Embryonic development and the principles of tissue engineering. Novartis Found. Symp. **249,** 17, 2003.

Address reprInt. requests to:
Arnold I. Caplan, Ph.D.
Skeletal Research Center
Department of Biology
Case Western Reserve University
2080 Adelbert Road, Millis Science Center, Room 118
Cleveland, OH 44106-7080

E-mail: ddb9@case.edu

This article has been cited by:

1. Kim Hynes, Danijela Menicanin, Stan Gronthos, P. Mark Bartold. 2012. Clinical utility of stem cells for periodontal regeneration. *Periodontology 2000* **59**:1, 203-227. [CrossRef]
2. Osamu Honmou, Rie Onodera, Masanori Sasaki, Stephen G. Waxman, Jeffery D. Kocsis. 2012. Mesenchymal stem cells: therapeutic outlook for stroke. *Trends in Molecular Medicine* **18**:5, 292-297. [CrossRef]
3. A. LIRAS, A. S. GABAN, E. C. RODRIGUEZ-MERCHAN. 2012. Cartilage restoration in haemophilia: advanced therapies. *Haemophilia* no-no. [CrossRef]
4. Nancy Parenteau , Janet Hardin-Young , William Shannon , Patrick Cantini , Alan Russell . 2012. Meeting the Need for Regenerative Therapies I: Target-Based Incidence and Its Relationship to U.S. Spending, Productivity, and Innovation. *Tissue Engineering Part B: Reviews* **18**:2, 139-154. [Abstract] [Full Text HTML] [Full Text PDF] [Full Text PDF with Links]
5. Sarvpreet Singh, Frank R. Kloss, Regina Brunauer, Magdalena Schimke, Angelika Jamnig, Brigitte Greiderer-Kleinlercher, Günter Klima, Julia Rentenberger, Thomas Auberger, Oliver Hächl, Michael Rasse, Robert Gassner, Günter Lepperdinger. 2012. Mesenchymal stem cells show radioresistance in vivo. *Journal of Cellular and Molecular Medicine* **16**:4, 877-887. [CrossRef]
6. Elena Torreggiani, Gina Lisignoli, Cristina Manferdini, Elisabetta Lambertini, Letizia Penolazzi, Renata Vecchiatini, Elena Gabusi, Pasquale Chieco, Andrea Facchini, Roberto Gambari, Roberta Piva. 2012. Role of Slug transcription factor in human mesenchymal stem cells. *Journal of Cellular and Molecular Medicine* **16**:4, 740-751. [CrossRef]
7. A. Leonida, A. Paiusco, G. Rossi, F. Carini, M. Baldoni, G. Caccianiga. 2012. Effects of low-level laser irradiation on proliferation and osteoblastic differentiation of human mesenchymal stem cells seeded on a three-dimensional biomatrix: in vitro pilot study. *Lasers in Medical Science* . [CrossRef]
8. Hae-Ryong Song, Swee-Hin Teoh, Jun-Ho Wang, Hak-Jun Kim, Ji-Hoon Bae, Sung Kim, Jerry Chan, Zhi-Yong Zhang, Chang-Wug OhEffect of Scaffolds with Bone Growth Factors on New Bone Formation 871-901. [CrossRef]
9. Eui Park, Hong-In Shin, Shin-Yoon KimAn Efficient ex vivo Expansion of Adult Mesenchymal Stem Cells in Scaffolds 833-853. [CrossRef]
10. Erin Salter , Brian Goh , Ben Hung , Daphne Hutton , Nalinkanth Ghone , Warren L. Grayson . 2012. Bone Tissue Engineering Bioreactors: A Role in the Clinic?. *Tissue Engineering Part B: Reviews* **18**:1, 62-75. [Abstract] [Full Text HTML] [Full Text PDF] [Full Text PDF with Links]
11. Sarah Ricco, Lindsey Boone, John F. PeroniRegenerative Medicine 85-97. [CrossRef]
12. Zhi-Yong Zhang, Swee-Hin Teoh, James H.P. Hui, Nicholas M. Fisk, Mahesh Choolani, Jerry K.Y. Chan. 2012. The potential of human fetal mesenchymal stem cells for off-the-shelf bone tissue engineering application. *Biomaterials* . [CrossRef]
13. Andreas Schmitt, Martijn van Griensven, Andreas B. Imhoff, Stefan Buchmann. 2012. Application of Stem Cells in Orthopedics. *Stem Cells International* **2012**, 1-11. [CrossRef]
14. N. Naveena, J. Venugopal, R. Rajeswari, S. Sundarrajan, R. Sridhar, M. Shayanti, S. Narayanan, S. Ramakrishna. 2012. Biomimetic composites and stem cells interaction for bone and cartilage tissue regeneration. *Journal of Materials Chemistry* . [CrossRef]
15. Zongbin Liu, Lidan Xiao, Baojian Xu, Yu Zhang, Arthur FT Mak, Yi Li, Wing-yin Man, Mo Yang. 2012. Covalently immobilized biomolecule gradient on hydrogel surface using a gradient generating microfluidic device for a quantitative mesenchymal stem cell study. *Biomicrofluidics* **6**:2, 024111. [CrossRef]
16. Adam A. Sassoon, Yasuhiro Ozasa, Takako Chikenji, Yu-Long Sun, Dirk R. Larson, Mary L. Maas, Chunfeng Zhao, Jin Jen, Peter C. Amadio. 2012. Skeletal muscle and bone marrow derived stromal cells: A comparison of tenocyte differentiation capabilities. *Journal of Orthopaedic Research* n/a-n/a. [CrossRef]
17. Ian Wimpenny, Hareklea Markides, Alicia J El Haj. 2012. Orthopaedic applications of nanoparticle-based stem cell therapies. *Stem Cell Research & Therapy* **3**:2, 13. [CrossRef]
18. Pandurangan Subash-Babu, Ali A. Alshatwi. 2012. Aloe-emodin inhibits adipocyte differentiation and maturation during in vitro human mesenchymal stem cell adipogenesis. *Journal of Biochemical and Molecular Toxicology* n/a-n/a. [CrossRef]
19. Hye-Joung Kim , Gun-Il Im . 2011. Electroporation-Mediated Transfer of SOX Trio Genes (SOX-5, SOX-6, and SOX-9) to Enhance the Chondrogenesis of Mesenchymal Stem Cells. *Stem Cells and Development* **20**:12, 2103-2114. [Abstract] [Full Text HTML] [Full Text PDF] [Full Text PDF with Links]
20. Pamela Gehron Robey . 2011. Cell Sources for Bone Regeneration: The Good, the Bad, and the Ugly (But Promising). *Tissue Engineering Part B: Reviews* **17**:6, 423-430. [Abstract] [Full Text HTML] [Full Text PDF] [Full Text PDF with Links]

