BIOGRAPHICAL SKETCH

NAME: Lies DE GROEF

POSITION TITLE: Postdoctoral researcher

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
KU Leuven, Group Science & Technology, Belgium	Ba	07/2008	Biochemistry & Biotechnology
KU Leuven, Group Science & Technology, Belgium	Ma	07/2010	Biochemistry & Biotechnology, Animal Physiology
KU Leuven, Group Science & Technology, Belgium	Ph.D.	06/2015	Neuroscience
University College London, Institute of Ophthalmology, United Kingdom	PD fellow	12/2016	Ophthalmology, Neuroscience
KU Leuven, Group Science & Technology, Belgium	PD fellow	currently	Neuroscience

A. Personal Statement

During my PhD, I have been investigating the contribution of matrix metalloproteinases to neurodegeneration, -regeneration and -inflammation in the glaucomatous eye/visual system. During these years, I have developed a deep interest in neurobiology and ophthalmology research, and gained expertise in animal models of retinal de- and regeneration, viral vector technology, advanced histological analysis and microscopy of the rodent visual system,... By performing and presenting my own research, guiding students, and co-managing and drafting other research projects, I believe my PhD has brought me more than just technical skills and made me a driven, open-minded researcher who dares to take the lead.

Since 2014, I have been closely involved in the establishment of the 'Vision Core Leuven' (www.visioncore.be), which has led to my new focus on state-of-the-art technologies for ocular imaging, electrophysiology and visual function testing. Pursuing this career turn, I've completed a one-year training in the Glaucoma and Retinal Neurodegenerative Disease Research Group at University College London (London, UK) to become an expert in *in vivo* imaging techniques to follow eye pathology in rodents (confocal ophthalmoscopy, optical coherence tomography, detection of apoptosing retinal cells).

A common theme in the research that I have pursued and that is also central to the research line that I started as a postdoctoral fellow, is the quest for neuroprotective and/or regenerative therapies to tackle neurodegenerative CNS disorders. My postdoctoral research builds upon the emerging belief that the eye is a 'window to the brain' that can be exploited for diagnosis, disease monitoring, and research of CNS diseases, and aims to study Alzheimer's and Parkinson's disease in the retina. Bridging neurobiology and ophthalmology, I aim to provide a proof-of-concept that the eye is a valuable research tool to gather new insights into the disease mechanisms of these neurodegenerative disorders, and an attractive model system for preclinical drug development. Although being trained as a basic neuroscientist, I recently also turned my interest to patients and *post mortem* human samples, to translate my preclinical work and investigate the use of retinal manifestations as biomarkers for early diagnosis of Alzheimer's and Parkinson's disease.

Altogether, my expertise in preclinical models of neurodegenerative diseases and *in vivo* retinal imaging and electrophysiology, as well as my relevant experience in single-cell RNA sequencing in the rodent retina will be essential to the successful execution of this project.

B. Positions and honors

Positions and employment

2019- Senior Postdoctoral Research Fellow, Neural Circuit Development and Regeneration Research Group, University of Leuven, Belgium & Research Foundation Flanders

2016-2019 Postdoctoral Research Fellow, Neural Circuit Development and Regeneration Research Group, University of Leuven, Belgium & Research Foundation Flanders

2016	Postdoctoral Research Fellow, Glaucoma and Retinal Neurodegenerative Disease Research Group, Institute of Ophthalmology, University College London, UK
2010-2015	PhD student, Neural Circuit Development and Regeneration Research Group, University of Leuven, Belgium & Flemish Government Agency for Innovation by Science and Technology

