Creation of evidence to establish diagnostic criteria and treatment guideline for anti-neurofasctin1 55 antibody- positive chronic inflammatory demyelinating polyneuropathy

Chronic inflammatory demyelinating polyneuropathy (CIDP) is an intractable neurologic disease affecting
peripheral nerves. The etiology ofCIDP remains to be established but it is regarded as a mixture ofheterogeneous conditions presenting a variety ofclinical and electrophysiological manifestations. Specific biomarkers for CIDP or any subtype ofCIDP are still unknown. We developed a sensitive and specific cell-based flow cytometric assay for anti-neurofascin155 (NF155) antibodies, and found about 20% ofour consecutive CIDP patients to have IgG4 class anti-NF155 antibodies. We disclosed that IgG4 anti-NF155 antibody-positive CIDP has very characteristic features, such as a younger onset age, higher frequency ofdistal muscle weakness and atrophy, longer distal and F wave
latencies, marked nerve root hypertrophy on MRI neurography, extremely high cerebrospinal fluid protein levels,
and absence ofinflammatory cell infiltrates and subperineural edema on biopsied sural nerves as compared with
anti-NF155 antibody-negative patients. We also found that anti-NF155 antibody-positive patients showed poor
response to intravenous immunoglobulins and required early administration ofcorticosteroids and immunosuppressants. So far we have established an ELISA assay for anti-NF155 antibodies which has excellent
concordance rates with the above-mentioned cell-based flow cytometric assay, and the tentative diagnostic criteria for anti-NF155 antibody-positive CIDP, and conducted the first round nation-wide survey ofpossible anti-NF155
antibody-positive CIDP patients. Based on these results, we aim to establish evidence for creating the first
diagnostic criteria for anti-NF155 antibody-positive CIDP and the treatment algorism and guideline for this
condition in the present study. For this purpose, we will carry out the following projects. 1) To validate the tentative diagnostic criteria for anti-NF155 antibody-positive CIDP by using the second round survey results ofthe nation-
wide survey, and based on this results, to establish the first diagnostic criteria for this condition. 2) To establish
pathogenicity ofanti-NF155 antibodies by investigating a corelation between a long term fluctuation ofanti- NF1 55 antibody titers and clinical and peripheral nerve electrophysiological findings of CIDP, and by
administrating anti-NF155 antibody-positive CIDP patients' IgG into experimental animals, 3) To identify antigenic epitopes ofanti-NF155 antibodies by using truncatedNF155 proteins, 4) To study background factors for
production ofanti-NF155 antibodies, such as HLAclass II gene alleles and environmental allergens, and 5) To
establish the most appropriate treatment algorism by using the second round nation-wide survey results. Through
these projects, we will establish anti-NF155 antibody-positive CIDP as a new disease entity and finalize the first
diagnostic criteria and treatment guideline.