

Press release

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Basic information

Name: Andreas Braae Holmgaard

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Department of: Biomedicine

Main supervisor: Professor Thomas Corydon

Title of dissertation: Fighting Retinal Diseases with RNA interference and CRISPR/Cas9 genome editing

Date for defence: October 2nd at (time of day): 14.00 Place: online at Zoom
(<https://aarhusuniversity.zoom.us/j/67702729132>)

Press release (Danish)

PhD forsvar: Fokus på behandling af retinale sygdomme igennem RNA interferens og CRISPR/Cas9 genom editering.

Et nyt ph.d.-projekt fra Aarhus Universitet, Health. Projektet er gennemført af Andreas Braae Holmgaard, der forsvare det d. 2/10

Vækstfaktoren Vegfa er involveret i patogenesen for aldersrelateret macula degeneration (AMD) og anti-VEGF terapi er påvist at øge synsstyrken hos patienter. Som alternativ til gentagne intraokulære injektioner undersøger vi potentialet i en genterapeutisk tilgang med Vegfa-knockdown og knockout. Vi viser at en multigen ekspressions kassette som udtrykker PEDF og anti-VEGF shRNA'er reducerer VEGF ekspressionen i en CNV-musemodel. For at udvide anvendeligheden af retinal genomeditering undersøgte vi om der var insertioner og deletioner (indels) i Vegfa genet i RPE celler efter levering af SpCas9 via lentivirale vektorer eller lipoplekser. Efter FACS isolation af eGFP-positive RPE celler fandt vi indels i Vegfa genet ved brug af lentivirale vektorer der indeholder tre forskellige sgRNA'er. Derudover påviste vi at RNP'er med kemisk modificerede sgRNA'er danner indels i Vegfa genet efter levering af non-virale lipoplekser til retina, dog med lav effektivitet. Sammenfattet demonstrerer vi som de første retinale indels efter levering af lentivirale vektorer og RNP'er med kemisk modificerede sgRNA'er.

Forsvaret af ph.d.-projektet er offentligt og finder sted den 2/10 kl. 14.00 online på Zoom (). Titlen på projektet er "Fighting Retinal Diseases with RNA interference and CRISPR/Cas9 genome editing". Yderligere oplysninger: Ph.d.-studerende Andreas Braae Holmgaard, e-mail: anho@biomed.au.dk, tlf. 28268737.

Bedømmelsesudvalg:

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Press release (English)

Fighting Retinal Diseases with RNA interference and CRISPR/Cas9 genome editing.

The Vegfa growth factor is involved in the pathogenesis of age-related macular degeneration (AMD) and anti-VEGF therapy has been demonstrated to increase visual acuity in patients. As an alternative

to repeated intraocular injections, we evaluate the potential of gene therapeutic targeting through Vegfa knockdown and knockout. We demonstrate that a multigenic expression cassette expressing PEDF and anti-VEGF shRNAs decrease VEGF expression in a CNV mice model. In order to expand the applicability of retinal genome editing, we evaluated whether insertions or deletions (indels) could be introduced into the Vegfa gene in RPE cells following delivery of SpCas9 by lentiviral vectors or lipoplexes. Following FACS isolation of eGFP-positive RPE cells, we demonstrate indel formation in the Vegfa gene using lentiviral vectors harboring three different sgRNAs. As well, we demonstrate that non-viral lipoplex-based retinal delivery of RNPs including chemically modified sgRNAs induce indels in the Vegfa gene, however, with lower efficacy. Consequently, we as the first demonstrate retinal indels using lentiviral delivery and using RNPs containing chemically modified sgRNAs. The project was carried out by Andreas Braae Holmgaard, who is defending his dissertation on October 2nd.

The defence is public and takes place on October 2nd at 2pm online at Zoom (<https://aarhusuniversity.zoom.us/j/67702729132>). The title of the project is "Fighting Retinal Diseases with RNA interference and CRISPR/Cas9 genome editing". For more information, please contact PhD student Andreas Braae Holmgaard, email: anho@biomed.au.dk, Phone +45 2826 8737.

Assessment committee:
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