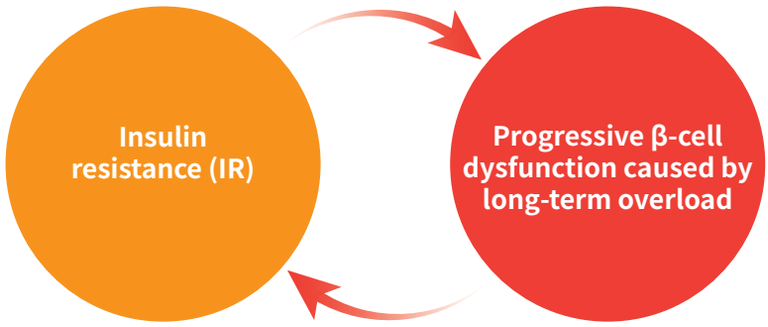
β-MSC — A dual-mechanism autologous MSC therapy for T2DM

Two principal pathophysiological mechanisms in T2DM

A reduced cellular responsiveness to insulin leads to impaired glucose utilization and a chronic decline in metabolic efficiency.



To maintain glycemic homeostasis, pancreatic β cells are forced to sustain excessive insulin secretion, which gradually results in cellular exhaustion and loss of functional capacity.

These two mechanisms mutually reinforce each other, driving a vicious cycle of worsening glycemic dysregulation. This ultimately leads to multi-organ complications involving the cardiovascular system, retina, kidneys, and nervous system, underscoring the severe burden of diabetes as one of the most prevalent metabolic diseases in modern society. Conventional therapies rely primarily on lowering blood glucose levels or supplementing insulin and do not fundamentally address the underlying cellular and metabolic pathology. As the disease progresses and complications accumulate, therapeutic options become increasingly limited, with diminishing ability to halt disease progression, making it difficult to achieve a true breakthrough at the root of the disorder.

HELENE's β-MSC Dual-Mechanism Therapeutic Approach

Building on the two fundamental pathological drivers described above, HELENE has leveraged its extensive expertise in regenerative medicine to develop a dual-mechanism stem cell therapeutic approach that targets both insulin resistance (IR) and pancreatic β-cell dysfunction

Mesenchymal stem cells (MSCs): targeting insulin resistance

At the metabolic level, MSCs support improved insulin sensitivity, enabling the body to utilize glucose more efficiently. This, in turn, reduces the chronic metabolic stress placed on the pancreatic islets over time.

Mechanisms by Which MSCs Improve Insulin Resistance

Within HELENE's dual-mechanism therapeutic platform, MSCs are specifically responsible for correcting the metabolic-side imbalance of type 2 diabetes. Their central mode of action lies in their paracrine activity, through which they exert systemic metabolic effects. MSCs secrete a broad spectrum of bioactive factors—including exosomes, cytokines, growth factors, and regulatory microRNAs (miRNAs)—that act on key metabolic tissues such as skeletal muscle and liver, leading to improved insulin sensitivity.

Key metabolic actions of MSCs

Ⅰ.**Fine-tuning of insulin signaling**
Exosomes released by MSCs deliver critical miRNAs to metabolic tissues, regulating the expression of insulin-related genes and thereby enhancing the stability and efficiency of insulin signaling pathways.

Ⅱ.**Support for enhanced insulin sensitivity**
Cytokines and growth factors secreted through MSC paracrine signaling improve intercellular responsiveness, promoting greater cellular glucose uptake and more efficient utilization of glucose as an energy source.

Ⅲ.**Improved glucose utilization in metabolic tissues**
MSC-derived bioactive factors act on muscle and liver to support more efficient glucose uptake, storage, and consumption, contributing to stabilization of blood-glucose fluctuations.

Ⅳ.**Reduction of long-term stress on pancreatic β cells**
As insulin sensitivity improves, the body's demand for insulin naturally decreases, relieving β cells from chronic hypersecretion and allowing them greater capacity for functional recovery.

Ⅴ.**Root-level suppression of insulin resistance through anti-inflammatory effects**
Chronic inflammation disrupts insulin signaling and is a major driver of insulin resistance. The anti-inflammatory paracrine activity of MSCs improves the inflammatory microenvironment and suppresses the underlying sources of insulin resistance at their origin.

IPC progenitor cells: addressing β-cell exhaustion

At the final stage of culture, MSCs possess the potential to differentiate into IPC progenitor cells (insulin-producing cell progenitors). When administered via intramuscular injection, these cells are expected to provide additional support to pancreatic islet function, helping to redistribute part of the workload borne by β cells.

Mechanisms by Which IPC Progenitor Cells Support Pancreatic Islet Function

To address the pancreatic islet–side dysfunction in type 2 diabetes, HELENE utilizes IPC progenitor cells differentiated from MSCs to complement and alleviate the long-term burden borne by endogenous β cells. These IPC progenitors retain regenerative potential for further maturation and already possess partial insulin-secreting and regulatory functions.

