AAO-01-01 A new antisense oligos targeting alpha-synuclein improves motor function in Parkinson's model mouse

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Objective: A familial form of Parkinson's disease (PD) induced by the multiplication of Alpha-synuclein (SNCA) gene is recognized that increases levels of SNCA protein is a significant risk of PD. Importantly, accumulation of SNCA protein in the CNS neurons is a major pathology of sporadic PD. However, the antipathogenic strategy has not been clearly demonstrated. In this study, we explored the effect of AmNA-ASO targeting SNCA on the behaviors of mice.

Methods: We used MRI, neuropathological method and western blotting to evaluate the effect of AmNA-ASO on the behaviors, we performed wire suspending test and pasta gnawing test of the mice. Results: AmNA-ASO could ameliorate motor function of Ataxin-1-KI mice. We performed behavioral analysis of AmNA-ASO treated mice.

Application: We crossed YAPdeltaC transgenic mice, which expression were increased from Tet-ON YAPdeltaC system in mutant Ataxin-1 knock-in (Atxn1-KI) mice. We performed behavioral analysis of AmNA-ASO treated mice.

Conclusion: AmNA-ASO significantly decreased the levels of SNCA protein in the brain of transgenic mice. We injected AmNA-ASO into intraventricular space of mice and examined its distribution in the brain. To examine the potency of AmNA-ASO, we measured levels of SNCA protein in the brain of transgenic mice expressing wild-type SNCA (Thy1:SNCA) mice by ELISA. To determine effects of AmNA-ASO on the behaviors, we performed wire suspending test and pasta gnawing test of the mice. Results: AmNA-ASO could ameliorate motor function of Ataxin-1-KI mice.

AAO-01-02 A new devise HANABI facilitates diagnosis of Synucleinopathies by sonication induced amplification

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Objective: Parkinson's disease (PD) and multiple systemic atrophy (MSA) share a common pathology caused by abnormal accumulation of alpha-synuclein (SNCA). Therefore, it is very important to be understood why the misfolded SNCA causes distinct clinical phenotypes. We have recently developed a new devise HANABI based on Real-Time Quaking-Induced Conversion (RT-QuIC) method to efficiently and detect misfolded SNCA in a very sensitive and specific manner. Our aim is to determine structure variations of SNCA accumulated in PD and MSA patients using HANABI. Methods: We performed RT-QuIC in cerebrospinal fluid (CSF) samples obtained from patients with PD and MSA to examine the structure and sensitivity of SNCA aggregation. Results: We analyzed and monitored kinetics of fibril amplification by HANABI. To determine correlation of the SNCA aggregation and disease progression, we compared kinetics with clinical scores and imaging data. To examine detailed structures of amplified SNCA fibrils, we also performed several biochemical and ultrastructural analyses, including protease K treatment, PT-IR and TEM. Results and Conclusions: The kinetics of PD and MSA patients were significantly faster than that of control. Interestingly, TEM and PT-IR analysis revealed that SNCA fibril amplification observed was distinct, suggesting the structural differences between two fibrils. Our data suggest that structure variations of SNCA causes distinct pathology of PD and MSA. HANABI will be useful for facilitating diagnosis of PD and MSA and allow us to understand a novel mechanism of disease associated with SNCA.
AO-02-1  Fc fusion protein as a novel treatment for myasthenia gravis

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【目的】重症筋無力症( MG) は神経伝達障害が原因で容易に筋力低下を伴う全身性の疾患で、治療法が限定されているため、新たな治療法の探索が求められている。MGはAChRの機能が欠損した状態で発症するが、AChRの欠損がAChRの受容体を介しての神経伝達障害と対応するものである。AChRの欠損が神経伝達障害を引き起こすが、AChRの欠損が神経伝達障害を引き起こすが、MGの治療法の探索が求められている。

【方法】MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探索は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治療法の探究は、MGの治
**AP-01-1** Brain-derived exosomes as potential blood biomarkers for Parkinson’s disease and parkinonism

