Curriculum vitae of Frans P.M. Cremers

Personal information:
Date of birth: 17-03-1960
Nationality: Netherlands

Degrees:
M.Sc., Biology, University of Nijmegen 18-12-1984
Ph.D., cum laude, Medical Sciences, University Hospital Nijmegen 18-04-1991
Title of thesis: Positional cloning of a candidate gene for choroideremia.
Promotores: Prof. Dr. H.H. Ropers and Prof. Dr. B. Wieringa

Employment record:
01/1985-12/1985: Research fellow at the Bloodbank Nijmegen
01/1986-05/1990: Department of Human Genetics: Ph.D student
06/1990-04/1991: Department of Human Genetics: Assistant Professor
05/1991-08/1992: Department of Human Genetics: Royal Netherlands Academy of Arts and Sciences (KNAW) fellow.
Co-head Molecular Genetics Division.
09/1992-08/1993: Department of Molecular Genetics, University of Texas, Southwestern Medical School, Dallas, TX. Guestfellow with Prof. M. Brown and Prof. J. Goldstein
09/1993-04/1996: Department of Human Genetics: KNAW-fellow.
Co-head Molecular Genetics Division.
05/1996-12/1999: Department of Human Genetics: Assistant Professor
Head of Molecular Genetics Division.
01/2000-06/2004: Department of Human Genetics: Associate Professor
Head of Molecular Genetics Division
07/2004-present: Department of Human Genetics: Full Professor in molecular biology of inherited eye disease; head of Molecular Genetics Division
04/2005-present Director of international research Masters: Molecular Mechanisms of Disease.

Honours:
- 'Student award' in the category 'predoctoral basic' at the 41st Annual Meeting of the American Society of Human Genetics', October 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.
- Royal Netherlands Academy of Arts and Sciences (KNAW) fellowship (1991 - 1996). Identification of novel genes for inherited retinal disorders.
- First European Vision Award October 2007, Portoroz, European Vision Institute.

Reviewing:

Manuscripts
Editorial board member of Ophthalmic Genetics (1/1995 – present) and Human Molecular Genetics (1/1997 – 12/2002).

Guest editor and reviewer for Investigative Ophthalmology & Visual Sciences

Additional reviewing for:
- American Journal of Clinical Genetics
- American Journal of Human Genetics
- American Journal of Medical Genetics
- Annals of Otology, Rhinology & Laryngology
- Archives of Ophthalmology
- Clinical Genetics
- European Journal of Human Genetics
- Genomics
- Human Genetics
- Human Mutation
- Journal of Clinical Investigation
- Journal of Medical Genetics
- Proceedings of the National Academy of Sciences USA
- Nature Genetics

Grants Reviewing
- British RP Society (UK)
- Deutsche Forschungsgemeinschaft: 'Gutachter' for the german 'DFG Sonderforschungsbereich 430: Zellulare Mechanismen sensorischer Prozesse und neuronaler interaktionen' (6/1999)(Germany)
- Foundation Fighting Blindness, Inc. USA
- Inserm Programme National de Recherche sur la Vision (France)
- The Netherlands Organisation for Scientific Research (ZonMw)
- Wellcome Trust (UK)

Miscellaneous
- 'X-chromosome editor' in the Human Genome Organisation (1993-1997)
- Member of Medical Advisory Board of the Dutch Retinitis Pigmentosa Society (1998 – 2007)
- Member of 'Educational Committee' Research School 'Institute of Cellular Signalling' (1997 – 2002).
- Member of the Nijmegen Center for Molecular Life Sciences research training committee M.Sc. "Molecular Mechanisms of Disease" (2004 – 2006).

<u>Educational activities:</u>
- Organiser of the 'Second EEC Course for Scientists in Ophthalmology', Nijmegen, December 1991.
- Lecturer at the 'Molecular Basis of Human Diseases' course in Lissabon, March 1995, July 1996, June 1997.

- Lecturer at the University Medical Center Nijmegen (2nd year Medicine and Health Science): Cell Biology: 1995.
- Coordinating lecturer of 2nd year Medicine and Health Science course B202 'Genetic and Immunologic Processes'; 1996 – 2001.
- Lecturer of 2nd year Medicine and Health Science course B202 'Genetic and Immunologic Processes'; 2001 – present.
- Programme Director of International Honours Master of Science programme entitled Molecular Mechanisms of Disease (03/05 – present).

Scientific accomplishments:

2008 Co-author in paper showing autosomal recessive inheritance of CFH variants in patients with basal laminar drusen.
2007 Co-author in paper describing identification of RPGRIP1L/Joubert syndrome gene.
2007 Co-senior author in paper describing identification of the LCA5/Lebercilin gene.
2006 Senior author on paper describing identification of the CEP290 gene, the most frequently mutated gene in LCA
2006 Senior author on paper describing for the first time CSPG2/Versican mutations in patients with erosive vitreoretinopathy
2005 Senior author on paper describing RPGRIP1-NPHP4 interaction
2004 Senior author on paper describing mapping benign concentric areolar macular dystrophy gene
2001 Senior author on paper describing involvement of CRB1 in Leber congenital amaurosis and RP with Coats' like exudative vasculopathy
2001 Senior author on paper describing functional conservation between cytoplasmic domains of human CRB1 and Drosophila Crumbs
2000 Senior author on paper describing that ABCA4 is the major gene involved in cone-rod dystrophy
2000 Co-supervisor of study in which RPGR interactor RPGRIP1 (LCA gene) is cloned.
1999 Corresponding author in paper describing cloning of RP12/LCA gene CRB1
1999 Senior author of candidate gene cloning autosomal deafness type 9 (DFNA9) gene (COCH)
1999 Detailed genotype-phenotype analysis ABCA4 in Stargardt disease; classification of ABCA4 mutations in mild, moderate, and severe categories
1998 First description of ABCA4 involvement in cone-rod dystrophy
1997 Senior author paper describing partial mouse choroideremia model
1996 Co-supervisor of positional cloning of X-linked RP3 gene (RPGR)
1996 Co-supervisor of identification of XRP3 microdeletions
1995 Senior author on positional cloning paper first non-syndromic deafness gene (POU3F4)
1995 Senior author on paper describing that 40% of mutations in DFN3 are deletions situated 800 kb proximal to POU3F4
1992 Co-supervisor of positional cloning Norrie disease gene
1990 Cloning of choroideremia gene: first retinal dystrophy gene identified by positional cloning

1987 Identification of first microdeletions associated with classic choroideremia

(Co)promoter of Ph.D studies:

- Dr. I. Huber: 'Cloning of a gene underlying X-linked mixed deafness'; 6-11-1995.
- Dr. S.M. van der Maarel: 'Cloning of a gene for X-linked deafness (DFN3) and cloning of a candidate gene for X-linked mental retardation'; 18-2-1997.
- Dr. R. Roepman: 'Elucidation of the molecular cause of retinitis pigmentosa type 3 (RP3); 4-12-2000.
- Dr. A.I. den Hollander: 'Identification of the crumbs homologue 1 gene and analysis of its role in autosomal recessive retinal dystrophies'; 8-3-2002.
- Dr. J.J.C. van Lith-Verhoeven: 'Clinical and molecular analysis of autosomal dominant retinal dystrophies'; 5-3-2004.
- Dr. B.J. Klevering, 'Retinal dystrophies caused by mutations in the ABCA4 gene. An evaluation of the clinical spectrum'; 26-11-2004.
- Dr. S.L. Go, 'Elucidation of the genetic causes of retinal detachment'; 10-3-2006.
- Dr. M.L.W. Luijendijk, 'Elucidation of the molecular genetic basis of inherited hearing impairment'; 4-4-2006.
- Mrs. S. Yzer, 'Ophthalmologic and molecular genetic studies of autosomal recessive retinal dystrophies'; 2-7-2007.
- Mrs. S. Dharmaraj, 'Clinical and molecular analysis of Leber congenital amaurosis' ; 2-7-2007.
- Mrs. I. Gosens: Composition and function of the Crumbs protein complex in the mammalian retina; 11-3-2008.

Research Grants:

British Retinitis Pigmentosa Society
Cloning and characterization of the full length candidate choroideremia gene and a homologous autosomal gene; F. Cremers / H. Ropers; EP 145.000; 09/1991 – 08/1994.

Construction of retina and RPE specific cDNA libraries by PCR coupled subtractive hybridization: application to dystrophies of the retinal pigment epithelium; F. Cremers / A. Deutman; EP 40.000; 09/1995 – 08/1997.

Elucidation of the molecular basis of autosomal recessive retinitis pigmentosa, cone-rod dystrophy, Stargardt disease, and age-related macular degeneration; F. Cremers / C. Hoyng; EP 33.460; 05/1998 – 04/1999.

Identification of novel genes for Usher syndrome through expression profiling and genomic mapping of cDNAs expressed in the retina, retinal pigment epithelium and cochlea; F. Cremers / C. Cremers; EP 34.650; 07/1999 – 06/2000.

Molecular pathology of X-linked retinitis pigmentosa (RP3); W. Berger / F. Cremers / H.H. Ropers; EP 135.000; 10/2000 - 9/2003.

Micro-array based high-throughput *ABCA4* mutation analysis in patients with autosomal recessive retinitis pigmentosa and cone-rod dystrophy; A. Maugeri / F. Cremers; EP 22.290,-; 7/2002 – 3/2003.

Identification of three genes involved in autosomal dominant retinal dystrophies; A. den Hollander / F. Cremers; EP 120.000; 1/2003 – 12/2005.

Dutch blindness foundations

Identification of genetic factors involved in central blindness; C.Hoyng / F.Cremers; NLG 200.000; 01/1998 – 12/1999.

Identification of genetic factors involved in ablatio retinae; F.Cremers / C.Hoyng; NLG 450.000; 01/2000 – 12/2003.

Molecular genetic studies of Wagner disease and exudative vitreoretinopathy; F.Cremers / C.Hoyng/N. Boonstra/EvNouhuijs; EURO 70.000; 09/2005 – 11/2006.

Inherited blindness, retinitis pigmentosa and cone-rod dystrophy: identification of molecular causes and genotype-phenotype correlation; L. van den Born, A. den Hollander, F. Cremers; 2005-13. EURO 276.000; 2/2007 – 1/2010.

Molecular genetic studies of Wagner disease and exudative vitreoretinopathy; F. Cremers, C. Hoyng, N. Boonstra, E. van Nouhuijs; EURO 195.000; 1/2007 – 12/2008.

European community

Biomed 2: Construction of an integrated transcriptional map of the human X-chromosome; H.Ropers / F.Cremers; NLG 160.000

Fifth framework/Neurosciences: Retinal degeneration and control of cell polarity; Wijnholds / Cremers / Knust / Broccoli / Rashbass / Le Bivic; Euro 1.950.000 (Euro 409.000,- for research F. Cremers)

Sixth framework/Marie Curie Research Training Network: European Retinal Research Network (RetNet). Manager: T. Wheeler-Schilling; participants: Bhattacharya, Humphries, Wissinger, Ballabio, Leveillard, Poch, Cremers, van Veen, Ueffing. Total budget: Euro 3.679.134,-; Nijmegen part: Euro 313.209,-; 7/2004-7/2006.