The core mechanisms of action include:

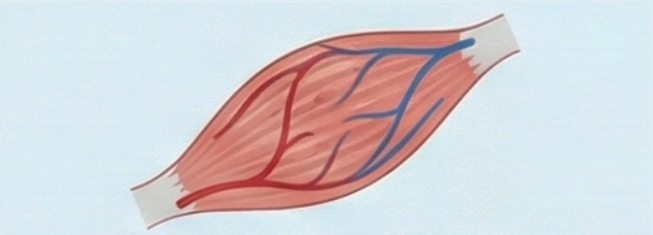
Ⅰ.**Improvement of the metabolic and inflammatory microenvironment through local paracrine effects**
IPC progenitor cells secrete bioactive factors such as IGF-1 and VEGF, which stabilize the tissue environment around the injection site and support cell survival. Through these local paracrine effects, the metabolic state and inflammatory microenvironment within muscle tissue are improved, enabling more effective cellular function.

Ⅱ.**Formation of a localized β-like micro-niche**
Following intramuscular administration, IPC progenitor cells take advantage of the highly vascularized and structurally supportive muscle tissue to remain locally and establish a small β-like supportive micro-niche. This creates a localized support hub capable of providing auxiliary responses to blood-glucose fluctuations, thereby offering multidimensional support to pancreatic islet function.

These two mechanisms act in a complementary manner to broadly target the core pathophysiology of diabetes. Rather than focusing solely on lowering blood glucose values, this therapy emphasizes the restoration of metabolic homeostasis and the long-term optimization of the internal biological environment, representing a fundamentally advanced therapeutic strategy.

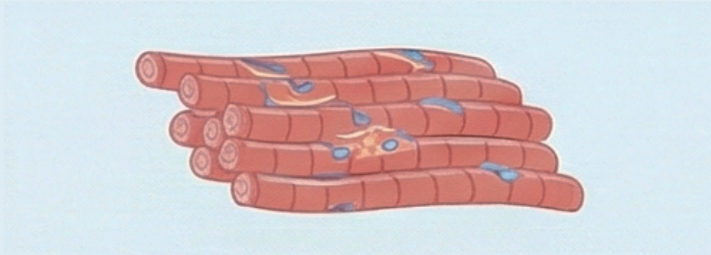
Advantages of Intramuscular (IM) Administration

Intramuscular (IM) injection is employed in this therapy because it offers multiple biological advantages that maximize the survival and functional performance of IPC progenitor cells.



Ensuring cell survival through abundant blood flow and nutrient supply

Compared with subcutaneous tissue, muscle tissue has a much richer blood supply, providing IPC progenitor cells with sufficient nutrients, oxygen, and an optimal metabolic exchange environment. This extensive vascular network prolongs local cell retention and supports stable, sustained cellular function.



Promotion of a functional microenvironment through stable tissue architecture

Muscle fibers are regularly organized and structurally stable, creating a physical framework that allows IPC progenitor cells to aggregate, adhere, and remain locally over the long term. This facilitates the formation of a β -like functional micro-niche, enabling the cell population to maintain consistent and durable biological activity.

Treatment Process

STEP1
Consultation

Please prepare and submit all relevant health documentation, including medical checkup reports, blood test results, and the patient questionnaire. After reviewing these materials, the physician will comprehensively assess your current health status and provide a detailed explanation of the stem cell therapy and the most appropriate treatment plan for you.

STEP2
Tissue Collection

Before blood testing, tissue collection is performed (in some cases, blood sampling may be done first depending on the situation). Under local anesthesia, approximately 5 mm of subcutaneous adipose tissue is collected from behind the ear. The procedure takes about 20 minutes. Afterward, a nurse will carefully inspect and treat the incision site and provide any necessary medications.

STEP3
Cell Cultivation at the HELENE Cell Processing Center (CPC)

Cell culture requires approximately four weeks. Throughout the entire process, HELENE's proprietary xeno-free culture medium, "HELENE MEDIUM," is used to ensure both safety and quality. After culture is completed, the following strict quality control and processing steps are carried out:

- **Selection and purification:** High-precision isolation and purification of MSCs using the autoMACS® Pro Separator (automated magnetic cell sorting system)
- **Quantification:** Accurate cell counting using the Countess® 3 FL automated cell counter
- **Viability and activity assessment:** Evaluation of cell activity and viability using a patented AI-based image analysis system
- **Sample preservation:** Collected tissue samples are cryopreserved long-term in liquid nitrogen at −196°C

STEP4
Treatment (Intravenous Infusion + Intramuscular Injection)

To ensure treatment is performed when the cells are at their peak activity, please arrive at the clinic on the designated date and time. Prior to administration, staff will show you your own cells, explain the stem cell quality certificate, and reconfirm the treatment details. The entire procedure takes approximately 90 minutes.