Objective Approximately 28% of familial ALS cases are caused by mutations in the Cu/Zn superoxide dismutase (SOD1) gene, which results in neurofilamentopathy and motor neuron degeneration. In ALS, oligodendrocyte precursor cells (OPCs) are shown to exhibit excessive proliferation with impaired functions. Then we tested a combination therapy of cell transplantation and antibody by injection of SOD1H46R rats antibody X, OPCs alone or scFv-X-OPCs and investigated the pathogenic role. [Methods] We examined autopsied brains from 5 PD patients and 9 control cases. We conducted phosphorylated-aSYN immunostaining to detect aSYN in Lewy bodies and adopted a proximity ligation assay (PLA) to examine the distribution of aSYN oligomers in PD brains. aSYN oligomers may distribute widely throughout the brain even in the earlier pathological course of PD.

Objective Neuron-centric view cannot explain all aspects of Alzheimer's disease (AD). Among non-neuronal cells, dysfunctional oligodendrocytes (OLs) and demyelination are reported to be observed in AD brains. OLs and patient-derived iPSC-derived oligodendrocyte precursor cells (OPCs) regulate neurovascular function by interacting with neuronal, vascular, glial, and immune system, pathological OLs/OLCs (OLs) could be involved in the astrogliosis and progression of AD. However, the mechanisms by which OLs/OPCs exacerbate AD remain elusive. Therefore, the aim of this study is to examine the roles of OLs on the pathogenesis of AD. [Methods] For in vitro studies, we examined the influence of Aβ40/42 on OLs and AD ADββ and Aβββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββββbeta
Complications and pregnancy in GNE myopathy patients: A nationwide repository survey in Japan


Department of Neuro muscular Research, National Institute of Neuroscience, National Center of Neurology and Psychiatry, Tokyo, Japan, Comprehensive Regenerative Medicine Research Center, School of Medicine and Dental Science, Keio University (Medicine), Tokyo Medical and Dental University, Tokyo, Japan.

Longitudinal analysis of at-risk cohort of Lewy body disease

Makoto Hatori, Katsunori Yokoi, Yuki Satake, Keita Hiraoka, Takagi Yuji, Watanabe Masa, Satoh Motokazu, Matsuhashi Akihiro, Horii Masakazu, Waki Keisuke, Suzuki Yutaka, Arashita Yukihiko, Washimi Noriyuki, Matsukawa Masahisa, Katsuno

Department of Neurology, Nagoya University Graduate School of Medicine, Japan. Lev D. Schaffer, Department of Neuroscience, The University of Texas Southwestern Medical Center, Dallas, TX, USA.

Establishment of diagnostic system for progressive supranuclear palsy using in vivo tau imaging

Hironobu Endo,Yuki Takada, Kenji Tagai, Matsuya Kuma, Manabu Kubota, Yumemori, Makoto Uno, Chiho Seki, Harumasa Nakamura, Masaki Oya, Yoko Iko, Katsunori Katsuzawa, Kenji Shishido, Kenichi Usui, Susumu Morii, Takahiko Toku, Hisotsu Shinnada, Makoto Higuchi

National Institute of Radiological Sciences, National Institutes for Quantum and Radiological Science and Technology, Japan. Department of Psychiatry, Kyoto University Graduate School of Medicine, Department of Oral and Maxillofacial Radiology, The Graduate School of Medical Science, Kyoto University, Japan.

The clinical features of small fiber neuropathy patients with anti-Plexin D1 antibodies

Takayuki Fujii, Ryo Yamasaki, Yukino Miyachi, Kyoko Iinuma, Ayako Sakoda, Fum-e Jae Lee, Young-min Lim, Kwanguk Kim, Jun-ichi Kira

Department of Neurology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan. Central Hospital, International University of Health and Welfare, Tokyo, Japan.

