News Release

Placenta-Derived Stem Cells Suppress Severe Autoimmune Kidney Disease Through a Novel Mechanism

—New therapeutic strategy targeting CD44 prevents inflammatory cells from becoming “trapped” in the kidney—

Key Points

- Researchers demonstrated in a rat model that amnion-derived mesenchymal stem cells (AMSCs)(*1), obtained from placental tissue that is normally discarded after childbirth, significantly ameliorate anti-glomerular basement membrane (anti-GBM) glomerulonephritis(*2).
- AMSCs reduced kidney injury by suppressing expression of the adhesion molecule CD44(*3) on neutrophils(*4), thereby preventing their accumulation within glomeruli(*5).
- The findings highlight the therapeutic potential of both AMSC-based cell therapy and CD44-targeted molecular therapies for severe autoimmune kidney diseases.

Summary

Anti-glomerular basement membrane (anti-GBM) glomerulonephritis is a severe autoimmune disease in which autoantibodies attack the glomeruli of the kidney, leading to rapidly progressive kidney dysfunction. Because current treatments are not sufficiently effective for many patients, the development of novel therapeutic approaches is urgently needed.

Researchers from the Department of Nephrology, Nagoya University Hospital, including Dr. Tomoya Nozaki, Assistant Professor Kumiko Fujieda, Associate Professor Kazuhiro Furuhashi, and Professor Shoichi Maruyama, investigated the therapeutic potential of amnion-derived mesenchymal stem cells (AMSCs), which can be isolated from placental amniotic membranes that are normally discarded after childbirth, in a rat model of anti-GBM glomerulonephritis. The researchers found that AMSC administration significantly improved both renal dysfunction and histological kidney injury. The therapeutic effects were comparable to, or greater than, those achieved with conventional bone marrow-derived mesenchymal stem cells (BMSCs).

The team further discovered that AMSCs regulate the activity of neutrophils, a major inflammatory cell type. Specifically, AMSCs reduced the expression of CD44, an adhesion molecule expressed on the surface of neutrophils. This

suppression prevented excessive accumulation and retention of neutrophils within glomeruli, thereby reducing inflammation and tissue injury. Intravital two-photon imaging further demonstrated that neutrophils co-cultured with AMSCs exhibited shorter residence times within glomeruli.

In addition, administration of a neutralizing anti-CD44 antibody produced renoprotective effects similar to those observed with AMSC treatment. These findings indicate that CD44-mediated regulation of neutrophil trafficking plays a critical role in the progression of anti-GBM glomerulonephritis.

This study demonstrates the potential of AMSCs derived from otherwise discarded placental tissue as a novel therapeutic strategy for anti-GBM glomerulonephritis. The findings also highlight CD44 as a promising therapeutic target for the development of new molecular-targeted treatments. To the best of the authors' knowledge, this is the first study to demonstrate that mesenchymal stem cells directly regulate neutrophil CD44 expression. Beyond kidney disease, these findings may have broader implications for the treatment of a variety of inflammatory disorders.

The study was published in the journal Stem Cell Research & Therapy on June 19, 2026. (Figure1)