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**Objective** There is still a substantial unmet need for blood-based biomarkers to make an objective diagnosis of Parkinson’s disease (PD) and parkinonism. The aim of this study is to determine whether enumeration of brain-derived exosomes in plasma is informative in the diagnosis of those diseases. **Method** We have developed a novel method to enumerate the plasma levels of neuron-, astrocyte-, and oligodendrocyte-derived exosomes (NDEs, ADEs, and ODEs, respectively) obtained from patients with PD, multiple system atrophy, progressive supranuclear palsy (PSP) and control subjects. Results: The plasma levels of NDEs, ADEs, and ODEs were individually and precisely quantified with our novel assay system using antibodies against neuron-, astrocyte- or oligodendrocyte-specific proteins combined with an antibody to the common exon marker CD81. The plasma levels of NDE, ADE and ODE were significantly higher in PD patients than in control samples, respectively (p<0.003 for NDE, p<0.021 for ADE, and p<0.008 for ODE). The plasma levels of ODE showed a significant correlation with UPDRS part III scores in the patients with MSA predominated in parkinsonism (MSA-P) (r=0.65, n=0.404) and those scores in the patients with PD (r=0.51, n=0.404), respectively. **Conclusion** This is the first report that enumerates NDE, ADE, and ODE in human plasma and shows the potential usefulness of these levels as biomarkers for PD. Our results suggest the capability of the plasma levels of ODE as a surrogate biomarker to monitor the severity of parkinsonism in MSA-P and PD.

**AP-01-3** alpha-synuclein propagation in brains via olfactory pathway in non-human primate model

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**Introduction** Parkinson’s disease (PD) is the neurodegenerative disease characterized by aggregation of α-synuclein (α-syn), a conserved, small, leucine rich protein. The α-syn aggregates are believed to propagate in brains in a prion-like fashion via two major pathways: the olfactory and vagal pathways. Recently, the common marmoset (Callithrix jacchus) has gathered a lot of attention in the field of neuroscience because of its useful characteristics as an animal model. In this study, we inoculated α-syn fibrils in the olfactory bulb of a common marmoset. We described our results in the following pathways. **Results** In Recombinant Olfactory (RO) mice, length marmoset α-syn was purified and incubated with agitation for a week to generate α-syn fibrils. A two-year-old female common marmoset was anesthetized with ketamine and isoflurane/oxygen mixture. Then, 80μl of fibrils solution (4mg/ml in sterile PBS) was stereotaxically injected using glass capillary at two sites in the unilateral olfactory bulb (OB). Three months after α-syn fibrils injection, the marmoset was sacrificed and perfused with PBS followed by 4% PFA in PBS. Eight-micron coronal sections were made and immunostained using phosphorylated α-syn (p-α-syn) antibody followed by DAB staining. Results: Wide-spread p-α-syn positive cells were observed in the immunostained brains. Alpha-synuclein propagation in brains via the olfactory pathway could be visualized in non-human primate brain.

**AP-01-5** Novel binding partner of dysferlin is a potential therapeutic target for dystroferylpathy

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**Background** Mutations in the dysferlin gene are responsible for adult-onset, progressive, and recessively inherited limb-girdle muscular dystrophy (MGMD) and other dysferlinopathies. The protein X is required for plasma-membrane repair and a potential therapeutic target for dysferlinopathy. **Methods and Results**: The protein X is required for plasma-membrane repair and a potential therapeutic target for dysferlinopathy. We previously reported over 50 different mutations across the entire dysferlin and are focusing on these dysferlin and dysferlin-related proteins. Mutations in the dysferlin gene are responsible for adult-onset, progressive, and recessively inherited limb-girdle muscular dystrophy (MGMD) and other dysferlinopathies. The protein X is required for plasma-membrane repair and a potential therapeutic target for dysferlinopathy.

**Conclusion** Binding partners of dysferlin, which can be working as the similar functional role, would be possible therapeutic targets to compensate the functional loss of the mutated dysferlin.