Respiratory event distribution predicts phenoconversion in idiopathic REM sleep behavior disorder

Kazuto Tsukita1,2, Yuko Oka3, Toshiaki Hamano1,3, Naoko Tachiban1

1Department of Neurology, Graduate School of Medicine, Kyushu University, Japan. 2Division of Sleep Medicine, Kansai Electric Power Research Institute, Japan. 3Laboratory of Biostatistics and Cell Biology, Graduate School of Frontier Biosciences, Osaka University, Japan. 4Division of Clinical Neurology, Kansai Electric Power Medical Research Institute.

Objective: Anti-Plexin D1 antibodies (Plexin D1-IgG) are associated with neuropathic pain (NP). Specifically, they are described in neuropathic pain due to root ganglion (DRG) inflammation. In this study, we evaluated the prevalence of Plexin D1-IgG in patients with idiopathic small fiber neuropathy (SFN) Method: We screened 38 patients with probable SFN (24 Koreans and 14 Japanese) and 55 healthy controls (30 Koreans and 25 Japanese) for serum Plexin D1-IgG using indirect enzyme-linked immunosorbent assay (ELISA) with recombinant human Plexin D1. The results were confirmed by a tissue-based assay with mouse IgG. Moreover, we retrospectively reviewed their demographic data, neurological findings, comorbidities, and SFN Symptom Inventory Questionnaire (SFN-SIQ). Results: The frequency of Plexin D1-IgG was higher in SFN patients than in the controls (33.8% vs. 0.0% (0/38) vs. 0.0% (0/55). p = 0.0036). Correlation analysis showed a significant positive correlation between the corrected-epidemiologic density value and disease duration in SFN patients with Plexin D1-IgG (Spearman’s Correlation, rs = 0.35, p = 0.001). In multivariate analysis of Plexin D1-IgG three had only IgG2, two had predominant IgG2 and weak IgG1, and one had only IgG1, which indicates IgG2 predominance (83.3%). (SFN) patients with Plexin D1-IgG showed late-middle-age onset (mean age 45.6 ± 14.9 years), abnormal sweating (70.0%), and burning pain (100%) in SFN-SIQ. Their NeP was characterized by burning (66.7%) and pricking (66.7%). Conclusion: We have demonstrated the presence of Plexin D1-IgG in a fraction of classical SFN patients.

LGI4 is a novel autoantigen targeting for nodal antigens in patients with non-familial anti-NMDA antibody encephalitis

Xu Zhang, Hidenori Ogata, Tomohiro Inamura, Takayuki Fujii, Ryo Yamasaki, Jun-ichi Kira

1Translational Neuroscience Research Center, Graduate School of Medicine, International University of Health and Welfare, Okawa, Japan. 2Department of Neurology, Neurological Institute, Graduate School of Medical Sciences, Kyusyu University, Fukuoka, Japan. 3School of Medicine, National Center of Neurology and Psychiatry, International University of Health and Welfare, Okawa, Japan. 4Department of Neurology, Brain and Nervous System Research Central Hospital, International University of Health and Welfare, Fukuoka, Japan.

Objectives: IgG antibodies to nodal proteins such as neurofascin 155 (NF155) and contactin-1 (CNTN1) are recently reported in a fraction of chronic inflammatory demyelinating polyneuropathy (CIDP) patients showing unique features. However, CIDP patients with similar features were occasionally negative for these antibodies. Therefore, we aim to discover novel autoantibodies in such seronegative CIDP patients with similar features. Methods: We screened sera to antibodies that bind to mouse sciatic nerves and dorsal root ganglia (DRG) by tissue-based indirect immunofluorescence assays (IFA) in 19 CIDP patients who were seronegative for anti NF155 and anti-CNTN1 antibodies. Results: Western blotting (WB) and cell-based RNA interference assay were used to identify the target antigens. Results: Sera from four CIDP patients selectively bound to intracellular regions of the sciatic nerves and satellite glia in DRG. The main IgG subtype was IgG1. The patients' IgG commonly stained a 60 kDa protein band on WB using mouse DRG and sciatic nerve lysates. Based on these features, we hypothesized Leucine Rich Repeat LGI Family Member 4 (LGI4) may be a target antigen in DRG and sciatic nerves. All four patients' IgG bound to LGI4-overexpression lysates. LGI4 siRNA effectively down-regulated LGI4 in LGI4-expressing melanoma cells and reduced the patients' IgG binding. Conclusion: LGI4 antibody-positive patients had very high cerebrospinal fluid protein amounts. Conclusion: Anti-LGI4 antibody is a novel autoantibody for nodal type CIDP.
AP-01-3  Treatment of Muscular Dystrophy Caused by Pseudoxon Insertion