21. Jong-Min Lee, Gun-Il Im. 2011. SOX trio-co-transduced adipose stem cells in fibrin gel to enhance cartilage repair and delay the progression of osteoarthritis in the rat. *Biomaterials* . [CrossRef]
22. Dr. Nancy Parenteau , Dr. Janet Hardin-Young , Dr. William Shannon , Mr. Patrick Cantini , Dr. Alan J. Russell . Meeting the Need for Regenerative Therapies I: Target-Based Incidence and Its Relationship to US Spending, Productivity and Innovation. *Tissue Engineering Part B: Reviews* **0**:ja. . [Abstract] [Full Text PDF] [Full Text PDF with Links]
23. ZhenHua Ren, JiaYin Wang, ChunLin Zou, YunQian Guan, Yu Alex Zhang. 2011. Labeling of cynomolgus monkey bone marrow-derived mesenchymal stem cells for cell tracking by multimodality imaging. *Science China Life Sciences* **54**:11, 981-987. [CrossRef]
24. Carmen Mariana Aanei , Pascale Flandrin , Florin Zugun Eloae , Eugen Carasevici , Denis Guyotat , Eric Wattel , Lydia Campos . Intrinsic Growth Deficiencies of Mesenchymal Stromal Cells in Myelodysplastic Syndromes. *Stem Cells and Development*, ahead of print. [Abstract] [Full Text HTML] [Full Text PDF] [Full Text PDF with Links]
25. Fei Peng, Hua Wu, Yadong Zheng, Xiqiang Xu, Jizhe Yu. 2011. The effect of noncoherent red light irradiation on proliferation and osteogenic differentiation of bone marrow mesenchymal stem cells. *Lasers in Medical Science* . [CrossRef]
26. Nermeen El-Motaz Bellah Ahmed, Eman Hassan Anwar Aboul-Ezz, Siza Yacoub Zakhary, Tarek Hamed El Badry, Magda Ismail Ramzy. 2011. Isolation of Dental Pulp Stem Cells and their In Vitro Differentiation into Odontoblast-like Cells. *Macedonian Journal of Medical Sciences* **4**:3, 253-260. [CrossRef]
27. T. Sakabe, T. Sakai. 2011. Musculoskeletal diseases--tendon. *British Medical Bulletin* **99**:1, 211-225. [CrossRef]
28. Yu Ren, Haiqing Wu, Xueyuan Zhou, Jianxun Wen, Muzi Jin, Ming Cang, Xudong Guo, Qinglian Wang, Dongjun Liu, Yuzhen Ma. 2011. Isolation, expansion, and differentiation of goat adipose-derived stem cells. *Research in Veterinary Science* . [CrossRef]
29. Matthew C. Stewart, Allison A. Stewart. 2011. Mesenchymal Stem Cells: Characteristics, Sources, and Mechanisms of Action. *Veterinary Clinics of North America: Equine Practice* **27**:2, 243-261. [CrossRef]
30. A.G.L. Alves, Allison A. Stewart, J. Dudhia, Y. Kasashima, A.E. Goodship, R.K.W. Smith. 2011. Cell-based Therapies for Tendon and Ligament Injuries. *Veterinary Clinics of North America: Equine Practice* **27**:2, 315-333. [CrossRef]
31. João L. Ellera Gomes, Ricardo Canquerini da Silva, Lúcia M. R. Silla, Marcelo R. Abreu, Roberto Pellanda. 2011. Conventional rotator cuff repair complemented by the aid of mononuclear autologous stem cells. *Knee Surgery, Sports Traumatology, Arthroscopy* . [CrossRef]
32. Jan C. Brune, Ariane Tormin, Maria C. Johansson, Pehr Rissler, Otte Brosjö, Richard Löfvenberg, Fredrik Vult von Steyern, Fredrik Mertens, Anders Rydholm, Stefan Scheding. 2011. Mesenchymal stromal cells from primary osteosarcoma are non-malignant and strikingly similar to their bone marrow counterparts. *International Journal of Cancer* **129**:2, 319-330. [CrossRef]
33. Dae Gyu Park, Kyung Gon Kim, Tae-Jin Lee, Joo-Young Kim, Eon Gi Sung, Myun-Whan Ahn, In-Hwan Song. 2011. Optimal supplementation of dexamethasone for clinical purposed expansion of mesenchymal stem cells for bone repair. *Journal of Orthopaedic Science* . [CrossRef]
34. Gun-Il Im, Hye-Joung Kim, Jin H. Lee. 2011. Chondrogenesis of adipose stem cells in a porous PLGA scaffold impregnated with plasmid DNA containing SOX trio (SOX-5,-6 and -9) genes. *Biomaterials* **32**:19, 4385-4392. [CrossRef]
35. Alexandra Peister, Maria A. Woodruff, Jarod J. Prince, Derwin P. Gray, Dietmar W. Hutmacher, Robert E. Guldberg. 2011. Cell sourcing for bone tissue engineering: Amniotic fluid stem cells have a delayed, robust differentiation compared to mesenchymal stem cells. *Stem Cell Research* **7**:1, 17-27. [CrossRef]
36. Virginia Pensabene, Silvia Taccola, Leonardo Ricotti, Gianni Ciofani, Arianna Menciassi, Francesca Perut, Manuela Salerno, Paolo Dario, Nicola Baldini. 2011. Flexible polymeric ultrathin film for mesenchymal stem cell differentiation. *Acta Biomaterialia* **7**:7, 2883-2891. [CrossRef]
37. Abbas Shafiee, Ehsan Seyedjafari, Masoud Soleimani, Naser Ahmadbeigi, Peyman Dinarvand, Nasser Ghaemi. 2011. A comparison between osteogenic differentiation of human unrestricted somatic stem cells and mesenchymal stem cells from bone marrow and adipose tissue. *Biotechnology Letters* **33**:6, 1257-1264. [CrossRef]
38. Benjamin Gantenbein-Ritter, Lorin M. Benneker, Mauro Alini, Sibylle Grad. 2011. Differential response of human bone marrow stromal cells to either TGF-#1 or rhGDF-5. *European Spine Journal* **20**:6, 962-971. [CrossRef]
39. Masoud Soleimani, Ehsan Abbasnia, Mehdi Fathi, Hedayat Sahraei, Yashar Fathi, Gholamreza Kaka. 2011. The effects of low-level laser irradiation on differentiation and proliferation of human bone marrow mesenchymal stem cells into neurons and osteoblasts—an in vitro study. *Lasers in Medical Science* . [CrossRef]

40. Brendon M. Baker , Roshan P. Shah , Alice H. Huang , Robert L. Mauck . 2011. Dynamic Tensile Loading Improves the Functional Properties of Mesenchymal Stem Cell-Laden Nanofiber-Based Fibrocartilage. *Tissue Engineering Part A* **17**:9-10, 1445-1455. [Abstract] [Full Text HTML] [Full Text PDF] [Full Text PDF with Links]
41. Benjamin Levi, Michael T. Longaker. 2011. Concise Review: Adipose-Derived Stromal Cells for Skeletal Regenerative Medicine. *STEM CELLS* **29**:4, 576-582. [CrossRef]
42. Tu-Lai Yew, Fang-Yao Chiu, Chih-Chien Tsai, Hen-Li Chen, Wei-Ping Lee, Yann-Jang Chen, Ming-Chau Chang, Shih-Chieh Hung. 2011. Knockdown of p21Cip1/Waf1 enhances proliferation, the expression of stemness markers, and osteogenic potential in human mesenchymal stem cells. *Aging Cell* **10**:2, 349-361. [CrossRef]
43. Jingting Li , Ming Pei . 2011. Optimization of an In Vitro Three-Dimensional Microenvironment to Reprogram Synovium-Derived Stem Cells for Cartilage Tissue Engineering. *Tissue Engineering Part A* **17**:5-6, 703-712. [Abstract] [Full Text HTML] [Full Text PDF] [Full Text PDF with Links]
44. Dominique J. Griffon, James P. Abulencia, Guillaume R. Ragetly, L. Page Fredericks, Sahraoui Chaieb. 2011. A comparative study of seeding techniques and three-dimensional matrices for mesenchymal cell attachment. *Journal of Tissue Engineering and Regenerative Medicine* **5**:3, 169-179. [CrossRef]
45. Nora G. Singer, Arnold I. Caplan. 2011. Mesenchymal Stem Cells: Mechanisms of Inflammation. *Annual Review of Pathology: Mechanisms of Disease* **6**:1, 457-478. [CrossRef]
46. Yi-Te Chen, Jyh-Ding Wei, Jung-Pan Wang, Hsieh-Hsing Lee, En-Rung Chiang, Hung-Chang Lai, Ling-Lan Chen, Yi-Ting Lee, Chih-Chien Tsai, Chien-Lin Liu, Shih-Chieh Hung. 2011. Isolation of mesenchymal stem cells from human ligamentum flavum. *Spine* 1. [CrossRef]
47. Raphael Lis, Cyril Touboul, Pejman Mirshahi, Fadoua Ali, Sharon Mathew, Daniel J. Nolan, Mahtab Maleki, Salma A. Abdalla, Christophe M. Raynaud, Denis Querleu, Eman Al-Azwani, Joel Malek, Massoud Mirshahi, Arash Rafii. 2011. Tumor associated mesenchymal stem cells protects ovarian cancer cells from hyperthermia through CXCL12. *International Journal of Cancer* **128**:3, 715-725. [CrossRef]
48. Nakia D. Spencer, Raymond Chun, Martin A. Vidal, Jeffrey M. Gimble, Mandi J. Lopez. 2011. In vitro expansion and differentiation of fresh and revitalized adult canine bone marrow-derived and adipose tissue-derived stromal cells. *The Veterinary Journal* . [CrossRef]
49. Khalid M. AlGhamdi, Ashok Kumar, Noura A. Moussa. 2011. Low-level laser therapy: a useful technique for enhancing the proliferation of various cultured cells. *Lasers in Medical Science* . [CrossRef]
50. C.-C. Tsai, Y.-J. Chen, T.-L. Yew, L.-L. Chen, J.-Y. Wang, C.-H. Chiu, S.-C. Hung. 2011. Hypoxia inhibits senescence and maintains mesenchymal stem cell properties through down-regulation of E2A-p21 by HIF-TWIST. *Blood* **117**:2, 459-469. [CrossRef]
51. B. Gantenbein-Ritter, D. SakaiBiomaterials for Intervertebral Disc Regeneration 161-169. [CrossRef]
52. Armando de Mattos Carvalho, Ana Liz Garcia Alves, Patrícia Galvão Gomes de Oliveira, Luis Emiliano Cisneros Álvarez, Renée Laufer Amorim, Carlos Alberto Hussni, Elenice Deffune. 2011. Use of Adipose Tissue-Derived Mesenchymal Stem Cells for Experimental Tendinitis Therapy in Equines. *Journal of Equine Veterinary Science* **31**:1, 26-34. [CrossRef]
53. Su-Hwan Kim, Young-Sung Kim, Su-Yeon Lee, Kyoung-Hwa Kim, Yong-Moo Lee, Won-Kyung Kim, Young-Kyoo Lee. 2011. Gene expression profile in mesenchymal stem cells derived from dental tissues and bone marrow. *Journal of Periodontal & Implant Science* **41**:4, 192. [CrossRef]
54. Miquel Gimeno-Fabra, Marianna Peroglio, David Eglin, Mauro Alini, Carole C. Perry. 2011. Combined release of platelet-rich plasma and 3D-mesenchymal stem cell encapsulation in alginate hydrogels modified by the presence of silica. *Journal of Materials Chemistry* **21**:12, 4086. [CrossRef]
55. Y. F. Zhang, Y.F. Zheng, L. Qin. 2011. The potential biohazards of nanosized wear particles at bone-prosthesis interface. *Asia-Pacific Journal of Chemical Engineering* n/a-n/a. [CrossRef]
56. Janet Zoldan, Thomas P. Kraehenbuehl, Abigail K. R. Lytton-Jean, Robert S. Langer, Daniel G. AndersonTissue Engineering for Stem Cell Mediated Regenerative Medicine 377-399. [CrossRef]
57. Wasim S. Khan, David S. Johnson, Timothy E. Hardingham. 2010. The potential of stem cells in the treatment of knee cartilage defects. *The Knee* **17**:6, 369-374. [CrossRef]
58. Jeong Min Seong, Byung-Chul Kim, Jae-Hong Park, Il Keun Kwon, Anathathios Mantalaris, Yu-Shik Hwang. 2010. Stem cells in bone tissue engineering. *Biomedical Materials* **5**:6, 062001. [CrossRef]