Functional Genomics of the Retina in Health and Disease (Evi-Genoret), Integrated Project LSHG-CT-2005-512036. Fourteen European groups participate. F. Cremers, R. Roepman et al. Total budget 10.000 kEUR – 330 kEUR Nijmegen; 1/2005 – 12/2008.

Foundation Fighting Blindness Inc

Isolation of novel retina and RPE specific cDNAs through subtraction hybridization-PCR I; F.Cremers / C.Hoyng / A.Deutman; USD 315.000; 9/1996 - 08/1999

Cloning of genes underlying X-linked retinitis pigmentosa type 2 and type 3; F.Cremers / W.Berger / H.Ropers; USD 303.000; 09/1996 - 08/1999.

Isolation of novel retina and RPE specific cDNAs through subtraction hybridization-PCR II; F.Cremers / C.Hoyng / A.Deutman; USD 204.800; 09/1999 - 08/2002.

Elucidation of the molecular processes underlying a severe form of autosomal recessive retinitis pigmentosa (RP12); A.den Hollander / F.Cremers; USD 178.000; 09/1999 - 08/2002.

Isolation of novel retina and RPE specific cDNAs through subtraction hybridization-PCR III; F.Cremers / A.den Hollander / C.Hoyng; USD 150.000; 06/2002 - 05/2005.

Foundation for Retinal Research
LCA5 (lebercilin): molecular genetic, functional, mouse KO, and gene rescue studies; J. Bennett, A. den Hollander, R. Koenekoop, P. Nishina, R. Roepman, F. Cremers; Total: 1078 kEUR; 498 kEUR Nijmegen; 1/2008 – 12/2011.

Macula Society
Linkage study in benign concentric annular macular dystrophy; F.Cremers / A.Deutman; USD 7.000

The Netherlands Organization for Scientific Research
Study of structure-function relationships for the choroideremia candidate gene located in Xq21; F.Cremers / H.Ropers / B.Wieringa; NLG 280.000; 11/1991 – 10/1995.

Molecular characterization of the Xq21 region: isolation of genes for mental retardation and deafness by positional cloning; H.Ropers / F.Cremers; NLG 400.000; 06/1992 – 05/1996.

Molecular and functional analysis of the X-linked mixed deafness (DFN3) gene encoding the POU domain transcription factor Brain 4; F.Cremers / H.Ropers; NLG 279.000; 06/1995 – 11/1997.

Choroideremia mice: embryo rescue through doxycycline inducible Rep-1 transgene expression; H.Ropers / F.Cremers; NLG 279.000; 09/1997 - 08/2000.

Research into the molecular causes of non-syndromal sensorineural deafness; C.Cremers / F.Cremers; NLG 400.000; 06/1998 – 05/2001

Cloning of genes involved in non-syndromic hearing impairment; F.Cremers; NLG 277.000; 05/1999 - 04/2003

University Medical Center Nijmegen
Molecular and functional characterization of two novel ABC transporters preferentially expressed in the RPE; F.Cremers / F.Russel; CAD 80.000; 08/2001 - 07/2003.

A new genetic approach: homozygosity mapping in patients with LCA in outbred populations; A. den Hollander, F. Cremers; 2008-19; Euro 205.000.

Forschung contra Blindheit, Initiative Usher Syndrom, e.V.
Development of Usher Syndrome Chip; Cremers / Kremer / Cremers; Euro 45,000,-; 11/2003 – 5/2004.

Summary of scientific accomplishments

Our research group over the last 15 years has been on the forefront of the elucidation of the molecular genetic causes of inherited blindness. Initially, we strongly focussed on X-linked chorioretinal diseases such as choroideremia, Norrie disease, X-linked retinitis pigmentosa (RP), and congenital stationary night blindness. In the last 10 years, we shifted our research towards the understanding of the most frequent causes of inherited autosomal retinal defects (e.g. Stargardt disease, autosomal recessive cone-rod dystrophy, autosomal recessive and dominant RP, Leber congenital amaurosis), and deaf-blindness (Usher syndrome). In the last 5 years, we introduced technology to perform functional genomics and proteomics in the area of inherited blindness and Usher syndrome.

Major accomplishments

i. Identification of the first retinal dystrophy gene (choroideremia gene) by positional cloning

Employing cytogenetically visible Xq21 deletions associated with syndromic forms of choroideremia, we mapped all (in 1988 known) 200 genomic X-chromosomal DNA clones using Southern blotting and were able to fine-map one particular probe that detected submicroscopic deletions in 3 patients with non-syndromic choroideremia. Genomic walking and jumping experiments enabled us to identify additional deletions, and finally, to clone the choroideremia gene. The choroideremia gene was the 6th human disease gene overall, and the 1st retinal disease gene, identified by means of positional cloning. Approximately 1/3 of choroideremia patients carry partial or whole gene mutations. The remainder of the choroideremia-associated mutations consistently result in CHM protein truncation. Through functional cloning, dr. M. Seabra and co-workers subsequently identified the choroideremia gene as a catalytic subunit of Rab geranylgeranyl transferase. We showed that the CHM gene, as well as an intronless homolog (CHML) on chromosome 1q are expressed ubiquitously and show overlapping enzymatic activity though there are differences in Rab substrate specificities. We showed that Chm knock-out mice are embryonic lethal due to vascular abnormalities of the placenta. The Chm defect cannot be transmitted through from heterozygous females to female offpring because of preferential paternal X-inactivation of the Chm gene. The underlying molecular cause of choroideremia remains enigmatic.

ii. Positional cloning of the Norrie disease gene

Employing deletion mapping, the Norrie disease protein (NDP) gene was identified. Norrie disease in 1/3 of cases is associated with deafness and mental retardation. Subsequent studies revealed that this gene also is a frequent cause of exudative vitreoretinopathy. The NDP gene recently was shown to be a ligand for the FZD4/LRP5 co-receptors, which are mutated in 20% and 15% of patients with familial exudative vitreoretinopathy.

iii. Positional cloning of the X-linked RP3 gene

In 1993 we focussed on the cloning of the elusive X-linked RP3 gene which had been refractory to cloning since the first genetic linkage studies in 1984 by dr. Bhattacharya and co-workers. Extensive genomic walking and mutation anaysis studies yielded the

retinitis pigmentosa GTPase regulator (RPGR) gene which is mutated in 70% of patients with X-linked RP. Subsequent studies revealed the RPGR gene also to be involved in a significant proportion of isolated males with RP or CRD, as well as X-linked recessive and dominant cone-rod dystrophy. Mutations in the RPGR gene, together with mutations in the ABCA4 and USH2A genes, are the most frequent cause of inherited blindness.

iv. Identification of the major gene (ABCA4) underlying autosomal recessive cone-rod dystrophy

Upon the identification of the ABCA4 gene by dr. R. Allikmets and colleagues, we found splice site mutations in a pseudo-automal dominant family with cone-rod dystrophy and retinitis pigmentosa. The predicted effect of these mutations enabled us and others to develop a genotype-phenotype model for ABCA4-associated retinal dystrophies, in which the residual ABCA4 activity is inversely correlated with the severity of retinal disease. Comprehensive mutational analysis of patients with STGD1 and arCRD corroborated this model and also revealed the presence of ethnic founder mutations in the ABCA4 gene.

v. Cloning of one of the most frequently mutated gene in patients with Leber congenital amaurosis (CRB1)

Through the construction of a subtraction cDNA library from the retina, we identified several novel retinal genes, one of which (CRB1), was found to be mutated in patients with arRP and preserved para-arteriolar RPE, RP and Coats' like vasculopathy, and most importantly, in Leber congenital amaurosis (LCA). In fact, mutations in CRB1 are the most frequent cause of LCA in the Netherlands, Belgium and Spain (15-30% of the cases). The CRB1 protein is a transmembrane protein located in a rim around the photoreceptor inner segments, at the outer limiting membrane, where it serves as an attachment point for a large complex of intracellular proteins (MPP5, MPP4, MUPP1, INADL) involved in photoreceptor cell maintenance and polarity.

vi. Cloning of the LCA gene RPGRIP1

By employing a YTH approach, we identified an interactor of RPGR, denoted RPGR-interacting protein 1, which together with RPGR is located at the photoreceptor connecting cilium and outer segments, and in several other retinal cell types. Others soon thereafter identified RPGRIP1 mutations in ~5% of patients with LCA.

vii. Identification of 51 novel exons of the major gene underlying Usher syndrome, USH2A

Sequence analysis of a sizeable cohort of patients with Usher syndrome type 2 revealed heterozygous USH2A gene mutations in a large proportion of patients. Detailed genomic sequence analysis enabled us to identify a second isoform which is encoded by 51 additional exons next to the 21 previously identified exons of the USH2A. This important finding not only has had a major impact on the molecular genetic analysis of Usher syndrome patients, but also has led to a re-appraisal of the putative function of the USH2A protein. The 3' end of the USH2A gene encodes a transmembrane domain as well as an 118-amino acid cytoplasmic domain which carries a PDZ-binding domain. Protein-protein interaction studies recently enabled us to link USH2A to Harmonin,

encoded by the USH1C gene, thereby establishing a molecular link between USH1 and USH2 proteins.

viii. Identification of molecular interaction between RPGRIP1 and NPHP4
YTH screening of a retinal library using the C2 domain of RPGRIP1 yielded cDNA fragments of NPHP4, encoding the nephronophtisis 4 protein. Mutations in NPHP4 were previously identified in patients with Senior-Løken syndrome, a combination of juvenile renal failure (nephronophtisis) and retinitis pigmentosa. LCA-associated missense mutations in the C2 domain of RPGRIP1, as well as Senior-Løken syndrome-associated missense mutations in the NPHP4 interacting domain, disrupted the RPGRIP1-NPHP4 interaction. These findings likely explain the retinal dystrophy in patients with Senior-Løken syndrome and open new research opportunities to elucidate the renal failure.

ix. Identification of CSPG2/Versican mutations in patients with Erosive vitreoretinopathy and Wagner disease
Upon the identification of a splice site mutation in CSPG2/Versican in one Japanese family with Wagner disease, we identified CSPG2/Versican splice site mutations in 6 additional Dutch families with Wagner disease and a family with erosive vitreoretinopathy. Moreover, we identified a consistent upregulation of mRNA splice variants V2 and V3 in patients with splice site mutations.

x. Identification of the most frequently mutated LCA gene
We identified the CEP290 gene by combining linkage results and published data. One particular splicing mutation resides deep intronic and activates a cryptic exon which, when spliced in the mRNA, results in a stopcodon. Mutations in CEP290 were found in ~1/5 of all LCA patients, rendering it the most frequently mutated LCA gene to date.

xi. Identification of the LCA5/Lebercilin gene
Homozygosity mapping combined with bioinformatics enabled us to identify the elusive LCA5 gene, encoding Lebercilin. Lebercilin, together with CEP290 and RPGRIP1, resides at the connecting cilium.

xii. Identification of an autosomal recessive mode of inheritance for basal laminar drusen
In 5 of 30 families with basal laminar drusen, we identified compound heterozygous variants in the most important AMD associated gene, *CFH.* In several families we found that *CFH* null alleles, combined with the His402 allele, underlie basal laminar drusen, an endophenotye of age-related macular degeneration.