Hiroaki Obara,1 Motoyasu Hosokawa,1 Tomonari Awaysa,2 Ryosuke Takahashi,1 Misako Nakata,1 Yuzi Ito,3 Ichizo Nishino4
1Department of Neurology, Kyoto University Graduate School of Medicine, Japan; 2Department of Anatomy and Developmental Biology, Kyoto University Graduate School of Medicine, Japan; 3Department of Neuroumscular Research, National Institute of Neuroscience, National Center of Neuroscience and Psychiatry; 4Department of Molecular Genetics, Research Institute of Molecular and Developmental Biology, The University of Tokyo, Japan

Objective: TAR DNA-binding protein 43 (TDP-43) is a common form of congenital muscular dystrophy in Japan. Recently, a de novo intronic mutation FKTN c.1974_1976delGT GTGT was discovered as the causative mutation in Japanese FCMD patients. This mutation induces pseudoxon inclusion within intron 5, which produces a non-functional shorter FKTN protein. In this report, we attempted to restore normal FKTN by modifying splicing patterns by small molecule compounds. (Methods and Result) Splicing reporters of FKTN (c67+2086C>T) was created to pick up small molecules that can skip the pseudoxon and restore the normal splicing pattern. By using this reporter, splicing factor 3b, subunit 1 (SF3B1) inhibitors and Cdc2-like kinases (CLKs) inhibitors were identified as the possible splicing modifiers for this mutation. (Conclusion) We have found several candidate splicing modifiers for this mutation. Inhibitors and Cdc2-like kinases (CLKs) inhibitors were identified as the possible treatment for FCMD patients by splicing modulation.

AP-01-4  Ablation of interleukin-19 improves motor function in a mouse model of amyotrophic lateral sclerosis

Hiroyasu Komiya,1 Hideyuki Takeuchi,2 Yuki Ogawa,3 Akihiro Ogawara, Keita Takahashi,4 Atsuko Katsumoto,5 Yasutaka Azuma,1 Shunta Hashiguchi,3 Misako Kumi,6 Kenichi Tanaka,7 Mikiko Tada,4 Hiroshi Doi,4 Fumika Sakaue6
4Department of Neurology, Shiga University of Medical Science, Japan

Objective: Neuroluimination by activated microglia and astrocytes plays a critical role in the disease progression of ALS. Interleukin-19 (IL-19) is a negative feedback regulator to limit proinflammatory response of microglia in autoregulatory manner, but it remains unclear how IL-19 contributes to the pathomechanism of ALS. In this study, we focused on the effect of IL-19 on the progression of ALS. (Method) We generated a G93A Tg mice with IL-19-/SOD1-/ or IL-19+/SOD1- mice. (Result) We found that IL-19 expression level was upregulated in the primary microglia and the lumbar spinal cords of SOD1 Tg mice compared to those of wild mice. Unexpectedly, IL-19+/SOD1- mice with IL-19 mice and evaluated disease progression, motor function, and survival rate as well as pathobiological and biochemical alterations. (Conclusion) We confirmed that IL-19 is one of the key factors that can be used for the treatment of ALS and can be used for the treatment of ALS.

