Detailed CV, including publications

NAME	POSITION TITLE
Léveillard, Thierry	Research Director INSERM
Born on April 26th 1960 in Veules-les-Roses (France)	

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	YEAR(s)	FIELD OF STUDY
Pierre and Marie Curie University, Paris, France	Msc	1985	Biochemistry
Rouen University, France	PhD	1989	Cellular Biology

A. Positions, Honors and patents.

Positions

- 1989-1991 Visiting post-graduated researcher, Center for Molecular Genetics (Pr. Peter Geiduschek), University of California, San Diego
- 1992 Research associate, Salk Institute (Pr. Inder Verma), San Diego, CA
- 1993-1996 Postdoctoral fellow, Institut de Génétique et de Biologie Moléculaire et Cellulaire (IGBMC directed by Pierre Chambon) (Dr. Bohdan Wasylyk), Strasbourg, France
- 1997- 1998 Postdoctoral fellow, Laboratoire de Physiopathologie Rétinienne, Inserm EMI 99-18, Strasbourg (Pr Sahel), France
- 1998-2002 Research Scientist Inserm (1st class), Laboratoire de Physiopathologie Rétinienne (Pr Sahel), Inserm EMI 99-18, Strasbourg, France
- 2002-2006 Research Scientist Inserm (1st class), Laboratoire de Physiopathologie cellulaire et moléculaire de la rétine, Inserm UMR592, Paris, France

2006-present Research Director Inserm, Institut de la Vision UMR-S 968, Paris, France

Honors

- 1997: IPSEN Award, Neuronal Plasticity
- 2005: Foundation Fighting Blindness (FFB), Trustee Award

Patents

- Disease-Associated Protein, 6 April 2001, foreign extension on 6 April 2002 (EP1379657)
- New neuronal viability factor and use therof, foreign extension on 5 June 2008 (BIO06385).
- Trophic factor for the treatment of retinal degenerative diseases (EP 07 109652.3)

B. Biographical narrative.

I (Thierry Léveillard) obtained my PhD at the University of Rouen (France) in 1989, following a Masters in Biochemistry at the University Pierre and Marie Curie in Paris. I spent three years as a post-doctoral researcher in San Diego (UCSD and the Salk Institute) and moved back to Strasbourg where I worked at the IGBMC for four years. My current project was initiated in Strasbourg where I was recruited as 'Chargé de recherche Inserm' in 1998 and ultimately continued in Paris where I was promoted 'Directeur de recherche' in 2006. The diverse influences of these different geographic locations translate to a broad expertise in molecular biology. I commenced my current medical project on signaling and the therapy of inherited retinal degeneration with José Sahel. It is ironic that within the field of neuroprotection, we try to promote the activity of the very same actors I was trying to inhibit in the field of cancer biology. Examples

include the growth factor GDNF, on which we published one paper in IOVS and two papers in Molecular Vision, and p53 shown to be activated in response to photoreceptor degeneration in a paper published in Molecular Neurosciences. One novel scientific achievement, the yields of which have occupied most of my time over the last ten years, was based on the observations made by Saddek Mohand-Saïd and José Sahel in a mouse model of retinitis pigmentosa (RP). The transplantation of rod photoreceptors in the eye of this mouse was found to prevent the secondary loss of cones, the more vital class of photoreceptors necessary for vision. In the degenerative disease RP, most patients carry a mutation in a gene (among many) expressed selectively in rods, hence preventing secondary cone loss by means of mimicking the effects of transplantation could be an effective and broadly applicable therapy. Two studies published respectively in PNAS and IOVS demonstrated that the molecules are proteins secreted by rods, but did not allow for their isolation. Using my broad expertise in molecular biology, I designed a protocol of systematic screening of a retinal library against primary cone cultures from chicken embryos. This strategy of expression cloning was inspired by the emerging concepts from the field of functional genomics. The identification of this novel member of the thioredoxin family, which we published in 2004 in Nature Genetics, resulted in our being honoured alongside José Sahel with the 2005 American foundation FFB award. We more recently published in BMC molecular Biology, RdCVF2 the paralogue of the first factor. We moved from Strasbourg to Paris in 2002, with the perspective of creating a new structure, the 'Institut de la Vision' designed within the spirit of the idiom "from bench to the bedside". We also created the company Fovea-Pharmaceuticals in 2005 to valorise our high content screening expertise for the identification of novel molecules for the treatment of retinal diseases.