<u>Minor accomplishments</u>
i. Contributions to the identification of retinal disease genes
We contributed in different ways to the identification of the X-linked RP2 gene (patient resources, co-supervision early phase of the study), the autosomal dominant RP type 13/PRPC8 gene (patient resources), and the autosomal recessive congenital stationary night blindness gene *GRM6* (patient resources).

ii. Co-development of high-throughput mutation analysis microarrays for STGD1/arCRD and LCA

Under the supervision of dr. R. Allikmets and in collaboration with Asper Biotech, we aided the development of allele-specific primer extension (APEX)-type mutation microarrays for the ABCA4 gene, the only gene mutated in autosomal recessive Stargardt disease (STGD1), and the major gene mutated in autosomal recessive CRD. The ABCA4 mutation microarray detects 60% of the theoretically expected mutations in STGD1 patients, in comparison to 80% of mutations detected by sequence analysis. Likewise, we contributed to the development of a mutation microarray for Leber congenital amaurosis, we detects mutations in 33% of LCA patients. Both microarrays have been implemented in routine molecular diagnostics.

iii. Development of high-throughput mutation analysis microarrays for Usher syndrome
In the last decade, 8 Usher syndrome genes have been identified which collectively contain approximately 350 protein-coding exons and 500 pathologic variants. In collaboration with Asper Biotech, we developed an APEX-type mutation microarray which detects mutations in ~50% of USH type 1 and 30% of USH type 2 patients. This microarray will be improved on a yearly basis and is available for routine molecular diagnostics.

Publications F.P.M. Cremers (up to 1-2-2008)

Boon, C. J. F., Klevering, B. J., Hoyng, C. B., Zonneveld-Vrieling, M. N., Nabuurs, S. B., Blokland, E., Cremers, F. P. M., & den Hollander, A. I. Basal laminar drusen caused by compound heterozygous variants in the CFH gene. (2008) *Am. J. Hum. Genet.* **82**, 516-523.

Frank, V., den Hollander, A. I., Bruchle, N. O., Zonneveld, M. N., Nurnberg, G., Becker, C., Bois, G. D., Kendziorra, H., Roosing, S., Senderek, J., Nurnberg, P., Cremers, F. P. M., Zerres, K. & Bergmann, C. Mutations of the CEP290 gene encoding a centrosomal protein cause Meckel-Gruber syndrome. (2008) *Hum. Mutat.* **29**, 45-52.

Arts, H. H., Doherty, D., van Beersum, S. E., Parisi, M. A., Letteboer, S. J., Gorden, N. T., Peters, T. A., Marker, T., Voesenek, K., Kartono, A., Ozyurek, H., Farin, F. M., Kroes, H. Y., Wolfrum, U., Brunner, H. G., Cremers, F. P. M., Glass, I. A., Knoers, N. V. A. M. & Roepman, R. Mutations in the gene encoding the basal body protein RPGRIP1L, a nephrocystin-4 interactor, cause Joubert syndrome. (2007) *Nat. Genet.* **39**, 882-888.

Boon, C. J. F., van Schooneveld, M. J., den Hollander, A. I., van Lith-Verhoeven, J. J., Zonneveld-Vrieling, M. N., Theelen, T., Cremers, F. P. M., Hoyng, C. B. & Klevering, B. J. Mutations in the peripherin/RDS gene are an important cause of multifocal pattern dystrophy simulating STGD1/fundus flavimaculatus. (2007) *Br. J. Ophthalmol.* **91**, 1504-1511.

Boon, C. J. F., Klevering, B. J., den Hollander, A. I., Zonneveld, M. N., Theelen, T., Cremers, F. P. M. & Hoyng, C. B. Clinical and genetic heterogeneity in multifocal vitelliform dystrophy. (2007) *Arch. Ophthalmol.* **125**, 1100-1106.

Collin, R. W., Kalay, E., Oostrik, J., Caylan, R., Wollnik, B., Arslan, S., den Hollander, A. I., Birinci, Y., Lichtner, P., Strom, T. M., Toraman, B., Hoefsloot, L. H., Cremers, C. W. R. J., Brunner, H. G., Cremers, F. P. M., Karaguzel, A. & Kremer, H. Involvement of DFNB59 mutations in autosomal recessive nonsyndromic hearing impairment. (2007) *Hum. Mutat.* **28**, 718-723.

den Hollander, A. I., van Lith-Verhoeven, J. J., Arends, M. L., Strom, T. M., Cremers, F. P. M. & Hoyng, C. B. Novel compound heterozygous TULP1 mutations in a family with severe early-onset retinitis pigmentosa. (2007) *Arch. Ophthalmol.* **125**, 932-935.

den Hollander, A.I., Lopez, I., Yzer, S., Zonneveld, M.N., Janssen, I.M., Strom, T.M., Hehir-Kwa, J.Y., Veltman, J.A., Arends, M.L., Meitinger, T., Musarella, M.A, Born, L.I. van den, Fishman, G.A., Maumenee, I.H, Rohrschneider, K., Cremers, F.P.M. & Koenekoop, R.K. Identification of novel mutations in patients with Leber congenital amaurosis and juvenile RP by genome-wide homozygosity mapping with SNP microarrays. (2007) *Invest. Ophthalmol. Vis. Sci.*, **48**, 5690-5698.

den Hollander, A. I., Koenekoop, R. K., Mohamed, M. D., Arts, H. H., Boldt, K., Towns, K. V., Sedmak, T., Beer, M., Nagel-Wolfrum, K., McKibbin, M., Dharmaraj, S., Lopez, I., Ivings, L., Williams, G. A., Springell, K., Woods, C. G., Jafri, H., Rashid, Y., Strom, T. M., van der, Z. B., Gosens, I., Kersten, F. F., van, W. E., Veltman, J. A., Zonneveld, M. N., van Beersum, S. E., Maumenee, I. H., Wolfrum, U., Cheetham, M. E., Ueffing, M., *Cremers, F. P. M., *Inglehearn, C. F. & *Roepman, R. Mutations in *LCA5*, encoding the ciliary protein lebercilin, cause Leber congenital amaurosis. (2007) *Nat. Genet.* **39**, 889-895. (*equal contributions)

Gosens, I., Sessa, A., Hollander, A.I. den, Letteboer, S.J.F., Belloni, V, Arends, M.L., Bivic, A. le, Cremers, F.P.M., Broccoli, V. & Roepman, R. FERM protein EPB41L5 is a novel member of the mammalian CRB-MPP5 polarity complex. (2007) *Exp. Cell Res.*, **313**, 3959-3970.

Gosens, I., van, W. E., Kersten, F. F., Krieger, E., van der, Z. B., Marker, T., Letteboer, S. J., Dusseljee, S., Peters, T., Spierenburg, H. A., Punte, I. M., Wolfrum, U., Cremers, F. P. M., Kremer, H. & Roepman, R.

MPP1 links the Usher protein network and the Crumbs protein complex in the retina. (2007) *Hum. Mol. Genet.* **16,** 1993-2003.

Hogewind, B.F.T., Gaplovska-Kysela, K, Theelen, T., Cremers, F.P.M., Yam, G.H, Hoyng, C.B. & Mukhopadhyay, A. Identification and functional characterization of a novel MYOC mutation in two primary open angle glaucoma families from The Netherlands. (2007**)** *Mol. Vision*, **13**, 1793-1801.

Koenekoop, R. K., Lopez, I., den Hollander, A. I., Allikmets, R. & Cremers, F. P. M. Genetic testing for retinal dystrophies and dysfunctions: benefits, dilemmas and solutions. (2007) *Clin. Experiment. Ophthalmol.* **35**, 473-485.

Koenekoop, R.K., Cremers, F.P.M. & den Hollander, A.I. Leber congenital amaurosis: ciliary proteins on the move. (2007) *Ophthalmic Genet.*, **28**, 111-112.

van den Hurk, J. A. J. M., Meij, I. C., del Carmen, S. M., Kano, H., Nikopoulos, K., Hoefsloot, L. H., Sistermans, E. A., de, W., I, Mukhopadhyay, A., Plomp, A. S., de Jong, P. T., Kazazian, H. H. & Cremers, F. P. M. L1 retrotransposition can occur early in human embryonic development. (2007) *Hum. Mol. Genet.* **16**, 1587-1592.

Yzer, S., Born, L.I. van den, Zonneveld, M.N., Lopez, I., Ayyagari, R, Teye-Botchway, L, Mota-Vieira, L, Cremers, F.P.M. & Koenekoop, R.K. Molecular and phenotypic analysis of a family with autosomal recessive cone-rod dystrophy and Stargardt disease. (2007) *Mol. Vision*, **13**, 1568-1572.

Cremers, F. P. M., Kimberling, W. J., Külm, M., De Brouwer, A. P., van Wijk, E., Te Brinke, H., Cremers, C. W. R. J., Hoefsloot, L. H., Banfi, S., Simonelli, F., Fleischhauer, J. C., Berger, W., Kelley, P. M., Haralambous, E., Bitner-Glindzicz, M., Webster, A. R., Saihan, Z., De Baere, E., Leroy, B. P., Silvestri, G., McKay, G. J., Koenekoop, R. K., Millan, J. M., Rosenberg, T., Joensuu, T., Sankila, E.-M., Weil, D., Weston, M. D., Wissinger, B. & Kremer, H. Development of a genotyping microarray for Usher syndrome. (2007) *J. Med. Genet.* **44,** 153-160.

Renner, A. B., Kellner, U., Cropp, E., Preising, M. N., MacDonald, I. M., van den Hurk, J. A. J. M., Cremers, F. P. M. & Foerster, M. H. Choroideremia: variability of clinical and electrophysiological characteristics and first report of a negative electroretinogram. (2006) *Ophthalmology* **113**, 2066-2073.

Richard, M., Roepman, R., Aartsen, W. M., van Rossum, A. G. S. H., den Hollander, A. I., Knust, E., Wijnholds, J. & Cremers, F. P. M. Towards understanding CRUMBS function in retinal dystrophies. (2006) *Hum. Mol. Genet.* **15**, R235-R243.

den Hollander, A. I., Koenekoop, R. K., Yzer, S., Lopez, I., Arends, M. L., Voesenek, K. E. J., Zonneveld, M. N., Strom, T. M., Meitinger, T., Brunner, H. G., Hoyng, C. B., van den Born, L. I., Rohrschneider, K. & Cremers, F. P. M. Mutations in the *CEP290* (*NPHP6*) gene are a frequent cause of Leber congenital amaurosis. (2006) *Am. J. Hum. Genet.* **79**, 556-561.