**AP-01-6** Creating mice models for sporadic Parkinson’s disease based on its genetic risk factors

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**Background** An animal model is essential not only to explore the pathogenesis of Parkinson’s disease (PD) but to also to validate the biomarker and validate the candidate drugs of PD. **Object** In this study, we try to generate a new appropriate animal model of PD. Material and Methods: Alpha synuclein (α-syn) is an important protein for the pathogenesis of PD. We previously generated α-syn bacterial artificial chromosome (BAC) transgenic mice harboring the entire human α-syn gene and its gene expression regulatory regions. We expressed 27-fold amount of α-syn with similar expression pattern to endogeneous α-syn. They manifested decreased anxiety-like behaviors which may reflect non-motor symptoms, but did not show dopaminergic neuronal loss. Recent genetic study showed that PD patients have higher prevalence of heterozygous GBA mutation, and reduced activity of GBA is presumed to affect accumulation of α-syn, although underlying mechanisms remain unclear. Here, we crossed wild-type α-syn BAC tg mice with GBA heterozygous knockout mice to investigate whether the infected OPC can secrete scFv-X. We investigated whether the infected OPC can secrete scFv-X. We also performed Immunohistochemical staining of SOD1 for OPGs. Result: The manifold expression vector expressing scFv-X derived from BAC was constructed and was subcloned into BAC vector. Primary OCs infected by the BAC vector, secreted scFv-X, which was recognized by the scFv-X specific antibody. Our results indicated that the scFv-X expression is a potential therapy due to its accelerated turnover. We succeeded in establishing a primary OCs expressing misfoldingspecific scFv. Further in vivo evaluation is expected to validate the effect of our combination therapy of OPGs and scFv.
**Development of a novel quantitative assay of p-tau and its application to the blood diagnosis of AD**

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**Introduction**

Alzheimer’s disease (AD) is a progressive, neurodegenerative disorder characterized by the formation of amyloid plaques and neurofibrillary tangles, leading to cognitive decline and memory loss. Early detection of AD is crucial for timely intervention and management. A reliable blood-based diagnostic marker is highly desirable to facilitate early diagnosis and monitor disease progression.

**Objectives**

The aims of this study were to develop a novel quantitative assay for p-tau and evaluate its diagnostic potential in the blood of AD patients.

**Methods**

A high-throughput screening approach was employed to identify antibodies that specifically bind to p-tau. The selected antibodies were further characterized for their specificity, sensitivity, and detection limit. The diagnostic performance of the p-tau assay was evaluated using a cohort of AD patients and healthy controls.

**Results**

The novel p-tau assay exhibited high specificity and sensitivity, allowing for accurate detection of p-tau levels in blood samples. The results demonstrated a statistically significant difference in p-tau levels between AD patients and healthy controls, indicating the potential of this assay as a blood-based diagnostic marker for AD.

**Conclusion**

The development of a novel quantitative p-tau assay represents a significant step towards the realization of blood-based diagnostic strategies for AD. Further validation studies are essential to establish its clinical utility and potential for personalized care.

**References**


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**Anti-glycolipid antibodies and clinical features in recurrent Guillain-Barré syndrome**

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**Objective**

To investigate the clinical features and anti-glycolipid antibody profiles in patients with recurrent Guillain-Barré syndrome (GBS) and to identify factors associated with recurrent GBS.

**Methods**

A retrospective study of 24 patients with recurrent GBS was conducted. Clinical features, anti-glycolipid antibody profiles, and genetic markers were analyzed.

**Results**

The recurrent GBS patients showed more severe neurologic deficits and a higher rate of cranial nerve involvement compared to the first GBS attack. Anti-GQ1b antibodies were positive in 17 (71%) patients, and anti-GM1 antibodies were positive in 10 (42%) patients. The presence of anti-GM1 antibodies was associated with a shorter interval between the first and recurrent GBS attacks.

**Conclusion**

Recurrent GBS patients had more severe clinical symptoms and a higher frequency of anti-GM1 antibodies compared to the first GBS attack. These findings highlight the importance of carefully monitoring patients with a history of GBS for recurrence and prompt treatment to minimize neurological sequelae.

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**Functional network features of visuoperceptual disturbances in Parkinson’s disease**

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**Objective**

This study aims to clarify the functional connectivity changes in the brain of patients with visuoperceptual disturbances in Parkinson’s disease (PD).

**Methods**

We evaluated 90 patients with non-demented Parkinson’s disease (PD) and 32 healthy control subjects (HC) using resting-state fMRI. Cognitive performances were assessed using the Mini-Mental State Examination, the Addenbrooke’s Cognitive Examination - Revised and the Visual Object and Space Perception Battery (VOSP).

**Results**

 Patients with visuoperceptual disturbances showed reduced connectivity in the dorsal visual stream, including the fusiform, parietal, and frontal regions. This finding was associated with clinical features such as anosognosia.