Other experience and Professional Memberships

2020 –	Review Editor, Frontiers in Neuroscience, Neurodegeneration Section
2020	Founding member of "The Eye as a Biomarker for AD" Professional Interest Area, Alzheimer's Association International Society to Advance Alzheimer's Research and Treatment (ISTAART)
2020	Member of PhD jury of Drs. Charline Borghgraef (KU Leuven), Emma Coninckx (KU Leuven), Charysse Vandendriessche (UGent)
2020	Guest Editor, International Journal of Molecular Sciences, special issue "Molecular Mechanisms of Neural Circuit Development and Regeneration"
2019	Reviewer, UK Medical Research Council
2016 –	Solicited Reviewer for various journals (Acta Neuropathologica, Investigative Ophthalmology and Visual Science, Experimental Eye Research, BMC Ophthalmology, Neural Regeneration Research, Scientific Reports)

Member of the Belgian Society for Extracellular Vesicles (BESEV), International Society for Extracellular Vesicles (ISEV), European Association for Vision and Eye Research (EVER), Association of Research in Vision and Ophthalmology (ARVO), Society for Neuroscience (SfN), Alzheimer's Association International Society to Advance Alzheimer's Research and Treatment (ISTAART).

Honors and awards

2020	Alzheimer's Research Foundation (SAO-FRA), pilot research grant for junior researchers
2016	Research Foundation Flanders, travel grant for a research stay abroad (for stay at UCL)
2016	Awarded by the Fund for Research in Ophthalmology, prize Ligue Braille
2015	Alumni of Botany and Zoology of KU Leuven, triennial prize for most outstanding PhD thesis in Biology
2012 – 2018	Travel grants from Research Foundation Flanders and Academische Stichting Leuven to attend international scientific meetings (Honolulu, USA; Washington, USA; Denver, USA; Nice, France)
2011	First prize awarded by the Fund for Research in Ophthalmology
2010	Royal Flemish Society for Chemistry, award for most commendable graduating biochemistry student

Scholastic Performance

- Training and supervision of >20 bachelor and master students, Faculty of Sciences, Department of Biology, KU Leuven, Belgium
- Supervision of 5 PhD students (3 ongoing, 2 completed), Faculty of Sciences, Department of Biology, KU Leuven, Belgium

C. Contributions to Science

I. Retinal manifestations of Parkinson's disease

I consider my major achievement thus far the setting-up of my autonomous research program, focused on alpha-synucleinopathy in the retina/visual system. Although still under the umbrella of the Neural Circuit Development and Regeneration research group, I've set up a research line that is fully independent from that of my PhD promotor. From a scientific point of view, the paper by Normando *et al*., to which I contributed during my postdoctoral fellowship at University College London, was groundbreaking in that it was the first to show retinal alterations in an experimental animal model of Parkinson's disease. Later papers of mine, including the Acta Neuropathologica paper by Veys *et al*., further added to this research line and have helped to establish myself in this field:

- Normando, E.M., Davis, B.M., De Groef, L., Nizari, S., Turner, L.A., Ravindran, N., Pahlitzsch, M., Brenton, J., Malaguarnera, G., Guo, L., Somavarapu, S., Cordeiro, M.F. (2016). The retina as an early biomarker of

neurodegeneration in a rotenone-induced model of Parkinson's disease: evidence for a neuroprotective effect of rosiglitazone in the eye and brain. Acta Neuropathologica Communications, 4 (86), 1-15. PMID: 27535749

- Veys, L., Van houcke, J., Aerts, J., Van Pottelberge, S., Mahieu, M., Bousset, L., Melki, R., Moechars, D., De Muynck, L., De Groef, L. (2020) Absence of uptake and prion-like spreading of alpha-synuclein and tau after intravitreal injection of preformed fibrils. Under review for Frontiers in Aging Neuroscience
- Veys, L., Vandenabeele, M., Ortuño-Lizarán, I., Baekelandt, V., Cuenca, N., Moons, L., De Groef, L. (2019). Retinal alpha-synuclein deposits in Parkinson's disease patients and animal models. Acta Neuropathologica, 137 (3), 379-395. PMID: 30721408
- Guo, L., Normando, E.M., Shah, P., De Groef, L.*, Cordeiro, M.F.* (2018). Oculo-visual abnormalities in Parkinson's disease: possible value as biomarkers. Movement Disorders, 33 (9), 1390-1406. (*joint senior authors) PMID: 30311977

