BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Cremers, Frans P.M.	Full professor in Ophthalmogenetics

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Radboud University Nijmegen, Nijmegen	M.Sc.	12/84	Biology
Radboud University Nijmegen, Nijmegen	Ph.D.	04/91	Molecular Genetics

A. Positions and Honors.

Positions and Employment

1986 - 1990	Department of Human Genetics: Ph.D. student.
1990 - 1991	Department of Human Genetics: Assistant Professor.
1991 - 1992	Department of Human Genetics: Royal Netherlands Academy of Arts and Sciences (KNAW) fellow. Co-head Molecular Genetics Division.
1992 - 1993	University of Texas, SW Medical School, Dallas. Fellow with drs. M. Brown & J. Goldstein.
1993 - 1996	Department of Human Genetics: KNAW-fellow. Co-head Molecular Genetics Division.
1996 - 1999	Department of Human Genetics: Assistant Professor. Head of Molecular Genetics Division.
2000 - 2004	Department of Human Genetics: Associate Professor. Head of Molecular Genetics Division.
2004 - present	Department of Human Genetics: Full Professor in molecular biology of inherited eye disease.
2005 - 2010	Director of international research Master Molecular Mechanisms of Disease.
2011 - 2016	Director of the Foundation Fighting Blindness USA Nijmegen Center Grant.
2017 - present	Director of the Foundation Fighting Blindness USA Nijmegen Program Project Award entitled 'Splice Modulation to Treat Inherited Retinal Diseases'.

Other Experience and Professional Memberships

1988 – present	Member of American Society of Human Genetics
1994 – present	Member of Association for Research in Vision and Ophthalmology
1995 – 2014	Editorial board member of Ophthalmic Genetics
1997 – 2002	Editorial board member Human Molecular Genetics
1998 – present	Member of the Retina International Scientific Advisory Committee
1998 – 2007	Member of Medical Advisory Board of Retina Netherlands
2003 – 2005	Guest editor for Investigative Ophthalmology & Visual Sciences
2004	Chairman Scientific Committee 13th World Congress of Retina International, Noordwijk, NL
2005 – 2010	Director of international research master RUMC 'Molecular Mechanisms of Disease'
2009 – 2013	Member of national research programme review committee (VIDI-ZonMw)
2009 – present	Adjunct Honorary Professor Comsats Institute of Information Technology, Islamabad, Pakistan.
2012 – 2020	Chairman Foundation Studyfund Radboud University Medical Center
2015 – present	Foundation Fighting Blindness USA Scientific Advisory Board member
2019 – 2021	Choroideremia Research Foundation Scientific Advisory Board member

Honors and Awards

- Student award' 'predoctoral basic'; 41st Annual Meeting; Am. Soc. Hum. Genet.', Oct. 1990, Cincinnati, USA.
- Retinitis Pigmentosa Award for the Prevention of Blindness 1990, February 1991, Essen, Germany.
- Cum laude Ph.D thesis: 'Positional cloning of a candidate gene for choroideremia', April 1991.
- First European Vision Award October 2007, Portoroz, European Vision Institute.
- Principal Investigator in the Radboud University Medical Center Nijmegen (2009-present).
- Principal Lecturer Star in the Radboud University Medical Center Nijmegen (2010).
- Internationalisations Award from the Radboud University Nijmegen (2010).
- Candle In The Dark - Childvision Research Award (2013).
- Guest professor at the Faculty of Medicine Universitas Indonesia in Jakarta (2014-2016; 2018-present).

- Ed Gollob Board of Directors Award; for the best publication in Ophthalmology in 2019 (2020).
- Retina International Lifetime Achievement Award (2021).