C. Responsabilities.

- Ministère des affaires étrangères ECO-NET 2007 and 2008 () PI
- Ministère des affaires étrangères ULYSSES 2007 and 2008 (RNA interference RdCVF) PI
- Région Ile de France Bourse posdoctorale 2006 (PI)
- RNG appel d'offres criblage 2007 (PI)
- ANR Maladies Rares 2006 (RdCVF targets) PI
- ANR Neuroscience 2005 (RdCVF2 Outside the Retina) PI
- ANR Maladies Neurologiques et Psychiatriques 2008 (RdCVF in Neurodegenerative Diseases) PI
- Contrat d'interface Inserm/CHNO 2005 (Preclinical Studies for RdCVF) PI
- Foundation Fighting Blindness TA-GT-0406-0332-UPA 2005 (AAV-RdCVF) PI: J. Bennett
- Foundation Fighting Blindness Centre Grant module I 2007 (RdCVF Therapeutic Approach) Co-PI
- Foundation Fighting Blindness Wynn's Grant 2008 (Neuroprotective molecules from natural sources) PI
- ANR Chaire d'Excellence 2005 (RdCVF Expression) PI: D. Zack
- European Union FP6, EVI-GENORET 2004 (Functional Genomics of the Retina in Health and Diseases) PI: J. Sahel
- European Union, Marie Curie Training Networks RETNET 2004 (Functional Genomics of the Retina) PI: S. Bhattacharrya
- Centre National de Genotypage 2003 and 2006 (GWAS for AMD) PI
- Centre National de Séquençage 2003 (Depp sequencing of cDNA libraries) PI

D. Publications (in chronological order).

1. Léveillard T, Sahel JA.
Rod-derived cone viability factor for treating blinding diseases: from clinic to redox signaling.
Sci Transl Med. 2010 Apr 7;2(26):26ps16.

2. Wunderlich KA, Léveillard T, Penkowa M, Zrenner E, Perez MT.
METALLOTHIONEINS I+II AND THEIR RECEPTOR MEGALIN ARE ALTERED IN INHERITED PHOTORECEPTOR DEGENERATION.
Invest Ophthalmol Vis Sci. 2010 Mar 31. [Epub ahead of print]

3. Cronin T, Raffelsberger W, Lee-Rivera I, Jaillard C, Niepon ML, Kinzel B, Clérin E, Petrosian A, Picaud S, Poch O, Sahel JA, Léveillard T.
The disruption of the rod-derived cone viability gene leads to photoreceptor dysfunction and susceptibility to oxidative stress.
Cell Death Differ. 2010 Feb 5. [Epub ahead of print]

4. Audo I, Kohl S, Leroy BP, Munier FL, Guillonneau X, Mohand-Saïd S, Bujakowska K, Nandrot EF, Lorenz B, Preising M, Kellner U, Renner AB, Bernd A, Antonio A, Moskova-Doumanova V, Lancelot ME, Poloschek CM, Drumare I, Defoort-Dhellemmes S, Wissinger B, Léveillard T, Hamel CP, Schorderet DF, De Baere E, Berger W, Jacobson SG, Zrenner E, Sahel JA, Bhattacharya SS, Zeitz C.
TRPM1 is mutated in patients with autosomal-recessive complete congenital stationary night blindness.
Am J Hum Genet. 2009 Nov;85(5):720-9.

5. Reichman S, Kalathur RK, Lambard S, Aït-Ali N, Yang Y, Lardenois A, Ripp R, Poch O, Zack DJ, Sahel JA, Léveillard T.
The homeobox gene CHX10/VSX2 regulates RdCVF promoter activity in the inner retina.
Hum Mol Genet. 2010 Jan 15;19(2):250-61.