59. Derek M. Doroski , Marc E. Levenston , Johnna S. Temenoff . 2010. Cyclic Tensile Culture Promotes Fibroblastic Differentiation of Marrow Stromal Cells Encapsulated in Poly(Ethylene Glycol)-Based Hydrogels. *Tissue Engineering Part A* **16**:11, 3457-3466. [Abstract] [Full Text HTML] [Full Text PDF] [Full Text PDF with Links]
60. Yue Xu , Preeti Malladi , Michael Chiou , Elena Bekerman , Amato J. Giaccia , Michael T. Longaker In Vitro Expansion of Adipose-Derived Adult Stromal Cells in Hypoxia Enhances Early Chondrogenesis 158-170. [Abstract] [Full Text PDF] [Full Text PDF with Links]
61. Peter C. Johnson , Antonios G. Mikos Stem Cells: State of the Art 3-11. [Citation] [Full Text PDF] [Full Text PDF with Links]
62. Ram I. Sharma, Jess G. Snedeker. 2010. Biochemical and biomechanical gradients for directed bone marrow stromal cell differentiation toward tendon and bone. *Biomaterials* **31**:30, 7695-7704. [CrossRef]
63. Guillaume Ragetly, Dominique J. Griffon, Yong Sik Chung. 2010. The effect of type II collagen coating of chitosan fibrous scaffolds on mesenchymal stem cell adhesion and chondrogenesis. *Acta Biomaterialia* **6**:10, 3988-3997. [CrossRef]
64. Sandra Shahab-Osterloh, Frank Witte, Andrea Hoffmann, Andreas Winkel, Sandra Laggies, Berit Neumann, Virginia Seiffart, Werner Lindenmaier, Achim D. Gruber, Jochen Ringe, Thomas Häupl, Fritz Thorey, Elmar Willbold, Pierre Corbeau, Gerhard Gross. 2010. Mesenchymal Stem Cell-Dependent Formation of Heterotopic Tendon-Bone Insertions (Osteotendinous Junctions). *STEM CELLS* **28**:9, 1590-1601. [CrossRef]
65. Oren Pleniceanu, Orit Harari-Steinberg, Benjamin Dekel. 2010. Concise Review: Kidney Stem/Progenitor Cells: Differentiate, Sort Out, or Reprogram?. *STEM CELLS* **28**:9, 1649-1660. [CrossRef]
66. Debby Gawlitta , Eric Farrell , Jos Malda , Laura B. Creemers , Jacqueline Alblas , Wouter J.A. Dhert . 2010. Modulating Endochondral Ossification of Multipotent Stromal Cells for Bone Regeneration. *Tissue Engineering Part B: Reviews* **16**:4, 385-395. [Abstract] [Full Text HTML] [Full Text PDF] [Full Text PDF with Links]
67. Lilia Araida Hidalgo-Bastida , Sarah H. Cartmell . 2010. Mesenchymal Stem Cells, Osteoblasts and Extracellular Matrix Proteins: Enhancing Cell Adhesion and Differentiation for Bone Tissue Engineering. *Tissue Engineering Part B: Reviews* **16**:4, 405-412. [Abstract] [Full Text HTML] [Full Text PDF] [Full Text PDF with Links]
68. Guillaume R. Ragetly, Dominique J. Griffon, Hae-Beom Lee, Yong Sik Chung. 2010. Effect of collagen II coating on mesenchymal stem cell adhesion on chitosan and on reacetylated chitosan fibrous scaffolds. *Journal of Materials Science: Materials in Medicine* **21**:8, 2479-2490. [CrossRef]
69. Gagandeep Kaur, Chao Wang, Jian Sun, Qian Wang. 2010. The synergistic effects of multivalent ligand display and nanotopography on osteogenic differentiation of rat bone marrow stem cells. *Biomaterials* **31**:22, 5813-5824. [CrossRef]
70. Brendon M. Baker, Ashwin S. Nathan, Albert O. Gee, Robert L. Mauck. 2010. The influence of an aligned nanofibrous topography on human mesenchymal stem cell fibrochondrogenesis. *Biomaterials* **31**:24, 6190-6200. [CrossRef]
71. Wei Wang, Bo Li, Yanglin Li, Yangzi Jiang, Hongwei Ouyang, Changyou Gao. 2010. In vivo restoration of full-thickness cartilage defects by poly(lactide-co-glycolide) sponges filled with fibrin gel, bone marrow mesenchymal stem cells and DNA complexes. *Biomaterials* **31**:23, 5953-5965. [CrossRef]
72. L.E. Flynn. 2010. The use of decellularized adipose tissue to provide an inductive microenvironment for the adipogenic differentiation of human adipose-derived stem cells. *Biomaterials* **31**:17, 4715-4724. [CrossRef]
73. Hugo Fernandes , Anouk Mentink , Ruud Bank , Reinout Stoop , Clemens van Blitterswijk , Jan de Boer . 2010. Endogenous Collagen Influences Differentiation of Human Multipotent Mesenchymal Stromal Cells. *Tissue Engineering Part A* **16**:5, 1693-1702. [Abstract] [Full Text HTML] [Full Text PDF] [Full Text PDF with Links] [Supplemental material]
74. Katrin Warstat , Diana Meckbach , Michaela Weis-Klemm , Anita Hack , Gerd Klein , Peter de Zwart , Wilhelm K. Aicher . 2010. TGF-# Enhances the Integrin #2#1-Mediated Attachment of Mesenchymal Stem Cells to Type I Collagen. *Stem Cells and Development* **19**:5, 645-656. [Abstract] [Full Text HTML] [Full Text PDF] [Full Text PDF with Links]
75. Paul T. Thevenot, Ashwin M. Nair, Jinhui Shen, Parisa Lotfi, Cheng-Yu Ko, Liping Tang. 2010. The effect of incorporation of SDF-1# into PLGA scaffolds on stem cell recruitment and the inflammatory response. *Biomaterials* **31**:14, 3997-4008. [CrossRef]
76. Hye-Joung Kim , Gun-Il Im . 2010. The Effects of ERK1/2 Inhibitor on the Chondrogenesis of Bone Marrow– and Adipose Tissue–Derived Multipotent Mesenchymal Stromal Cells. *Tissue Engineering Part A* **16**:3, 851-860. [Abstract] [Full Text HTML] [Full Text PDF] [Full Text PDF with Links]
77. Jun-Beom Park. 2010. Use of Cell-Based Approaches in Maxillary Sinus Augmentation Procedures. *Journal of Craniofacial Surgery* **21**:2, 557-560. [CrossRef]
78. Caren E. Petrie Aronin, Rocky S. Tuan. 2010. Therapeutic potential of the immunomodulatory activities of adult mesenchymal stem cells. *Birth Defects Research Part C: Embryo Today: Reviews* **90**:1, 67-74. [CrossRef]