B. Biography

Prof. Cremers is professor of ophthalmogenetics in the Department of Human Genetics and the Donders Institute for Brain, Cognition and Behaviour in the Radboudumc in Nijmegen, The Netherlands. He performed his PhD study, entitled 'positional cloning of the choroideremia gene', in Nijmegen, under the supervision of Prof. B. Wieringa and Prof. H-H. Ropers. He headed the Division of Molecular Genetics from 1992 – 2011 and was the director of the master program Molecular Mechanisms of Disease from 2005 – 2010.
He published 347 peer-reviewed papers and 15 book chapters on molecular genetics of inherited retinal diseases (IRDs). He supervised 34 PhD students and 8 postdocs, of whom 7 are now full professors (among which Camiel Boon, Rob Collin, Anneke den Hollander, Ronald Roepman) or assistant professor (Susanne Roosing).
He initiated and coordinated national (RD5000) and international (European Retinal Disease Consortium) collaborations in the IRD field. He is the director of the Foundation Fighting Blindness USA Program Project Award entitled 'Splice Modulation to Treat Inherited Retinal Diseases' and is co-chairing the Genetic Diagnostics Transworkgroup in ERN-EYE.
His team was significantly involved in the identification of 32 IRD-associated genes, among which the X-linked choroideremia and RP3/*RPGR* gene, genes associated with Leber congenital amaurosis (*CEP290, CRB1, LCA5),* autosomal recessive retinitis pigmentosa *(EYS, USH2A*), autosomal recessive cone dystrophy (*PDE6C, POC1B*), as well as familial exudative vitreoretinopathy (*TSPAN12, ZNF408)*. He also discovered the first hearing impairment gene, *POU3F4*, implicated in X-linked DFN3.
Recently, he published on the genetic landscape of Stargardt disease. He discovered hidden intronic mutations in the *ABCA4* gene by sequencing >3.000 Stargardt disease probands and employing stem cell technology and transcriptomics.

In the 2020-2024 period, he is performing three very large international studies Website link.:
1. IRD variant & cases collection for 200 genes:
He coordinates 12 international teams that collect all gene variants published in 200 IRD-associated genes, as well as the IRD cases in whom the variants were found. These teams will then go on to interpret and classify all variants according to their pathogenicity and upload all variants in open access databases (LOVD, ClinVar).
2. Genotyping of 3,000 macula disease probands:
Employing an adapted smMIPs-based targeted sequencing technology, 3,000 macula disease (MD) cases and controls will be sequenced for exonic and known causal deep-intronic variants in 105 genes implicated in inherited MD and age-related MD. By comparing the frequency of variants in cases and controls, he aims to shed light on putative overlapping genetic factors and modifiers for these MDs. The inherited MD cases are unsolved probands from the STGD-MD *ABCA4* 'complete gene' smMIPs study ascertained by 25 international collaborators.
3. Genotyping of 4,000 retinitis pigmentosa and Leber congenital amaurosis probands:
Employing an adapted smMIPs-based targeted sequencing technology, 4,000 RP and LCA probands will be sequenced for exonic and known causal deep-intronic variants in 110 genes implicated in RP and LCA, with special emphasis on the *RPE65* gene, for which a gene therapy is available. These probands also have been ascertained by >25 collaborators worldwide.
Both genotyping platforms will be instrumental to cost-effectively sequence a significant fraction of unsolved MD, RP and LCA cases. He considers that these two gene sequencing platforms encompass >90% of the genetic defects for these conditions, so the ultimate goal is to solve >90% of the MD, RP and LCA cases by 2025.

C. Research grants (current)

Novartis. Cost-effective identification of causal variants in 110 genes underlying Leber congenital amaurosis and retinitis pigmentosa in 4,000 probands, with a special focus on *RPE65*; PI, F.P.M. Cremers; co-PIs: S. Roosing, A. Hoischen; € 597,158; 01/2021 – 04/2024.

Health Research Charities Ireland – Health Research Board. High-throughput sequencing of inherited and multifactorial macula disease-associated genes and risk factors allows identification of genetic interactions and modifiers; co-applicants: F.P.M. Cremers, G.J. Farrar, A.I. den Hollander, S. Roosing, C.-M. Dhaenens; € 300.000; [Nijmegen € 150.000]; 06/2021 – 05/2024.

Stichting voor Ooglijders, ProRetina, Stichting Blindenhulp, Oogfonds; Pilot study: High-throughput sequence analysis of maculopathy probands employing smMIPs for all reported inherited and multifactorial maculopathy-associated genes and risk factors. PI F.P.M. Cremers and co-PIs Prof. dr. A.I. den Hollander, Dr. C-M. Dhaenens, Dr. S. Roosing; € 120.000; 05/2020 – 09/2020.

European Joint Programme on Rare Diseases (EJPRD) - ZonMw. Solving missing heritability in inherited retinal diseases using integrated omics and gene editing in human cellular and animal models (Solve-RET). PI: E. de Baere; co-PIs: S. Banfi, F.P.M. Cremers, H. Dollfus, J.L. Gomez-Skarmeta, P. Liskova, M. Spielmann, C. Rivolta. Total budget: € 1,654,600; Nijmegen part: € 250,000; 06/2020 – 05/2023.

