FINAL PROGRAM

International Parkinson and Movement Disorder Society
Asian & Oceanian Section

8th Asian and Oceanian Parkinson's Disease and Movement Disorders Congress

MARCH 17-19, 2023

Kolkata, INDIA

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Building research capacity through training in the Global Parkinson's Genetics Program (GP2)

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Objective: To establish a virtual 'center of excellence' with resources and expertise to serve the training needs of the Global Parkinson's Genetics Program (GP2; www.gp2.org) and its collaborators.

Background: GP2 is an international collaborative effort to drive forward research into the genetic basis of Parkinson's disease (PD). Alongside developing strong links with global partners, training and collaboration are vital aspects to accelerate and diversify research efforts.

Methods: The Training, Networking and Communication working group has divided training opportunities into 'individuals' and 'groups' to broaden knowledge and reach impact. For groups, we developed a free and accessible web-based learning platform (https://training.gp2.org/) to establish foundational knowledge on PD genetics, bioinformatics, medical statistics and molecular biology. For individuals, tailored research training opportunities, from short courses to graduate programs and placement opportunities, have been offered to clinicians and scientists from traditionally underrepresented regions in PD research to develop skills and build local capacity.

Results: To date, seven courses have been launched on the GP2 learning platform, including beginner and intermediate bioinformatics, using Terra for data analysis, PD genetics for non-geneticists, research methods, and bioinformatics training workshop; currently accessed by over 600 students. Courses focusing on an introduction to Python, functional biology, and advanced bioinformatics are in development. More than 30 trainees have been supported to attend graduate courses in bioinformatics and data science at the Foundation for Advanced Education in the Sciences at the NIH. 4 PhD and 7 master's fellowships have been awarded to individuals in Africa, Asia and Latin America, and sabbatical training opportunities at GP2 centers have started. A trainee network of 118 worldwide members has been created to streamline training and employment opportunities, provide direct expertise to the places where it is needed and to facilitate data access and analyses across GP2.

Conclusion: Training the next generation of PD researchers worldwide is a priority for GP2. As GP2 gains momentum, our reach will expand to ensure local research capacity is generated and to support the growing network of trainees and researchers worldwide to further the understanding of the genetic basis of PD.

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Polygenic risk score of Alzheimer's disease is associated with dementia in Parkinson's disease.

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Objective: We investigated the association of Alzheimer's disease (AD) or Parkinson's disease (PD) polygenic risk scores (PRS) with dementia in the PD patient cohort.

Background: Recent genome-wide association studies revealed genetic variants associated with PD susceptibility. Cognitive decline is one of the most crucial non-motor symptoms in patients with PD, which negatively affects patients' quality of life, and increases the caregiver burden. Little is known about genetic factors associated with dementia in PD (PDD). Alzheimer's disease and PDD shares substantial overlap in pathologic and clinical presentation, and a few studies demonstrated common genetic factors between PD and AD.

Methods: We recruited 1,024 patients with PD between January 2009 and December 2016 and performed genomic analysis using a Korean chip. Using electric medical records, we reviewed the year of PD diagnosis, the development of dementia, the year of dementia diagnosis or the latest year of follow-up. Clinical data were collected until August 2022. PRS was constructed with variants obtained from previous genome-wide association studies for PD and AD in Asian populations. We compared PRS between patients with PDD and PD patients without dementia using Wilcoxon signed-rank test. The association between PRS and dementia incidence was evaluated with multivariable Cox proportional hazard models.

Results: Among the 1,024 final study population, 225 patients were diagnosed with dementia after a median of 10 years of follow-up. Patients with PDD showed higher AD-PRS than PD patients without dementia (P=0.0016). The association was significant after adjusting for age and education (P=0.0013). However, PD-PRS was not significantly different between patients with PDD and PD patients without dementia (P=0.75). Participants with AD-PRS in the top quartile were at higher risk of developing PD after adjusting for age and education than participants with AD-PRS in the lowest quartile (hazard ratio, 1.70; 95% confidence interval, 1.16–2.48, P=0.006).

Conclusion: We identified that AD-PRS, not PD-PRS was significantly associated with dementia development in PD. This could help elucidate pathogenic mechanisms and potential treatments strategy for dementia in PD.

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Hereditary And Geneological Characteristics Of Parkinson's Disease Depending On The Clinical Forms

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Objective: Study of the genetic characteristics of Parkinson's disease and their role in early detection of the disease

Background: Predictors of PK have been studied for many years, but taking into account the genetic-degenerative characteristics of the disease, finding predictors of early detection of the disease in the Uzbek population and developing principles of prognosis is a very important and urgent issue.

Methods: To achieve the goal of the study, 106 patients with various forms of PD were enrolled. The age of patients in the main group was from 18 to 70 years, and the average was 56.04±10.9. The average duration of the disease is 5.56±6.2 years. 55 (51.8%) of the examined patients in the main group were men and 51 (48.2%) were women.

Results: PD is considered a genetic degenerative disease and can be passed from one generation to another in an autosomal dominant or autosomal recessive type, and often occurs sporadically. The results obtained on the basis of genetic and anamnestic data showed that 21 patients (19.8%) were autosomal dominant, 38 patients (35.8%) were autosomal recessive, and 47 patients (44.8%) were known to meet sporadically. it happened. At the next stage, we analyzed the types of breeding according to the clinical forms of the disease. It was found that 18 (85.7%) patients with autosomal dominant type had akinetic-rigid form, and 3 (14.3%) suffered from tremor form. It was found that 21 (55.2%) patients with autosomal recessive type had tremor and 17 (44.8%) had mixed PD. It was found that 17 (36.1%) of the sporadic patients had tremors and 30 (63.9%) had mixed forms. It should be emphasized that in the autosomal-dominant type, the rpoband male, the female patient, and the proband female were bred from the male patient.

Conclusion: The type of reproduction of PD disease is closely related to the clinical forms of the disease, the akinetic-rigid form is more autosomal-dominant, the tremor form is relatively autosomal recessive, and the mixed form can be reproduced almost uniformly from generation to generation.

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Exploring Vitamin D as a NOS inhibitor in Parkinson's Disease using in-silico methodologies

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Objective: To unravel the anti-inflammatory actions of vitamin D in Parkinson's disease (PD) by studying interactions between NOS (Neuronal Nitric oxide synthase-nNOS and Inducible Nitric oxide synthase -iNOS) with vitamin D (calcidiol, ergocalciferol and calcitriol).

Background: Neuroinflammation is evident in PD with elevated NOS levels in substantia nigra. nNOS and iNOS are the only enzymes producing NO in the brain and reportedly linked with the bulk of sporadic and familial PD. Both nNOS and iNOS have potential implications in neurodegeneration and glial response occurring in PD. Conversely, vitamin D is known to regulate macrophage transition, the major inflammatory stimuli and has anti-inflammatory activity, and hence vitamin D-NOS interactions need to be assessed.