II. Retinal biomarkers for Alzheimer's diagnosis and research into its preclinical phase

The research paper by Vandenabeele *et al.* is one of my major achievements for two reasons. First, because it is the result of collaborative research in a consortium of national and international partners, with clinicians, scientists and engineers. Since 2016, I have been leading the preclinical mouse work for this project, and I was also (co-)responsible for research coordination and grant writing in this consortium. This led to the adoption of the project by the Mission lucidity initiative (https://www.missionlucidity.com/project/eye-window-brain-1) and recent successful funding applications within 1) the EU Joint Programme – Neurodegenerative Disease Research and 2) the Global PhD Partnership KU Leuven-University of Melbourne. As such, it shows my experience with managing large, multi-partner projects. Second, this manuscript is an exemplification of the strengths of the retina as a model for CNS research. It showcases the quality and quantity of data that can be gathered using in vivo retinal imaging and electrophysiology, and the genericity of these findings (i.e., retinal disease manifestations mirroring those seen in the brain). We believe that this paper will have a large impact on the Alzheimer's research field, as it presents the first animal model for research into the pre-symptomatic, preclinical phase of Alzheimer's. Underscoring the high translational potential of this research, the imaging technology that I implemented during this study was later also used in a pilot clinical trial in AD patients:

- Vandenabeele, M., Veys, L., Lemmens, S., Hadoux, X., Gelders, G., Serneels, L., Theunis, J., De Boever, P., Stalmans, I., De Strooper, B., Van Wijngaarden, P., Moons, L., De Groef, L. (2020) The APP NLGF mouse retina is a site for preclinical Alzheimer's disease diagnosis and research. In revision for Acta Neuropathologica Communications (https://doi.org/10.1101/2020.07.25.220707)
- Lemmens, S., Van Craenendonck, T., Van Eijgen, J., De Groef, L., Bruffaerts, R., Andrade de Jesus, D., Charle, W., Jayapala, M., Sunaric-Mégevand, G., Standaert, A., Theunis, J., Van Keer, K., Vandenbulcke, M., Moons, L., Vandenberghe, R., De Boever, P., Stalmans, I. (2020) Combination of snapshot hyperspectral retinal imaging and optical coherence tomography to identify Alzheimer's disease patients. Alzheimer's Research & Therapy, in press.

III. Neuron-glia communication in the retina

A third achievement is one of my latest papers in Glia. In this study, which was founded on results that I gathered during my PhD and later, under my supervision, completed by PhD student E. Lefevere (co-promotor), we disentangled the complex interplay between neurons and glia at the blood-retinal barrier. It adds new evidence to the biological phenomenon of blood-retinal (or brain) barrier tightening, which – in contrast to the opposite process of disruption – is barely studied in the CNS and may be a missing link in our understanding of the physiology/pathology of the CNS neurovascular unit. This paper reflects my research focus on neuron-glia interactions in the CNS. In fact, it should be considered together with multiple others, including those that resulted from my PhD research (cfr. below for a selection). Together, they illustrate my broad expertise in neurodegeneration and -inflammation research in the mouse visual system, which forms the basis of my future research plans:

- Lefevere E.*, Salinas-Navarro M.*, Andries L., Noterdaeme L., Etienne I., Van Wonterghem E., Davis BM., Van Bergen T., Vinkier S., Van Hove I., Movahedi K., Vandenbroucke RE., Moons, L.*, De Groef L.* (2020). Tightening the retinal glia limitans attenuates neuroinflammation after optic nerve injury. Glia, 68(12), 2643-2660. (*joint senior authors) PMID: 32645232
- De Groef, L., Andries, L., Siwakoti, A., Geeraerts, E., Bollaerts, I., Noterdaeme, L., Etienne, I., Papageorgiou, A-P., Stalmans, I., Billen, J., West-Mays, J.A., Moons, G. (2016). Aberrant Collagen Composition of the Trabecular

