Use of MDFc19, a Stem Cell Derived Supplement, in New Skin Care Products

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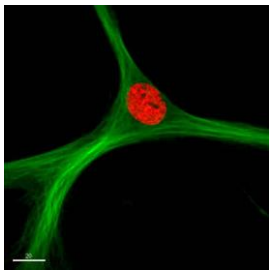
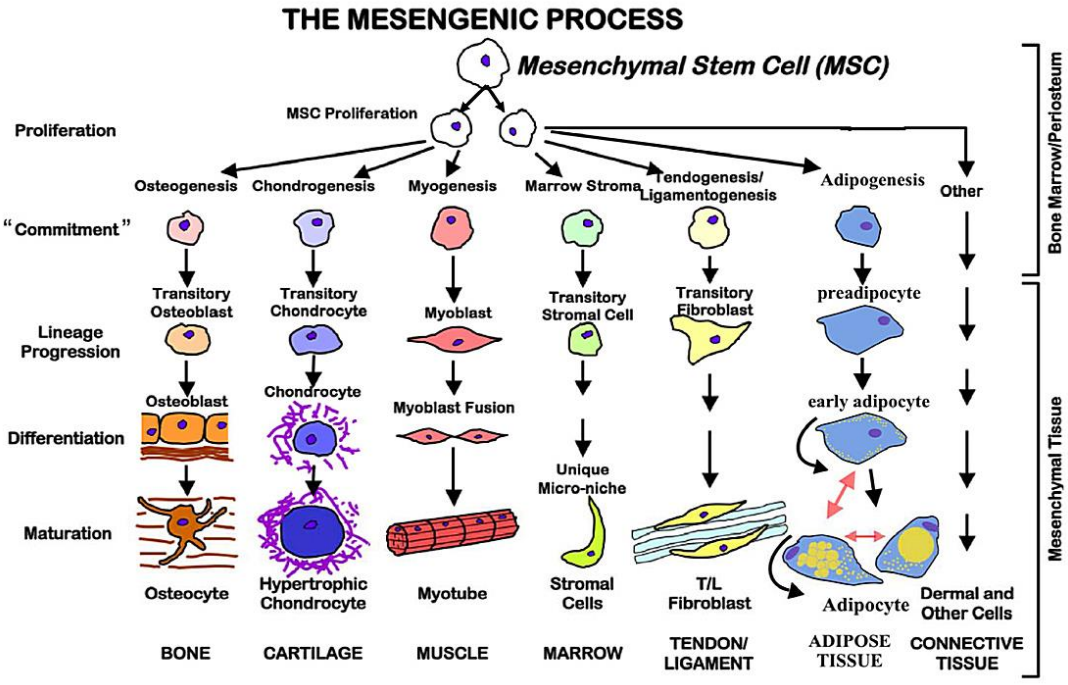
What are These Human Adult Stem Cells



Human Adult Mesenchymal Stem Cell (MSC)

There are many types of human adult stem cells located in all of our organs that provide a variety of functions in maintaining, replacing, and healing the multitude of different cell types in the human body. (1,2) One of the most important types of Adult Stem Cells is the Human Mesenchymal Stem Cell or MSC for short. It circulates in the blood and is located in all of our tissues. Normally it waits in a restful state until stimulated by signals resulting from damage or changes in the body from different types of diseases or disorders. Upon this proper signaling, the Human Adult MSC's begin to multiply and release different signals to bring in other inflammatory and immune cells to aid in the battle. The MSC's can also differentiate or change into many different types of cells important to the structure and function of the body. (3,4) As shown below, the different types of cells that can be produced by the MSC's include bone, cartilage muscle, heart muscle, tendons and ligaments, connective tissues, and fat. (5) In addition to these cell types, MSC's can also develop into all of the different types of blood cells from the bone marrow and spleen as well as the blood vessels themselves.

Human Adult Mesenchymal Stem Cell (MSC) Differentiation into Tissues (5)



It is also important to understand what the MSC's are not able to do. They cannot make skin, nerve, spinal cord, or brain cells. They also are not able to make the different organs in the body such as lung, liver, pancreas, and kidneys. Nor can they make ovarian or testicular reproductive cells. Most importantly, the MSC's are definitely not in any way the same as Human Embryonic Stem Cells (ESC's) that are the cause of a great deal of controversy. (6) Human ESC's can be produced in the test tube from human eggs that are

fertilized *in vitro* by human sperm that can then grow into small spherical structures (blastula) that contain a small number of undifferentiated ESC's. (7) Only if these blastula successfully implant into the uterus, can the blastula differentiate into a placenta that can support the human ESC's ability to differentiate into a human fetus that is capable of growing into a fully developed human. (8) If undifferentiated or partially differentiated human ESC's are implanted directly into adult tissue, they will form tumors. (9) MSC's cannot form fetuses or tumors when implanted into the body. MSC's are limited in their differentiation only to the formation of the tissues shown in the table above and then only under very specific conditions and signals.

