# Novel Application Method for Mesenchymal Stem Cell Therapy Utilizing Its Attractant-Responsive Accumulation Property

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| 論　文　名 | Novel Application Method for Mesenchymal Stem Cell Therapy Utilizing Its Attractant–Responsive Accumulation Property<br>（創傷治癒促進を目指した間葉系幹細胞の新規投与法についての検討） |
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## 論　文　審　査　の　結　果　の　要　旨

Objectives: Stem cell therapy is an emerging treatment modality for various diseases. Because mesenchymal stem cells (MSCs) are known to accumulate at the site of damage, their possible clinical application has been investigated. MSCs are usually administered using intravenous injection, but this route carries a risk of pulmonary embolism. We developed a remote administration method that uses collagen gel as a scaffold and investigated the effect of this scaffold on the retention of stemness, homing ability, and therapeutic effect using a mouse tooth extraction model.

Materials and Methods: MSCs isolated from the bone marrow of green fluorescent protein (GFP)-expressing donor mice were expanded for 3 weeks in three-dimensional (3-D) culture using a collagen gel scaffold and evaluated to confirm the efficacy of the scaffold. Next, MSCs suspended in collagen gel were subcutaneously administered into the backs of mice. Two days later, extraction of the maxillary first molar was carried out. Numbers of MSCs in scaffolds, migration and accumulation around the extracted tooth cavity, extraction site healing, and presence of MSCs in vital organs were evaluated.

Results: MSCs cultured in the collagen gel scaffold maintained stemness for 2 weeks. After subcutaneous administration, numbers of MSCs in scaffolds decreased over time, but cells survived for 2 weeks. After tooth extraction, GFP-expressing MSCs were confirmed in the surrounding mucosa of the extracted tooth cavity; in the scaffold group, numbers of MSCs increased over time and fewer were observed in lung tissue. Wound healing was enhanced by injection of MSCs via the tail vein or into the back compared with the untreated control group.

Conclusions: Delivery in a collagen gel could maintain the characteristics of MSCs, which migrated to the damaged area and promoted wound healing without side effects occurring with conventional administration methods.

The paper has included novel data clarifying the functional effects of collagen scaffold for sustainable supply of MSCs. Therefore, it could be recommended for a DOCTOR OF PHILOSOPHY (Dental Science) in Kyushu University.