Pressemeddelelse: Erhvervs ph.d.-projekt i samarbejde med Lundbeck

Et nyt PhD projekt samarbejde mellem Health, Aarhus University og H. Lundbeck A/S, viser at hæmningen af leucine rich repeat kinase 2 (LRRK2) normaliserer Parkinsons syge-lignende forandringer af subthalamiske neuroner i en model for Parkinsons syge.

Parkinsons syge (PD) er den hyppigst forekommende neurodegenerative sygdom, der også påvirker bevægelsesfunktionen. Der findes ingen behandling, som kan bremse eller stoppe sygdomsudviklingen. Protein ophobninger i hjernen også kaldet Lewy bodies og Lewy neurites er særlige histopatologiske kendetegn for PD. Proteinet α-synuclein er en stor bestanddel af disse ophobninger. Udover dets rolle i sygdomspatologien er genet der koder for α-synuclein også associeret med dominant nedarvet PD. Arvelige mutationer i LRRK2 genet er den mest almindelige genetiske årsag til PD og i bestemte etniske populationer ses en prævalens på op til 30-40 % i arvelig PD. Den patologiske effekt af LRRK2 antages at være koblet til dets enzymatiske aktivitet.

I hans netop færdiggjorte PhD projekt, viser Michael Andersen at viral induceret overudtryk af α-synuclein i midthjernen af en dyremodel for PD fører til en elektrofysiologisk fænotype af glutamaterge subthalamiske neuroner, som deler ligheder med patofysiologiske karakteristika der også ses i hjernen hos PD patienter. Overudtryk af α-synuclein medfører en øget neuronal burst fyring. I studiet blev der også vist at en akut hæmning af LRRK2's enzymatiske aktivitet fuldstændig normaliserede fyringsmønsteret af disse subthalamiske neuroner. Disse fund indikerer at et samspil mellem α-synuclein og LRRK2 kan være relevant for sygdomsudviklingen i PD og at hæmningen af LRRK2's enzymatiske aktivitet kan være et potentielt lægemiddelprincip der kan føre til udvikling af nye behandlinger af PD.¨

Forsvaret af ph.d.-projektet er offentligt og finder sted den 26/4 kl. 10:30 hos H. Lundbeck A/S Ottiliavej 9, 2500 Valby. Titlen på projektet er athophysiological interplay between leucine-rich-repeat-kinase-2 and α-synuclein in the mechanisms leading to neuronal dysfunction and neurodegeneration in Parkinson's disease. Yderligere oplysninger: Ph.d.-studerende Michael Aagaard Andersen, e-mail:aaga@lundbeck.com, tlf. 27147772. Ved ønske om deltagelse i forsvaret skal jeg vide det senest d. 24/4 at 12:00, da De skal registreres.

A new PhD project from Health, Aarhus University in collaboration with H. Lundbeck A/S, shows that inhibition of leucine rich repeat kinase 2 (LRRK2) normalises Parkinson's disease-like changes of subthalamic neurones in an model of PD.

Parkinson's disease (PD) is the most common neurodegenerative disease that also affects motor function. There is no existing disease-modifying treatment available. Protein aggregates in the brain called Lewy bodies and Lewy neurites are histopathological hallmarks of PD. The protein α-synuclein is a major part of those aggregates. Beside its role in disease pathology, mutations in the α-synuclein gene are associated with autosomally dominant inherited PD. Inheritable mutations in leucine rich repeat kinase (LRRK2) are the most common genetic cause of PD in certain ethnic populations, with a prevalence of 30-40%. The pathological effect of LRRK2 is hypothesized to be linked to enzymatic activity.

In his recently completed PhD project, Michael Andersen shows that viral induced overexpression of α-synuclein in the midbrain of an animal model of PD induces an electrophysiological phenotype in glutamatergic subthalamic neurones resembling the pathophysiological characteristics found in PD

patients. Overexpression of α-synuclein leads to increased neuronal burst firing. Importantly, it was discovered that acute inhibition of LRRK2 completely normalized the firing pattern in the subthalamic neurones and that the inhibition of LRRK2 enzymatic activity might be a potential treatment principle that can lead to development of new treatments of PD.

The defence is public and takes place on 26/4 at 10:30 at H. Lundbeck A/S Ottiliavej 9, 2500 Valby. The title of the project is Pathophysiological interplay between leucine-rich-repeat-kinase-2 and α-synuclein in the mechanisms leading to neuronal dysfunction and neurodegeneration in Parkinson's disease. For more information, please contact PhD student Michael Aagaard Andersen, email: aaga@lundbeck.com, Phone +45 2714 7772. If You want to attend will need to know no latter than the 24/4 at 12:00, as You need to be registrated.