Human Clinical Trials Injecting Adult Human MSC's for Treating Diseases and Disorders

Currently, the Federal Drug Administration (FDA) has approved 290 clinical trials taking viable adult human MSC's from donors and permitting their injection into humans for a large variety of diseases and disorders. (10) One of these approved studies is injecting human MSC's into people with recent heart attacks and finding that those receiving the MSC injections have a 50% reduction in permanent damage and function of the heart after the attack compared to those that only received saline injections. (11,12) Injecting these Adult Human MSC's from one donor into humans with different diseases without using immunosuppression is possible due to the fact that these unique stem cells do not express human transplant antigens on their surfaces. (13) Thus, the recipient's immune system does not recognize them as foreign and accepts them as their own cells. After injection these MSC's go about their business of recognizing damaged tissues and attempting to repair them. While it may be possible that the injected MSC's can differentiate into the cells needed to replace the damaged ones, the effectiveness of this MSC differentiation during repair is not entirely clear. But it is certainly well accepted that the injected MSC's release an impressive amount of different types of bioactive molecules that can clearly be aiding the repair and recovery of the different types of tissue damage. (14) These bioactive substances released by MSC's while they are expanding and responding to the tissue damage include a variety of cytokines, anti-oxidants, pro-angiogenic factors, and growth factors. (15) In addition, they release substances that limit stress responses and reduce signals that cause the damaged cells to go into controlled cell death or apoptosis. The summation of this varied MSC response to damaged and diseased tissues through the release of such a variety of "healing" substances stimulates researchers to try to discover and identify these agents that may eventually be utilized as specific drugs. (16) Until that happens, the MSC's will continue to be implanted into patients in ongoing clinical trials.

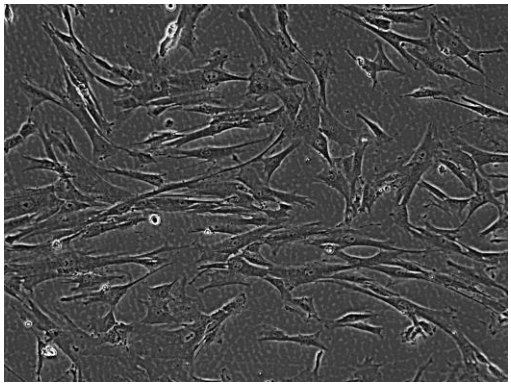
Development of Mesenchymal Derived Factor Complex (MDFc19) for Skin Care Products

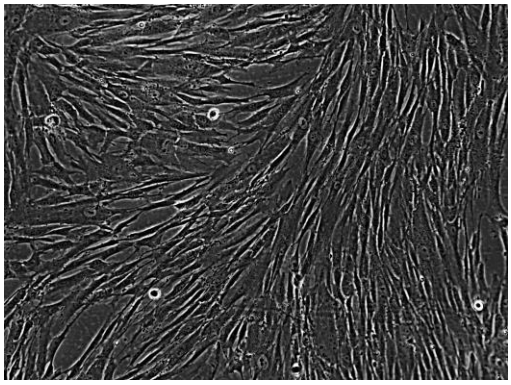
Dr. Scharp postulated that when adult human MSC's are rapidly growing in the laboratory, one may simultaneously stimulate the formation and release of a number of these so far un-identified, critical "healing" factors into the culture media used to grow the MSC's. Thus, the concept of MDFc19 was developed and tested as the basis to provide these important compounds as a critical supplement for skin care formulations and products. (17, 18) Adult human MSC's were grown in a proprietary medium at Scharp Technologies. Under controlled conditions, the MSC's are removed, and the conditioned medium is combined into lots containing equal quantities of the growth condition variables. This conditioned medium is then added to skin care formulations as MDFc19. To assure these peptides can cross the epidermis to gain access to the dermis, carrier constituents are included in the formulation. (19) Safety testing was completed without evidence of toxicity. A number of different trials in patients have also been completed, demonstrating a clear response on small winkles, skin thickness, UV light damage, hyperpigmentation, age related changes, and other parameters.

Preliminary Research Findings from MSC Cultures with Human Dermal Fibroblasts

Since the active components in MDFc19 have not been identified, Scharp Technologies has established research protocols for these active components using human dermal fibroblast cell lines. Previous studies have shown that direct MSC contact and even paracrine signals from MSC's induce dermal fibroblasts to respond to injury by proliferation, increase in collagen production, closure of induced gaps in their confluent cell growth, and migration towards MSC's. (20,21) The Scharp Technology tissue culture results compared with both positive and negative controls show that just inclusion of MDFc19 without MSC's in the culture of these human dermal fibroblasts significantly increase their collagen production, their growth, and their rapid ability to close experimental gaps created in growing layers of these cells. Additional studies continue towards elucidating the mechanisms involved. The final goal of this research is to actually identify the specific peptides through genomic and proteomic studies that are being released from the MSC's. A collaborative research program is underway with Evan Snyder, MD, PhD, of the Sanford Consortium of Regenerative Medicine at the Sanford Burnham Medical Research Institute in La Jolla, CA, to identify the markers and genes involved in the MSC's while producing the un-identified components of MDFc-19. (22,23) The final goal is to isolate and purify the most potent of the active components of MDFc-19 that may be further developed into specific new products for skin care and damaged skin repair. Scharp Technologies recently converted a provisional patent with the USPTO to a formal application on their novel culture of MSC's and their effects on dermal fibroblasts.

Testing of Cultured Human Dermal Fibroblasts Grown in MDFc19





Potential Markets Beyond Skin Care Products

The cosmeceutical market is quite substantial in size and rapidly accepts new products that deliver observable improvements that have actual scientific backing. (24-26) Yet there are a number of additional medical conditions to be considered that can be developed that may benefit from using the MDFc19 components. During the preliminary clinical testing of the skin care products containing MDFc19, it was observed that there may be positive reductions in the clinical skin conditions of eczema, rosacea, and psoriasis. It is expected that higher concentrations of MDFc19 may be required in potential new products to initiate clinical testing of these types of skin disorders to confirm these early observations. Since major changes in these conditions could be observed in products that are more potent, the product classification may have to be increased in order to remain in compliance with the FDA and FTC regulations. Scharp Technologies is in discussion with relevent university based clinical programs to consider their potential testing of new products for these disorders.

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