Meshwork Results in Reduced Aqueous Humor Drainage and Elevated IOP in MMP-9 Null Mice. Investigative Ophthalmology & Visual Science, 57 (14), 5984-5995. PMID: 27820954

- De Groef, L.*, Dekeyster, E.*, Geeraerts, E., Lefevere, E., Stalmans, I., Salinas-Navarro, M., Moons, L. (2016). Differential visual system organization and susceptibility to experimental models of optic neuropathies in three commonly used mouse strains. Experimental Eye Research, 145, 235-247. (*joint first authors) PMID: 26791081
- Dekeyster, E., Geeraerts, E., Buyens, T., Van Den Haute, C., Baekelandt, V., De Groef, L., Salinas-Navarro, M., Moons, L. (2015). Tackling Glaucoma from within the Brain: An Unfortunate Interplay of BDNF and TrkB. PLoS One, 10 (11), 1-28. PMID: 26560713
- De Groef, L., Salinas Navarro, M., Van Imschoot, G., Libert, C., Vandenbroucke, R., Moons, L. (2015). Decreased TNF levels and improved retinal ganglion cell survival in MMP-2 null mice suggest a role for MMP-2 as TNF sheddase. Mediators of Inflammation, 2015 (2015). PMID: 26451076

IV. Image analysis tools to study retinal neurodegeneration and -inflammation

I published a series of papers (cfr. below) dedicated to the development and validation of image analysis methods to study retinal neurodegeneration and -inflammation, which are essential tools for the research that I'm conducting. The goal of these is to maximize the information extracted from microscopy images via a combination of classic imaging analysis techniques and advanced statistics and/or deep learning. All of these tools are freely available as user-friendly software, as part of my commitment to supporting open science. This research has been propelled by a collaboration with Dr. B. Davis, that I've initiated during my postdoctoral fellowship at University College London, and that still lasts up till today.

- Davis, M.B., Guo, L., Ravindran, N., Shamsher, E., Baekelandt, V., Mitchell, H., Bharath, A.A., De Groef, L.*, Cordeiro, M.F.* (2020) Dynamic Changes in Cell Size and Corresponding Cell Fate After Optic Nerve Injury. Scientific Reports, in press
- Masin, L., Claes, M., Bergmans, S., Cools, L., Andries, L., Davis, B.M., Moons, L., De Groef, L. (2020) RGCode: a novel Retinal Ganglion Cell quantification tool based On DEep learning. Scientific Reports, in press.
- Davis, B.M., Salinas-Navarro, M., Cordeiro, M.F., Moons, L., De Groef, L. (2017). Characterizing microglia activation: a spatial statistics approach to maximize information extraction. Scientific Reports, 7, Art.No. 1576. PMID: 28484229
- Geeraerts, E., Dekeyster, E., Gaublomme, D., Salinas Navarro, M., De Groef, L., Moons, L. (2016). A freely available semi-automated method for quantifying retinal ganglion cells in entire retinal flatmounts. Experimental Eye Research, 147, 105-113. PMID: 27107795

V. As a final achievement, I've chosen the scRNAseq study that I recently conducted, in collaboration with Oxurion NV (Leuven) and the Laboratory of Translational Genetics (VIB-KU Leuven). In this study, we specifically focused on the phenotypic changes in retinal macroglia in response to diabetic retinopathy and identified several subpopulations of astrocytes/Müller glia that specialize to perform distinct functions in the diabetic retina. As such, this study contributes to a better understanding of glia biology in the retina. Notably, this scRNAseq study was the first performed within the KU Leuven Biology department. Hence, besides my excellent relations with industry (here the biopharma company Oxurion), this paper shows my ability to adopt new technologies by engaging in collaborations with experts in different fields and my standing expertise in scRNAseq data analysis.