79. Xuan Guo, Hansoo Park, Simon Young, James D. Kretlow, Jeroen J. van den Beucken, L. Scott Baggett, Yasuhiko Tabata, F. Kurtis Kasper, Antonios G. Mikos, John A. Jansen. 2010. Repair of osteochondral defects with biodegradable hydrogel composites encapsulating marrow mesenchymal stem cells in a rabbit model. *Acta Biomaterialia* **6**:1, 39-47. [CrossRef]
80. Seal Hwangbo, Jongok Kim, Sungho Her, Hyekyung Cho, Jongho Lee. 2010. Therapeutic Potential of Human Adipose Stem Cells in a Rat Myocardial Infarction Model. *Yonsei Medical Journal* **51**:1, 69. [CrossRef]
81. Jennifer E. Phillips, Timothy A. Petrie, Francis P. Creighton, Andrés J. García. 2010. Human mesenchymal stem cell differentiation on self-assembled monolayers presenting different surface chemistries. *Acta Biomaterialia* **6**:1, 12-20. [CrossRef]
82. Kenneth K. Y. Wong, Xuelai Liu. 2010. Silver nanoparticles—the real "silver bullet" in clinical medicine?. *MedChemComm* **1**:2, 125. [CrossRef]
83. H. LI, J. H. ELISSEEFFScaffolds for musculoskeletal tissue engineering 301-329. [CrossRef]
84. C Zilkens, T Lögters, B Bittersohl, R Krauspe, S Lensing-Höhn, M Jäger. 2010. Spinning around or stagnation - what do osteoblasts and chondroblasts really like?. *European Journal of Medical Research* **15**:1, 35. [CrossRef]
85. Su-Hwan Kim, Kyoung-Hwa Kim, Byoung-Moo Seo, Ki-Tae Koo, Tae-Il Kim, Yang-Jo Seol, Young Ku, In-Chul Rhyu, Chong-Pyoung Chung, Yong-Moo Lee. 2009. Alveolar Bone Regeneration by Transplantation of Periodontal Ligament Stem Cells and Bone Marrow Stem Cells in a Canine Peri-Implant Defect Model: A Pilot Study. *Journal of Periodontology* **80**:11, 1815-1823. [CrossRef]
86. John D. Kisiday , David D. Frisbie , C. Wayne McIlwraith , Alan J. Grodzinsky . 2009. Dynamic Compression Stimulates Proteoglycan Synthesis by Mesenchymal Stem Cells in the Absence of Chondrogenic Cytokines. *Tissue Engineering Part A* **15**:10, 2817-2824. [Abstract] [Full Text HTML] [Full Text PDF] [Full Text PDF with Links]
87. Lin Peng, Min Liu, Ya-Nan Xue, Shi-Wen Huang, Ren-Xi Zhuo. 2009. Transfection and intracellular trafficking characteristics for poly(amidoamine)s with pendant primary amine in the delivery of plasmid DNA to bone marrow stromal cells. *Biomaterials* **30**:29, 5825-5833. [CrossRef]
88. James D. Kretlow, Simon Young, Leda Klouda, Mark Wong, Antonios G. Mikos. 2009. Injectable Biomaterials for Regenerating Complex Craniofacial Tissues. *Advanced Materials* **21**:32-33, 3368-3393. [CrossRef]
89. Manitha B. Nair, Anne Bernhardt, Anja Lode, Christiane Heinemann, Sebastian Thieme, Thomas Hanke, Harikrishna Varma, Michael Gelinsky, Annie John. 2009. A bioactive triphasic ceramic-coated hydroxyapatite promotes proliferation and osteogenic differentiation of human bone marrow stromal cells. *Journal of Biomedical Materials Research Part A* **90A**:2, 533-542. [CrossRef]
90. Tobias D. Henning, Michael F. Wendland, Daniel Golovko, Elizabeth J. Sutton, Barbara Sennino, Farbod Malek, Jan S. Bauer, Donald M. McDonald, Heike Daldrup-Link. 2009. Relaxation effects of ferucarbotran-labeled mesenchymal stem cells at 1.5T and 3T: Discrimination of viable from lysed cells. *Magnetic Resonance in Medicine* **62**:2, 325-332. [CrossRef]
91. Gina Lisignoli, Katia Codeluppi, Katia Todoerti, Cristina Manferdini, Anna Piacentini, Nicoletta Zini, Francesco Grassi, Luca Cattini, Roberta Piva, Vittorio Rizzoli, Andrea Facchini, Nicola Giuliani, Antonino Neri. 2009. Gene array profile identifies collagen type XV as a novel human osteoblast-secreted matrix protein. *Journal of Cellular Physiology* **220**:2, 401-409. [CrossRef]
92. Merel Koning, Martin C. Harmsen, Marja J. A. van Luyn, Paul M. N. Werker. 2009. Current opportunities and challenges in skeletal muscle tissue engineering. *Journal of Tissue Engineering and Regenerative Medicine* **3**:6, 407-415. [CrossRef]
93. In-Hwan Song, Arnold I. Caplan, James E. Dennis. 2009. In vitro dexamethasone pretreatment enhances bone formation of human mesenchymal stem cells in vivo. *Journal of Orthopaedic Research* **27**:7, 916-921. [CrossRef]
94. Yi Tang, Xiangwei Wu, Weiqi Lei, Lijuan Pang, Chao Wan, Zhenqi Shi, Ling Zhao, Timothy R Nagy, Xinyu Peng, Junbo Hu, Xu Feng, Wim Van Hul, Mei Wan, Xu Cao. 2009. TGF-#1–induced migration of bone mesenchymal stem cells couples bone resorption with formation. *Nature Medicine* **15**:7, 757-765. [CrossRef]
95. Nancy L Parenteau. 2009. Commercial development of cell-based therapeutics: strategic considerations along the drug to tissue spectrum. *Regenerative Medicine* **4**:4, 601-611. [CrossRef]
96. Hyun-Jun Shin, Woo-Teak Lee, Suk-Hoon Park, Sun-Hwa Lee, Jung-Ho Park, Yong-San Yoon, Jennifer H. Shin. 2009. Development of a Tensile Cell Stimulator to Study the Effects of Uniaxial Tensile Stress on Osteogenic Differentiation of Bone Marrow Mesenchymal Stem Cells. *Transactions of the Korean Society of Mechanical Engineers A* **33**:7, 629-636. [CrossRef]
97. Arnold I. Caplan . 2009. New Era of Cell-Based Orthopedic Therapies. *Tissue Engineering Part B: Reviews* **15**:2, 195-200. [Abstract] [Full Text HTML] [Full Text PDF] [Full Text PDF with Links]