AP-01-5  Ablation of interleukin-19 improves motor function in a mouse model of amyotrophic lateral sclerosis

Hiroyasu Komiya,1 Hideyuki Takeuchi,2 Yuki Ogawa,3 Akihiro Ogawara, Keita Takahashi,4 Atsuko Katsumoto,5 Yasutaka Azuma,1 Shunta Hashiguchi,3 Misako Kumi,6 Kenichi Tanaka,7 Mikiko Tada,4 Hiroshi Doi,4 Fumika Sakaue6
4Department of Neurology, Shiga University of Medical Science, Japan

Objective: Neuroluimination by activated microglia and astrocytes plays a critical role in the disease progression of ALS. Interleukin-19 (IL-19) is a negative feedback regulator to limit proinflammatory response of microglia in autoregulatory manner, but it remains unclear how IL-19 contributes to the pathomechanism of ALS. In this study, we focused on the effect of IL-19 on the progression of ALS. (Method) We generated a G93A Tg mice with IL-19-/SOD1-/ or IL-19+/SOD1- mice. (Result) We found that IL-19 expression level was upregulated in the primary microglia and the lumbar spinal cords of SOD1 Tg mice compared to those of wild mice. Unexpectedly, IL-19+/SOD1- mice with IL-19 mice and evaluated disease progression, motor function, and survival rate as well as pathobiological and biochemical alterations. (Conclusion) We confirmed that IL-19 is one of the key factors that can be used for the treatment of ALS and can be used for the treatment of ALS.

AP-01-6  Ablation of interleukin-19 improves motor function in a mouse model of amyotrophic lateral sclerosis

Hiroyasu Komiya,1 Hideyuki Takeuchi,2 Yuki Ogawa,3 Akihiro Ogawara, Keita Takahashi,4 Atsuko Katsumoto,5 Yasutaka Azuma,1 Shunta Hashiguchi,3 Misako Kumi,6 Kenichi Tanaka,7 Mikiko Tada,4 Hiroshi Doi,4 Fumika Sakaue6
4Department of Neurology, Shiga University of Medical Science, Japan

Objective: Neuroluimination by activated microglia and astrocytes plays a critical role in the disease progression of ALS. Interleukin-19 (IL-19) is a negative feedback regulator to limit proinflammatory response of microglia in autoregulatory manner, but it remains unclear how IL-19 contributes to the pathomechanism of ALS. In this study, we focused on the effect of IL-19 on the progression of ALS. (Method) We generated a G93A Tg mice with IL-19-/SOD1-/ or IL-19+/SOD1- mice. (Result) We found that IL-19 expression level was upregulated in the primary microglia and the lumbar spinal cords of SOD1 Tg mice compared to those of wild mice. Unexpectedly, IL-19+/SOD1- mice with IL-19 mice and evaluated disease progression, motor function, and survival rate as well as pathobiological and biochemical alterations. (Conclusion) We confirmed that IL-19 is one of the key factors that can be used for the treatment of ALS and can be used for the treatment of ALS.
Whole-exome sequencing of leukoencephalopathy without NOTCH3 mutation (Cadasil mimics)

【結論】CADASIL mimicsにおいてNOTCH3以外の病原性あるいは感受性遺伝子を同定する機会をえた。

【目的】CADASILは最も頻度の高い遺伝性脳小血管病であり、若年性脳梗塞や頭蓋内出血を引き起こす重要な疾患である。本研究の目的は、CADASILの診断が難しい症例に対する新たな解析法の開発を試みることである。

【方法】Hodgesらの診断基準を満たすTGAの2症例で、急性期および回復期（2週間後）に撮影されたMRIを解析した。確定診断に至らなかった症例を対象に、NOTCH3以外の遺伝性脳小血管病の症例に対してエキソーム解析を行い、NOTCH3以外の遺伝性脳小血管病の関与を明らかにした。遺伝性脳小血管病における遺伝的多様性が示唆された。

【結果】急性期の3T, 7T DWIで症例1は一過性に海馬に点状高信号を認め、確定診断に役立つ。症例2は57歳女性で、発症翌日に3T MRIを第4病日に7T MRIを撮影した。

【結論】TGAの診断が難しい症例に対してエキソーム解析を行い、NOTCH3以外の遺伝性脳小血管病の関与を明らかにした。

Cadasil mimics in which NOTCH3 is not involved

【目的】Cadasil mimicsの診断が難しい症例に対して新たな解析法の開発を試みることである。

【方法】Hodgesらの診断基準を満たすTGAの2症例で、急性期および回復期（2週間後）に撮影されたMRIを解析した。確定診断に至らなかった症例を対象に、NOTCH3以外の遺伝性脳小血管病の症例に対してエキソーム解析を行い、NOTCH3以外の遺伝性脳小血管病の関与を明らかにした。遺伝性脳小血管病における遺伝的多様性が示唆された。