6. Lambert JC, Heath S, Even G, Campion D, Sleegers K, Hiltunen M, Combarros O, Zelenika D, Bullido MJ, Tavernier B, Letenneur L, Bettens K, Berr C, Pasquier F, Fiévet N, Barberger-Gateau P, Engelborghs S, De Deyn P, Mateo I, Franck A, Helisalmi S, Porcellini E, Hanon O; European Alzheimer's Disease Initiative Investigators, de Pancorbo MM, Lendon C, Dufouil C, Jaillard C, Léveillard T, Alvarez V, Bosco P, Mancuso M, Panza F, Nacmias B, Bossù P, Piccardi P, Annoni G, Seripa D, Galimberti D, Hannequin D, Licastro F, Soininen H, Ritchie K, Blanché H, Dartigues JF, Tzourio C, Gut I, Van Broeckhoven C, Alpérovitch A, Lathrop M, Amouyel P.
Genome-wide association study identifies variants at CLU and CR1 associated with Alzheimer's disease.
Nat Genet. 2009 Oct;41(10):1094-9.

7. Bujakowska K, Maubaret C, Chakarova CF, Tanimoto N, Beck SC, Fahl E, Humphries MM, Kenna PF, Makarov E, Makarova O, Paquet-Durand F, Ekström PA, van Veen T, Léveillard T, Humphries P, Seeliger MW, Bhattacharya SS.
Study of gene-targeted mouse models of splicing factor gene Prpf31 implicated in human autosomal dominant retinitis pigmentosa (RP).
Invest Ophthalmol Vis Sci. 2009 Dec;50(12):5927-33.

8. Fridlich R, Delalande F, Jaillard C, Lu J, Poidevin L, Cronin T, Perrocheau L, Millet-Puel G, Niepon ML, Poch O, Holmgren A, Van Dorsselaer A, Sahel JA, Léveillard T.
The thioredoxin-like protein rod-derived cone viability factor (RdCVFL) interacts with TAU and inhibits its phosphorylation in the retina.
Mol Cell Proteomics. 2009 Jun;8(6):1206-18.

9. Yang Y, Mohand-Said S, Danan A, Simonutti M, Fontaine V, Clerin E, Picaud S, Léveillard T, Sahel JA.
Functional cone rescue by RdCVF protein in a dominant model of retinitis pigmentosa.
Mol Ther. 2009 May;17(5):787-95.

10: Kalathur RK, Gagniere N, Berthommier G, Poidevin L, Raffelsberger W, Ripp R, Léveillard T, Poch O.
RETINOBASE: a web database, data mining and analysis platform for gene expression data on retina.
BMC Genomics. 2008 May 5;9:208.

11: Chalmel F, Léveillard T, Jaillard C, Lardenois A, Berdugo N, Morel E, Koehl P, Lambrou G, Holmgren A, Sahel JA, Poch O.
Rod-derived Cone Viability Factor-2 is a novel bifunctional-thioredoxin-like protein with therapeutic potential.
BMC Mol Biol. 2007 Aug 31;8:74.

12: Calza S, Raffelsberger W, Ploner A, Sahel J, Léveillard T, Pawitan Y.
Filtering genes to improve sensitivity in oligonucleotide microarray data analysis.
Nucleic Acids Res. 2007;35(16):e102.

13: Fradot M, Lorentz O, Wurtz JM, Sahel JA, Léveillard T.
The loss of transcriptional inhibition by the photoreceptor-cell specific nuclear receptor (NR2E3) is not a necessary cause of enhanced S-cone syndrome.
Mol Vis. 2007 Apr 6;13:594-601.

14: Cronin T, Léveillard T, Sahel JA.
Retinal degenerations: from cell signaling to cell therapy; pre-clinical and clinical issues.
Curr Gene Ther. 2007 Apr;7(2):121-9.

15: Léveillard T, Mohand-Saïd S, Sahel JA.
[Retinal repair by transplantation of photoreceptor precursors]
Med Sci (Paris). 2007 Mar;23(3):240-2. French.

16: Lorentz O, Sahel J, Mohand-Saïd S, Léveillard T.
Cone survival: identification of RdCVF.
Adv Exp Med Biol. 2006;572:315-9.

17: Hanein S, Perrault I, Gerber S, Dollfus H, Dufier JL, Feingold J, Munnich A, Bhattacharya S, Kaplan J, Sahel JA, Rozet JM, Léveillard T.
Disease-associated variants of the rod-derived cone viability factor (RdCVF) in Leber congenital amaurosis. Rod-derived cone viability variants in LCA.
Adv Exp Med Biol. 2006;572:9-14.

