AAN 2022 Updates

Biomarkers for Parkinson's Disease

Parkinson's disease (PD) is a neurodegenerative disorder where motor symptoms arise due to loss of dopaminergic neurons. Neurodegeneration predates onset of motor symptoms by several years. Identification of subclinical/ early disease with the help of biomarkers is likely to improve disease outcomes.

Early biochemical changes in α-synuclein (αSyn) in the central and enteric nervous system in PD

αSyn aggregates are the main components of Lewy bodies found in the brain and the enteric nervous system of PD patients. Pathological changes and accompanying neurodegeneration may precede clinical diagnosis by years. It has previously been shown that membrane-bound αSyn is protected from aggregation, while cytosolic, soluble αSyn tends to aggregate.

Reduced membrane-binding of αSyn in brain and gut in the mouse model and in post-mortem cortex of PD patients was demonstrated. Additionally, a trend toward increased membrane-binding of αSyn in the colon tissue obtained during routine screening colonoscopy of human PD patients vs healthy controls was observed.

Biochemical assessment of αSyn in the human gut tissue suggests that biochemical changes in αSyn in the gut may serve as a biomarker of disease.[1]

Mitochondrial Antigen Presentation (MitAP) correlates to PD-like Symptoms

Mitochondrial dysfunction and T cell autoimmunity have been implicated in PD pathogenesis. Pathological loss of dopaminergic neurons in PD has been attributed to the accumulation of dysfunctional mitochondria resulting in oxidative stress and death of dopaminergic neurons. T cell infiltration, high levels of pro-inflammatory cytokines and inflammation are also associated with PD. PTEN-induced kinase 1 (PINK1) gene is a repressor of the immune system and helps in clearing damaged mitochondria, thereby repressing the MitAP. Mutations of this gene have been linked to early PD.

The role of MitAP and mitochondrial specific T cell (mitoT cells) was assessed in a murine model of PD by transfer of activated mitoT cells into wild type and PINK1-KO mice. Introduction of infection led to MitAP engagement and establishment of autoreactive T cells in the periphery and brain of the PINK1 KO mice. The transfer of mitoT cells triggered PD like symptoms and these motor symptoms were reversed after L-DOPA administration, thereby highlighting the impact of mitoT cells on the dopaminergic system.

PINK1 has a likely role in the regulation of immune system. These autoreactivity events occur very early in the disease process when compared to the onset of motor symptoms. MitoT cells could serve as potential early biomarkers for PD.[2]

With the SMARTImmunology Insights Series you will better understand the implications of the future disease landscape and be equipped with the knowledge to inform clinical investment decisions. As commercial and clinical teams plan strategies for differentiation and success, they rely on the series for up-to-date, key data-driven insights, across more than 20 immunology and neurology indications.

References

1. V. Gao, L. Komer, J. Briano, et. al. Early biochemical changes in α-synuclein in the central and enteric nervous system in Parkinson's disease. Neurology. 2022;98 (Supplement 18):2295.
2. M. Badr, A. Laplante, D. Matheoud. Mitochondrial antigen presentation in correlation to Parkinson's disease-like symptoms. Neurology. 2022;98 (Supplement 18):3547.

Please contact:
John.L'Ecuyer@smartanalyst.com

GLOBAL HEADQUARTERS
(New York, USA)
285 Madison Ave
22nd Floor, New York
NY 10017
Mobile: +1 (646) 852-5097

EUROPE
(London, UK)
1.04 Power Road Studios 114
Power Road, Chiswick London
W3 5PY
Mobile.: +44-(0)-752-163-8242
Mobile.: +44-(0)-772-574-429

ASIA PACIFIC
(Gurgaon, INDIA)
First Floor, DLF Plaza Tower
DLF Qutub Enclave, DLF City
Phase-I, Gurgaon 122002
Haryana, India
Tel.: 91-124-4313800