98. Weihua Hu, Fengjing Guo, Feng Li, Hui Huang, Weikai Zhang, Anmin Chen. 2009. Construction of Sox9 gene eukaryotic expression vector and its inductive effects on directed differentiation of bone marrow stromal cells into precartilaginous stem cells in rats. *Journal of Huazhong University of Science and Technology [Medical Sciences]* **29**:3, 291-295. [CrossRef]
99. Qian Fang, Denglong Chen, Zhiming Yang, Min Li. 2009. In vitro and in vivo research on using Antheraea pernyi silk fibroin as tissue engineering tendon scaffolds. *Materials Science and Engineering: C* **29**:5, 1527-1534. [CrossRef]
100. Bo Fang , Yi-Zao Wan , Ting-Ting Tang , Chuan Gao , Ke-Rong Dai . 2009. Proliferation and Osteoblastic Differentiation of Human Bone Marrow Stromal Cells on Hydroxyapatite/Bacterial Cellulose Nanocomposite Scaffolds. *Tissue Engineering Part A* **15**:5, 1091-1098. [Abstract] [Full Text HTML] [Full Text PDF] [Full Text PDF with Links]
101. Xuan Guo, Hansoo Park, Guangpeng Liu, Wei Liu, Yilin Cao, Yasuhiko Tabata, F. Kurtis Kasper, Antonios G. Mikos. 2009. In vitro generation of an osteochondral construct using injectable hydrogel composites encapsulating rabbit marrow mesenchymal stem cells. *Biomaterials* **30**:14, 2741-2752. [CrossRef]
102. Lisley I. Mambelli , Enrico J.C. Santos , Paulo J.R. Frazão , Mariana B. Chaparro , Alexandre Kerkis , André L.V. Zoppa , Irina Kerkis . 2009. Characterization of Equine Adipose Tissue–Derived Progenitor Cells Before and After Cryopreservation. *Tissue Engineering Part C: Methods* **15**:1, 87-94. [Abstract] [Full Text HTML] [Full Text PDF] [Full Text PDF with Links]
103. Tsai-Sheng Fu, Wen-Jer Chen, Lih-Huei Chen, Song-Shu Lin, Shih-Jung Liu, Steve W.N. Ueng. 2009. Enhancement of posterolateral lumbar spine fusion using low-dose rhBMP-2 and cultured marrow stromal cells. *Journal of Orthopaedic Research* **27**:3, 380-384. [CrossRef]
104. Shannon M. Rush, Graham A. Hamilton, Lynn M. Ackerson. 2009. Mesenchymal Stem Cell Allograft in Revision Foot and Ankle Surgery: A Clinical and Radiographic Analysis. *The Journal of Foot and Ankle Surgery* **48**:2, 163-169. [CrossRef]
105. Daniela Franco Bueno , Irina Kerkis , André Mendonça Costa , Marília T. Martins , Gerson Shigeru Kobayashi , Eder Zucconi , Roberto Dalto Fanganiello , Felipe T. Salles , Ana Beatriz Almeida , Cássio Eduardo Raposo do Amaral , Nivaldo Alonso , Maria Rita Passos-Bueno . 2009. New Source of Muscle-Derived Stem Cells with Potential for Alveolar Bone Reconstruction in Cleft Lip and/or Palate Patients. *Tissue Engineering Part A* **15**:2, 427-435. [Abstract] [Full Text HTML] [Full Text PDF] [Full Text PDF with Links] [Supplemental material]
106. In-Hwan Song, Arnold I. Caplan, James E. Dennis. 2009. Dexamethasone inhibition of confluence-induced apoptosis in human mesenchymal stem cells. *Journal of Orthopaedic Research* **27**:2, 216-221. [CrossRef]
107. Min-Ju Jhin, Young-Sung Kim, Su-Hwan Kim, Kyoung-Hwa Kim, Chul-Woo Lee, Ki-Tae Koo, Tae-Il Kim, Yang-Jo Seol, Young Ku, In-Chul Rhyu, Chong-Pyoung Chung, Yong-Moo Lee. 2009. Investigation of postnatal stem cells from canine dental tissue and bone marrow. *The Journal of the Korean Academy of Periodontology* **39**:2, 119. [CrossRef]
108. Sinan Karaoglu, Cengiz Celik, Petek Korkusuz. 2009. The effects of bone marrow or periosteum on tendon-to-bone tunnel healing in a rabbit model. *Knee Surgery Sports Traumatology Arthroscopy* **17**:2, 170. [CrossRef]
109. Ji Sun Park, Dae Gyun Woo, Han Na Yang, Hye Jin Lim, Kyong Mi Park, Kun Na, Keun-Hong Park. 2009. Chondrogenesis of human mesenchymal stem cells encapsulated in a hydrogel construct: Neocartilage formation in animal models as both mice and rabbits. *Journal of Biomedical Materials Research Part A* **9999A**, NA-NA. [CrossRef]
110. Laura Baumgartner, Stefan Arnhold, Klara Brixius, Klaus Addicks, Wilhelm Bloch. 2009. Human mesenchymal stem cells: Influence of oxygen pressure on proliferation and chondrogenic differentiation in fibrin glue in vitro. *Journal of Biomedical Materials Research Part A* **9999A**, NA-NA. [CrossRef]
111. Likun Guo, Naoki Kawazoe, Takashi Hoshiba, Tetsuya Tateishi, Guoping Chen, Xingdong Zhang. 2008. Osteogenic differentiation of human mesenchymal stem cells on chargeable polymer-modified surfaces. *Journal of Biomedical Materials Research Part A* **87A**:4, 903-912. [CrossRef]
112. Huihui Xu, Shadi F. Othman, Richard L. Magin. 2008. Monitoring Tissue Engineering Using Magnetic Resonance Imaging. *Journal of Bioscience and Bioengineering* **106**:6, 515-527. [CrossRef]
113. R. J. W. Hoogendoorn, Z. F. Lu, R. J. Kroeze, R. A. Bank, P. I. Wuisman, M. N. Helder. 2008. Adipose stem cells for intervertebral disc regeneration: current status and concepts for the future. *Journal of Cellular and Molecular Medicine* **12**:6a, 2205-2216. [CrossRef]
114. Jian-feng Hou, Hao Zhang, Xin Yuan, Jun Li, Ying-jie Wei, Sheng-shou Hu. 2008. In vitro effects of low-level laser irradiation for bone marrow mesenchymal stem cells: Proliferation, growth factors secretion and myogenic differentiation. *Lasers in Surgery and Medicine* **40**:10, 726-733. [CrossRef]
115. Kris R. Jatana, Stephen P. Smith. 2008. The Scientific Basis for Lipotransfer: Is It the Ideal Filler?. *Facial Plastic Surgery Clinics of North America* **16**:4, 443-448. [CrossRef]

116. Kuangshin Tai , Gadi Pelled , Dima Sheyn , Anna Bershteyn , Lin Han , Ilan Kallai , Yoram Zilberman , Christine Ortiz , Dan Gazit . 2008. Nanobiomechanics of Repair Bone Regenerated by Genetically Modified Mesenchymal Stem Cells. *Tissue Engineering Part A* **14**:10, 1709-1720. [Abstract] [Full Text HTML] [Full Text PDF] [Full Text PDF with Links]

117. Danielle S. W. Benoit, Michael P. Schwartz, Andrew R. Durney, Kristi S. Anseth. 2008. Small functional groups for controlled differentiation of hydrogel-encapsulated human mesenchymal stem cells. *Nature Materials* **7**:10, 816-823. [CrossRef]

118. Katharina Schallmoser , Eva Rohde , Andreas Reinisch , Christina Bartmann , Daniela Thaler , Camilla Drexler , Anna C. Obenauf , Gerhard Lanzer , Werner Linkesch , Dirk Strunk . 2008. Rapid Large-Scale Expansion of Functional Mesenchymal Stem Cells from Unmanipulated Bone Marrow Without Animal Serum. *Tissue Engineering Part C: Methods* **14**:3, 185-196. [Abstract] [Full Text PDF] [Full Text PDF with Links] [Supplemental material]

119. M. Pei, J. Luo, Q. Chen. 2008. Enhancing and maintaining chondrogenesis of synovial fibroblasts by cartilage extracellular matrix protein matrilins1. *Osteoarthritis and Cartilage* **16**:9, 1110-1117. [CrossRef]

120. Young-Ju Kim, Hye-Joung Kim, Gun-Il Im. 2008. PTHrP promotes chondrogenesis and suppresses hypertrophy from both bone marrow-derived and adipose tissue-derived MSCs. *Biochemical and Biophysical Research Communications* **373**:1, 104-108. [CrossRef]

121. R. Rollín, F. Marco, E. Camafeita, E. Calvo, L. López-Durán, J.Á. Jover, J.A. López, B. Fernández-Gutiérrez. 2008. Differential proteome of bone marrow mesenchymal stem cells from osteoarthritis patients. *Osteoarthritis and Cartilage* **16**:8, 929-935. [CrossRef]

122. Tobias Winkler , Philipp von Roth , Maria Rose Schumann , Katharina Sieland , Gisela Stoltenburg-Didinger , Matthias Taupitz , Carsten Perka , Georg N. Duda , Georg Matziolis . 2008. In Vivo Visualization of Locally Transplanted Mesenchymal Stem Cells in the Severely Injured Muscle in Rats. *Tissue Engineering Part A* **14**:7, 1149-1160. [Abstract] [Full Text PDF] [Full Text PDF with Links]