Kalay, E., Li, Y., Uzumcu, A., Uyguner, O., Collin, R. W., Caylan, R., Ulubil-Emiroglu, M., Kersten, F. F., Hafiz, G., van, W. E., Kayserili, H., Rohmann, E., Wagenstaller, J., Hoefsloot, L. H., Strom, T. M., Nurnberg, G., Baserer, N., den Hollander, A. I., Cremers, F. P. M., Cremers, C. W. R. J., Becker, C., Brunner, H. G., Nurnberg, P., Karaguzel, A., Basaran, S., Kubisch, C., Kremer, H. & Wollnik, B. Mutations in the lipoma HMGIC fusion partner-like 5 (LHFPL5) gene cause autosomal recessive nonsyndromic hearing loss. (2006) *Hum. Mutat.* **27**, 633-639.

Mukhopadhyay, A., Nikopoulos, K., Maugeri, A., De Brouwer, A. P., van Nouhuys, C. E., Boon, C. J., Perveen, R., Zegers, H. A., Wittebol-Post, D., van den Biesen, P. R., van der Velde-Visser SD, Brunner, H. G., Black, G. C., Hoyng, C. B. & Cremers, F. P. M. Erosive vitreoretinopathy and wagner disease are caused by intronic mutations in CSPG2/Versican that result in an imbalance of splice variants. (2006) *Invest. Ophthalmol. Vis. Sci.* **47**, 3565-3572.

van Wijk, E., van der Zwaag, B., Peters, T., Zimmermann, U., Te Brinke, H., Kersten, F. F., Marker, T., Aller, E., Hoefsloot, L. H., Cremers, C. W. R. J., Cremers, F. P. M., Wolfrum, U., Knipper, M., Roepman, R. & Kremer, H. The DFNB31 gene product whirlin connects to the Usher protein network in the cochlea and retina by direct association with USH2A and VLGR1. (2006) *Hum. Mol. Genet.* **15**, 751-765.

Yzer, S., Fishman, G. A., Racine, J., Al-Zuhaibi, S., Chakor, H., Dorfman, A., Szlyk, J., Lachapelle, P., van den Born, L. I., Allikmets, R., Lopez, I., Cremers, F. P. M. & Koenekoop, R. K. CRB1 heterozygotes with regional retinal dysfunction: Implications for genetic testing of Leber congenital amaurosis. (2006) *Invest. Ophthalmol. Vis. Sci.* **47**, 3736-3744.

Yzer, S., Leroy, B. P., De Baere, E., de Ravel, T. J., Zonneveld, M. N., Voesenek, K., Kellner, U., Martinez Ciriano, J. P., de Faber, J.-T. H. N., Rohrschneider, K., Roepman, R., den Hollander, A. I., Cruysberg, J. R., Meire, F., Casteels, I., van Moll-Ramirez, N. G., Allikmets, R., van den Born, L. I. & Cremers, F. P. M. Microarray-based mutation detection and phenotypic characterization of patients with Leber congenital amaurosis. (2006) *Invest. Ophthalmol. Vis. Sci.* **47**, 1167-1176.

Roepman, R., Letteboer, S. J., Arts, H. H., van Beersum, S. E., Lu, X., Krieger, E., Ferreira, P. A. & Cremers, F. P. M. Interaction of nephrocystin-4 and RPGRIP1 is disrupted by nephronophthisis or Leber congenital amaurosis (LCA)-associated mutations. (2005) *Proc Natl Acad Sci USA* **102**, 18520-18525.

Zeitz, C., van Genderen, M., Neidhardt, J., Luhmann, U. F., Hoeben, F., Forster, U., Wycisk, K., Matyas, G., Hoyng, C. B., Riemslag, F., Meire, F., Cremers, F. P. & Berger, W. Mutations in GRM6 cause autosomal recessive congenital stationary night blindness with a distinctive scotopic 15-Hz flicker electroretinogram (2005) *Invest. Ophthalmol. Vis. Sci.* **46**, 4328-4335.

De Brouwer, A. P., Kunst, H. P., Krebsova, A., van Asseldonk, K., Reis, A., Snoeckx, R. L., van Camp, G., Cremers, C. W. R. J., Cremers, F. P. M. and Kremer, H. Fine mapping of autosomal dominant nonsyndromic hearing impairment DFNA21 to chromosome 6p24.1-22.3. (2005) *Am. J. Med. Genet.* **137**, 41-46.

Zernant, J., Kulm, M., Dharmaraj, S., den Hollander, A. I., Perrault, I., Preising, M. N., Lorenz, B., Kaplan, J., Cremers, F. P. M., Maumenee, I., Koenekoop, R. K. and Allikmets, R. Genotyping microarray (disease chip) for Leber congenital amaurosis: detection of modifier alleles. (2005) *Invest. Ophthalmol. Vis. Sci.* **46**, 3052-3059.

Kemperman, M. H., De Leenheer, E. M., Huygen, P. L., van Duijnhoven, G., Morton, C. C., Robertson, N. G., Cremers, F. P. M., Kremer, H. and Cremers, C. W. R. J. Audiometric, vestibular, and genetic aspects of a DFNA9 family with a G88E COCH mutation (2005) *Otol. Neurotol.* **26**, 926-933.

Yang, Z., Alvarez, B. V., Chakarova, C., Jiang, L., Karan, G., Frederick, J. M., Zhao, Y., Sauve, Y., Li, X., Zrenner, E., Wissinger, B., Hollander, A. I., Katz, B., Baehr, W., Cremers, F.P.M., Casey, J. R., Bhattacharya, S. S. & Zhang, K. Mutant carbonic anhydrase 4 impairs pH regulation and causes retinal photoreceptor degeneration (2005) *Hum. Mol. Genet.* **14**, 255-265.

Klevering, B. J., Deutman, A. F., Maugeri, A., Cremers, F. P. M. & Hoyng, C. B. The spectrum of retinal phenotypes caused by mutations in the ABCA4 gene (2005) *Graefes Arch. Clin. Exp. Ophthalmol.* **243**, 90-100.

Kohl, S., Varsanyi, B., Antunes, G. A., Baumann, B., Hoyng, C. B., Jagle, H., Rosenberg, T., Kellner, U., Lorenz, B., Salati, R., Jurklies, B., Farkas, A., Andreasson, S., Weleber, R. G., Jacobson, S. G., Rudolph, G., Castellan, C., Dollfus, H., Legius, E., Anastasi, M., Bitoun, P., Lev, D., Sieving, P. A., Munier, F. L., Zrenner, E., Sharpe, L. T., Cremers, F. P. M. & Wissinger, B. CNGB3 mutations account for 50% of all cases with autosomal recessive achromatopsia (2005) *Eur. J. Hum. Genet.* **13**, 302-308.

Zeitz, C., Minotti, R., Feil, S., Matyas, G., Cremers, F. P. M., Hoyng, C. B. & Berger, W. Novel mutations in CACNA1F and NYX in Dutch families with X-linked congenital stationary night blindness (2005) *Mol. Vis.* **11**, 179-183.

van den Hurk, J. A., Rashbass, P., Roepman, R., Davis, J., Voesenek, K. E., Arends, M. L., Zonneveld, M. N., van Roekel, M. H., Cameron, K., Rohrschneider, K., Heckenlively, J. R., Koenekoop, R. K., Hoyng, C. B., Cremers, F. P. M. & den Hollander, A. I. Characterization of the Crumbs homolog 2 (CRB2) gene and analysis of its role in retinitis pigmentosa and Leber congenital amaurosis (2005) *Mol. Vis.* **11**, 263-273.

Kantardzhieva, A., Gosens, I., Alexeeva, S., Punte, I. M., Versteeg, I., Krieger, E., Neefjes-Mol, C. A., den Hollander, A. I., Letteboer, S. J., Klooster, J., Cremers, F. P. M., Roepman, R. & Wijnholds, J. MPP5 Recruits MPP4 to the CRB1 Complex in Photoreceptors (2005) *Invest. Ophthalmol. Vis. Sci.* **46**, 2192-2201.

Klevering, B. J., Yzer, S., Rohrschneider, K., Zonneveld, M., Allikmets, R., van den Born, L. I., Maugeri, A., Hoyng, C. B. & Cremers, F. P. M. Microarray-based mutation analysis of the *ABCA4* (ABCR) gene in autosomal recessive cone-rod dystrophy and retinitis pigmentosa (2004) *Eur. J. Hum. Genet.* **12**, 1024-1032.

Maugeri, A., Meire, F., Hoyng, C. B., Vink, C., van Regemorter, N., Karan, G., Yang, Z., Cremers, F. P. M. & Zhang, K. A novel mutation in the ELOVL4 gene causes autosomal dominant Stargardt-like macular dystrophy (2004) *Invest. Ophthalmol. Vis. Sci.* **45**, 4263-4267.

Bischoff, A. M. L. C., Luijendijk, M. W. J., Huygen, P. L. M., van Duijnhoven, G., De Leenheer, E. M. R., Oudesluijs, G. G., Van Laer, L., Cremers, F. P. M., Cremers, C. W. R. J. & Kremer, H. A novel mutation identified in the DFNA5 gene in a Dutch family: a clinical and genetic evaluation (2004) *Audiol. Neurootol.* **9**, 34-46.

Cremers, F. P. M., Maugeri, A., den Hollander, A. I. & Hoyng, C. B. (2004) in *Retinal Dystrophies: functional genomics to gene therapy*, eds. Bock, G., Chader, G., & Goode, J. (John Wiley & Sons, Chichester, UK), pp. 68-79.

Cremers, F. P. M. & Cremers, C. W. R. J. (2004) in *Molecular Basis of Inborn Errors of Development; The Molecular Basis of Clinical Disorders of Morphogenesis*, eds. Epstein, C., Erickson, R., & Wynshaw-Boris, A. (Oxford University Press, San Francisco), pp. 792-797.

den Hollander, A. I., Davis, J., van der Velde-Visser, S. D., Zonneveld, M. N., Pierrottet, C. O., Koenekoop, R. K., Kellner, U., van den Born, L. I., Heckenlively, J. R., Hoyng, C. B., Handford, P. A., Roepman, R. & Cremers, F. P. M. CRB1 mutation spectrum in inherited retinal dystrophies (2004) *Hum. Mutat.* **24**, 355-369.

den Hollander, A. I., Lith-Verhoeven, J. J., Kersten, F. F., Heister, J. G., de Kovel, C. G., Deutman, A. F., Hoyng, C. B. & Cremers, F. P. M. Identification of novel locus for autosomal dominant butterfly shaped macular dystrophy on 5q21.2-q33.2 (2004) *J. Med. Genet.* **41**, 699-702.

Kemperman, M. H., De Leenheer, E. M. R., Huygen, P. L. M., van Wijk, E., van Duijnhoven, G., Cremers, F. P. M., Kremer, H. & Cremers, C. W. R. J. A Dutch family with hearing loss linked to the DFNA20/26 locus: longitudinal analysis of hearing impairment (2004) *Arch. Otolaryngol. Head Neck Surg.* **130**, 281-288.

Klevering, B. J., Maugeri, A., Wagner, A., Go, S. L., Vink, C., Cremers, F. P. M. & Hoyng, C. B. Three families displaying the combination of Stargardt's disease with cone-rod dystrophy or retinitis pigmentosa (2004) *Ophthalmology* **111**, 546-553.