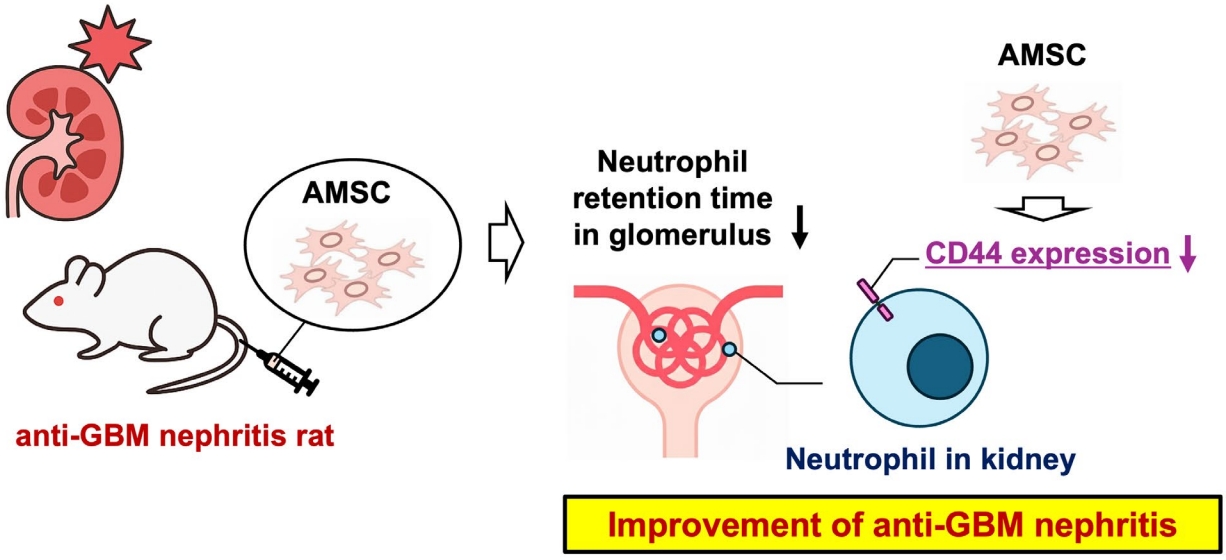

Figure 1. Proposed Renoprotective Mechanism of AMSCs Identified in This Study

Research Background

Mesenchymal stem cells (MSCs) have attracted considerable attention in regenerative medicine because of their immunomodulatory and tissue-repair properties. Bone marrow-derived MSCs (BMSCs) are the most extensively studied and clinically utilized MSC population; however, bone marrow harvesting is invasive and obtaining sufficient numbers of cells from healthy donors can be challenging.

To overcome these limitations, the research team focused on amnion-derived mesenchymal stem cells (AMSCs), which can be isolated noninvasively from placental amniotic membranes that are routinely discarded after childbirth. AMSCs have been reported to exhibit greater proliferative capacity and stronger immunomodulatory effects than BMSCs. However, their therapeutic efficacy and molecular mechanisms in anti-GBM glomerulonephritis have remained largely unexplored.

Anti-GBM glomerulonephritis is a severe autoimmune disease caused by autoantibodies directed against the glomerular basement membrane (GBM). The disease often progresses rapidly, resulting in crescentic glomerulonephritis and severe kidney dysfunction. Although current treatments—including plasma exchange, corticosteroids, and immunosuppressive agents—can improve outcomes, many patients still progress to kidney failure requiring dialysis. Therefore, new therapeutic approaches are urgently needed.

In this study, the researchers evaluated the therapeutic effects of AMSCs in experimental anti-GBM glomerulonephritis and investigated the underlying mechanisms responsible for their renoprotective actions.

Research Results

1. AMSCs exert dose-dependent renoprotective effects comparable to or greater than those of BMSCs

Intravenous administration of human AMSCs to rats with anti-GBM glomerulonephritis significantly suppressed elevations in serum creatinine and blood urea nitrogen (BUN) levels. Histological analyses revealed significant improvements in crescent formation scores and tubular injury scores.

These renoprotective effects were enhanced in a dose-dependent manner with repeated administration and were comparable to, or greater than, those observed with BMSCs. (Figure2)