123. Gert J. Meijer, Joost D. de Bruijn, Ron Koole, Clemens A. van Blitterswijk. 2008. Cell based bone tissue engineering in jaw defects. *Biomaterials* **29**:21, 3053-3061. [CrossRef]

124. Alan J. Nixon, Linda A. Dahlgren, Jennifer L. Haupt, Amy E. Yeager, Daniel L. Ward. 2008. Effect of adipose-derived nucleated cell fractions on tendon repair in horses with collagenase-induced tendinitis. *American Journal of Veterinary Research* **69**:7, 928-937. [CrossRef]

125. Brandon C. Perry , Dan Zhou , Xiaohua Wu , Feng-Chun Yang , Michael A. Byers , T.-M. Gabriel Chu , J. Jeffrey Hockema , Erik J. Woods , W. Scott Goebel . 2008. Collection, Cryopreservation, and Characterization of Human Dental Pulp–Derived Mesenchymal Stem Cells for Banking and Clinical Use. *Tissue Engineering Part C: Methods* **14**:2, 149-156. [Abstract] [Full Text PDF] [Full Text PDF with Links]

126. Stefan Bajada, Irena Mazakova, James B. Richardson, Nureddin Ashammakhi. 2008. Updates on stem cells and their applications in regenerative medicine. *Journal of Tissue Engineering and Regenerative Medicine* **2**:4, 169-183. [CrossRef]

127. Brian Stevens, Yanzhe Yang, Arunesh Mohandas, Brent Stucker, Kytai Truong Nguyen. 2008. A review of materials, fabrication methods, and strategies used to enhance bone regeneration in engineered bone tissues. *Journal of Biomedical Materials Research Part B: Applied Biomaterials* **85B**:2, 573-582. [CrossRef]

128. Tobias Winkler, Philipp Von Roth, Maria Rose Schumann, Katharina Sieland, Gisela Stoltenburg-Didinger, Matthias Taupitz, Carsten Perka, Georg N. Duda, Georg Matziolis. 2008. In Vivo Visualization of Locally Transplanted Mesenchymal Stem Cells in the Severely Injured Muscle in Rats. *Tissue Engineering Part A*, ahead of print080423075413219. [CrossRef]

129. Lisa A. Fortier, Roger K.W. Smith. 2008. Regenerative Medicine for Tendinous and Ligamentous Injuries of Sport Horses. *Veterinary Clinics of North America: Equine Practice* **24**:1, 191-201. [CrossRef]

130. Venkata Lokesh Battula, Sabrina Treml, Harald Abele, Hans-Jörg Bühring. 2008. Prospective isolation and characterization of mesenchymal stem cells from human placenta using a frizzled-9-specific monoclonal antibody. *Differentiation* **76**:4, 326-336. [CrossRef]

131. L. Mazzucco, V. Balbo, E. Cattana, P. Borzini. 2008. Platelet-rich plasma and platelet gel preparation using Plateltex®. *Vox Sanguinis* **94**:3, 202-208. [CrossRef]

132. Paolo Bianco, Pamela Gehron Robey, Paul J. Simmons. 2008. Mesenchymal Stem Cells: Revisiting History, Concepts, and Assays. *Cell Stem Cell* **2**:4, 313-319. [CrossRef]

133. Danièle Noël, David Caton, Stéphane Roche, Claire Bony, Sylvain Lehmann, Louis Casteilla, Christian Jorgensen, Béatrice Cousin. 2008. Cell specific differences between human adipose-derived and mesenchymal–stromal cells despite similar differentiation potentials. *Experimental Cell Research* **314**:7, 1575-1584. [CrossRef]

134. John D. Kisiday, Paul W. Kopesky, Christopher H. Evans, Alan J. Grodzinsky, C. Wayne McIlwraith, David D. Frisbie. 2008. Evaluation of adult equine bone marrow- and adipose-derived progenitor cell chondrogenesis in hydrogel cultures. *Journal of Orthopaedic Research* **26**:3, 322-331. [CrossRef]

135. Gwendolyn M. Hoben, Eugene J. Koay, Kyriacos A. Athanasiou. 2008. Fibrochondrogenesis in Two Embryonic Stem Cell Lines: Effects of Differentiation Timelines. *Stem Cells* **26**:2, 422-430. [CrossRef]

136. Veronika S. Urbán, Judit Kiss, János Kovács, Elen Gócza, Virág Vas, E#va Monostori, Ferenc Uher. 2008. Mesenchymal Stem Cells Cooperate with Bone Marrow Cells in Therapy of Diabetes. *Stem Cells* **26**:1, 244-253. [CrossRef]

137. A LJUNGQVIST, M SCHWELLNUS, N BACHL, M COLLINS, J COOK, K KHAN, N MAFFULLI, Y PITSILADIS, G RILEY, G GOLSPINK. 2008. International Olympic Committee Consensus Statement: Molecular Basis of Connective Tissue and Muscle Injuries in Sport. *Clinics in Sports Medicine* **27**:1, 231-239. [CrossRef]

138. Maik Stiehler, Cody Bünger, Anette Baatrup, Martin Lind, Moustapha Kassem, Tina Mygind. 2008. Effect of dynamic 3-D culture on proliferation, distribution, and osteogenic differentiation of human mesenchymal stem cells. *Journal of Biomedical Materials Research Part A* . [CrossRef]

139. AI Caplan. 2008. Why are MSCs therapeutic? New data: new insight. *The Journal of Pathology* n/a-n/a. [CrossRef]

140. Annie John, Manitha B. Nair, H. K. Varma, Anne Bernhardt, Michael Gelinsky. 2008. Biodegradation and Cytocompatibility Studies of a Triphasic Ceramic-Coated Porous Hydroxyapatite for Bone Substitute Applications. *International Journal of Applied Ceramic Technology* **5**:1, 11-19. [CrossRef]

141. Jose Diaz-Romero, Dobrila Nesic, Shawn Patrick Grogan, Paul Heini, Pierre Mainil-Varlet. 2008. Immunophenotypic changes of human articular chondrocytes during monolayer culture reflect bona fide dedifferentiation rather than amplification of progenitor cells. *Journal of Cellular Physiology* **214**:1, 75-83. [CrossRef]

142. Kevin Lee, Casey K. Chan, Nilesh Patil, Stuart B. Goodman. 2008. Cell therapy for bone regeneration-Bench to bedside. *Journal of Biomedical Materials Research Part B: Applied Biomaterials* **9999B**, NA-NA. [CrossRef]

143. Yinze Diao, Qingjun Ma, Fuzhai Cui, Yanfeng Zhong. 2008. Human umbilical cord mesenchymal stem cells: Osteogenesis in vivo as seed cells for bone tissue engineering. *Journal of Biomedical Materials Research Part A* **9999A**, NA-NA. [CrossRef]

144. Catherine Gérard, Karine Blouin, André Tchernof, Charles J. Doillon. 2008. Adipogenesis in Nonadherent and Adherent Bone Marrow Stem Cells Grown in Fibrin Gel and in the Presence of Adult Plasma. *Cells Tissues Organs* **187**:3, 186-198. [CrossRef]

145. Jeffrey M. Gimble, Farshid Guilak, Mark E. Nuttall, Solomon Sathishkumar, Martin Vidal, Bruce A. Bunnell. 2008. In vitro Differentiation Potential of Mesenchymal Stem Cells. *Transfusion Medicine and Hemotherapy* **35**:3, 228-238. [CrossRef]

146. Yue Xu , Preeti Malladi , Michael Chiou , Elena Bekerman , Amato J. Giaccia , Michael T. Longaker . 2007. In Vitro Expansion of Adipose-Derived Adult Stromal Cells in Hypoxia Enhances Early Chondrogenesis. *Tissue Engineering* **13**:12, 2981-2993. [Abstract] [Full Text PDF] [Full Text PDF with Links]

147. Mary B. Goldring, Steven R. Goldring. 2007. Osteoarthritis. *Journal of Cellular Physiology* **213**:3, 626-634. [CrossRef]

148. S. Heinemann, C. Heinemann, H. Ehrlich, M. Meyer, H. Baltzer, H. Worch, T. Hanke. 2007. A Novel Biomimetic Hybrid Material Made of Silicified Collagen: Perspectives for Bone Replacement. *Advanced Engineering Materials* **9**:12, 1061-1068. [CrossRef]