【結果】急性期の3T, 7T DWIで症例1は一過性に海馬に点状高信号を認め、確定診断に役立つ。症例2は57歳女性で、発症翌日に3T MRIを第4病日に7T MRIを撮影した。

【結論】TGAの診断が難しい症例に対してエキソーム解析を行い、NOTCH3以外の遺伝性脳小血管病の関与を明らかにした。

Impact of dyskinesia onset on non-motor symptoms and quality of life in Parkinson’s disease patients

【目的】PD患者の非運動症状（NMS）の改善とQoL向上のための非運動症状の管理に、運動症状の管理を前提とした治療戦略が推奨される。

【方法】Pacific Parkinsonism, Movement Disorder, and Neurological Disorders Division, Department of Neuropsychology, Sapporo University School of Medicine, Sapporo, Japan

【結果】本研究は、PD患者の非運動症状とQoLを評価し、運動症状の管理が非運動症状の改善とQoL向上に与える影響を解析することを目的とした。

【結論】本研究の結果は、PD患者の非運動症状とQoLの改善に運動症状の管理が重要であることを示唆している。
**Methods:** A large population of PD patients. To evaluate the altered expression of peripheral clock genes and their correlation with the sleep-wake phenotypes including representative PD cohort. To evaluate the altered expression of peripheral BMAL1, CLOCK, CRY1, PER1, and PER2 in the peripheral blood mononuclear cells (PBMCs) of patients with PD (n=326), and healthy controls (HC, n=314) using real-time quantitative PCR. Then we performed comprehensive association analyses on the sleep characteristics and the PBMCs clock gene expression.

**Results:** We determined the expression levels of BMAL1, CLOCK, CRY1, PER1, and PER2 were significantly decreased in the PBMCs of PD as compared with that of HC (P<0.05). Statistical analyses revealed that a combination of five clock genes could reach a high diagnostic performance (areas under the curves, 92%) for PD comorbid probable RBD, as well as the risk predictive of sleep and wakefulness disturbances in PD patients.

**Conclusions:** Our study demonstrates that peripheral BMAL1, CLOCK, CRY1, PER1, and PER2 levels are altered in PD patients and may serve as endogenous predictors for sleep and wakefulness disturbances of PD.

---

**Objective:** The sleep disturbance in Alzheimer’s disease (NCD-AD) patients is multifactorial due to a combination of tDCS and cognitive training, sham tDCS, or tDCS. Primary outcomes included sleep quality (measured by PSQI) and global cognition (measured by ADAS-Cog) at 4th week, 8th week, and 12th week. Results: Compared to combined modality, mild NCD-AD patients who received tDCS only demonstrated prominent enhancement on sleep quality at 12th week (t=4.95, p<0.001). Within the tDCS group (n=60), we defined poor sleepers as baseline PSQI total score larger than 5 and good sleepers as PSQI total score less than 5. After a 4-week course of tDCS treatment, poor sleepers showed significantly enhanced sleep quality than 5 and good sleepers as PSQI total score less than 5. After a 4-week course of tDCS, poor sleepers as PSQI total score less than 5 and good sleepers as PSQI total score less than 5. After a 4-week course of tDCS treatment, poor sleepers showed significantly enhanced sleep quality than 5 and good sleepers as PSQI total score less than 5. After a 4-week course of tDCS, poor sleepers showed significantly enhanced sleep quality than 5 and good sleepers as PSQI total score less than 5.

**Conclusion:** These results suggest that the overexpressed astroglial Cx43 in chronic EAE and MS lesions exacerbate neuroinflammation. Thus, astroglial Cx43 is a novel promising therapeutic target for chronic progressive MS, in which no highly efficient drugs are available.