**Conclusion**

Visuoperceptual disturbances in PD are associated with functional connectivity changes in the dorsal visual stream, which could serve as a biomarker for disease severity.

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Ape-01-1  Association analysis of SNPs near the DYT3 locus to dystonic symptoms in XDP

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BACKGROUND: X-linked Dystonia-Parkinsonism (XDP, DYT, Leigh Disease, OMIM 312495) is an inherited degenerative disease with variable expression. OBJECTIVES: To elucidate the association between phenotypes and four SNPs of interest: ChrX:71102421C>G, ChrX:71653235C>T, rs41484056, rs41438158.

RESULTS: The ChrX:71102421C>G polymorphism had a significant effect on the presence of neck/shoulder dystonia (p=0.001). Logistic regression analysis showed that none of the SNPs influence age at onset of symptoms. Z-test was used to compare proportions of patients. RESULTS: The ChrX:71102421C>G polymorphism had a significant effect on the presence of neck/shoulder dystonia (p=0.001). Logistic regression analysis showed that none of the SNPs influence age at onset of symptoms. Z-test was used to compare proportions of patients.

Ape-01-2  Altered gamma delta T cell repertoire correlates with disability in untreated multiple sclerosis

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Purpose: We reported that the deletion-type copy number variation at T cell receptor (TCR) α and γ loci increased the susceptibility to multiple sclerosis (MS), which was mediated by a decreased rearrangement of TCR γ and α loci, respectively. However, it remains unclear whether the alteration of γ δ T cell repertoire in MS patients.

Methods: Comprehensive flow cytometric immunophenotyping was performed in 36 MS patients with no disease-modifying therapies (DMTs) in 36 MS patients treated with immunosuppressives (ISs) and healthy controls (HCs). Results: The frequencies of regulatory CD4+ T (Treg) cells (CD56CD45R0+) among CD4+ T cells, Vγ2Vδ2+ γδ T cells (CD56CD4+ T cells) in MS patients treated with IFN-β (p=0.003, p<0.001, respectively) were significantly decreased in MS patients with no DMTs compared to ISs (p<0.001, p=0.001, respectively) and healthy controls (p=0.001, p<0.001, respectively). The frequency of Vδ1Vγ2+ γδ T cells was decreased (p<0.001) and Vδ1Vγ2+ γδ T cells were increased compared to ISs (p=0.001, p<0.001). The Vδ1/Vδ2 ratio was significantly increased in both MS patients with no DMTs and those treated with IFN-β compared with HCs (p=0.003, p=0.001, respectively). The frequency of Vδ1Vγ2+ γδ T cells negatively correlated with disease severity defined by Expanded Disability Status Scale scores in MS patients with no DMTs (r=0.60, p=0.056), but not in those treated with IFN-β (r=0.002, p=0.992). Conclusion: MS patients had distinct γ δ T cell repertoire compared to HCs and the altered γδ T cell parameters were robustly associated with disease severity only in MS patients with no DMTs.

Ape-01-3  GWAS based on ATN system identifies new susceptibility loci for Alzheimer disease

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Purpose: To identify new susceptibility loci for Alzheimer’s disease (AD) and provide mechanisms by which these novel variants modulate disease. Method We conducted a case-control genome-wide association studies (GWAS) based on “A/T/N” system from 699 participants in Alzheimer’s Disease Neuroimaging Initiative (ADNI) cohort. Meanwhile, we studied the novel loci with MRI measures, abnormal glucose metabolism, and β-amyloid (A β) deposition on neuroimaging in ADNI database. Results: We observed significant association between phenotypes and four SNPs of interest: ChrX:71102421C>G, rs41484056, rs41438158 and ChrX:71653235C>T. Logistic regression analysis showed that none of the SNPs influence age at onset of symptoms. Z-test was used to compare proportions of patients.

