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Kidswell Bio Corporation (TSE:4584)

S-Quatre Corporation

Research on SHED for Osteonecrosis Published in an International Scientific Journal — New Findings Highlight the Potential of SHED for Refractory Bone Diseases —

Tokyo, September 14, 2026 – S-Quatre Corporation, a subsidiary of Kidswell Bio Group, is engaged in the research and development of novel cell-based therapies (regenerative medicine products) using stem cells from human exfoliated deciduous teeth (SQ-SHED), with the aim of developing new treatments for pediatric and rare diseases for which no effective therapies currently exist.

Research findings on a radiation-induced osteonecrosis model, based on a collaborative study between Dokkyo Medical University and S-Quatre, have been published in the *Journal of Orthopaedic Research*, an international journal in the field of orthopaedics. The study demonstrated the potential of SHED to promote bone repair and provided insights into the mechanisms underlying these actions.

Background of the Study

Osteonecrosis is a group of disorders characterized by the death of bone tissue due to impaired blood supply or other causes. One representative condition, idiopathic osteonecrosis of the femoral head (designated in Japan as Intractable Disease No. 71), most commonly affects adults in their 30s to 50s. As the disease progresses, the affected bone may collapse, resulting in significant deterioration of hip joint function. Although an increasing number of cases are now diagnosed at an early stage, no effective treatment has yet been established to regenerate necrotic bone itself. In particular, for younger patients, there is a strong need for new treatment options that can preserve their natural joints for as long as possible and delay or avoid total hip replacement.

To explore the potential of a novel regenerative treatment for refractory osteonecrosis, this study evaluated the bone repair effects of SHED using a rat model of radiation-induced osteonecrosis. Bone marrow-derived mesenchymal stromal cells (MSCs), which have conventionally been used in bone regeneration research, present several challenges to clinical application in regenerative medicine, including the physical burden associated with cell harvesting and the limited number of cells that can be obtained. SHED, by contrast, have been reported to possess not only the characteristics of MSCs but also a high proliferative capacity and the ability to secrete various factors involved in tissue repair. Using a rat model of radiation-induced osteonecrosis, the study compared the bone regeneration-promoting effects of SHED with those of bone marrow-derived MSCs and investigated the mechanisms underlying the effects of SHED.

Key Research Findings

In this study, a rat model of osteonecrosis was established by irradiating the tibia. A scaffold containing SHED was implanted into the osteonecrotic area, and the bone repair process was monitored over an eight-week period. Cell culture assays, imaging analyses, histological analyses, and gene expression analyses of the repaired tissue were conducted, yielding the following findings:

- SHED were confirmed to secrete factors involved in angiogenesis. In cell culture experiments, conditioned medium from SHED significantly promoted the migration of macrophage-like cells involved in tissue repair compared with conditioned medium from bone marrow-derived MSCs.
- When SHED were transplanted into the rat model of radiation-induced osteonecrosis, the SHED group showed a significantly higher bone repair rate than the scaffold-only group at all time points evaluated—4, 6, and 8 weeks after transplantation. In contrast, no significant difference was observed between the bone marrow-derived MSC group and the scaffold-only group. The SHED group showed a significantly higher bone repair rate than the bone marrow-derived MSC group from 4 weeks onward.
- At the SHED transplantation area, newly formed bone and bone marrow, as well as periosteal proliferation, were observed. The area occupied by blood vessels was also significantly greater than in both the scaffold-only group and the bone marrow-derived MSC group.
- Gene expression analysis of the repaired tissue in the SHED group showed changes consistent with the activation of gene sets and signaling pathways associated with angiogenesis and the recruitment of immune cells.
- The cells comprising the newly formed bone and blood vessels were confirmed to be predominantly of rat origin. These findings suggest that, rather than directly differentiating into bone or vascular cells, transplanted SHED may promote bone regeneration by secreting factors that act on surrounding cells and facilitate tissue repair.

Collectively, these findings suggest that, in a radiation-induced osteonecrosis model, SHED may promote bone repair through paracrine mechanisms, whereby SHED-derived factors act on surrounding cells to enhance angiogenesis and recruit host-derived reparative cells.

Since blood flow is reduced in osteonecrotic lesions, these areas generally provide an environment in which bone regeneration is difficult to achieve. This study is positioned as a preclinical proof of concept (PoC), demonstrating the potential of SHED to promote angiogenesis and surrounding tissue repair responses and thereby facilitate bone regeneration even under such challenging conditions.

The findings of this study represent an important research outcome with the potential to contribute to the development of new treatments for refractory osteonecrosis. Going forward, further studies, including evaluations using models that more closely reflect clinical pathology, will be conducted with the aim of developing new therapeutic options for refractory bone diseases. In parallel, basic and translational research will continue to further elucidate the characteristics and mechanisms of action of SHED, while its therapeutic potential is evaluated in collaboration with external research institutions.

■ Published Paper

Murakami T et al., “Stem cells from human exfoliated deciduous teeth as a potent cell therapy for radiation-induced osteonecrosis model”, *Journal of Orthopaedic Research*, August 19, 2026

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