18: Lardenois A, Chalmel F, Bianchetti L, Sahel JA, Léveillard T, Poch O.
PromAn: an integrated knowledge-based web server dedicated to promoter analysis.
Nucleic Acids Res. 2006 Jul 1;34(Web Server issue):W578-83.

19: Delyfer MN, Forster V, Neveux N, Picaud S, Léveillard T, Sahel JA.
Evidence for glutamate-mediated excitotoxic mechanisms during photoreceptor degeneration in the rd1 mouse retina.
Mol Vis. 2005 Sep 1;11:688-96.

20: Delyfer MN, Simonutti M, Neveux N, Léveillard T, Sahel JA.
Does GDNF exert its neuroprotective effects on photoreceptors in the rd1 retina through the glial glutamate transporter GLAST?
Mol Vis. 2005 Sep 1;11:677-87.

21: Galy A, Roux MJ, Sahel JA, Léveillard T, Giangrande A.
Rhodopsin maturation defects induce photoreceptor death by apoptosis: a fly model for RhodopsinPro23His human retinitis pigmentosa.
Hum Mol Genet. 2005 Sep 1;14(17):2547-57.

22: Sahel JA, Mohand-Said S, Léveillard T.
[Neuroprotection of photoreceptor cells in rod-cone dystrophies: from cell therapy to cell signalling]
C R Biol. 2005 Feb;328(2):163-8. Review. French.

23: Chalmel F, Lardenois A, Thompson JD, Muller J, Sahel JA, Léveillard T, Poch O.
GOAnno: GO annotation based on multiple alignment.
Bioinformatics. 2005 May 1;21(9):2095-6.

24: Léveillard T, Mohand-Saïd S, Poch O, Sahel JA.
[Rod-derived cone viability factor: a clue for therapy of retinitis pigmentosa?]
Med Sci (Paris). 2005 Jan;21(1):22-4. French.

25: Hackam AS, Strom R, Liu D, Qian J, Wang C, Otteson D, Gunatilaka T, Farkas RH, Chowers I, Kageyama M, Léveillard T, Sahel JA, Campochiaro PA, Parmigiani G, Zack DJ.

Identification of gene expression changes associated with the progression of retinal degeneration in the rd1 mouse.
Invest Ophthalmol Vis Sci. 2004 Sep;45(9):2929-42.

26: Menu dit Huart L, Lorentz O, Goureau O, Léveillard T, Sahel JA.
DNA repair in the degenerating mouse retina.
Mol Cell Neurosci. 2004 Jul;26(3):441-9.

27: Léveillard T, Mohand-Saïd S, Lorentz O, Hicks D, Fintz AC, Clérin E, Simonutti M, Forster V, Cavusoglu N, Chalmel F, Dollé P, Poch O, Lambrou G, Sahel JA.
Identification and characterization of rod-derived cone viability factor.
Nat Genet. 2004 Jul;36(7):755-9.

28: Delyfer MN, Léveillard T, Mohand-Saïd S, Hicks D, Picaud S, Sahel JA.
Inherited retinal degenerations: therapeutic prospects.
Biol Cell. 2004 May;96(4):261-9. Review.

29: Léveillard T, Mohand-Saïd S, Fintz AC, Lambrou G, Sahel JA.
The search for rod-dependent cone viability factors, secreted factors promoting cone viability.
Novartis Found Symp. 2004;255:117-27; discussion 127-30, 177-8.

30: Cavusoglu N, Thierse D, Mohand-Saïd S, Chalmel F, Poch O, Van-Dorsselaer A, Sahel JA, Léveillard T.
Differential proteomic analysis of the mouse retina: the induction of crystallin proteins by retinal degeneration in the rd1 mouse.
Mol Cell Proteomics. 2003 Aug;2(8):494-505.

31: Fintz AC, Audo I, Hicks D, Mohand-Said S, Léveillard T, Sahel J.
Partial characterization of retina-derived cone neuroprotection in two culture models of photoreceptor degeneration.
Invest Ophthalmol Vis Sci. 2003 Feb;44(2):818-25.