149. 2007. LVMH Recherche Symposium VII Stem Cells and Skin: Present and Future. *Journal of Cosmetic Dermatology* **6**:4, 283-297. [CrossRef]

150. Andrea Hoffmann, Gerhard Gross. 2007. Tendon and ligament engineering in the adult organism: mesenchymal stem cells and gene-therapeutic approaches. *International Orthopaedics* **31**:6, 791-797. [CrossRef]

151. Arnold I. Caplan. 2007. Adult mesenchymal stem cells for tissue engineering versus regenerative medicine. *Journal of Cellular Physiology* **213**:2, 341-347. [CrossRef]

152. Karin A Corsi, Jonathan B Pollett, Julie A Phillippi, Arvydas Usas, Guangheng Li, Johnny Huard. 2007. Osteogenic Potential of Postnatal Skeletal Muscle–Derived Stem Cells Is Influenced by Donor Sex. *Journal of Bone and Mineral Research* **22**:10, 1592-1602. [CrossRef]

153. Karin A. Corsi, Edward M. Schwarz, David J. Mooney, Johnny Huard. 2007. Regenerative medicine in orthopaedic surgery. *Journal of Orthopaedic Research* **25**:10, 1261-1268. [CrossRef]

154. Nazish Ahmed, William L. Stanford, Rita A. Kandel. 2007. Mesenchymal stem and progenitor cells for cartilage repair. *Skeletal Radiology* **36**:10, 909-912. [CrossRef]

155. Andre F. Steinert , Glyn D. Palmer , Ramille Capito , Jochen G. Hofstaetter , Carmencita Pilapil , Steven C. Ghivizzani , Myron Spector , Christopher H. Evans . 2007. Genetically Enhanced Engineering of Meniscus Tissue Using Ex Vivo Delivery

of Transforming Growth Factor-#1 Complementary Deoxyribonucleic Acid. *Tissue Engineering* **13**:9, 2227-2237. [Abstract] [Full Text PDF] [Full Text PDF with Links]

156. Gail E. Kilroy, Sandra J. Foster, Xiying Wu, Joseph Ruiz, Sonya Sherwood, Aaron Heifetz, John W. Ludlow, Dawn M. Stricker, Suma Potiny, Patrick Green, Yuan-Di C. Halvorsen, Bentley Cheatham, Robert W. Storms, Jeffrey M. Gimble. 2007. Cytokine profile of human adipose-derived stem cells: Expression of angiogenic, hematopoietic, and pro-inflammatory factors. *Journal of Cellular Physiology* **212**:3, 702-709. [CrossRef]
157. PG Buxton, MT Cobourne. 2007. Regenerative approaches in the craniofacial region: manipulating cellular progenitors for oro-facial repair. *Oral Diseases* **13**:5, 452-460. [CrossRef]
158. Huiqi Xie, Fuchun Yang, Li Deng, Jingcong Luo, Tingwu Qin, Xiuqun Li, Guang-Qian Zhou, Zhiming Yang. 2007. The performance of a bone-derived scaffold material in the repair of critical bone defects in a rhesus monkey model. *Biomaterials* **28**:22, 3314-3324. [CrossRef]
159. Kazunori Shimizu, Akira Ito, Tatsuro Yoshida, Yoichi Yamada, Minoru Ueda, Hiroyuki Honda. 2007. Bone tissue engineering with human mesenchymal stem cell sheets constructed using magnetite nanoparticles and magnetic force. *Journal of Biomedical Materials Research Part B: Applied Biomaterials* **82B**:2, 471-480. [CrossRef]
160. M. Bue, S. Riccò, V. Conti, E. Merli, R. Ramoni, S. Grolli. 2007. Platelet Lysate Promotes in Vitro Proliferation of Equine Mesenchymal Stem Cells and Tenocytes. *Veterinary Research Communications* **31**:S1, 289-292. [CrossRef]
161. D. McGonagle, A. English, E.A. Jones. 2007. (iii) The relevance of mesenchymal stem cells in vivo for future orthopaedic strategies aimed at fracture repair. *Current Orthopaedics* **21**:4, 262-267. [CrossRef]
162. Harold Castano-Izquierdo, José Álvarez-Barreto, Juliette van den Dolder, John A. Jansen, Antonios G. Mikos, Vassilios I. Sikavitsas. 2007. Pre-culture period of mesenchymal stem cells in osteogenic media influences theirin vivo bone forming potential. *Journal of Biomedical Materials Research Part A* **82A**:1, 129-138. [CrossRef]
163. Markus M. Wilke, Daryl V. Nydam, Alan J. Nixon. 2007. Enhanced early chondrogenesis in articular defects following arthroscopic mesenchymal stem cell implantation in an equine model. *Journal of Orthopaedic Research* **25**:7, 913-925. [CrossRef]
164. Hansoo Park, Johnna S. Temenoff, Yasuhiko Tabata, Arnold I. Caplan, Antonios G. Mikos. 2007. Injectable biodegradable hydrogel composites for rabbit marrow mesenchymal stem cell and growth factor delivery for cartilage tissue engineering. *Biomaterials* **28**:21, 3217-3227. [CrossRef]
165. Marc M. Thibault , Caroline D. Hoemann , Michael D. Buschmann . 2007. Fibronectin, Vitronectin, and Collagen I Induce Chemotaxis and Haptotaxis of Human and Rabbit Mesenchymal Stem Cells in a Standardized Transmembrane Assay. *Stem Cells and Development* **16**:3, 489-502. [Abstract] [Full Text PDF] [Full Text PDF with Links]
166. Rachel Rivkin , Alon Ben-Ari , Ibrahim Kassis , Lior Zangi , Elena Gaberman , Lilia Levdansky , Gerard Marx , Raphael Gorodetsky . 2007. High-Yield Isolation, Expansion, and Differentiation of Murine Bone Marrow-Derived Mesenchymal Stem Cells Using Fibrin Microbeads (FMB). *Cloning and Stem Cells* **9**:2, 157-175. [Abstract] [Full Text PDF] [Full Text PDF with Links]
167. Liu Hong , Aylin Colpan , Ioana A. Peptan , Joseph Daw , Anne George , Carla A. Evans . 2007. 17-# Estradiol Enhances Osteogenic and Adipogenic Differentiation of Human Adipose-Derived Stromal Cells. *Tissue Engineering* **13**:6, 1197-1203. [Abstract] [Full Text PDF] [Full Text PDF with Links]
168. Véronique Viateau, Geneviève Guillemin, Valérie Bousson, Karim Oudina, Didier Hannouche, Laurent Sedel, Delphine Logeart-Avramoglou, Hervé Petite. 2007. Long-bone critical-size defects treated with tissue-engineered grafts: A study on sheep. *Journal of Orthopaedic Research* **25**:6, 741-749. [CrossRef]
169. Vivian H. Fan, Ada Au, Kenichi Tamama, Romie Littrell, Llewellyn B. Richardson, John W. Wright, Alan Wells, Linda G. Griffith. 2007. Tethered Epidermal Growth Factor Provides a Survival Advantage to Mesenchymal Stem Cells. *Stem Cells* **25**:5, 1241-1251. [CrossRef]
170. Humberto Filho Cerruti, Irina Kerkis, Alexandre Kerkis, Nelson Hidekazu Tatsui, Adriana da Costa Neves, Daniela Franco Bueno, Marcelo Cavenaghi Pereira da Silva. 2007. Allogenous Bone Grafts Improved by Bone Marrow Stem Cells and Platelet Growth Factors: Clinical Case Reports. *Artificial Organs* **31**:4, 268-273. [CrossRef]
171. R. Rollín, R. Álvarez-Lafuente, F. Marco, J.A. Jover, C. Hernández-García, C. Rodríguez-Navas, L. López-Durán, B. Fernández-Gutiérrez. 2007. Human parvovirus B19, varicella zoster virus, and human herpesvirus-6 in mesenchymal stem cells of patients with osteoarthritis: analysis with quantitative real-time polymerase chain reaction. *Osteoarthritis and Cartilage* **15**:4, 475-478. [CrossRef]

