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Kidswell Bio Corporation (TSE:4584)  
S-Quatre Corporation  
PR Release

## **Publication of Research Paper on the Application of SHED in the Treatment of Peripheral Nerve Injuries**

Tokyo, August 14, 2025 - Kidswell Bio Group is engaged in the research and development of novel cell-based therapies (regenerative medicine products) utilizing stem cells from human exfoliated deciduous teeth (SHED), with the aim of developing new treatments for pediatric and rare diseases for which no effective therapies currently exist.

Our group company S-Quatre Corporation and the Department of Neurosurgery in Nagoya University have been conducting joint research on cell-based therapies using SHED, with the goal of developing groundbreaking treatments for spinal cord injuries and peripheral nerve injuries.

As part of this ongoing research, the teams previously published a research paper in January 2024 demonstrating the therapeutic efficacy and mechanisms of SHED in a spinal cord injury model. Following on those findings, the latest research has now successfully clarified the effects of SHED in a peripheral nerve injury model. These new results have been published in the peer-reviewed journal *Stem Cells and Development*.

### **Background of the Study**

Peripheral nerve injuries occur when the nerves in the arms or legs are cut or compressed due to various causes, leading to reduced motor or sensory function, or even paralysis. In particular, when large bundles of motor nerves are severely damaged—for example, as a result of a major accident—existing treatments such as nerve suturing or artificial nerve conduits are often insufficient for full functional recovery. This highlights the urgent need for new regenerative therapies to achieve more effective outcomes.

Although previous studies have reported that transplantation of dental pulp stem cells can promote peripheral nerve regeneration, the underlying mechanisms have not yet been fully elucidated. Therefore, this study focused on the anti-inflammatory properties of SHED, with the objective of clarifying the mechanisms by which they contribute to peripheral nerve regeneration.

### Highlights of the Research Findings

- In a rat model, the sciatic nerve was transected and sutured, after which the suture site was wrapped with a cellulose membrane soaked in a suspension of SHED. Compared to rats treated with a cellulose membrane without SHED, the SHED-treated group showed significant improvement in motor function beginning four weeks after treatment, with further marked improvement observed over the following eight weeks.
- Analysis of the central spinal cord following sciatic nerve injury revealed activation of STAT3—a key mediator of inflammatory responses—in neurons between 12 and 48 hours post-injury. However, this activation was significantly suppressed in rats treated with SHED.
- A similar phenomenon was observed at the peripheral injury site, where an increase in the pro-inflammatory cytokine IL-6 and upregulation of importin  $\beta$ 1—known to be involved in the retrograde transport of intracellular proteins toward the central nerves—were also detected. Notably, both increases in IL-6 and importin  $\beta$ 1 were significantly suppressed in the SHED-treated group.
- Furthermore, in SHED-treated group, significant activation of the ERK signaling pathway—known to be involved in myelination—was observed in Schwann cells at the injury site on day 4 post-injury.
- These findings suggest that the recovery of motor function induced by SHED may involve multiple mechanisms: 1) attenuation of peripheral nerve inflammation through suppression of IL-6 expression and regulation of STAT3 activation, 2) reduction of central nerve inflammation via inhibition of importin  $\beta$ 1 expression, thereby suppressing the retrograde transport of activated STAT3; and 3) promotion of remyelination at the peripheral injury site through activation of ERK signaling in Schwann cells.

### Published Papers

Oyama T et.al., "Stem Cells from Human Exfoliated Deciduous Teeth Improve Motor Function after Sciatic Nerve Injury Through Suppression of Inflammation" *Stem Cells and Development* 12 August 2025

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