32: Sahel JA, Mohand-Said S, Léveillard T, Hicks D, Picaud S, Dreyfus H.
Rod-cone interdependence: implications for therapy of photoreceptor cell diseases.
Prog Brain Res. 2001;131:649-61. Review.

33: Mohand-Said S, Hicks D, Léveillard T, Picaud S, Porto F, Sahel JA.
Rod-cone interactions: developmental and clinical significance.
Prog Retin Eye Res. 2001 Jul;20(4):451-67.

34: Fuhrmann V, Kinkl N, Léveillard T, Sahel J, Hicks D.
Fibroblast growth factor receptor 4 (FGFR4) is expressed in adult rat and human retinal photoreceptors and neurons.
J Mol Neurosci. 1999 Aug-Oct;13(1-2):187-97.

35: Frasson M, Picaud S, Léveillard T, Simonutti M, Mohand-Said S, Dreyfus H, Hicks D, Sabel J.
Glial cell line-derived neurotrophic factor induces histologic and functional protection of rod photoreceptors in the rd/rd mouse.
Invest Ophthalmol Vis Sci. 1999 Oct;40(11):2724-34.

36: Mohand-Said S, Deudon-Combe A, Hicks D, Simonutti M, Forster V, Fintz AC, Léveillard T, Dreyfus H, Sahel JA.
Normal retina releases a diffusible factor stimulating cone survival in the retinal degeneration mouse.
Proc Natl Acad Sci U S A. 1998 Jul 7;95(14):8357-62.

37: Léveillard T, Gorry P, Niederreither K, Wasylyk B.
MDM2 expression during mouse embryogenesis and the requirement of p53.
Mech Dev. 1998 Jun;74(1-2):189-93.

38: Bloch-Zupan A, Léveillard T, Gorry P, Fausser JL, Ruch JV.
Expression of p21(WAF1/CIP1) during mouse odontogenesis.
Eur J Oral Sci. 1998 Jan;106 Suppl 1:104-11.

39: Léveillard T, Wasylyk B.
The MDM2 C-terminal region binds to TAFII250 and is required for MDM2 regulation of the cyclin A promoter.
J Biol Chem. 1997 Dec 5;272(49):30651-61.

40: Léveillard T, Andera L, Bissonnette N, Schaeffer L, Bracco L, Egly JM, Wasylyk B.
Functional interactions between p53 and the TFIIH complex are affected by tumour-associated mutations.
EMBO J. 1996 Apr 1;15(7):1615-24.

41: Léveillard T, Kassavetis GA, Geiduschek EP.
Repression and redirection of Saccharomyces cerevisiae tRNA synthesis from upstream of the transcriptional start site.
J Biol Chem. 1993 Feb 15;268(5):3594-603.

42: Léveillard T, Verma IM.
Diverse molecular mechanisms of inhibition of NF-kappa B/DNA binding complexes by I kappa B proteins.
Gene Expr. 1993;3(2):135-50.

43: Léveillard T, Kassavetis GA, Geiduschek EP.
Saccharomyces cerevisiae transcription factors IIIB and IIIC bend the DNA of a tRNA(Gln) gene.
J Biol Chem. 1991 Mar 15;266(8):5162-8.

44: Diarra-Mehrpour M, Bourguignon J, Sesboüé R, Salier JP, Léveillard T, Martin JP.
Structural analysis of the human inter-alpha-trypsin inhibitor light-chain gene.
Eur J Biochem. 1990 Jul 20;191(1):131-9.

45: Léveillard T, Sirugo G, Hanauer A, Sesboüé R, Bourguignon J, Diarra-Mehrpour M, Salier JP, Martin JP.
An hypervariable polymorphism detected in the human inter-alpha-trypsin inhibitor heavy chain gene ITIH2.
Nucleic Acids Res. 1990 Mar 11;18(5):1319.

46: Léveillard T, Diarra-Mehrpour M, Salier JP, Sesboüe R, Bourguignon J, Martin JP.
Bgl I reveals two polymorphic sites in the human inter-alpha-trypsin inhibitor heavy chain gene ITI H2.
Nucleic Acids Res. 1990 Jan 25;18(2):386.

47: Léveillard T, Salier JP, Sesboüé R, Bourguignon J, Diarra-Mehrpour M, Martin JP.
Dra I polymorphism in the human inter-alpha-trypsin inhibitor heavy chain gene ITIH1.
Nucleic Acids Res. 1989 Jul 11;17(13):5419.

