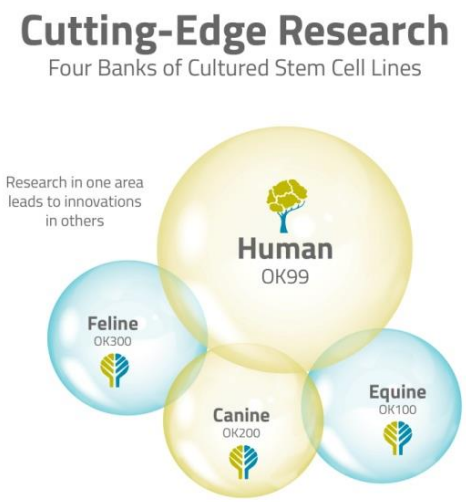
The Science Behind Celavie Biosciences

Through a purposeful union of science, medicine, technology and the marketplace, Celavie Biosciences LLC catalyzes the natural healing power intrinsic to the biology of cells to advance regenerative medicine and relieve suffering worldwide. We believe Celavie's stem cells carry humanity's best hope for curing many of the world's most devastating conditions, which will intensify in tandem with the growth and graying of the world's population.



Through continuous innovation, we strive to increase the effectiveness and reach of Celavie's proprietary stem cell products and technologies. Our technology facilitates the commercial-scale production and banking of our cells across four mammalian lines. We have shown in vitro that our stem cells are capable of maturing into a wide range of adult stem cells that can be applied to a number of degenerative and under-addressed diseases, both human and veterinary.

Our goal is to develop cells that are hypo-immunogenic and do not cause tumors. Unlike embryonic stem cells, human OK99 cells have not produced tumors when implanted into immunodeficient rats.

A first-in-human Phase I clinical trial for Parkinson's disease carried out in Mexico City at Hospital Angeles de Pedegral with permission of COFEPRIS (Mexico's FDA) just reached its two-year follow-up. Conducted on seven patients, the trial has not revealed any lasting adverse effects or complications over a period of more than two years. Protocol for a larger controlled single-blinded randomized trial in US is in progress. Preparation of materials for IND application is in progress.

Our veterinary subsidiary, Celavet Inc., focuses on animal-based applications for our stem cell technology. Our equine open label study with 400 cases treated did not reveal any tumor formation at the three-year follow-up. Clinically, the horses demonstrated a return-to-normal function. Ultrasound examination showed reconstruction of lesions with anatomically correct fiber alignment and absence of scar tissue.

Changing the Paradigm of Stem Cell Technology

The theoretical premise of Celavie's approach is that undifferentiated stem cells are pluripotent and can read cues in the micro-environment into which they are injected. They can become any cell type required to rapidly restore, remodel, and renew tissues that have been damaged by chronic disease, use, or trauma.

The foundational theory for using Celavie's undifferentiated cells is that they will:

- Migrate to the site of the disorder;
- Read the micro-environment into which they are transplanted;
- Multiply and differentiate according to the nature and severity of the disorder;
- Mature into multiple cell types that address the deficiency in its entirety; and,
- Restore function and structure.

"Cell therapies are not efficiently used as a 'last-ditch effort.' They should be considered proactively during the early healing phases."

Source: John Peroni, DVM, MS, Dipl. ACVS, Univ. of Georgia, "Stem Cells and Tissue Healing in Horses", June 2011, *The Horse Magazine*

Both Celavie and Celavet use the latest technological breakthroughs to produce large banks of undifferentiated stem cells with uniform qualities utilizing closed-system bioreactors. The cells are grown in a specialized patented medium that allows them to maintain their sterility and genetic stability over the course of the manufacturing process. Sterility and the integrity of the process are facilitated through the use of the closed-system bioreactor and automated separation and dispensing systems. The manufacturing process utilizes an industry-accepted, multi-tier cell banking system. Every bank of cells is required to meet stringent requirements for viability, genetic stability, and absence of infectious agents prior to release. A single cell line can lead to 13 million therapeutic doses. When required for treatment, our cells are thawed, reintroduced to the transportation medium, and shipped to the clinical location overnight.

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Celavet uses the same standardized and controlled production methods to establish equine, canine, and feline stem cell lines as those used by Celavie Biosciences in the manufacture of human cells. Stem cell lines from different species all express standard stem cell characteristics and are available to address pathologies in their respective species.

Applications

Driven by their innate therapeutic intelligence and regenerative capability, our allogeneic, pluripotent cells will allow for more natural healing for a wide range of disorders. We are developing restorative stem cell treatments for Parkinson's disease (PD), Huntington's disease, Friedreich's ataxia (FA), amyotrophic lateral sclerosis (ALS), epilepsy, cerebellar ataxia and other disorders, such as type 1 diabetes. Celavie is currently conducting preclinical trials of OK99 undifferentiated stem cells in animal models of diabetes mellitus type 1, and further studies of cerebellar ataxia (effect of stem cell treatment on the animals' longevity) in collaboration with California State University, Northridge. The manuscript, "Efficacy of Two Delivery Routes for Transplanting Human Neural Progenitor Cells (NPC) Into the Spastic Hans Wistar Rat, a Model of Ataxia," was published in *Cell Transplantation Journal* in February 2017.

Celavet develops stem cell-based therapies for the treatment and prevention of orthopedic injuries and diseases in large and small animals, restoring health and mobility. Utilizing Celavie's proprietary technology, we are able to transplant allogeneic stem cells into the ligaments and tendons of injured horses, enabling them to regain their fullest potential as competitors, performers, workers or companions. With noticeable tissue repair observed in trials conducted on nearly 500 horses treated at more than 35 veterinary centers around the US in multiple trials, this application allows a faster path to market.

Celavet has received approval from the Center for Veterinary Medicine (CVM) for our donor selection criteria and product characterization of our equine OK100 stem cells. These approvals mark critical progress towards pivotal studies for the OK100 stem cells, proposed to treat tendinitis (e.g., tendon injuries, bowed tendons, etc.) in horses. Celavet's R&D team is accumulating evidence that Celavet stem cells are hypo- or non-immunogenic and do not cause an immune response. Celavet expects to obtain approval by early 2018 for Target Animal Safety (TAS) and clinically controlled studies on OK100 for the Treatment of Equine Musculoskeletal Injuries (INAD 011792).

Celavie & Celavet Stem Cells vs. Other Cells

Cell type	Potency	Healing potential	Tumorigenicity	Turnaround time	Percent stem cells in final formulation
Autologous Adult Stem Cells	Multipotent	Limited	No	Long	Low
Embryonic Stem Calls	Pluripotent	High	YES	Short	High
Induced Pluripotent Cells	Pluripotent	High	YES	Long	Varies
Celavie/Celavet Stem Cells	Pluripotent	High	No	Short	High

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