Luijendijk, M. W., van Wijk, E., Bischoff, A. M., Krieger, E., Huygen, P. L., Pennings, R. J., Brunner, H. G., Cremers, C. W., Cremers, F. P. M. & Kremer, H. Identification and molecular modelling of a mutation in the motor head domain of myosin VIIA in a family with autosomal dominant hearing impairment (DFNA11) (2004) *Hum. Genet.* **115**, 149-156.

Pennings, R. J., Te Brinke, H., Weston, M. D., Claassen, A., Orten, D. J., Weekamp, H., van Aarem, A., Huygen, P. L., Deutman, A. F., Hoefsloot, L. H., Cremers, F. P. M., Cremers, C. W., Kimberling, W. J. & Kremer, H. USH2A mutation analysis in 70 Dutch families with Usher syndrome type II (2004) *Hum. Mutat.* **24**, 185.

Shi, W., van den Hurk, J. A., Alamo-Bethencourt, V., Mayer, W., Winkens, H. J., Ropers, H. H., Cremers, F. P. M. & Fundele, R. Choroideremia gene product affects trophoblast development and vascularization in mouse extra-embryonic tissues (2004) *Dev. Biol.* **272**, 53-65.

Theelen, T., Go, S. L., Tilanus, M. A., Klevering, B. J., Deutman, A. F., Cremers, F. P. M. & Hoyng, C. B. Autosomal dominant rhegmatogenous retinal detachment-clinical appearance and surgical outcome (2004) *Graefes Arch. Clin. Exp. Ophthalmol*. **242**, 892-897.

van Lith-Verhoeven, J. J. C., Hoyng, C. B., van den Helm, B., Deutman, A. F., Brink, H. M. A., Kemperman, M. H., de Jong, W. H. M., Kremer, H. & Cremers, F. P. M. The benign concentric annular macular dystrophy (BCAMD) locus maps to 6p12.3-q16 (2004) *Invest. Ophthalmol. Vis. Sci.* **45**, 30-35.

van Wijk, E., Pennings, R. J. E., Te, B. H., Claassen, A., Yntema, H. G., Hoefsloot, L. H., Cremers, F. P. M., Cremers, C. W. R. J. & Kremer, H. Identification of 51 novel exons of the Usher syndrome type 2A (USH2A) gene that encode multiple conserved functional domains and that are mutated in patients with Usher syndrome type II (2004) *Am. J. Hum. Genet.* **74**, 738-744.

De Brouwer, A. P., Pennings, R. J., Roeters, M., Van Hauwe, P., Astuto, L. M., Hoefsloot, L. H., Huygen, P. L., Van Den, H. B., Deutman, A. F., Bork, M., Kimberling, W. J., Cremers, F. P. M., Cremers, C. W. & Kremer, H. Mutations in the calcium-binding motifs of CDH23 and the 35delG mutation in GJB2 cause hearing loss in one family (2003) *Hum. Genet.* **112**, 156-163.

Go, S. L., Maugeri, A., Mulder, J. J. S., van Driel, M. A., Cremers, F. P. M. & Hoyng, C. B. Autosomal dominant rhegmatogenous retinal detachment associated with an Arg453Ter mutation in the *COL2A1* gene (2003) *Invest. Ophthalmol. Vis. Sci.* **44**, 4035-4043.

Jaakson, K., Zernant, J., Kulm, M., Hutchinson, A., Tonisson, N., Hawlina, M., Ravnic-Glavac, M., Meltzer, M., Caruso, R., Testa, F., Maugeri, A., Hoyng, C. B., Gouras, P., Simonelli, F., Lewis, R. A., Lupski, J. R., Cremers, F. P. M. & Allikmets, R. Genotyping microarray (gene chip) for the *ABCR* (*ABCA4*) gene (2003) *Hum. Mutation* **22**, 395-403.

Luijendijk, M. W. J., van de Pol, T. J. R., van Duijnhoven, G., den Hollander, A. I., ten Caat, J., van Limpt, V., Brunner, H. G., Kremer, H. & Cremers, F. P. M. Cloning, characterization and mRNA expression analysis of novel human fetal cochlea cDNAs (2003) *Genomics* **82**, 480-490.

van den Hurk, J. A. J. M., van de Pol, D. J. R., Wissinger, B., van Driel, M. A., Hoefsloot, L. H., de Wijs, I. J., van den Born, L. I., Heckenlively, J. R., Brunner, H. G., Zrenner, E., Ropers, H. H. & Cremers, F. P. M. Novel types of mutation in the *choroideremia* (*CHM*) gene: a full-length L1 insertion and an intronic mutation activating a cryptic exon (2003) *Hum. Genet.* **113**, 268-275.

van Lith-Verhoeven, J. J. C., Cremers, F. P. M., Van Den, H. B., Hoyng, C. B. & Deutman, A. F. Genetic heterogeneity of butterfly-shaped pigment dystrophy of the fovea (2003) *Mol. Vis.* **9**, 138-143.

van Lith-Verhoeven, J. J. C., van den Helm, B., Deutman, A. F., Bergen, A. A., Cremers, F. P. M., Hoyng, C. B. & de Jong, P. T. V. M. A peculiar autosomal dominant macular dystrophy is caused by an Asparagine deletion at codon 169 in the *peripherin/RDS* gene (2003) *Arch. Ophthalmol.* **121**, 1452-1457.

van Wijk, E., Krieger, E., Kemperman, M. H., De Leenheer, E. M. R., Huygen, P. L. M., Cremers, C. W. R. J., Cremers, F. P. M. & Kremer, H. A mutation in the gamma actin 1 (ACTG1) gene causes autosomal dominant hearing loss (DFNA20/26) (2003) *J. Med. Genet.* **40**, 879-884.

Yzer, S., van den Born, L. I., Schuil, J., Kroes, H. Y., van Genderen, M. M., Boonstra, N., van den Helm, B., Brunner, H. G., Koenekoop, R. K. & Cremers, F. P. M. A Tyr368His *RPE65* founder mutation is associated with early-onset retinal dystrophy with variable expression and progression in 10 families of a genetically isolated population (2003) *J. Med. Genet.* **40**, 709-713.

Cremers, C. W. R. J., Snik, A. F., Huygen, P. L., Joosten, F. B. & Cremers, F. P. M. X-linked mixed deafness syndrome with congenital fixation of the stapedial footplate and perilymphatic gusher (DFN3) (2002) *Adv. Otorhinolaryngol.* **61**, 161-167.

Cremers, F. P. M., Maugeri, A., Klevering, B. J., Hoefsloot, L. H. & Hoyng, C. B. [From gene to disease: from the ABCA4 gene to Stargardt disease, cone- rod dystrophy and retinitis pigmentosa] (2002) *Ned. Tijdschr. Geneeskd.* **146**, 1581-1584.

Cremers, F. P. M., van den Hurk, J. A. J. M. & den Hollander, A. I. Molecular genetics of Leber congenital amaurosis (2002) *Hum. Mol. Genet.* **11**, 1169-1176.

den Hollander, A. I., Knust, E. & Cremers, F. P. M. (2002) in *The Encyclopedia of Molecular Medicine*, ed. Creighton, T. E. (John Wiley & Sons, New York), pp. 940-942.

den Hollander, A. I., Ghiani, M., de Kok, Y., Wijnholds, J., Ballabio, A., Cremers, F. P. M. & Broccoli, V. Isolation of *Crb1*, a mouse homologue of *Drosophila crumbs*, and analysis of its expression pattern in eye and brain (2002) *Mech. Dev.* **110**, 203-207.

Klevering, B. J., Blankenagel, A., Maugeri, A., Cremers, F. P. M., Hoyng, C. B. & Rohrschneider, K. Phenotypic spectrum of autosomal recessive cone-rod dystrophies caused by mutations in the ABCA4 (ABCR) gene (2002) *Invest. Ophthalmol. Vis. Sci.* **43**, 1980-1985.

Klevering, B. J., van Driel, M., van Hogerwou, A. J., van de Pol, T. J. R., Deutman, A. F., Pinckers, A. J., Cremers, F. P. M. & Hoyng, C. B. Central areolar choroidal dystrophy associated with dominantly inherited drusen (2002) *Br. J. Ophthalmol.* **86**, 91-96.

Maugeri, A., Flothmann, K., Hemmrich, N., Ingvast, S., Jorge, P., Paloma, E., Patel, R., Rozet, J. M., Tammur, J., Testa, F., Balcells, S., Bird, A. C., Brunner, H. G., Hoyng, C. B., Metspalu, A., Simonelli, F., Allikmets, R., Bhattacharya, S. S., D'Urso, M., Gonzalez-Duarte, R., Kaplan, J., te Meerman, G. J., Santos, R., Schwartz, M., van Camp, G., Wadelius, C., Weber, B. H. & Cremers, F. P. M. The ABCA4 2588G>C Stargardt mutation: single origin and increasing frequency from South-West to North-East Europe (2002) *Eur. J. Hum. Genet.* **10**, 197-203.

Schulz, H. L., Stoehr, H., White, K., van Driel, M. A., Hoyng, C. B., Cremers, F. P. M. & Weber, B. H. Genomic structure and assessment of the retinally expressed RFamide- related peptide gene in dominant cystoid macular dystrophy (2002) *Mol. Vis.* **8**, 67-71.

van den Hurk, J. A. J. M., Seabra, M. & Cremers, F. P. M. (2002) in *The Encyclopedia of Molecular Medicine*, ed. Creighton, T. E. (John Wiley & Sons, New York), pp. 750-752.

van Lith-Verhoeven, J. J. C., van der Velde-Visser SD, Sohocki, M. M., Deutman, A. F., Brink, H. M., Cremers, F. P. M. & Hoyng, C. B. Clinical characterization, linkage analysis, and PRPC8 mutation analysis

of a family with autosomal dominant retinitis pigmentosa type 13 (RP13) (2002) *Ophthalmic Genet.* **23**, 1-12.

Bom, S. J., De Leenheer, E. M., Lemaire, F. X., Kemperman, M. H., Verhagen, W. I., Marres, H. A., Kunst, H. P., Ensink, R. J., Bosman, A. J., van Camp, G., Cremers, F. P. M., Huygen, P. L. & Cremers, C. W. Speech recognition scores related to age and degree of hearing impairment in DFNA2/KCNQ4 and DFNA9/COCH (2001) *Arch. Otolaryngol. Head Neck Surg.* **127**, 1045-1048.

Cremers, F. P. M. & Ropers, H.-H. (2001) in *The Metabolic and Molecular Bases of Inherited Disease*, eds. Scriver, C. R., Beaudet, A. L., Sly, W. S., Valle, D., Childs, B., Kinzler, K. W., & Vogelstein, B. (McGraw-Hill, New York), pp. 5935-5946.

den Hollander, A. I., Heckenlively, J. R., van den Born, L. I., de Kok, Y. J. M., van der Velde-Visser, S. D., Kellner, U., Jurklies, B., van Schooneveld, M. J., Blankenagel, A., Rohrschneider, K., Wissinger, B., Cruysberg, J. R. M., Deutman, A. F., Brunner, H. G., Apfelstedt-Sylla, E., Hoyng, C. B. & Cremers, F. P. M. Leber congenital amaurosis and retinitis pigmentosa with Coats-like exudative vasculopathy are associated with mutations in the crumbs homologue 1 (*CRB1*) gene (2001) *Am. J. Hum. Genet.* **69**, 198-203.

den Hollander, A. I., Johnson, K., de Kok, Y., Klebes, A., Brunner, H. G., Knust, E. & Cremers, F. P. M. CRB1 has a cytoplasmic domain that is functionally conserved between human and *Drosophila* (2001) *Hum. Mol. Genet.* **10**, 2767-2773.