Foundation Fighting Blindness USA. Comprehensive registry and in silico assessment of variants associated with non-syndromic inherited retinal diseases, Bardet-Biedl syndrome and Usher syndrome; PI: Prof. dr. J.T. den Dunnen (Leiden) and Prof. dr. F.P.M. Cremers (Nijmegen); co-PIs: Dr. S. Roosing (Nijmegen) and I.F.A.C. Fokkema (Leiden), FFB Award Number: BR-GE-0120-0775-LUMC; total budget for all 12 teams involved: $ 585,211; Nijmegen part $ 88,224; 01/2020-12/2022.

RadboudUMC project. Solving the unsolved sensory diseases by combining transcriptome sequencing of sensory progenitor cells and WGS; PIs: H. Kremer, F. Cremers; € 206.000; 05/2017-06/2021.

RetinaUK-Macular Society. Natural exon skipping in *ABCA4* mRNA and its modulation as a novel genetic therapy for Stargardt disease; PI: R.W.J. Collin; co-PI: F.P.M. Cremers; £ 120.000; 11/2018 – 10/2021. [https://retinauk.org.uk/research/research-we-fund/innovation-fund-projects/]

European Union. Horizon 2020, Marie Sklodowska-Curie Innovative Training Network entitled 'European Training Network to Diagnose, Understand and Treat Stargardt Disease, a Frequent Inherited Blinding Disorder'-'StarT' (813490). PI: E. de Baere, Ghent. Co-PIs: K. Vleminckx, F. Coppieters, Ghent; F.P.M. Cremers, R.W.J. Collin, Nijmegen; S. Banfi, A. Auricchio, Naples; S. Kohl, Tuebingen; C. Toomes, Leeds; J-L. Gomez-Skarmeta, Barcelona; G.J. Farrar, Dublin; M.E. Cheetham, London. Commercial partners: M. Lako, NewCells, Newcastle and P. Adamson, ProQR, Leiden. Partner organizations: Retina International, Fighting Blindness Ireland, 20Med Therapeutics, F. Hofmann – La Roche Ltd. and the European Vision Institute. Total budget: € 3.776.714; F.P.M. Cremers part: € 265.620; 11/2018 – 10/2022. [https://www.startn.eu/]

Velux Foundation. Identification and treatment of non-coding USH2A variants underlying Usher syndrome and retinitis pigmentosa; PIs, H. Kremer, F.P.M. Cremers, E. van Wyk, S. Roosing; € 397,000; 05/2018 – 04/2022. [https://veluxstiftung.ch/foundation/#foundation4; see Annual Report 2017]

Foundation Fighting Blindness USA Project Program Award entitled 'Splice Modulation to Treat Inherited Retinal Diseases'; PI: F.P.M. Cremers; co-PIs: R.W.J. Collin, H.A.R. van Wijk, A. Garanto, C.B. Hoyng, S. Roosing, S. Albert, R. van Huet, total budget: $ 2.500.000; module 1 budget $ 542.800,-.; 05/2017 – 04/2022. [https://www.fightingblindness.org/funded-grants]

Foundation Fighting Blindness USA Individual Investigator Award entitled 'Deciphering the mechanisms underlying variable expression and non-penetrance of Stargardt disease'; PI: F.P.M. Cremers; co-PI: S. Roosing; budget: $ 299.147,-; 06/2018 – 05/2022. [https://www.fightingblindness.org/funded-grants]

Fighting Blindness Ireland. Shedding light on unexplained inherited retinal diseases in Ireland and the Netherlands; co-PIs: J. Farrar, F.P.M. Cremers, S. Roosing, M. Carrigan; € 340.000; 03/2018 – 12/2021. [https://www.fightingblindness.ie/shedding-light-on-unexplained-inherited-retinal-diseases-in-ireland-and-the-netherlands/]

