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Research director, INSERM (French National Institute for Health and Medical Research), DR2.

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EDUCATION AND DIPLOMAS

1996 Ph.D., Louis Pasteur University, Strasbourg, France.
2003 Habilitation à Diriger les Recherches, Université Paris XI, Orsay, France.

RESEARCH EXPERIENCE

1991-96 **Graduate student:** Dr. JM Egly's laboratory, Institut de Génétique et de Biologie Moléculaire et Cellulaire, Strasbourg, France.
1996-99 **Postdoctoral fellow:** Dr. LH Tsai's laboratory, Harvard Medical School, Boston, USA.
1999-01 **Postdoctoral fellow:** Dr. F. Saudou's laboratory, Institut Curie - UMR146 CNRS, Orsay, France.
2001-05 **Junior Scientist:** INSERM, Chargé de Recherche 2^{ème} Classe
2005-10 **Senior Scientist:** INSERM, Chargé de Recherche 1^{ère} Classe.
2007-10 Clinical research contract - Interface clinique INSERM/AP-HP.
2009-2014 **Group leader,** Institut Curie - CNRS 3306 - INSERM U1005, Orsay, France.
2010-now **Research director:** INSERM, DR2.
2015-now **Group leader,** GIN - INSERM U836 - UGA, Grenoble, France.

PUBLICATIONS

1. Fischer L, Gerard M, Chalut C, Lutz Y, **Humbert S**, Kaso M, Chambon P and Egly JM (1992). Cloning of the 62-kilodalton component of basic transcription factor BTF2. *Science*, 257, 1392-1395.
2. Lepage P, Heckel C, **Humbert S**, Stahl S and Rautmann G (1993). Recombinant technology as an alternative to chemical peptide synthesis: expression and characterization of HIV-1 Rev recombinant peptides. *Anal Biochem*, 213, 40-48.
3. Schaeffer L, Roy R, **Humbert S**, Moncollin V, Vermeulen W, Hoeijmakers JHJ, Chambon P and Egly JM (1993). DNA repair helicase: a component of BTF2 (TFIIH) basic transcription factor. *Science*, 260, 58-63.
4. Roy R, Schaeffer L, **Humbert S**, Vermeulen W, Weeda G and Egly JM (1993). The DNA-dependent ATPase activity associated with the class II transcription factor BTF2/TFIIH. *J Biol Chem*, 269, 9826-9832.
5. van Vuuren AJ, Vermeulen W, Ma L, Weeda G, Appeldoorn E, Jaspers NGJ, van der Eb AJ, Bootsma D, Hoeijmakers JHJ, **Humbert S**, Schaeffer L and Egly JM (1994). Correction of xeroderma pigmentosum repair defect by basal transcription factor BTF2 (TFIIH). *EMBO J*, 13, 1645-1653.
6. **Humbert S**, van Vuuren H, Lutz Y, Hoeijmakers JHJ, Egly JM and Moncollin V (1994). p44 and p34 subunits of the BTF2/TFIIH transcription factor have homologies with SSL1, a yeast protein involved in DNA repair. *EMBO J*, 13, 2393-2398.
7. van Vuuren AJ, Appeldoorn E, Odijk H, **Humbert S**, Eker APM, Jaspers NGJ, Egly JM and Hoeijmakers JHJ (1995). Characterization of a subunit and partial purification of the nucleotide excision repair complex, containing the correcting activities of ERCC1, ERCC4, ERCC11 and XP-F. *Mutation Research*, 337, 25-39.
8. **Humbert S**, Dhavan R and Tsai LH (2000). p39 activates cdk5 in neurons, and is associated with the actin cytoskeleton. *J Cell Sci*, 113, 975-983.
9. **Humbert S**, Lanier LM and Tsai LH (2000). Synaptic localization of p39, a neuronal activator of cdk5. *Neuroreport*, 11, 2213-2216.
10. Zuckeberg, L.R., Patrick, G.N., Nikolic, M., **Humbert S**, Wu, C.L., Lanier, L.M., Gertler, F.B., Vidal, M., Van Etten, R.A., and Tsai, L.-H. (2000). Cables links Cdk5 and c-Abl and facilitates Cdk5 tyrosine phosphorylation, kinase upregulation, and neurite outgrowth. *Neuron*, 26, 633-646.
11. Ko J[§], **Humbert S**[§], Bronson RT, Takahashi S, Kulkarni AB, Li E and Tsai LH (2001). p35 and p39 are essential for cyclin-dependent kinase 5 function during neurodevelopment. *J Neurosci*, 21, 6758-6771. [§] equal first authors.
12. **Humbert S**, Bryson EA, Cordelières FP, Connors NC, Datta SR, Finkbeiner S, Greenberg ME and Saudou F (2002). The IGF-1/Akt pathway is neuroprotective in Huntington's disease and involves huntingtin phosphorylation by Akt. *Dev Cell*, 2, 831-837.
13. Holbert S, Dedeoglu A, **Humbert S**, Saudou F, Ferrante RJ and Néri C (2003). The Cdc42-interacting protein 4 binds to huntingtin: neuropathologic and biological evidence for a role in Huntington's disease pathogenesis. *Proc Natl Acad Sci*, 100, 2712-2717.