Fransen, E., Verstreken, M., Bom, S. J., Lemaire, F., Kemperman, M. H., de Kok, Y. J. M., Wuyts, F. L., Verhagen, W. I., Huygen, P. L., McGuirt, W. T., Smith, R. J., Van Maldergem, L. V., Declau, F., Cremers, C. W. R. J., van de Heyning, P. H., Cremers, F. P. M. & van Camp, G. A common ancestor for COCH related cochleovestibular (DFNA9) patients in Belgium and The Netherlands bearing the P51S mutation (2001) *J. Med. Genet.* **38**, 61-65.

Kirschner, R., Erturk, D., Zeitz, C., Sahin, S., Ramser, J., Cremers, F. P. M., Ropers, H. H. & Berger, W. DNA sequence comparison of human and mouse retinitis pigmentosa GTPase regulator (RPGR) identifies tissue-specific exons and putative regulatory elements (2001) *Hum. Genet.* **109**, 271-278.

McKie, A. B., McHale, J. C., Keen, T. J., Tarttelin, E. E., Goliath, R., van Lith-Verhoeven, J. J., Greenberg, J., Ramesar, R. S., Hoyng, C. B., Cremers, F. P. M., Mackey, D. A., Bhattacharya, S. S., Bird, A. C., Markham, A. F. & Inglehearn, C. F. Mutations in the pre-mRNA splicing factor gene *PRPC8* in autosomal dominant retinitis pigmentosa (RP13) (2001) *Hum. Mol. Genet.* **10**, 1555-1562.

Shah, Z. H., Toompuu, M., Hakkinen, T., Rovio, A. T., van Ravenswaay, C., De Leenheer, E. M., Smith, R. J., Cremers, F. P. M., Cremers, C. W. & Jacobs, H. T. Novel coding-region polymorphisms in mitochondrial seryl-tRNA synthetase (SARSM) and mitoribosomal protein S12 (RPMS12) genes in DFNA4 autosomal dominant deafness families (2001) *Hum. Mutat.* **17**, 433-434.

Wissinger, B., Gamer, D., Jagle, H., Giorda, R., Marx, T., Mayer, S., Tippmann, S., Broghammer, M., Jurklies, B., Rosenberg, T., Jacobson, S. G., Sener, E. C., Tatlipinar, S., Hoyng, C. B., Castellan, C., Bitoun, P., Andreasson, S., Rudolph, G., Kellner, U., Lorenz, B., Wolff, G., Verellen-Dumoulin, C., Schwartz, M., Cremers, F. P. M., Apfelstedt-Sylla, E., Zrenner, E., Salati, R., Sharpe, L. T. & Kohl, S. CNGA3 mutations in hereditary cone photoreceptor disorders (2001) *Am. J. Hum. Genet.* **69**, 722-737.

Allikmets, R., Maugeri, A., van Driel, M. A., Hoyng, C. B., Cremers, F. P. M. & et al. Further evidence for an association of ABCR alleles with age-related macular degeneration. The International ABCR Screening Consortium (2000) *Am. J. Hum. Genet.* **67**, 487-491.

Cremers, F. P. M., Cremers, C. W. R. J. & Ropers, H.-H. (2000) in *Genetics in Oto-Rhino-Laryngology*, eds. Kitamura, K. & Steel, K. P. (S. Karger AG, Basel), pp. 184-195.

Maugeri, A., Klevering, B. J., Rohrschneider, K., Blankenagel, A., Brunner, H. G., Deutman, A. F., Hoyng, C. B. & Cremers, F. P. M. Mutations in the *ABCA4* (*ABCR*) gene are the major cause of autosomal recessive cone-rod dystrophy (2000) *Am. J. Hum. Genet.* **67**, 960-966.

Roepman, R., Bernoud-Hubac, N., Schick, D., Maugeri, A., Berger, W., Ropers, H.-H., Cremers, F. P. M. & Ferreira, P. A. The Retinitis Pigmentosa GTPase Regulator (RPGR) interacts with novel transport-like proteins in the outer segments of rod photoreceptors (2000) *Hum. Mol. Genet.* **9**, 2095-2105.

Bom, S. J., Kunst, H. P., Huygen, P. L., Cremers, F. P. M. & Cremers, C. W. Non-syndromal autosomal dominant hearing impairment: ongoing phenotypical characterization of genotypes (1999) *Br. J. Audiol.* **33**, 335-348.

Bom, S. J. H., Kunst, H. P. M., Huygen, P. L. M., Cremers, F. P. M. & Cremers, C. W. R. J. Nonsyndromic autosomal dominant hearing impairment: ongoing phenotypical characterisation of genotypes (1999) *Br J Audiol* **33**, 335-348.

Bom, S. J. H., Kemperman, M. H., de Kok, Y. J. M., Huygen, P. L. M., Verhagen, W. I. M., Cremers, F. P. M. & Cremers, C. W. R. J. Progressive cochleovestibular impairment caused by a point mutation in the *COCH* gene at DFNA9 (1999) *Laryngoscope* **109**, 1525-1530.

de Kok, Y. J. M., Bom, S. J. H., Brunt, T. M., Kemperman, M. H., van Beusekom, E., van der Velde-Visser, S. D., Robertson, N. G., Morton, C. C., Huygen, P. L. M., Verhagen, W. I. M., Brunner, H. G., Cremers, C. W. R. J. & Cremers, F. P. M. A Pro51Ser mutation in the *COCH* gene is associated with late-onset autosomal dominant progressive hearing loss with vestibular defects (1999) *Hum Mol Genet* **8**, 361-366.

den Hollander, A. I., van Driel, M. A., de Kok, Y. J. M., van de Pol, T. J. R., Hoyng, C. B., Brunner, H. G., Deutman, A. F. & Cremers, F. P. M. Isolation and mapping of novel candidate genes for retinal disorders using suppression subtractive hybridization (1999) *Genomics* **58**, 240-249.

den Hollander, A. I., ten Brink, J. B., de Kok, Y. J. M., van Soest, S., van den Born, L. I., van Driel, M. A., van de Pol, T. J. R., Payne, A. M., Bhattacharya, S. S., Kellner, U., Hoyng, C. B., Westerveld, A., Brunner, H. G., Bleeker-Wagemakers, E. M., Deutman, A. F., Heckenlively, J. R., Cremers, F. P. M. & Bergen, A. A. B. Mutations in a human homologue of *Drosophila crumbs* cause retinitis pigmentosa (RP12) (1999) *Nature Genet* **23**, 217-221.

den Hollander, A. I., van der Velde-Visser, S. D., Pinckers, A. J. L. G., Hoyng, C. B., Brunner, H. G. & Cremers, F. P. M. Refined mapping of the gene for autosomal dominant retinitis pigmentosa (RP17) on chromosome 17q22 (1999) *Hum Genet* **104**, 73-76.

Gong, Y., Krakow, D., Marcelino, J., Wilkin, D., Chitayat, D., Babul-Hirji, R., Hudgkins, L., Cremers, C. W. R. J., Cremers, F. P. M., Brunner, H. G., Reinker, K., Rimoin, D. L., Cohn, D. H., Goodman, F. R., Reardon, W., Patton, M., Francomano, C. A. & Warman, M. L. Heterozygous mutations in the gene encoding noggin affect human joint morphogenesis (1999) *Nature Genet* **21**, 302-304.

Kirschner, R., Rosenberg, T., Schultz-Heienbrok, R., Lenzner, S., Feil, S., Roepman, R., Cremers, F. P. M., Ropers, H.-H. & Berger, W. *RPGR* transcription studies in mouse and human tissues reveal a retina-specific isoform that is disrupted in a patient with X-linked retinitis pigmentosa (1999) *Hum Mol Genet* **8**, 1571-1578.

Klevering, B. J., van Driel, M., van de Pol, T. J. R., Pinckers, A. J. L. G., Cremers, F. P. M. & Hoyng, C. B. Phenotypic variations in a retinal dystrophy family as result of different mutations in the ABCR gene (1999) *Brit J Ophthalmol* **83**, 914-918.

Maugeri, A., van Driel, M. A., van de Pol, T. J. R., Klevering, B. J., van Haren, F. J. J., Tijmes, N., Bergen, A. A. B., Rohrschneider, K., Blankenagel, A., Pinckers, A. J. L. G., Dahl, N., Brunner, H. G., Deutman, A.

F., Hoyng, C. B. & Cremers, F. P. M. The 2588G>C mutation in the *ABCR* gene is a mild frequent founder mutation in the western European population and allows the classification of *ABCR* mutations in patients with Stargardt disease (1999) *Am J Hum Genet* **64**, 1024-1035.

van Kasteren, Y. M., Hundscheid, R. D., Smits, A. P., Cremers, F. P. M., van Zonneveld, P. & Braat, D. D. Familial idiopathic premature ovarian failure: an overrated and underestimated genetic disease? (1999) *Hum. Reprod.* **14**, 2455-2459.

Cremers, F. P. M. Genetic causes of hearing loss (1998) *Curr Opin Neurol* **11**, 11-16.

Cremers, F. P. M., van de Pol, T. J. R., van Driel, M., den Hollander, A. I., van Haren, F. J. J., Knoers, N. V. A. M., Tijmes, N., Bergen, A. A. B., Rohrschneider, K., Blankenagel, A., Pinckers, A. J. L. G., Deutman, A. F. & Hoyng, C. B. Autosomal recessive retinitis pigmentosa and cone-rod dystrophy caused by splice site mutations in the Stargardt's disease gene *ABCR* (1998) *Hum Mol Genet* **7**, 355-362.

Eib, D. W., Merkx, G. F., Martens, G. J. & Cremers, F. P. M. Assignment of H7365 (C9orf2) to human chromosome band 9q31 by somatic cell hybrid analysis and fluorescence in situ hybridization (1998) *Cytogenet Cell Genet* **81**, 180-181.

Gerber, S., Rozet, J. M., van de Pol, T. J. R., Hoyng, C. B., Munnich, A., Blankenagel, A., Kaplan, J. & Cremers, F. P. M. Complete exon-intron structure of the retina specific ATP binding transporter gene (*ABCR*) allows the identification of novel mutations underlying Stargardt disease (1998) *Genomics* **48**, 139-142.