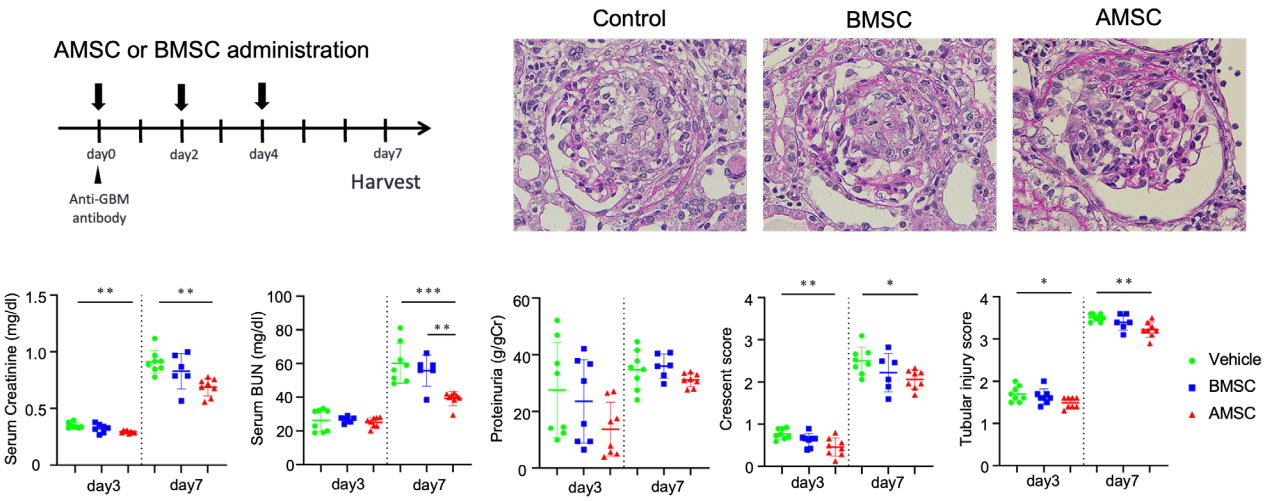

Figure2. Therapeutic Effects of AMSC Administration in Anti-GBM Glomerulonephritis

2. AMSCs reduce neutrophil accumulation in the kidney by downregulating the adhesion molecule CD44

Flow cytometric and histological analyses revealed that AMSC treatment selectively reduced neutrophil accumulation within inflamed glomeruli. Mechanistically, CD44 expression was significantly decreased in neutrophils that had infiltrated the kidney.

In contrast, no significant changes were observed in the expression of other adhesion molecules, including VLA-4, CD11b, LFA-1, and PSGL-1. Furthermore, CD44 expression in circulating peripheral blood neutrophils remained unchanged, indicating that the effect was localized to inflammatory sites within the kidney.

To directly examine neutrophil behavior in vivo, the researchers employed two-photon microscopy(*6). Neutrophils co-cultured with AMSCs exhibited significantly shorter residence times within glomerular capillaries than control neutrophils, demonstrating that AMSCs directly suppress neutrophil adhesion and retention within inflamed glomeruli. (Figure3)

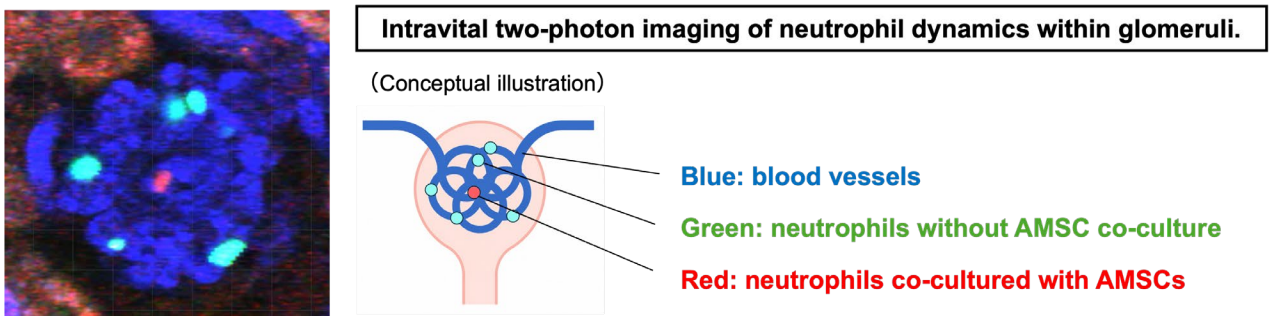

Figure3. AMSCs Suppress Neutrophil Retention Within Glomeruli

3. Neutralization of CD44 ameliorates anti-GBM glomerulonephritis

To determine whether CD44 itself could serve as a therapeutic target, the researchers administered a neutralizing anti-CD44 antibody to rats with anti-GBM glomerulonephritis.

Anti-CD44 treatment significantly improved serum creatinine, BUN, urinary protein excretion, and crescent formation scores. Histological analyses also demonstrated reduced neutrophil infiltration within glomeruli.

These findings provide direct evidence that regulation of neutrophil trafficking through CD44 contributes to renal protection and suggest that CD44 may represent a novel therapeutic target for anti-GBM glomerulonephritis. (Figure4)

