Abstract Information

First Name :	Toshihide
Last Name :	Yamashita
Email :	yamashita@molneu.med.osaka-u.ac.jp
Address :	Graduate School of Medicine, Osaka University

Participation :	symposium
Title of the Symposium :	Unravelling Neurodegeneration: Insights into Parkinson's Disease and Related Disorders in AfrArabia and Beyond
Category :	Invited Speakers
Thematic Area :	Neurodegeneration, Neuroplasticity, and Repair
Title :	Repulsive guidance molecule regulates glial and immune function under neurological diseases

Co-Authors :	Department of Molecular Neuroscience, Graduate School of Medicine, Osaka University

Abstract :

Repulsive guidance molecule-a (RGMa), which is a glycosylphosphatidylinositol-linked glycoprotein, is expressed in glial cells and immune cells. RGMa was previously recognized as the protein that regulates axon growth negatively in the adult central nervous system (CNS). Enhanced recovery of skilled forelimb movement as well as neural rewiring was observed after spinal cord injury (SCI) in adult macaque monkey following anti-RGMa antibody treatment. Based on the findings by the preclinical studies, the international clinical trials of humanized anti-RGMa monoclonal antibody (Unasnemab) for SCI is ongoing currently.

Furthermore, RGMa was shown to be involved in immune regulation. RGMa expressed in dendritic cells promotes activation of T cells, leading to deterioration of autoimmune encephalomyelitis. Further, under the condition of neuromyelitis optica (NMO), anti-RGMa antibody treatment significantly suppressed neutrophil infiltration, and decreased the expression of neutrophil chemoattractants. The multiple modes of actions of anti-RGMa antibody may explain the potent effects on the neurodegenerative and neuroimmune diseases as well as the CNS injuries. The clinical trial of Unasnemab for HTLV-1-associated myelopathy is also ongoing.

We recently reported that RGMa regulates blood-brain barrier integrity and cell survival in the CNS. Intravenous, administration of anti-RGMa antibodies reduced the loss of tyrosine hydroxylase (TH)-positive neurons and accumulation of Iba1-positive microglia/macrophages in the substantia nigra (SN) in a mouse model of Parkinson?s disease (PD). Selective expression of RGMa in TH-positive neurons in the SN induced neuronal loss/degeneration and inflammation, resulting in a progressive movement disorder. Increased RGMa expression upregulated pro-inflammatory cytokine expression in microglia. Our observations suggest that

the upregulation of RGMa is associated with the PD pathology; furthermore, inhibitory RGMa antibodies are a potential therapeutic option.