News Release

Title
Development of a novel therapy for treating multiple sclerosis using conditioned medium (CM) from the stem cells of human exfoliated deciduous teeth (SHED)

Key Points
○ A single intravenous administration of SHED-CM at the disease peak of experimental autoimmune encephalomyelitis (EAE), a mouse model of multiple sclerosis, markedly improved neurological deficits.
○ SHED-CM significantly reduced inflammatory cell infiltration, pro-inflammatory cytokine expression and induced tissue-repairing macrophages in the central nervous system of EAE mice, resulting in significant reduction of demyelination and axonal injury.
○ Treatment of EAE mice with the secreted ectodomain of sialic acid-binding Ig-like lectin-9 (ED-Siglec-9), a major component of SHED-CM, recapitulated the therapeutic effects of SHED-CM.
○ Our study suggests that SHED-CM and ED-siglec-9 may be a promising therapeutic strategy for autoimmune diseases such as multiple sclerosis.

Summary
Graduate student Chiaki Shimojima and Associate Professor Akihito Yamamoto (Department of Oral and Maxillofacial Surgery/Protective Care for Masticatory Disorders of Nagoya University Graduate School of Medicine, Dean: Masahide Takahashi) and Assistant Professor Hideyuki Takeuchi (Department of Neuroimmunology, Research Institute of Environmental Medicine, Nagoya University; currently Associate Professor of Department of Neurology and Stroke Medicine, Yokohama City University Graduate School of Medicine) found that a single intravenous administration of SHED-CM at the disease peak of experimental autoimmune encephalomyelitis (EAE), a mouse model of multiple sclerosis, markedly improved neurological deficits. SHED-CM significantly reduced inflammatory cell infiltration, pro-inflammatory cytokine expression and induced tissue-repairing macrophages in the central nervous system of EAE mice, resulting in significant reduction of demyelination and axonal injury. Treatment of EAE mice with the secreted ectodomain of sialic acid-binding Ig-like lectin-9 (ED-Siglec-9), a major component of SHED-CM, recapitulated the therapeutic effects of SHED-CM.
acid-binding Ig-like lectin-9 (ED-Siglec-9), a major component of SHED-CM, recapitulated the therapeutic effects of SHED-CM. Our data suggest that SHED-CM and ED-siglec-9 may be a promising therapeutic strategy for autoimmune diseases such as multiple sclerosis. This work has been carried out as a collaboration study with Professor Emeriti Ueda Minoru and Akio Suzumura, and it is published online in the official journal of the American Association of Immunologists, *The Journal of Immunology*, in XXXXX, XX, XX.

**Research Background**

Multiple sclerosis (MS) and its animal model experimental autoimmune encephalomyelitis (EAE), are autoimmune neurological diseases of the central nervous system (CNS). In MS and EAE, autoreactive Th1/Th17 cells infiltrate the CNS, leading to microglia/macrophage activation that induces inflammatory demyelination and subsequent neuronal damage, and results in a wide range of clinical features, including sensory and motor paralysis, blindness, pain, incontinence, and dementia.

We previously reported that SHED-CM improved animal models of spinal cord injury, liver inflammation, lung fibrosis and Alzheimer's disease. Here we investigated the efficacy of SHED-CM and the secreted ectodomain of sialic acid-binding Ig-like lectin-9 (ED-Siglec-9), a major component of SHED-CM, on experimental autoimmune encephalomyelitis (EAE).

**Research Results**

A single intravenous administration of SHED-CM at the peak of EAE markedly improved neurological deficits. SHED-CM significantly reduced inflammatory cell infiltration, pro-inflammatory cytokine expression and induced tissue-repairing macrophages in the central nervous system of EAE mice, resulting in significant reduction of demyelination and axonal injury. Treatment of EAE mice with the secreted ectodomain of sialic acid-binding Ig-like lectin-9 (ED-Siglec-9), a major component of SHED-CM, recapitulated the therapeutic effects of SHED-CM.

**Research Summary and Future Perspective**

Our data suggest that SHED-CM and ED-siglec-9 may be a promising therapeutic strategy for autoimmune diseases such as MS. The goal of our study is to develop the novel anti-autoimmune drug based on the SHED-CM or ED-siglec-9.

**Publication**


**Japanese ver.**