48: Léveillard T, Bourguignon J, Salier JP, Diarra-Mehrpour M, Sesboüé R, Martin JP.
Two RFLPs in human inter-alpha-trypsin inhibitor heavy chain gene ITIH2 on chromosome 10.
Nucleic Acids Res. 1989 Jul 11;17(13):5418.

49: Léveillard T, Sesboüé R, Salier JP, Bourguignon J, Le Gueult LC, Diarra-Mehrpour M, Martin JP.
An Apa I polymorphism for the human inter-alpha-trypsin inhibitor heavy chain gene ITIH1 on chromosome 3.
Nucleic Acids Res. 1989 Apr 11;17(7):2875.

50: Léveillard T, Diarra-Mehrpour M, Bourguignon J, Sesboüé R, Salier JP, Martin JP.
Eco O 109 reveals two polymorphic sites in the human inter-alpha-trypsin inhibitor light chain gene, ITI L.
Nucleic Acids Res. 1989 Feb 11;17(3):1272.

51: Léveillard T, Salier JP, Sesboüé R, Bourguignon J, Diarra-Mehrpour M, Martin JP.
Sst I RFLP in the human inter-alpha-trypsin inhibitor heavy chain gene ITIH1.
Nucleic Acids Res. 1988 Dec 23;16(24):11852.

52: Léveillard T, Bourguignon J, Sesboüé R, Hanauer A, Salier JP, Diarra-Mehrpour M, Martin JP.
BstXI RFLP in the human inter-alpha-trypsin inhibitor light chain gene.
Nucleic Acids Res. 1988 Mar 25;16(6):2744.

E. Invited lectures.

Lund, European PRO-AGE-RET meeting February 2004 ; Paris, Ecole Normale Supérieure, Avril 2004 ; Paris, Académie des sciences May 2004 ; Noordwijk, Retina International World Congress July 2004 ; Sydney, XVI International Congress of Eye Research September 2004 ; Dublin, All Ireland Retinal Research Network Meeting September 2004-09-22; Berlin, 102nd Annual meeting of the German Society of ophthalmology, September 2004 ; Bienne, 25ème anniversaire de Retina Suisse, Octobre 2004 ; Philadelphia, University of Pennsylvania November 4th 2004 ; Bilbao, Final meeting of the Pro-aged Ret European consortium March 15th 2005 ; Fort Lauderdale, ARVO May 2nd 2005 ; Helsinki, RETNET annual meeting June 10th 2005 ; Dublin, EVI-GENORET therapeutic component meeting June 15th 2005; Berne, Meeting of the Biozentrum consortium June 21rst 2005 ; Munchen, EVI-GENORET functional genomics component meeting September 9th 2005 ; Berlin, Annual meeting of the German ophthalmology society September 29th 2005 ; London, EVI-GENORET therapeutic component meeting November 23rd 2005 ; Postdam, Proretina annual meeting April 7th 2006 ; Munchen, EVI-GENORET functional genomics component meeting January 20th 2006 ; Paris, Salpétrière Proteomic network meeting May 18th 2006 ; Cambridge, International Society of Ocular Biology meeting September 6th 2006 ; Buenos-Aires, XVII International Congress of Eye Research October 30th ; Venezia, Euro-RETNET annual meeting November 20th 2006 ; Tuebingen, EVI-GENORET therapeutic component meeting November 29th 2006 ; Paris, Institut Pasteur December 5th 2006 ; Paris, Annual meeting of the EVI-GENORET consortium March 16th 2007; Fort Lauderdale, ARVO May 8th 2007 ; St Petersbourg, ECO-NET network August 27th 2007; Lyons ENS December 14th 2007 ; Moscow ECO-NET network December 18th 2007, Beijing XVIII International Congress of Eye Research October 2008, Yerevan Internal minisymposium Defense mechanisms of the retina October 2008, Paris, October 6th 2009Ministère des finances, Colloque des Instituts Carnot, Barcelona, November 24th 2009, ESF-UB Conference in Biomedicine in association with Eurovisionnet and Fondation Voir et Entendre, Paris, November 27th Cité des Sciences de Paris la Villette ANR.