

**A GUIDE FOR PATIENTS**

# **LITERATURE**

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literature page



# ❖ Lupus

## ➤ **Allogeneic Mesenchymal Stem Cell Transplantation in Severe and Refractory Systemic Lupus Erythematosus: 4 Years of Experience**

Mesenchymal stem cells (MSCs) are multipotential nonhematopoietic progenitors and are capable of differentiating into several tissues of mesenchymal origin. We have shown that bone marrow-derived MSCs from both SLE patients and lupus-prone MRL/lpr mice are defective structurally and functionally. Here we observe the long-term safety and efficacy of allogeneic MSC transplantation (MSCT) in treatment-resistant SLE patients. Eighty-seven patients with persistently active SLE who were refractory to standard treatment or had life-threatening visceral involvement were enrolled. Allogeneic bone marrow or umbilical cord-derived MSCs were harvested and infused intravenously ( $1 \times 10^6$  cells/kg of body weight). Primary outcomes were rates of survival, disease remission and relapse, as well as transplantation-related adverse events.



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## ➤ Additive Therapeutic Effects of Mesenchymal Stem Cells and IL-37 for Systemic Lupus Erythematosus

Although mesenchymal stem cells might have potential for treating SLE, their immunoregulatory plasticity renders their therapeutic effects unpredictable. The authors genetically modified mesenchymal stem cells to overexpress IL-37—a protein with immunosuppressive activity—and assessed the modified cells' effects on immune suppression *in vitro*, as well as the effects of transplanting such cells into a mouse model of SLE. Mice transplanted with IL-37-overexpressing cells displayed improved survival and reduced signs of SLE compared with controls. Expression of IL-37 by mesenchymal stem cells can maintain higher serum levels of IL-37, and these cells had prolonged survival after transplantation, perhaps through IL-37 suppressing the inflammatory microenvironment. The additive therapeutic effects of this approach might offer a way to enhance the stability and effectiveness of mesenchymal stem cells in treating SLE.

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## ➤ Mesenchymal stem cell therapy induces FLT3L and CD1c<sup>+</sup> dendritic cells in systemic lupus erythematosus patients

Allogeneic mesenchymal stem cells (MSCs) exhibit immunoregulatory function in human autoimmune diseases such as systemic lupus erythematosus (SLE), but the underlying mechanisms remain incompletely understood.

Here we show that the number of peripheral tolerogenic CD1c<sup>+</sup> dendritic cells (DCs) and the levels of serum FLT3L are significantly decreased in SLE patients especially with lupus nephritis, compared to healthy controls. Transplantation of allogeneic umbilical cord-derived MSCs (UC-MSCs) significantly up-regulates peripheral blood CD1c<sup>+</sup>DCs and serum FLT3L. Mechanistically, UC-MSCs express FLT3L that binds to FLT3 on CD1c<sup>+</sup>DCs to promote the proliferation and inhibit the apoptosis of tolerogenic CD1c<sup>+</sup>DCs. Conversely, reduction of FLT3L with small interfering RNA in MSCs abolishes the up-regulation of tolerogenic CD1c<sup>+</sup>DCs in lupus patients treated with MSCs. Interferon- $\gamma$  induces FLT3L expression in UC-MSCs through JAK/STAT signaling pathway. Thus, allogeneic MSCs might suppress inflammation in lupus through up-regulating tolerogenic DCs.

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## ➤ **Allogeneic Mesenchymal Stem Cell Transplantation in Severe and Refractory Systemic Lupus Erythematosus: 4 Years of Experience**

Mesenchymal stem cells (MSCs) are multipotential nonhematopoietic progenitors and are capable of differentiating into several tissues of mesenchymal origin. We have shown that bone marrow-derived MSCs from both SLE patients and lupus-prone MRL/lpr mice are defective structurally and functionally. Here we observe the long-term safety and efficacy of allogeneic MSC transplantation (MSCT) in treatment-resistant SLE patients. Eighty-seven patients with persistently active SLE who were refractory to standard treatment or had life-threatening visceral involvement were enrolled. Allogeneic bone marrow or umbilical cord-derived MSCs were harvested and infused intravenously ( $1 \times 10^6$  cells/kg of body weight).

Primary outcomes were rates of survival, disease remission and relapse, as well as transplantation-related adverse events.

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### ➤ **Umbilical cord mesenchymal stem cell transplantation in active and refractory systemic lupus erythematosus: a multicenter clinical study**

In our present single-center pilot study, umbilical cord (UC)-derived mesenchymal stem cells (MSCs) had a good safety profile and therapeutic effect in severe and refractory systemic lupus erythematosus (SLE). The present multicenter clinical trial was undertaken to assess the safety and efficacy of allogeneic UC MSC transplantation (MSCT) in patients with active and refractory SLE

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### ➤ **Systematic review: the effects of autologous stem cell therapy for patients with liver disease**

As morbidity and mortality from liver disease continues to rise, new strategies are necessary. Liver transplantation is not only an expensive resource committing the patient to lifelong immunosuppression but also suitable donor organs are in short supply.

Against this background, autologous stem cell therapy has emerged as a potential treatment option

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### ➤ **Mesenchymal Stem Cell Therapy: Hope for Patients With Systemic Lupus Erythematosus**

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease. Although previous studies have demonstrated that SLE is related to the imbalance of cells in the immune system, including B cells, T cells, and dendritic cells, etc., the mechanisms underlying SLE pathogenesis remain unclear.

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### ➤ **An Overview of the Safety, Efficiency, and Signal Pathways of Stem Cell Therapy for Systemic Lupus Erythematosus**

Systemic lupus erythematosus (SLE) is an autoimmune disease that affects multiple organs and tissues. Mesenchymal stem cells (MSCs) are considered a good source for autoimmune disease and hematological disease therapy.

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## ➤ Stem Cell Therapy Shows Early Promise for the Treatment of Lupus

A newly published [study](#) reviewing the current body of scientific evidence on the safety and efficacy of stem cell therapy to treat rheumatic disease highlights the potential benefits of mesenchymal stromal cells (MSCs) – a type of stem cell – for the treatment of lupus..

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