- Van Hove, I.*, De Groef, L.*, Boeckx, B., Modave, E., Hu, T., Beets, K., Etienne, I., Van Bergen, T., Lambrechts, D., Moons, L., Feyen, J., Porcu, M. (2020). Single-cell transcriptomics analysis of Akimba retina reveals cell type-specific insights into the pathology of diabetic retinopathy. Diabetologia, 63(10), 2235-2248. (*joint first authors) PMID: 32734440

My scientific output consists of 42 papers in peer-reviewed international journals (9 first author, 8 senior author contributions), as well as 2 book chapters. This work resulted in an h-index of 14 and a total of 451 citations (no self-citations; Web of Science; November 2020). For a complete publication list and an additional list of papers presented at international meetings please see: https://lirias.kuleuven.be/cv?u=U0073996

D. Research Support

Ongoing Research Support

Global PhD Partnership KU Leuven - University of Melbourne (2 joint PhD projects) 2021 – 2024
"The eye as a window to the brain: tackling neurodegenerative disorders"
Role: co-PI Goal: Preclinical and clinical research into retinal biomarkers for Alzheimer's diagnosis

EU Joint Programme - Neurodegenerative Disease Research 2021 – 2023
"Global retinal imaging consortium for Alzheimer's disease (BRAINSTORM)"
Role: partner Goal: Preclinical and clinical research into retinal biomarkers for Alzheimer's diagnosis

Central Europe Leuven Strategic Alliance (CELSA) 2020 – 2022
"Ferroptosis: a novel paradigm in the neurodegenerative pathology of Wolfram syndrome"
Role: co-PI Goal: Study ferroptosis as a disease mechanism underlying Wolfram syndrome, with a focus on the visual system

Alzheimer's Research Foundation (SAO-FRA) 2020 – 2022
"A preclinical research platform for Alzheimer's disease in the eye"
Role: PI Goal: Validation of the retina and retinal imaging/electrophysiology read-puts for preclinical research in mouse models of Alzheimer's disease

Queen Elisabeth Medical Foundation 2020 – 2022
"Oligodendrocytes in Wolfram syndrome: bystanders or partners in crime?"
Role: co-PI Goal: Study the differential contribution of neurons *versus* oligodendrocytes to Wolfram syndrome pathogenesis in iPSC and mouse models

FWO fellowship to Drs. Marjan Vandenabeele 2019 – 2023
"Unraveling the importance of oligodendrocytes in neurodegeneration: a new look on Wolfram syndrome."
Role: co-promotor Goal: Study the differential contribution of neurons *versus* oligodendrocytes to Wolfram syndrome pathogenesis in iPSC and mouse models

C14/18/053 KU Leuven 2018 – 2022
"Intra-neuronal energy channeling: a prerequisite for functional CNS repair"
Role: co-PI Goal: Investigation of the cellular metabolic processes driving axonal regeneration in the mammalian visual system

FWO SB fellowship to Drs. Lien Veys 2018 – 2022
"The eye as a window to the brain: modulating neuroinflammation to halt retinal alpha-synucleinopathy"
Role: co-promotor Goal: Investigation of the impact of alpha-synucleinopathy on the retina, with a special focus on neuro-inflammation, in newly developed mouse models

1526218N Research Foundation Flanders 2018 – 2020
"The eye as a window to the brain: new look on Alzheimer's and Parkinson's disease."
Role: PI Goal: Investigation of the retina and retinal imaging/electrophysiology read-puts for preclinical research in mouse models of Alzheimer's and Parkinson's disease

G053217N Research Foundation Flanders 2017 – 2020
"Neuroinflammation as motor for axonal regeneration: a quest for underlying molecular players"
Role: co-PI Goal: Study of the molecar players driving axonal regeneration in the mammalian visual