Schwahn, U., Lenzner, S., Dong, J., Feil, S., Hinzmann, B., van Duijnhoven, G., Kirschner, R., Hemberger, M., Bergen, A. A. B., Rosenberg, T., Pinckers, A. J. L. G., Fundele, R., Rosenthal, A., Cremers, F. P. M., Ropers, H.-H. & Berger, W. Positional cloning of the gene for X-linked retinitis pigmentosa 2 (1998) *Nature Genet* **19**, 327-332.

van Driel, M. A., Maugeri, A., Klevering, B. J., Hoyng, C. B. & Cremers, F. P. M. *ABCR* unites what ophthalmologists divide(s) (1998) *Ophthalmic Genet* **19** , 117-122.

de Kok, Y. J. M., Cremers, C. W. R. J., Ropers, H.-H. & Cremers, F. P. M. The molecular basis of X-linked deafness type 3 (DFN3) in two sporadic cases: Identification of a somatic mosaicism for a *POU3F4* missense mutation (1997) *Hum Mutation* **10**, 207-211.

van den Hurk, J. A. J. M., Schwartz, M., van Bokhoven, H., van de Pol, T. J. R., Bogerd, L., Pinckers, A. J. L. G., Bleeker-Wagemakers, E. M., Pawlowitzki, I. H., Rüther, K., Ropers, H.-H. & Cremers, F. P. M. Molecular basis of choroideremia (CHM): mutations involving the Rab escort protein-1 (*REP-1*) gene (1997) *Hum Mutation* **9**, 110-117.

van den Hurk, J. A. J. M., Hendriks, W., van de Pol, T. J. R., Oerlemans, F., Jaissle, G., Rüther, K., Kohler, K., Hartmann, J., Zrenner, E., van Bokhoven, H., Wieringa, B., Ropers, H.-H. & Cremers, F. P. M. Mouse choroideremia gene mutation causes photoreceptor cell degeneration and is not transmitted through the female germline. (1997) *Hum Mol Genet* **6**, 851-858.

de Kok, Y. J. M., Vossenaar, E. R., Cremers, C. W. R. J., Dahl, N., Laporte, J., Hu, L. J., Lacombe, D., Fischel-Ghodsian, N., Friedman, R. A., Parnes, L. S., Thorpe, P., Bitner-Glindzicz, M., Pander, H.-J., Heilbronner, H., Gravelin, J., den Dunnen, J. T., Brunner, H. G., Ropers, H.-H. & Cremers, F. P. M. Identification of a hot spot for microdeletions in patients with X-linked deafness (DFN3) 900 kb proximal to the DFN3 gene *POU3F4* (1996) *Hum Mol Genet* **5**, 1229-1235.

Hoyng, C. B., Poppelaars, F., van de Pol, T. J. R., Kremer, H., Pinckers, A. J. L. G., Deutman, A. F. & Cremers, F. P. M. Genetic fine mapping of the gene for recessive Stargardt disease (1996) *Hum Genet* **98**, 500-504.

Roepman, R., van Duynhoven, G., Rosenberg, T., Pinckers, A. J. L. G., Bleeker-Wagemakers, E. M., Bergen, A. A. B., Post, J., Beck, A., Reinhardt, R., Ropers, H.-H., Cremers, F. P. M. & Berger, W. Positional cloning of the gene for X-linked retinitis pigmentosa: homology with the guanine-nucleotide-exchange factor RCC1 (1996) *Hum Mol Genet* **5**, 1035-1041.

Roepman, R., Bauer, D., Rosenberg, T., van Duynhoven, G., van de Vosse, E., Platzer, M., Rosenthal, A., Ropers, H.-H., Cremers, F. P. M. & Berger, W. Identification of a gene disrupted by a microdeletion in a patient with X-linked retinitis pigmentosa (1996) *Hum Mol Genet* **5**, 827-833.

van Bokhoven, H., Rawson, R. B., Merkx, G. F. M., Cremers, F. P. M. & Seabra, M. C. cDNA cloning and chromosomal localization of the genes encoding the α- and β-subunits of human rab geranylgeranyl transferase: the 3' end of the α-subunit gene overlaps with the transglutaminase 1 gene promoter (1996) *Genomics* **38**, 133-140.

van Bokhoven, H., van den Hurk, J. A. J. M., Bogerd, L., van de Pol, T. J. R., Ropers, H.-H. & Cremers, F. P. M. A highly polymorphic microsatellite marker located within the choroideremia gene (1996) *Ophthalmic Genet* **17**, 119-121.

van der Maarel, S. M., Scholten, I. H. J. M., Huber, I., Philippe, C., Suijkerbuijk, R. F., Gilgenkrantz, S., Kere, J., Cremers, F. P. M. & Ropers, H.-H. Cloning and characterization of *DXS6673E*, a candidate gene for X-linked mental retardation in Xq13.1 (1996) *Hum Mol Genet* **5**, 887-897.

Berger, W., van Duijnhoven, G., Pinckers, A., Smits, A., Ropers, H.-H. & Cremers, F. P. M. Linkage analysis in a Dutch family with X-linked recessive congenital stationary night blindness (XL-CSNB) (1995) *Hum Genet* **95**, 67-70.

Bitner-Glindzicz, M., Turnpenny, P., Höglund, P., Kääriäinen, H., Sankila, E.-M., van der Maarel, S. M., de Kok, Y. J. M., Ropers, H.-H., Cremers, F. P. M., Pembrey, M. & Malcolm, S. Further mutations in *Brain 4* (POU3F4) clarify the phenotype in the X-linked deafness, DFN3 (1995) *Hum Mol Genet* **4**, 1467-1469.

Cremers, F. P. M. & Ropers, H.-H. (1995) in *The Metabolic Basis of Inherited Disease*, eds. Scriver, C. R., Beaudet, A. L., Sly, W. S., & Valle, D. (McGraw-Hill, Inc., pp. 4311-4323.

Cremers, F. P. M., Bitner-Glindzicz, M., Pembrey, M. E. & Ropers, H.-H. Mapping and cloning hereditary deafness genes (1995) *Curr Opin Genet Dev* **5**, 371-375.

de Kok, Y. J. M., van der Maarel, S. M., Bitner-Glindzicz, M., Huber, I., Monaco, A. P., Malcolm, S., Pembrey, M. E., Ropers, H.-H. & Cremers, F. P. M. Association between X-linked mixed deafness and mutations in the POU domain gene POU3F4 (1995) *Science* **267** , 685-688.

de Kok, Y. J. M., Merkx, G. F. M., van der Maarel, S. M., Huber, I., Malcolm, S., Ropers, H.-H. & Cremers, F. P. M. A duplication/paracentric inversion associated with familial X-linked deafness (DFN3) suggests the presence of a regulatory element more than 400 kb upstream of the *POU3F4* gene (1995) *Hum Mol Genet* **4**, 2145-2150.

Nelson, D. L., Ballabio, A., Cremers, F. P. M., Monaco, A. P. & Schlessinger, D. Report of the sixth international workshop on X chromosome mapping 1995 (1995) *Cytogenet Cell Genet* **71**, 307-342.

Philippe, C., Arnould, C., Sloan, F., van Bokhoven, H., van der Velde-Visser, S. D., Chery, M., Ropers, H.-H., Gilgenkrantz, S., Monaco, A. P. & Cremers, F. P. M. A high resolution interval map of the q21 region of the human X chromosome (1995) *Genomics* **27**, 539-543.

Ponjavic, V., Abrahamson, M., Andréasson, S., van Bokhoven, H., Cremers, F. P. M., Ehinger, B. & Fex, G. Phenotype variations within a choroideremia family lacking the entire CHM gene (1995) *Ophthalmic Genet* **16**, 143-150.

van der Maarel, S. M., Scholten, I. H. J. M., Maat-Kievit, J. A., Huber, I., de Kok, Y. J. M., de Wijs, I., van de Pol, T. J. R., van Bokhoven, H., den Dunnen, J. T., van Ommen, G. J. B., Philippe, C., Monaco, A. P., Smeets, H. J. M., Ropers, H.-H. & Cremers, F. P. M. Yeast artificial chromosome cloning of the Xq13.3-q21.31 region and fine mapping of a deletion associated with choroideremia and nonspecific mental retardation (1995) *Eur J Hum Genet* **3**, 207-218.

Bitner-Glindzicz, M., de Kok, Y., Summers, D., Huber, I., Cremers, F. P. M., Ropers, H.-H., Reardon, W., Pembrey, M. E. & Malcolm, S. Close linkage of a gene for X linked deafness to three microsatellite repeats at Xq21 in radiologically normal and abnormal families (1994) *J Med Genet* **31**, 916-921.

Cremers, F. P. M. & Ropers, H.-H. (1994) in *Molecular Genetics of Inherited Eye Disorders*, eds. Wright, A. & Jay, B. (Harwood Academic Publishers GMBH, pp. 303-319.

Cremers, F. P. M., Armstrong, S. A., Seabra, M. C., Brown, M. S. & Goldstein, J. L. REP-2, a Rab escort protein encoded by the choroideremia-like gene (1994) *J Biol Chem* **269**, 2111-2117.

Huber, I., Bitner-Glindzicz, M., de Kok, Y. J. M., van der Maarel, S. M., Ishikawa-Brush, Y., Monaco, A. P., Robinson, D., Malcolm, S., Pembrey, M. E., Brunner, H. G., Cremers, F. P. M. & Ropers, H.-H. X-linked mixed deafness (DFN3): cloning and characterization of the critical region allows the identification of novel microdeletions (1994) *Hum Mol Genet* **3**, 1151-1154.

Röhme, D., Sidén, T., van der Maarel, S. M., Cremers, F. P. M., Tantravahi, U., Marinoni, J.-C., Ropers, H.-H. & Schwartz, C. E. Radiation hybrids for the proximal long arm of the X chromosome and their use in the derivation of an ordered set of cosmid markers from a defined subregion in proximal Xq13.1 (1994) *Somat Cell Mol Genet* **20**, 1-10.

van Bokhoven, H., van Genderen, C., Ropers, H.-H. & Cremers, F. P. M. Dinucleotide repeat polymorphism within the choroideremia gene at Xq21.2 (1994) *Hum Mol Genet* **3**, 1446.

van Bokhoven, H., van Genderen, C., Molloy, C. M., van de Pol, T. J. R., Cremers, C. W. R. J., van Aarem, A., Schwartz, M., Rosenberg, T., Geurts van Kessel, A. H. M., Ropers, H.-H. & Cremers, F. P. M. Mapping of the choroideremia-like (CHML) gene at 1q42-qter and mutation analysis in patients with Usher syndrome type II (1994) *Genomics* **19**, 385-387.

van Bokhoven, H., Schwartz, M., Andréasson, S., van den Hurk, J. A. J. M., Bogerd, L., Jay, M., Rüther, K., Jay, B., Pawlowitzki, I. H., Sankila, E.-M., Wright, A., Ropers, H.-H., Rosenberg, T. & Cremers, F. P. M. Mutation spectrum in the CHM gene of Danish and Swedish choroideremia patients (1994) *Hum Mol Genet* **3**, 1047-1051.

van Bokhoven, H., van den Hurk, J. A. J. M., Bogerd, L., Philippe, C., Gilgenkrantz, S., de Jong, P., Ropers, H.-H. & Cremers, F. P. M. Cloning and characterization of the human choroideremia gene (1994) *Hum Mol Genet* **3**, 1041-1046.

