ERASMUS UNIVERSITEIT ROTTERDAM

Erasmus University Rotterdam, the Netherlands
CSC PhD 2015 Project Description

School/Department:	**Department of Ophthalmology and Epidemiology** **Erasmus Medical Center, Rotterdam** Research schools: **Molecular Medicine research school (www.molmed.nl)** **Netherlands Institute for Health Sciences (NIHES; www.nihes.nl).**
Project Title:	**Systems-level analysis of myopia-relevant pathways**
Abstract:	Myopia (near-sightedness) is a growing public health issue due to its rapidly rising prevalence all over the world. In particular high myopia carries a significant risk of blindness for which there are no treatment options. The disease etiology of this trait is complex and largely unknown. Using genetic data of large study cohorts we recently identified over 100 disease loci and genes that are correlated with myopia. A simple search for the function of these genes provide important clues for pathways involved in myopiagenesis and include neurotransmission, ion channelling, retinoic acid metabolism, extracellular matrix formation, and eye development. How these genes integrate in a network at the cellular level (systems biology) is unknown and is crucial for the next step in defining disease mechanisms and is the main goal for this research. The project will be performed in close collaboration with Prof. Luis Serrano and Dr. Christina Kiel (CRG, Barcelona) and Prof. Phil Luthert (London) who have pioneered systems biology approaches and are harnessing them to solve the challenges of complex disorders. A systems representation of the pathways, cells and extracellular compartments of significance in myopia will provide important clues to identify of putative targets for further therapeutic research and prevention modules. Relevant literature: • Verhoeven VJM, Hysi PG, ……. , Stambolian D, **Klaver CCW***, Hammond CJ. *Genome-wide meta-analyses of multiancestry cohorts identify multiple new susceptibility loci for refractive error and myopia.* Nature Genetics. 2013;45(3):314-8. ***Klaver CCW** shared last, and corresponding author • Verhoeven VJM, Buitendijk GHS, Rivadeneira F, Uitterlinden AG, Vingerling JR, Hofman A, **Klaver CCW**. *Education influences the*

	role of genetics in myopia. European Journal of Epidemiology. 2013;28(12):973-80. • Kiel C, Serrano, L. Structural Data in Synthetic Biology Approaches for Studying General Design Principles of Cellular Signaling Networks. Structure. 2012; 20(11):1806 • Serrano, L. Synthetic biology: promises and challenges. Molecular systems biology. 2007; 3: 158
Requirements of candidate:	The candidate should have a degree in **biology, molecular biology, (bio)medical sciences or general medicine** and needs to have **affinity for working with large datasets.** Master degree: Yes IELTS Grade: 7.0 *(minimal 6.0 per component)* *or* TOEFL: *100 (minimal 20 per component)*
Supervisor information:	Name: Prof.dr. C.C.W. Klaver Email: m.meester-smoor@erasmusmc.nl (postdoc) website: www.myopiestudie.nl (in dutch) her research group is embedded in: Molecular Medicine research school (www.molmed.nl) Netherlands Institute for Health Sciences (NIHES; www.nihes.nl). Short CV including publications: see on following pages.

Curriculum Vitae

Name, first name and initials:	Klaver, Caroline C.W.
Date of birth:	May 5, 1967
Nationality:	Dutch
URL web site:	www.myopiestudie.nl (in dutch)

Academic Degrees

2000 PhD Erasmus Medical Center (MC) Rotterdam; *cum laude*
1997 MSc Clinical Epidemiology; Netherlands Institute for Health Sciences, Rotterdam
1993 MD General Medicine; Erasmus MC Rotterdam; *cum laude*

International training

2002-2003 Post-doc Retina & Genetics, Columbia University & VRM Consultants, New York
2001 (5 mo) Post-doc Ophthalmic Genetics & Pathology, University of Iowa
1997 (1 mo) PhD student; AMD-classification system, University of Madison, Wisconsin
1989 (9 mo) Master student; Neonatal Tolerance, Dept. Immunology; University of Miami

Appointments

2012-now Professor of Ophthalmology and Epidemiology, Erasmus MC, Rotterdam
2008-2011 Associate Professor, Erasmus MC, Rotterdam
2003-now Ophthalmologist and Clinical Researcher (0.8-0.9 fte), Erasmus MC, Rotterdam
2003-2006 Senior Researcher (0.2 fte), Netherlands Institute for Neuroscience, Amsterdam

Present Activities

- Research (50%):
Main research themes: clinical and genetic epidemiology, and mechanisms of 4 eye disorders: *refractive error/myopia; age-related macular degeneration; retinal dystrophies; primary open-angle glaucoma*. My group focuses on identification of risk factors; gene finding; gene-environment interaction; imaging and phenotyping; prognostic modelling; pathway annotation; functional studies in animal models.

- Clinical work (40%):
Clinical ophthalmologist - expert on ophthalmic genetics; retina; paediatric ophthalmology.

- Teaching (10%):
Senior lecturer at Erasmus Medical School; supervisor of Master students in Ophthalmology.

Leadership and organization

- Research Team:
Promotor and supervisor of 9 PhD students; expected PhD degree in 2014 (1x); 2015 (2x); 2016 (2x); 2017 (2); supervisor of 1 Post-doc, 1 MSc student, and 4 research assistants. Two PhD students graduated in 2008 and 2011, respectively.