Ape-01-4  MIR-132 EXPRESSION IN PLASMA OF PARKINSON’S DISEASE

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Purpose: microRNAs (miRNAs) are small, evolutionarily conserved and non-coding small RNAs involved in posttranscriptional gene regulation. miR-132 has been reported to regulate nuclear receptor related 1 protein (Nurrl), which plays a key role in the maintenance of the dopaminergic system of the brain and mutations in this gene has been associated with disorders like Parkinson’s disease, schizophrenia, and manic depression. The mir-132 expression level in plasma is correlated to neurologic symptoms, such as motor controls (NC) and healthy controls (HC) has not been reported yet. Therefore, we determine whether mir-132 expression is altered in patients with PD we measured its expression in human plasma in 240 patients with PD, 218 HC, and 200 NDC by reverse transcription real-time quantitative PCR (RT-qPCR) in the form of single-blind, using artificial synthetic external miRNA as control. miR-132 expression levels was significantly increased nearly 2-folds in patients with PD as compared with HC (p < 0.001) and has a increased trend as compared with NDC. When adjusted for gender, age, higher levels of miR-132 expression were associated with significantly increased risk for PD in men, and whose frequency was highest in the dementia group. When adjusted for disease stage, symptom, and medication, the observed high miR-132 expression in plasma indicates possible systemic involvement in PD, and the finding may help identify individuals with PD and other neurological disorders. Our study levels in plasma is expected to be used as a potential biomarker aiding in diagnosis and prognosis of PD.

Ape-01-5  Rehabilitation and Readmission/Mortality Risks in Patients with Stroke or Transient Ischemic Attack

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Objective: The high-dose stroke rehabilitation induces greater functional improvement and lower stroke re-admissions. The impact of the dose of stroke rehabilitation on subsequent readmission/mortality risks remains unclear. The objective of this study was thus to investigate the associations between the dose of stroke rehabilitation and risks of 3 outcome events (OEs) in patients with stroke or transient ischemic attack (TIA). Methods: The Taiwan National Health Insurance database was used. Information on 4594 patients with first-ever acute stroke or TIA was collected with the averaged follow-up duration of 32 months. Three OEs were investigated: vascular readmissions/all-cause mortality (VE), all-cause readmissions/mortality (OE1), and stroke readmissions/mortality (OE2). Three doses were used in Model 1 (None, Low-dose, and High-dose) and 4 doses were used in Model 2 (None, Inpatient plus/ or Outpatient). Results: Comparing to None, Low-dose was related to lower risks of VE (Hazard Ratio (HR) 0.77, 95% Confidence Interval (CI) 0.65-0.93; p=0.002), and OE1 (HR 0.79, 95% CI 0.71-0.88; p=0.001) and OE2 (HR 0.56, 95% CI 0.48-0.64; p<0.001). The Low-dose was related to lower risks of VE (HR 0.55, 95% CI 0.47-0.65; p=0.001) and OE2 (HR 0.60, 95% CI 0.53-0.67; p=0.045). Conclusions: Rehabilitation was associated with reduced readmission/mortality in patients with stroke or TIA.

Ape-01-6  Interactions between caffeine intake and LRRK2 gene in Parkinson’s Disease

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Objective: We investigated the gene-environment interaction between caffeine consumption and genetic susceptibility to PD, specifically at the LRRK2 gene. Studies of multiple risk factors of PD have been implicated in PD but gene-environment interactions have not been studied in detail. Caffeine has been associated with reduced PD risk. The LRRK2 gene encodes a large multiprotein kinase with a putative autoinhibitory domain, the dominant familial form of PD, and the S1647T variant is a risk factor for PD and an increased risk of Parkinson’s disease, schizophrenia, and manic depression. The mir-132 expression level in plasma is correlated to neurologic symptoms, such as motor controls (NC) and healthy controls (HC) has not been reported yet. Therefore, we determine whether mir-132 expression is associated with significantly increased risk for PD in men, and whose frequency was highest in the dementia group.

Results: Compared to caffeine consumers with low genetic susceptibility, non-coffee consumers with high genetic susceptibility (homozygous recessive Intender) and OE1 (HR 0.67, 95% CI 0.59-0.75; p=0.001) had almost four times higher risk (OR 39.99, 95% CI 158.84; p < 0.001), with greater effect seen in the Chinese population [OR 4.54, 95% CI (214, 962), p<0.001]. There was no significant dose-response interaction. Conclusion: There is evidence that caffeine consumption significantly reduces the risk of PD in cases with high genetic susceptibility compared to those with low genetic susceptibility at the LRRK2 5167Tloci. Future studies can investigate the interactions with other genetic risk variants of PD.

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