Willard, H. F., Cremers, F. P. M., Mandel, J. L., Monaco, A. P., Nelson, D. L. & Schlessinger, D. Report of the fifth international workshop on human X chromosome mapping 1994 (1994) *Cytogenet Cell Genet* **67**, 295-358.

Andres, D. A., Seabra, M. C., Brown, M. S., Armstrong, S. A., Smeland, T. E., Cremers, F. P. M. & Goldstein, J. L. cDNA cloning of component A of Rab geranylgeranyl transferase and demonstration of its role as a Rab escort protein (1993) *Cell* **73**, 1091-1099.

Herzberg, N. H., van Schooneveld, M. J., Bleeker-Wagemakers, E. M., Zwart, R., Cremers, F. P. M., van der Knaap, M. S., Bolhuis, P. A. & de Visser, M. Kearns-Sayre syndrome with a phenocopy of choroideremia instead of pigmentary retinopathy (1993) *Neurology* **43**, 218-221.

Philippe, C., Cremers, F. P. M., Chery, M., Bach, I., Abbadi, N., Ropers, H.-H. & Gilgenkrantz, S. Physical mapping of DNA markers in the q13-q22 region of the human X chromosome (1993) *Genomics* **17**, 147-152.

Schwartz, M., Rosenberg, T., van den Hurk, J. A. J. M., van de Pol, T. J. R. & Cremers, F. P. M. Identification of mutations in Danish choroideremia families (1993) *Hum Mutation* **2**, 43-47.

Traupe, H., Vetter, U., Happle, R., Fisher, L. W., Cremers, F. P. M., Landry, S. J., Pankav, R. & Ropers, H.-H. Exclusion of the biglycan (BGN) gene as a candidate gene for the Happle syndrome employing an intragenic single-strand conformational polymorphisn (1993) *Hum Genet* **91**, 89-90.

Bach, I., Robinson, D., Thomas, N., Ropers, H.-H. & Cremers, F. P. M. Physical fine mapping of genes underlying X-linked deafness and non fra(X)-X-linked mental retardation at Xq21 (1992) *Hum Genet* **89**, 620-624.

Bach, I., Brunner, H. G., Beighton, P., Ruvalcaba, R. H. A., Reardon, W., Pembrey, M. E., van der Velde-Visser, S. D., Bruns, G. A. P., Cremers, C. W. R. J., Cremers, F. P. M. & Ropers, H.-H. Microdeletions in patients with gusher-associated, X-linked mixed deafness (DFN3) (1992) *Am J Hum Genet* **50**, 38-44.

Berger, W., van de Pol, T. J. R., Warburg, M., Gal, A., Bleeker-Wagemakers, E. M., de Silva, H., Meindl, A., Meitinger, T., Cremers, F. P. M. & Ropers, H.-H. Mutations in the candidate gene for Norrie disease (1992) *Hum Mol Genet* **1**, 461-465.

Berger, W., Meindl, A., de Leeuw, B., de Roos, A., van de Pol, T. J. R., Meitinger, T., van der Velde-Visser, S. D., Achatz, H., Geurts van Kessel, A. H. M., Cremers, F. P. M. & Ropers, H.-H. Generation and characterization of radiation reduced cell hybrids and isolation of probes from the proximal short arm of the human X chromosome (1992) *Hum Genet* **90**, 243-246.

Berger, W., Meindl, A., van de Pol, T. J. R., Cremers, F. P. M., Ropers, H.-H., Dörner, C., Monaco, A., Bergen, A. A. B., Lebo, R., Warburg, M., Zergollern, L., Lorenz, B., Gal, A., Bleeker-Wagemakers, E. M. & Meitinger, T. Isolation of a candidate gene for Norrie disease by positional cloning (1992) *Nature Genet* **1**, 199-203.

Cremers, F. P. M., Molloy, C. M., van de Pol, T. J. R., van den Hurk, J. A. J. M., Bach, I., Geurts van Kessel, A. H. M. & Ropers, H.-H. An autosomal homologue of the choroideremia gene colocalizes with the Usher syndrome type II locus on the distal part of chromosome 1q (1992) *Hum Mol Genet* **1**, 71-75.

Meindl, A., Berger, W., Meitinger, T., van de Pol, T. J. R., Achatz, H., Dörner, C., Haasement, M., Hellebrand, H., Gal, A., Cremers, F. P. M. & Ropers, H.-H. Norrie disease is caused by mutations in an extracellular protein resembling C-terminal globular domain of mucins (1992) *Nature Genet* **2**, 139-143.

Molloy, C. M., van de Pol, T. J. R., Brohet, R. M., Ropers, H.-H. & Cremers, F. P. M. Three RFLPs for pZ11 (DXS540) in the choroideremia gene at Xq21.2 (1992) *Nucleic Acids Res* **20**, 1434.

Sankila, E.-M., Tolvanen, R., van den Hurk, J. A. J. M., Cremers, F. P. M. & de la Chapelle, A. Aberrant splicing of the CHM gene is a significant cause of choroideremia (1992) *Nature Genet* **1**, 109-113.

Traupe, H., Müller, D., Atherton, D., Chester Kalter, D., Cremers, F. P. M., van Oost, B. A. & Ropers, H.-H. Exclusion mapping of the X-linked dominant chondrodysplasia punctata/ichthyosis/cataract/short stature (Happle) syndrome: possible implication of an unstable pre-mutation (1992) *Hum Genet* **89**, 659-665.

van den Hurk, J. A. J. M., van Zandvoort, P. M., Brunsmann, F., Pawlowitzki, I. H., Holzgreve, W., Szabo, P., Cremers, F. P. M. & van Oost, B. A. Prenatal exclusion of choroideremia (1992) *Am J Med Genet* **44**, 822-823.

van den Hurk, J. A. J. M., van de Pol, T. J. R., Molloy, C. M., Brunsmann, F., Rüther, K., Zrenner, E., Pinckers, A. J. L. G., Pawlowitzki, I. H., Bleeker-Wagemakers, E. M., Wieringa, B., Ropers, H.-H. & Cremers, F. P. M. Detection and characterization of point mutations in the choroideremia candidate gene by PCR-SSCP analysis and direct DNA sequencing (1992) *Am J Hum Genet* **50**, 1195-1202.

Sankila, E.-M., Sistonen, P., Cremers, F. P. M. & de la Chapelle, A. Choroideremia: linkage analysis with physically mapped close DNA- markers (1991) *Hum Genet* **87**, 348-352.

Cremers, F. P. M., van de Pol, T. J. R., van Kerkhoff, E. P. M., Wieringa, B. & Ropers, H.-H. Cloning of a gene that is rearranged in patients with choroideraemia (1990) *Nature* **347**, 674-677.

Cremers, F. P. M., Brunsmann, F., Berger, W., van Kerkhoff, E. P. M., van de Pol, T. J. R., Wieringa, B., Pawlowitzki, I. H. & Ropers, H.-H. Cloning of the breakpoints of a deletion associated with choroideremia (1990) *Hum Genet* **86**, 61-64.

Cremers, F. P. M., Sankila, E.-M., Brunsmann, F., Jay, M., Jay, B., Wright, A., Pinckers, A. J. L. G., Schwartz, M., van de Pol, T. J. R., Wieringa, B., de la Chapelle, A., Pawlowitzki, I. H. & Ropers, H.-H. Deletions in patients with classical choroideremia vary in size from 45 kb to several megabases (1990) *Am J Hum Genet* **47**, 622-628.

Shiloh, Y., Lidvak, G., Ziv, Y., Lehner, T., Sandkuyl, L., Hildesheimer, M., Buchris, V., Cremers, F. P. M., Szabo, P., White, B. N., Holden, J. J. A. & Ott, J. Genetic mapping of X-linked albinism-deafness syndrome (ADFN) to Xq26.3-q27.1 (1990) *Am J Hum Genet* **47**, 20-27.

van de Pol, T. J. R., Cremers, F. P. M., Brohet, R. M., Wieringa, B. & Ropers, H.-H. Derivation of clones from the choroideremia locus by preparative field inversion gel electrophoresis (1990) *Nucleic Acids Res* **18**, 725-731.

Cremers, F. P. M., van de Pol, T. J. R., Wieringa, B., Collins, F. S., Sankila, E.-M., Siu, V. M., Flintoff, W. F., Brunsmann, F., Blonden, L. A. J. & Ropers, H.-H. Chromosomal jumping from the DXS165 locus allows molecular characterization of four microdeletions and a de novo chromosome X/13 translocation associated with choroideremia (1989) *Proc Natl Acad Sci USA* **86**, 7510-7514.

Cremers, F. P. M., van de Pol, T. J. R., Diergaarde, P. J., Wieringa, B., Nussbaum, R. L., Schwartz, M. & Ropers, H.-H. Physical fine mapping of the choroideremia locus using Xq21 deletions associated with complex syndromes (1989) *Genomics* **4**, 41-46.

den Dunnen, J. T., van Neck, J. W., Cremers, F. P. M., Lubsen, N. H. & Schoenmakers, J. G. G. Nucleotide sequence of the rat gamma-crystallin gene region and comparison with an orthologous human region (1989) *Gene* **78**, 201-213.

Cremers, F. P. M., van de Pol, T. J. R., Wieringa, B., Hofker, M. H., Pearson, P. L., Pfeiffer, R. A., Mikkelsen, M., Tabor, A. & Ropers, H.-H. Molecular analysis of male-viable deletions and duplications allows ordering of 52 DNA probes on proximal Xq (1988) *Am J Hum Genet* **43**, 452-461.

Cremers, F. P. M., Brunsmann, F., van de Pol, T. J. R., Pawlowitzki, I. H., Paulsen, K., Wieringa, B. & Ropers, H.-H. Deletion of the DXS165 locus in patients with classical choroideremia (1987) *Clin Genet* **32**, 421-423.

Cremers, F. P. M., Pfeiffer, R. A., van de Pol, T. J. R., Hofker, M. H., Kruse, T. A., Wieringa, B. & Ropers, H.-H. An interstitial duplication of the X chromosome in a male allows physical fine mapping of probes from the Xq13-q22 region (1987) *Hum Genet* **77**, 23-27.

den Dunnen, J. T., Moormann, R. J. M., Cremers, F. P. M. & Schoenmakers, J. G. G. Two human gamma-crystallin genes are linked and riddled with *Alu*-repeats (1985) *Gene* **38**, 197-204.

van Kuppevelt, T. H. M. S. M., Cremers, F. P. M., Domen, J. G. W., van Beuningen, H. M., van den Brule, A. J. C. & Kuyper, C. M. A. Ultrastructural localisation of proteoglycans in human lung alveoli (1985) *Eur J Cell Biol* **36**, 74-80.

van Kuppevelt, T. H. M. S. M., Cremers, F. P. M., Domen, J. G. W. & Kuyper, C. M. A. Staining of proteoglycans in mouse lung alveoli. II. Characterization of the cuprolinic blue-positive, anionic sites (1984) *Histochem J* **16**, 671-686.