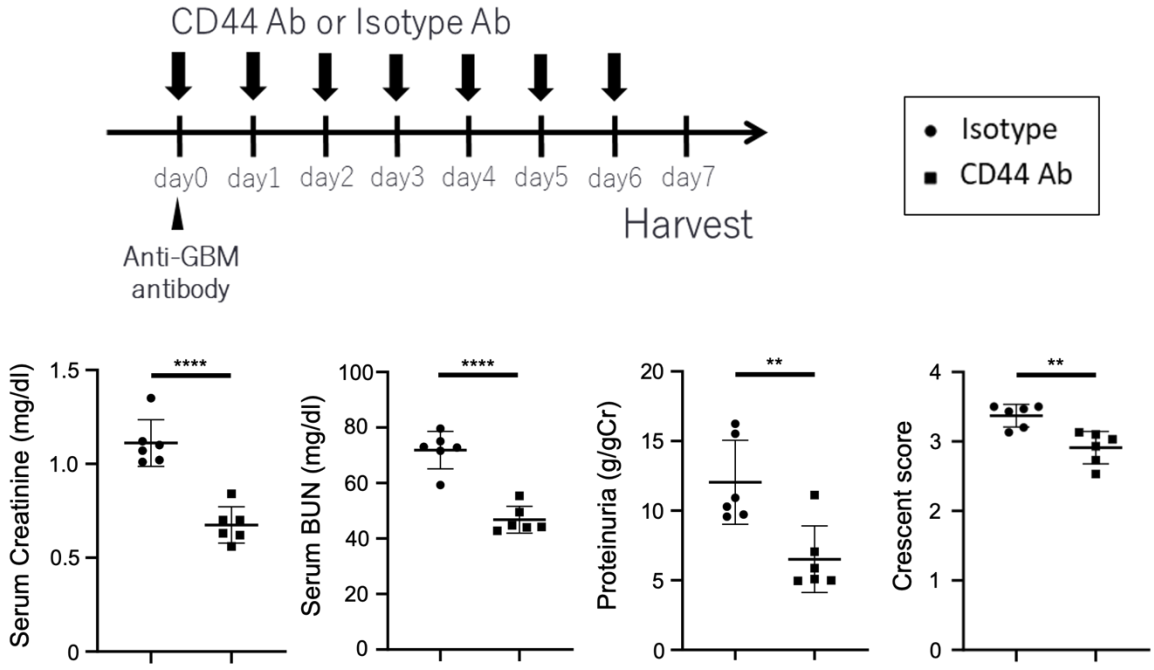

Figure4. Improvement of Anti-GBM Glomerulonephritis Through CD44 Inhibition

Research Summary and Future Perspective

This study demonstrates that AMSCs, which can be obtained noninvasively from placental tissue that is routinely discarded after childbirth, are effective in treating anti-GBM glomerulonephritis.

Importantly, the researchers identified a previously unrecognized mechanism underlying this therapeutic effect: AMSCs suppress CD44 expression on kidney-infiltrating neutrophils, thereby reducing their retention and accumulation within glomeruli and limiting inflammatory kidney injury. To the best of the authors' knowledge, this is the first study to demonstrate that mesenchymal stem cells can directly regulate neutrophil CD44 expression.

In addition to establishing AMSCs as a promising and readily available cell source for regenerative therapy, the findings identify CD44 itself as a potential therapeutic target. Future studies will be needed to evaluate the safety and efficacy of AMSC-based therapies and CD44-targeted interventions in clinical settings. These findings may contribute to the development of novel cell-based and molecular-targeted therapies for anti-GBM glomerulonephritis and other inflammatory kidney diseases.

Glossary

∗1) Amnion-derived mesenchymal stem cells (AMSCs): Mesenchymal stem cells isolated from the amniotic membrane of the placenta. Because the placenta is normally discarded after childbirth, AMSCs can be obtained noninvasively and in large quantities. They possess immunomodulatory and tissue-repair properties.

∗2) Anti-glomerular basement membrane (anti-GBM) glomerulonephritis: A severe autoimmune kidney disease caused by autoantibodies directed against the glomerular basement membrane (GBM). The disease often progresses rapidly and can result in kidney failure requiring dialysis.

∗3) CD44: A cell-surface adhesion molecule involved in cell adhesion, migration, and inflammatory responses.

∗4) Neutrophils: A type of white blood cell that plays a central role in innate immunity. Excessive accumulation and adhesion of neutrophils at sites of inflammation can promote tissue injury.

*5) **Glomerulus:** A specialized network of capillaries within the kidney that filters blood to produce urine. In anti-GBM glomerulonephritis, glomeruli become major sites of inflammatory injury.

*6) **Intravital two-photon microscopy:** An advanced imaging technique that enables high-resolution visualization of cellular behavior within living organs. In this study, fluorescently labeled neutrophils were observed in real time within glomeruli of living rats.

Publication

Stem Cell Research & Therapy

Amnion-derived Mesenchymal Stem Cells Attenuate Anti-GBM Glomerulonephritis via Regulation of Neutrophil CD44 Expression

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