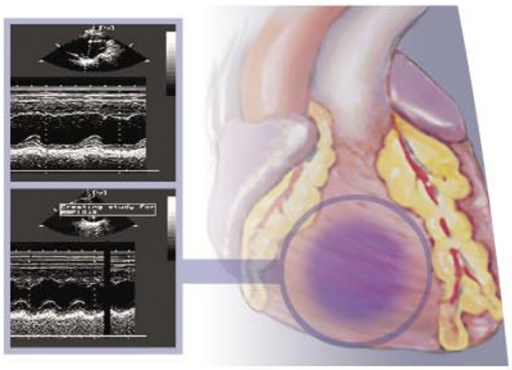
Leaders In Stem Cell Medicine

Applications of Mesenchymal Stem Cells

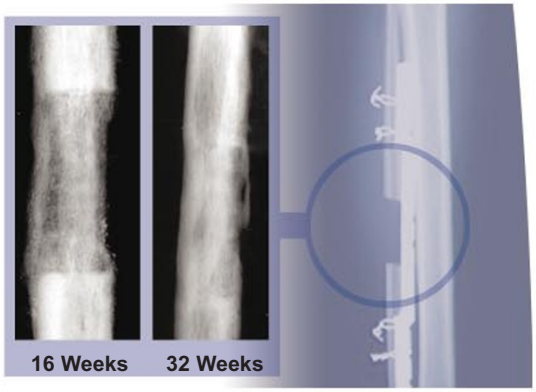
Cardiac Muscle Repair

CardioCel™ is a product candidate that uses "off-the-shelf" MSCs to regenerate damaged or diseased heart muscle. It is targeted primarily to post-myocardial infarct patients. Osiris has demonstrated robust engraftment and cardiac differentiation of allogeneic MSCs in both pig and mouse infarction models. Delivery of allogeneic porcine MSCs improved left ventricular function in a reperfusion infarct model. Clinical trials are anticipated for early 2002.



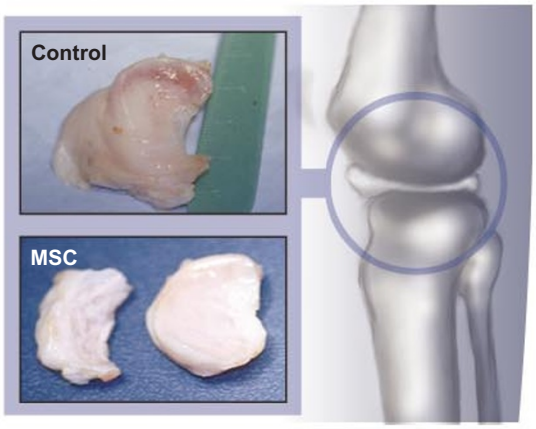
Bone Regeneration

The OsteoCel™ product candidate combines off-the-shelf human MSCs with an appropriate biocompatible matrix to regenerate bone that has been injured, diseased or degenerated. The figure illustrates critical gap repair in a baboon model, using allogeneic baboon MSCs on a supporting matrix. A Phase I clinical trial is underway and Phase II trials are planned for early 2002. Osiris seeks to address not only segmental gap cases, but also smaller non-unions, cavitary defects, spinal repair and craniofacial reconstruction.



Joint Repair

Chondrogen™ is a product candidate comprising off-the-shelf human MSCs delivered in liquid suspension by intra-articular injection. The aim is to regenerate a severely damaged meniscus, thus delaying or halting the progression of osteoarthritis in the knee joint. Osiris has established a goat model for the induction of osteoarthritis that includes a complete medial menisectomy. The figure shows the regeneration of the medial meniscus six weeks after a single intra-articular injection of 10 million allogeneic goat MSCs. Clinical trials are anticipated for early 2002.



Osiris develops off-the-shelf cellular products based on the human mesenchymal stem cell (hMSC). These products start with donor material that is expanded in vitro using Osiris' proprietary process. The expanded cells are cryopreserved in the undifferentiated stem cell state, shipped to and stored at the clinical site, then thawed for administration. Once delivered, the cells receive host signals that direct appropriate differentiation. Osiris' basic science and pre-clinical research have confirmed the ability to use MSCs in a fully allogeneic context without MHC matching or immunosuppression. Other clinical applications for hMSCs include support of hematopoietic stem cell transplantation (Phase II clinical trials).

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When The Body Can t Heal Itself

This is an exciting time for the field of stem cell biology. It would have been difficult to predict four years ago the tremendous progress that the field has seen both in basic research discoveries, as well as in therapeutic potential. From the first descriptions of the human embryonic and germ stem cells to the multipotentiality of adult stem cells, dramatic developments have occurred on all fronts. These developments have taken place under heightened awareness from scientists, the medical community, elected officials and interested citizens. All of us know much more about stem cells today than at any previous time, yet the foreseeable future promises even more exciting breakthroughs, including the discovery of new adult stem cells, and greater plasticity of these cells. Osiris is delighted to support this Nature Insight on the biology and potential of stem cells.

Almost 20 years ago the field of stem cell therapeutics was launched with the isolation of the hematopoietic stem cell. It took another 10 years before the mesenchymal stem cell was identified and utilized in the repair of connective tissues in pre-clinical models. Subsequently, fetal neural stem cells were used to treat patients with Parkinson's disease and adult liver stem cells have been identified. The search for other adult stem cells, such as those giving rise to pancreatic islets, continues. Preclinical and clinical studies have shown that the *in vivo* environment provides the necessary cues for tissue-appropriate differentiation and regulation of adult mesenchymal stem cells (MSCs). Additionally, recent studies have shown that MSCs are an "immune privileged" cell type and therefore do not stimulate an immune response *in vitro* or *in vivo* and can be used clinically without immunosuppression. Whether other adult or even embryonic stem cells will demonstrate the same immune privilege remains to be shown. Osiris' scientists and collaborators have demonstrated in several large animal models that the use of fully mismatched, donor-derived MSCs repaired bone, cardiac muscle and meniscus without evidence of immune rejection. The use of stem cells in such an "off-the-shelf" manner could make stem cell based cellular therapies feasible and cost-effective in the acute injury setting as well as in chronic disease states. The era of cellular and tissue regeneration for the treatment of disease and the effects of aging has indeed begun.

Though the articles in this publication can only touch on the possibilities that stem cell biology may provide, we can be certain that continued research will enhance significantly our understanding of human development. Through the dedication of many individuals, research teams and institutions, physicians and healthcare professionals, and in cooperation with industry and regulatory agencies, we are confident that stem cell biology will beneficially impact healthcare for all mankind.

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