172. Andrea Augello, Roberta Tasso, Simone Maria Negrini, Ranieri Cancedda, Giuseppina Pennesi. 2007. Cell therapy using allogeneic bone marrow mesenchymal stem cells prevents tissue damage in collagen-induced arthritis. *Arthritis & Rheumatism* **56**:4, 1175-1186. [CrossRef]
173. S. Grässel, N. Ahmed. 2007. Einsatz von mesenchymalen Knochenmarkstammzellen für die Ex-vivo-Knorpelregeneration. *Der Orthopäde* **36**:3, 227-235. [CrossRef]
174. Dennis McGonagle, Cosimo De Bari, Peter Arnold, Elena Jones. 2007. Lessons from musculoskeletal stem cell research: The key to successful regenerative medicine development. *Arthritis & Rheumatism* **56**:3, 714-721. [CrossRef]
175. Jeffrey A. HubbellPolymers in Tissue Engineering 2719-2742. [CrossRef]
176. H. Zheng, J. A. Martin, Y. Duwayri, G. Falcon, J. A. Buckwalter. 2007. Impact of Aging on Rat Bone Marrow-Derived Stem Cell Chondrogenesis. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences* **62**:2, 136-148. [CrossRef]
177. Xi Chen, Angela McClurg, Guang-Qian Zhou, Mervyn McCaigue, Marilyn Ann Armstrong, Gang Li. 2007. Chondrogenic Differentiation Alters the Immunosuppressive Property of Bone Marrow-Derived Mesenchymal Stem Cells, and the Effect Is Partially due to the Upregulated Expression of B7 Molecules. *Stem Cells* **25**:2, 364-370. [CrossRef]
178. Philipp Niemeyer , Martin Kornacker , Alexander Mehlhorn , Anja Seckinger , Jana Vohrer , Hagen Schmal , Philip Kasten , Volker Eckstein , Norbert P. Südkamp , Ulf Krause . 2007. Comparison of Immunological Properties of Bone Marrow Stromal Cells and Adipose Tissue–Derived Stem Cells Before and After Osteogenic Differentiation In Vitro. *Tissue Engineering* **13**:1, 111-121. [Abstract] [Full Text PDF] [Full Text PDF with Links]
179. Regina Ebert, Norbert Schütze, Tatjana Schilling, Lothar Seefried, Meike Weber, Ulrich Nöth, Jochen Eulert, Franz Jakob. 2007. Influence of hormones on osteogenic differentiation processes of mesenchymal stem cells. *Expert Review of Endocrinology & Metabolism* **2**:1, 59. [CrossRef]
180. P. Wo#niak, A. J. El HajBone regeneration and repair using tissue engineering 294-318. [CrossRef]
181. A. Scutt, E. M. Williamson. 2007. Cannabinoids Stimulate Fibroblastic Colony Formation by Bone Marrow Cells Indirectly via CB2 Receptors. *Calcified Tissue International* **80**:1, 50-59. [CrossRef]
182. Florence Fioretti, Corinne Lebreton-DeCoster, Farida Gueniche, Myriam Yousfi, Philippe Humbert, Gaston Godeau, Karim Senni, Alexis Desmoulière, Bernard Coulomb. 2007. Human bone marrow-derived cells: An attractive source to populate dermal substitutes. *Wound Repair and Regeneration*, ahead of print071106213451001. [CrossRef]
183. Philipp Niemeyer, Martin Kornacker, Alexander Mehlhorn, Anja Seckinger, Jana Vohrer, Hagen Schmal, Philip Kasten, Volker Eckstein, Norbert P. Südkamp, Ulf Krause. 2007. Comparison of Immunological Properties of Bone Marrow Stromal Cells and Adipose Tissue?Derived Stem Cells Before and After Osteogenic Differentiation In Vitro. *Tissue Engineering* **13**:1, 111-121. [CrossRef]
184. K. A. Corsi, J. HuardMusculoskeletal tissue engineering with skeletal muscle-derived stem cells 172-186. [CrossRef]
185. Philipp Niemeyer, Martin Kornacker, Alexander Mehlhorn, Anja Seckinger, Jana Vohrer, Hagen Schmal, Philip Kasten, Volker Eckstein, Norbert P. Südkamp, Ulf Krause. 2006. Comparison of Immunological Properties of Bone Marrow Stromal Cells and Adipose Tissue?Derived Stem Cells Before and After Osteogenic Differentiation in Vitro. *Tissue Engineering*, ahead of print061220075423031. [CrossRef]
186. Stuart B. Goodman, Ting Ma, Richard Chiu, Ravi Ramachandran, R. Lane Smith. 2006. Effects of orthopaedic wear particles on osteoprogenitor cells. *Biomaterials* **27**:36, 6096-6101. [CrossRef]
187. Hans Klingemann. 2006. Discarded stem cells with a future?. *Expert Opinion on Biological Therapy* **6**:12, 1251-1254. [CrossRef]
188. Koichiro Iohara, Li Zheng, Masataka Ito, Atsushi Tomokiyo, Kenji Matsushita, Misako Nakashima. 2006. Side Population Cells Isolated from Porcine Dental Pulp Tissue with Self-Renewal and Multipotency for Dentinogenesis, Chondrogenesis, Adipogenesis, and Neurogenesis. *Stem Cells* **24**:11, 2493-2503. [CrossRef]
189. Philipp Mayer-Kuckuk, Adele L. Boskey. 2006. Molecular imaging promotes progress in orthopedic research. *Bone* **39**:5, 965-977. [CrossRef]
190. Liu Hong , Aylin Colpan , Ioana A. Peptan . 2006. Modulations of 17-# Estradiol on Osteogenic and Adipogenic Differentiations of Human Mesenchymal Stem Cells. *Tissue Engineering* **12**:10, 2747-2753. [Abstract] [Full Text PDF] [Full Text PDF with Links]
191. MARTIN A. VIDAL, GAIL E. KILROY, JILL R. JOHNSON, MANDI J. LOPEZ, RUSTIN M. MOORE, JEFFREY M. GIMBLE. 2006. Cell Growth Characteristics and Differentiation Frequency of Adherent Equine Bone Marrow?Derived Mesenchymal Stromal Cells: Adipogenic and Osteogenic Capacity. *Veterinary Surgery* **35**:7, 601-610. [CrossRef]

192. M GOLDRING. 2006. Update on the biology of the chondrocyte and new approaches to treating cartilage diseases. *Best Practice & Research Clinical Rheumatology* **20**:5, 1003-1025. [CrossRef]

193. Liu Hong, Aylin Colpan, Ioana A. Peptan. 2006. Modulations of 17-? Estradiol on Osteogenic and Adipogenic Differentiations of Human Mesenchymal Stem Cells. *Tissue Engineering*, ahead of print060928131519001. [CrossRef]

194. Timothy A. Moseley, Min Zhu, Marc H. Hedrick. 2006. Adipose-Derived Stem and Progenitor Cells as Fillers in Plastic and Reconstructive Surgery. *Plastic and Reconstructive Surgery* **118**:Suppl, 121S-128S. [CrossRef]

195. Andrea Hoffmann, Gerhard Gross. 2006. Tendon and ligament engineering: from cell biology to in vivo application. *Regenerative Medicine* **1**:4, 563-574. [CrossRef]

196. Pierre J Marie, Olivia Fromigué. 2006. Osteogenic differentiation of human marrow-derived mesenchymal stem cells. *Regenerative Medicine* **1**:4, 539-548. [CrossRef]

197. Jean-Thomas Vilquin, Philippe Rosset. 2006. Mesenchymal stem cells in bone and cartilage repair: current status. *Regenerative Medicine* **1**:4, 589-604. [CrossRef]

198. Mary B. Goldring. 2006. Are bone morphogenetic proteins effective inducers of cartilage repair? Ex vivo transduction of muscle-derived stem cells. *Arthritis & Rheumatism* **54**:2, 387-389. [CrossRef]

199. Curtis L. Cetrulo. 2006. Cord-blood mesenchymal stem cells and tissue engineering. *Stem Cell Reviews* **2**:2, 163. [CrossRef]

200. Irina Kerkis, Alexandre Kerkis, Dmitri Dozortsev, Gaëlle Chopin Stukart-Parsons, Sílvia Maria Gomes Massironi, Lygia V. Pereira, Arnold I. Caplan, Humberto F. Cerruti. 2006. Isolation and Characterization of a Population of Immature Dental Pulp Stem Cells Expressing OCT-4 and Other Embryonic Stem Cell Markers. *Cells Tissues Organs* **184**:3-4, 105-116. [CrossRef]

201. Raymund E. Horch. 2006. Future perspectives in tissue engineering: ?Tissue Engineering? Review Series. *Journal of Cellular and Molecular Medicine* **10**:1, 4-6. [CrossRef]