- Principal Investigator:
PI of Ophthalmology in population-based Rotterdam Study (N=10,000); in family-based ERF study (N=2,600); in Generation R (N=7,000); PI and founder of Rotterdam studies on high myopia (N=1,200); retinal dystrophies (N=1,000); of CORRBI biobank for genetic eye diseases (N=2,000); of GIGA study on Glaucoma in Africa (N=2,000).

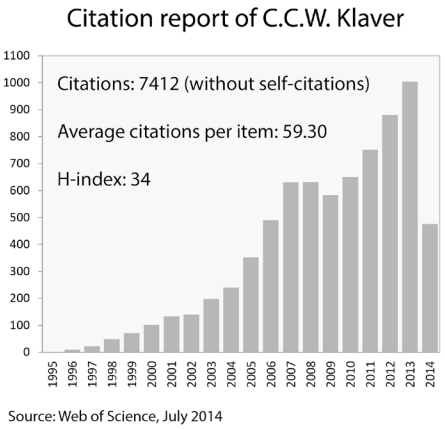
- **Initiation and organization:**
Founder of the international CREAM consortium for refractive error and myopia (38 studies; N=63,000). Initiator and organizer of 2-yearly Lowlands Ophthalmogenetic meetings (2011-now); organizing team for the yearly consortium meetings of CREAM and E3 (2011-now); steering committee of the National Workgroup for Medical Retina (2010-now); initiator of teaching seminars for eye care professionals in NL (2009-now).

Publications

- 133 publications, 5 reviews, 5 book chapters, 2 invited editorials

- 114 publications in first Quartile (Q1)

- H-index: 34



List of top 10 publications

- Verhoeven VJM, Hysi PG, Wojciechowski R, Fan Q, Guggenheim JA, Höhn R, . . ., **Klaver CCW***, Hammond CJ. Genome-wide meta-analyses of multiancestry cohorts identify multiple new susceptibility loci for refractive error and myopia. *Nature Genetics*. 2013;45:314-8.
  ***Klaver CCW** shared last and corresponding author [IF 35.21; Q1; Citations (without self) 25]
- Cheng CY, Schache M, Ikram MK, Young TL, Guggenheim JA, Vitart V, . . . **Klaver CCW***. . . Baird PN. Nine loci for ocular axial length identified through genome-wide association studies, including shared loci with refractive error. *Am J Hum Genet.* 2013;93:264-77.
  ***Klaver CCW** shared last author [IF 11.20; Q1; Citations 2]
- Fritsche LG, Chen W, Schu M, Yaspan BL, Yu Y, Thorleifsson G, . . ., **Klaver CCW,** . . . Abecasis GR. Seven new loci associated with age-related macular degeneration. *Nature Genetics.* 2013;45:433-9. [IF 35.21; Q1; Citations 33]
- Solouki AM, Verhoeven VJM, Van Duijn CM, Verkerk AJMH, Ikram MK, Hysi PG, . . . **Klaver CCW**. A genome-wide association study identifies a susceptibility locus for refractive errors and myopia at 15q14. *Nature Genetics.* 2010;42:897-901. [IF 35.21; Q1; Citations 73]
- Hysi PG, Young TL, MacKey DA, Andrew T, Fernández-Medarde A, Solouki AM, . . ., **Klaver CCW**, Hammond CJ. A genome-wide association study for myopia and refractive error identifies a susceptibility locus at 15q25. *Nature Genetics.* 2010;42:902-5. [IF 35.21; Q1; Citations 78]
- Thiadens AAHJ, den Hollander AI, Roosing S, Nabuurs SB, Zekveld-Vroon RC, Collin RW, De Baere E, Koenekoop RK, van Schooneveld MJ, Strom TM, van Lith-Verhoeven JJ, Lotery AJ, van Moll-Ramirez N, Leroy BP, van den Born LI, Hoyng CB, Cremers FP, **Klaver CCW.** Homozygosity mapping reveals PDE6C mutations in patients with early-onset cone disorders. *Am J Hum Genet* 2009;85:240-7. [IF 11.20; Q1; Citations 48]
- Despriet DD, van Duijn CM, Oostra AG, Hofman A, Wright AF, ten Brink JB, Bakker A, de Jong PT, Vingerling JR, Bergen AA, **Klaver CCW.** Complement component C3 and risk of age-related macular degeneration. *Ophthalmology*. 2009;116:474-480. [IF 5.45; Q1; Citations 40]
- Despriet DDG, **Klaver CCW**, Witteman JCM, Bergen AAB, Kardys I, de Maat MPM, Boekhoorn SS, Vingerling JR, Hofman A, Oostra BA, Uitterlinden AG, Stijnen T, van Duijn CM, de Jong PTVM. Complement factor H,polymorphism, complement activators, and risk of age-related macular degeneration. *JAMA.* 2006;296:301-309 [IF 30.01; Q1; Citations 178]
- Hageman GS, Anderson DH, Johnson LV, Hancox LS, Taiber AJ, Hardisty LI, . . ., **Klaver CCW,** . . . , Dean M, Allikmets R. A common haplotype in the complement regulatory gene factor H (HF1/CFH) predisposes individuals to age-related macular degeneration. *Proc Natl Acad Sci*. 2005;102:7227-32. [IF 9.68; Q1; Citations 951]
- **Klaver CCW,** Kliffen M, van Duijn CM, Hofman A, Cruts M, Grobbee DE, van Broeckhoven C, de Jong PTVM. Genetic association of apolipoprotein E with age-related macular degeneration. *Am J Hum Genet.* 1998;63:200-6. [IF 11.20; Q1; Citations 225]