

Press release

Please fill in this form and return it to graduateschoolhealth@au.dk in Word format no later than three weeks prior to your defence.

Basic information

Name: Zongpei Zhao Email: zongpeizhao@biomed.au.dk Phone: +86 18222296829

Department of: Biomedicine

Main supervisor: Dr. Monika Golas, Associate Professor

Title of dissertation: Characterization of Macromolecular Complexes Involved in Neuronal Development

Date for defence: December 17, 2018 at (time of day): 14:00 Place: 1232-115 Large Anatomical Auditorium.

Press release (Danish)

Karakterisering af makromolekylære komplekser involveret i neuronal udvikling

Dette projekt er blevet udført af Zongpei Zhao, som forsvare sin afhandling den 17. december, 2018.

Et hovedtræk ved neurodegenerative sygdomme er, at nerveceller mister deres funktioner og henfalder. I neuroner spiller makromolekylære proteinkomplekser væsentlige roller i en række cellulære processer herunder signalering, kontrol af genudtryk, receptor aktivering, intracellulær transport samt transmission af signaler imellem nerveceller. I Huntingtons sygdom – en neurodegenerativ sygdom – er det centrale huntingtin-REST/NRSF makromolekylære proteinkompleks destabiliseret, hvilket vides at reducere udtrykket af gener, som er specifikke for neuroner. For at kunne beskrive de intramolekylære interaktioner i dette kompleks, har vi produceret disse proteiner rekombinant. Herved har vi kunne lave analyser der bidrager til at forstå interaktionerne i huntingtin-REST/NRSF komplekset.

Ved binding af den lysin-specifikke demethylase CoREST samt proteinerne histidin demethylase 1 eller 2 til det C-terminale repressor domæne af REST/HRSF dannes der det C-terminale transkriptions repressor kompleks (CRC). Dette kompleks er centralt for den transkriptionel repression i neuroner. Men strukturen af CRC komplekset er ikke velbeskrevet, og vi har derfor dannet dette kompleks for at kunne studere aktiviteten og for at karakterisere mekanismen af to nye små-molekyle inhibitorer. Ydermere har vi ved hjælp af kemisk krydsbinding og massespektrometri har vi fået indsigt i strukturen af CRC komplekset.

Forsvaret er offentligt og finder sted 17. december 2018 klokken 14:00 i Store Anatomiske Auditorium på Aarhus Universitet (Bygning 1232, lokale 115). Projektets titel er: Characterization of Macromolecular Complexes Involved in Neuronal Development. For yderligere information kontakt PhD-studerende Zhogpei Zhao; e-mail:zongpeizhao@biomed.au.dk; Telefon: +86 18222296829

Bedømmelsesudvalg: Dr. Michael Lund Nielsen, Professor, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark

Dr. Johan Jakobsson, Senior Lecturer, Lund Stem Cell Center, Lund University, Lund, Sweden

Dr. Helle H. Damkier, Associated Professor, Department of Biomedicine, Aarhus University, Aarhus, Denmark

Press release (English)

Characterization of Macromolecular Complexes Involved in Neuronal Development

The project was carried out by Zongpei Zhao, who is defending his dissertation on the 17th of December 2018.

The main characteristics of neurodegenerative diseases are known as dysfunction and death of neurons. Neuronal macromolecular complexes play a key role in signaling pathways and other cellular

processes including e.g. signal transduction, regulation of the gene expression profile, receptor activation, intracellular transport, and synaptic transmission. In Huntington disease, a neurodegenerative disorder, the central huntingtin-REST/NRSF protein complex is destabilized, which results in the repression of neuronal genes. We have produced each protein of the huntingtin complex and probed the interaction network within the complex. Our results provide insights into the organization of the huntingtin-REST/NRSF complex.

Furthermore, CoREST, the lysine specific demethylase 1, and the histone deacetylase 1 or 2 bind to the C-terminal repressor domain of REST/NRSF and form the C-terminal transcriptional repressor complex (CRC). The CRC is critical to understand the transcriptional repression mechanism. The structure of fully assembled CRC is poorly understood. Thus, we have produced the fully assembled CRC, studied its functional activity and used it to determine the drug mechanism of two newly developed small-molecule inhibitors. By using cross-linking coupled mass spectrometry, we have obtained insights into the structural organization of the CRC.

The defence is public and takes place on the 17th of Dec at 2 pm in the Large Anatomical Auditorium, Aarhus University, Building 1232 Room 115. The title of the project is "Characterization of Macromolecular Complexes Involved in Neuronal Development". For more information, please contact PhD student Zongpei Zhao, email: zongpeizhao@biomed.au.dk, Phone +86 18222296829

Assessment committee: Dr. Michael Lund Nielsen, Professor, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark

Dr. Johan Jakobsson, Senior Lecturer, Lund Stem Cell Center, Lund University, Lund, Sweden

Dr. Helle H. Damkier, Associated Professor, Department of Biomedicine, Aarhus University, Aarhus, Denmark

Permission

By sending in this form:

- I hereby grant permission to publish the above Danish and English press releases.
- I confirm that I have been informed that any applicable inventions shall be treated confidentially and shall under no circumstances whatsoever be published, presented or mentioned prior to submission of a patent application, and that I have an obligation to inform my head of department and the university's Patents Committee if I believe I have made an invention in connection with my work. I also confirm that I am not aware that publication violates any other possible holders of a copyright.