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

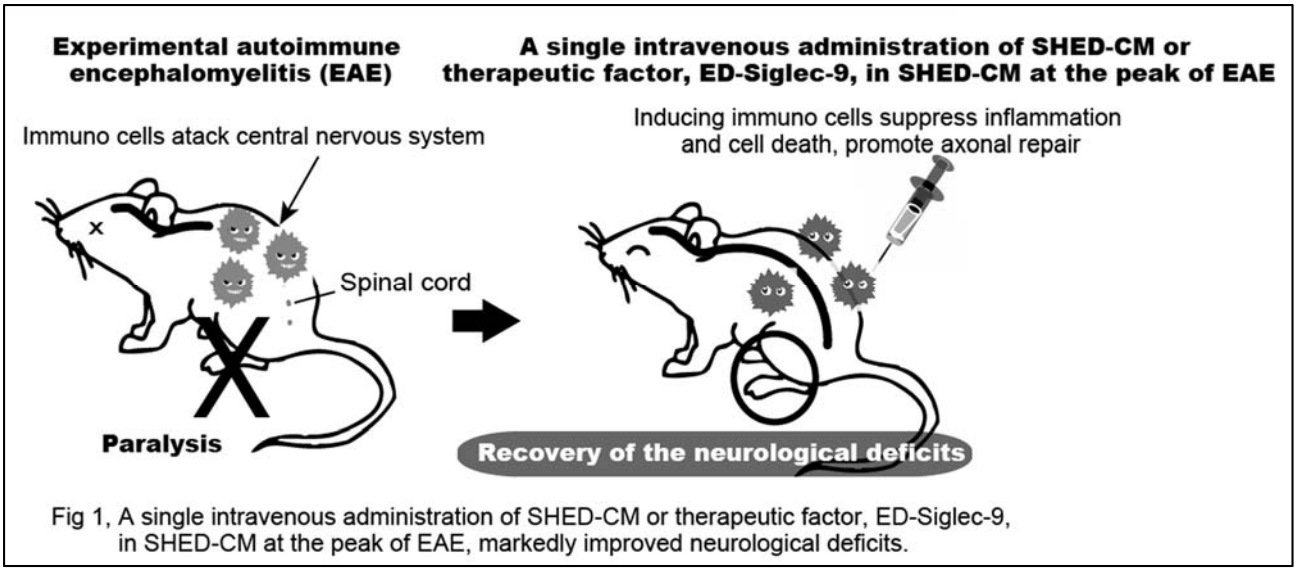

Fig 1, A single intravenous administration of SHED-CM or therapeutic factor, ED-Siglec-9, in SHED-CM at the peak of EAE, markedly improved neurological deficits.

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

Chiaki Shimojima, Hideyuki Takeuchi, Shijie Jin, Bijay Parajuli, Hisashi Hattori, Akio Suzumura, Hideharu Hibi, Minoru Ueda, Akihito Yamamoto. Conditioned Medium from the Stem Cells of Human Exfoliated Deciduous Teeth Ameliorates Experimental Autoimmune Encephalomyelitis. *The Journal of Immunology*, Published online before print April 6, 2016.

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