D. Selected peer-reviewed Publications (from 2012 – present; from 347 peer-reviewed publications)

1. Estrada-Cuzcano, A., Neveling, K., [17 co-authors], the ERDC, den Hollander, A.I., Klevering, B.J. & **Cremers, F.P.M.** Mutations in C8orf37, encoding a ciliary protein, are associated with autosomal-recessive retinal dystrophies with early macular involvement. (2012) *Am. J. Hum. Genet.* **90**, 102-109.
2. Collin, R.W.J., Nikopoulos, K., Dona, M., Gilissen, C., [18 co-authors], Veltman, J.A., van Wijk, E. & **Cremers, F.P.M.** *ZNF408* is mutated in familial exudative vitreoretinopathy and crucial for the development of zebrafish retinal vasculature (2013). *Proc. Natl. Acad. Sci. USA,* **110**, 9856-9861.
3. *Roosing, S., *Lamers, I.J.C., *de Vrieze, E., *van den Born, L.I., [7 co-authors and study group], #van Wijk, E., #Roepman, R., #den Hollander, A.I. & #**Cremers, F.P.M.** Disruption of the basal body protein POC1B results in autosomal recessive cone-rod dystrophy (2014). *Am. J. Hum. Genet.* **95**, 131-142. *Shared first authors; #shared senior authors.
4. Sangermano, R., Bax, N.M., Bauwens, M., van den Born, L.I., De Baere, E., Garanto, A., Collin, R.W.J., Goercharn-Ramlal, A.S.A., den Engelsman-van Dijk, A.H.A., Rohrschneider, K., Hoyng, C.B., ***Cremers, F.P.M.**, *Albert, S. Photoreceptor progenitor mRNA analysis reveals exon skipping due to the *ABCA4* c.5461-10T>C mutation in Stargardt disease. (2016) *Ophthalmology*. **123**:1375-1385. *Shared senior authors.
5. Sangermano, R., Khan, M., Cornelis, S.S., Richelle, V., Albert, S., Garanto, A., Elmelik, D., Qamar, R., Lugtenberg, D., van den Born, L.I., Collin, R.W.J., **Cremers, F.P.M.** *ABCA4* midigenes reveal the full splice spectrum of all reported noncanonical splice site variants in Stargardt disease. (2018) *Genome Res*. **28**:100-110.
6. *Albert, A., *Garanto, A., Sangermano, R., Khan, M., Bax, N.M., Hoyng, C.B., Zernant, J., Lee, W., Allikmets, R., #Collin, R.W.J., #**Cremers, F.P.M.** Identification and rescue of splice defects caused by two neighboring deep-intronic *ABCA4* mutations underlying Stargardt disease. (2018) *Am. J. Hum. Genet.*, **102**, 517-527. *Shared first authors; #shared senior authors.
7. *Sangermano, R., *Garanto, A., *Khan, M., Runhart, E. H., Bauwens, M., Bax, N. M., van den Born, L. I., Khan, M. I., Cornelis, S. S., ….[9 co-authors] ….. Arno, G., Fakin, A., Carss, K. J., Raymond, F. L., Webster, A. R., Dhaenens, C-M., Stöhr, H., Grassmann, F., Weber, B. H. F., Hoyng, C. B., de Baere, E., Albert, S., **Collin, R. W. J., ****Cremers, F. P. M.** (2019) Identification and rescue of splice defects due to deep-intronic *ABCA4* variants in Stargardt disease. *Genet Med.* **21**:1751-1760. *Shared first authors; **shared senior authors.
8. Khan, M., Cornelis, S. S., del Pozo-Valero, M., Whelan, L., Runhart, E. H., Mishra, K., Bults, F., AlSwaiti, Y., AlTabishi, A., De Baere, E., Banfi, S., Banin, E., Bauwens, M., Ben-Yosef, T., Boon, C. J. F., van den Born, L. I., Defoort, S., Devos, A., Dockery, A., Dudakova, L., Fakin, A., Farrar, G. J., Ferraz Sallum, J. M., Fujinami, K., Gilissen, C., Glavač, D., Gorin, M. B., Greenberg, J., Hayashi, T., Hettinga, Y., Hoischen, A., Hoyng, C. B., Hufendiek, K., Jägle, H., Kamakari, S., Karali, M., Kellner, U., Klaver, C. C. W., Kousal, B., Lamey, T., MacDonald, I. M., Matynia, A., McLaren, T., Mena, M. D., Meunier, I., Miller, R., Newman, H., Ntozini, B., Oldak, M., Pieterse, M., Podhajcer, O.L., Puech, B., Ramesar, R., Rüther, K., Salameh, M., Vallim Salles, M., Sharon, D., Simonelli, F., Spital, G., Steehouwer, M., Szaflik, J. P., Thompson, J. A., Thuillier, C., Tracewska, A. M., van Zweeden, M., Vincent, A. L., Zanlonghi, X., Liskova, P., Stöhr, H., De Roach, J., Ayuso, C., Roberts, L., Weber, B. H. F., Dhaenens, C-M.*, **Cremers, F. P. M.*** Resolving the dark matter of *ABCA4* for 1,054 Stargardt disease probands through integrated genomics and transcriptomics. (2020) *Genet. Med.,* **22**:1235-1246. *Shared senior authors.
9. **Cremers, F. P. M.**, Lee, W., Collin, R. W. J., Allikmets, R. Clinical spectrum, genetic complexity and therapeutic approaches for retinal disease caused by *ABCA4* mutations. (2020) *Prog. Retin. Eye Res.* Apr 9:100861. doi: 10.1016/j.preteyeres. 100861. [Epub ahead of print] Review.