AARHUS UNIVERSITY

Press release

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Basic information

Name: Juan Yuan Email: juan@biomed.au.dk Phone: 81922685

Department of: Biomedicine

Main supervisor: Associate Professor Monika Golas

Title of dissertation: Characterization of mechanisms in neurogenesis and neuronal diseases

Date for defence: 7 December at (time of day): 13:00 Place: Lille Anatomisk Auditorium, Aarhus University, Building 1231, room 424, Wilhelm Meyers Alle 3, Aarhus

Press release (Danish)

Karakterisering af mekanismer i neurogenese og neuronale sygdomme

Et nyt ph.d.-projekt fra Aarhus Universitet, Health. Projektet er gennemført af Juan Yuan, der forsvarer sin afhandling den 7 December 2018.

Neurogenesen er processen for differentiering af neuroner fra neurale stamceller. Differentieringen af neurale stamceller til neuroner reguleres af et præcist reguleret netværk af transskriptionelle repressorer og aktivatorer. Repressor element 1 silencing transskriptionsfaktor (REST), også kaldet neuron-restriktiv silencing faktor (NSRF), er en nøgle regulator for mange neuronale gener. REST/NSRF er involveret i Huntingtons sygdoms (HD) udviklingen. Celletransplantationer har lovende udsigter for at erstatte de beskadige medium spiny neuroner (MSNer) i striatum hos HD-patienter. Celle ressourcer til transplantation er imidlertid begrænsede. I dette ph.d.-studie har vi udarbejdet effektive metoder til at differentiere humane neurale stamceller til modne og funktionelle MSNer. Vi validerede metoden ved at undersøge MSN fænotypiske markører samt ekspressionen og funktionen af MSN-berigede receptorer. De differentierede MSNer bidrager med en pålidelig ressource til en fremtidig udvikling af en celle terapi til HD-patienter. REST/NSFR har også været impliceret i cancer patogenese, så som medulloblastomaer. Epigenetiske lægemidler har vist sig at have en anti-cancer effekt på hjernetumorer. Vi undersøgte anti-cancer effekten af histone deacetylase (HDAC) hæmmere og en DNA methyltransferase 1 (DNMT1) hæmmer på medulloblastom cellelinjer. Kombinationen af HDAC-hæmmere og DNMT1-hæmmer er forslået at have en synergistisk anti-cancer effekt i medulloblastom-celler. Derudover har vi generet en cellelinje, der kan anvendes til at undersøge potentielle inhibitorer som lægemiddel kandidater rettet mod REST/NSFR i medulloblastomaer.

Forsvaret er offentligt og finder sted den 7 December kl 13:00 i Lille Anatomisk Auditorium, Aarhus Universitet, Bygning 1231, lokale 424, Wilhelm Meyers Allé 3, Aarhus C. Titlen på projektet er "Karakterisering af mekanismer i neurogenese og neuronale sygdomme". For mere information, kontakt venligst ph.d.-studerende Juan Yuan, e-mail: juan@biomed.au.dk, Telefon +45 81922685.

Bedømmelsesudvalg:

Lektor Mai Marie Holm (formand for udvalget og moderator for forsvaret)
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Lektor Kate Lykke Lambertsen
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Lektor Fredrik J. Swartling
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Press release (English)
Characterization of mechanisms in neurogenesis and neuronal diseases

The project was carried out by Juan Yuan, who is defending her dissertation on 7 December 2018.

Neurogenesis is the process of differentiation of neurons from neural stem cells. The differentiation of neurons from neural stem cells is precisely regulated by a network of transcriptional repressors and activators. The repressor element 1 silencing transcription factor (REST), also called neuron-restrictive silencer factor (NRSF), is a key regulator of many neuronal genes. REST/NRSF is involved in the pathogenesis of Huntington disease (HD). Cell transplantation holds promise to replace medium spiny neurons (MSNs) in the striatum of HD patients. However, cell resources for grafting are limited. In this PhD study, we have set up efficient methods to differentiate human neural progenitor cells into mature and functional MSNs. We validated the methods by studying MSN phenotype markers as well as the expression and function of MSN-enriched receptors. The differentiated MSNs provide reliable resources for the development of future cell therapies in HD. REST/NRSF has also been implicated in cancer pathogenesis such as medulloblastoma. Epigenetic drugs have been demonstrated to display an anti-cancer effect on brain tumors. We studied the anti-cancer effects of histone deacetylases (HDAC) inhibitors and a DNA methyltransferase 1 (DNMT1) inhibitor on medulloblastoma cell lines. The combination of an HDAC inhibitor and a DNMT1 inhibitor was suggested to mediate a synergistic anti-cancer effect in medulloblastoma cells. We also generated a cell line used to screen potential inhibitors as drug candidates for medulloblastoma with the aim to target REST/NRSF.

The defence is public and takes place on the 7 December 2018 at 13:00 in Lille Anatomisk Auditorium, Aarhus University, Building 1231, room 424, Wilhelm Meyers Alle 3, Aarhus C. The title of the project is "Characterization of mechanisms in neurogenesis and neuronal diseases". For more information, please contact PhD student Juan Yuan, email: juan@biomed.au.dk, Phone +45 81922685.

Assessment committee:

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