14. Bizat N, Hermel JM, **Humbert S**, Jacquard C, Creminon C, Escartin C, Saudou F, Krajewski S, Hantraye P and Brouillet E (2003). In vivo calpain/caspase cross-talk during 3-nitropropionic acid-induced striatal degeneration: Implication of a calpain-mediated cleavage of active caspase-3. *J Biol Chem*, 278, 43245-43253.
15. Rangone H, Poizat G, Troncoso J, Ross CA, MacDonald ME, Saudou F and **Humbert S** (2004). The serum and glucocorticoid induced kinase SGK inhibits mutant huntingtin-induced toxicity by phosphorylating serine 421 of huntingtin. *Eur J Neurosci*, 19, 273-279.
16. Gauthier LR, Charrin BC, Borell-Pagès M, Dompierre JP, Rangone H, Cordelieres FP, de Mey J, MacDonald, ME, Lessman V, **Humbert S** and Saudou F (2004). Huntingtin controls neurotrophic support and survival of neurons by enhancing BDNF vesicular transport along microtubules. *Cell*, 118, 127-138.
17. Colin E, Régulier E, Perrin V, Dürr A, Brice A, Aebischer P, Déglon N, **Humbert S** and Saudou F (2005). Akt is altered in an animal model of Huntington's disease and in patients. *Eur J Neurosci*, 21, 1478-1488.
18. Rangone H, Pardo R, Colin E, Girault JA, Saudou F and **Humbert S** (2005). S260 phosphorylation of arfaptin 2 by Akt inhibits polyQ-huntingtin-induced toxicity by rescuing proteasomal impairment. *J Biol Chem*, 280, 22021-22028.
19. Pardo R, Colin E, Régulier E, Aebischer P, Déglon N, **Humbert S** and Saudou F (2006). Inhibition of calcineurin by FK506 protects against polyQ-huntingtin toxicity through an increase of huntingtin phosphorylation at S421. *J Neurosci*, 26, 1635-1645.
20. Borrell-Pagès M, Canals JM, Cordelières FP, Parker JA, Pineda JR, Grange G, Bryson EA, Guillemier M, Hirsch E, Hantraye P, Cheetham ME, Néri C, Alberch J, Brouillet E, Saudou, F and **Humbert S** (2006). Cystamine and cysteamine increase brain levels of BDNF in Huntington's disease through HSJ1b and transglutaminase. *J Clin Invest*, 116, 1410-1424.
21. Dompierre J, Godin JD, Charrin BC, Cordelières FP, King SJ, **Humbert S** and Saudou F (2007). HDAC6 Inhibition Compensates for the Transport Deficit in Huntington's Disease by Increasing Tubulin Acetylation. *J Neurosci*, 27, 3571-3583.
22. Anne S, Saudou F and **Humbert S** (2007). Phosphorylation of huntingtin by Cdk5 is induced by DNA damage and regulates wild-type and mutant huntingtin toxicity in neurons. *J Neurosci*, 27, 7318-7328.
23. Roze E, Betuing S, Deyts C, Marcon E, Brami-Cherrier K, Pagès C, **Humbert S**, Mérienne K, Caboche J (2007). Mitogen- and stress-activated protein kinase-1 deficiency is involved in expanded-huntingtin-induced transcriptional dysregulation and striatal death. *FASEB J*, 22, 1083-1093.
24. Colin E, Zala D, Rangone H, Liot G, Li XJ, Saudou F and **Humbert S** (2008). Huntingtin phosphorylation acts as a molecular switch for anterograde/retrograde transport in neurons. *EMBO J*, 27, 2124-2134.
25. Zala D, Colin E, Rangone H, **Humbert S** and Saudou F (2008). Phosphorylation of mutant huntingtin at S421 restores anterograde and retrograde transport in neurons. *Hum Mol Genet*, 17, 3837-3846.
26. Pineda JR, Pardo R, Zala D, Yu H, **Humbert S** and Saudou F (2009). Genetic and Pharmacological inhibition of calcineurin corrects the BDNF transport defect in Huntington's disease. *Mol Brain*, 2, 33-44.
27. Twelvetrees AE, Yuen E, Arancibia-Carcamo IL, Rostaing P, Lumb MJ, **Humbert S**, Triller A, Saudou F, Yan Z and Kittler JT (2010). Mutant huntingtin disrupts a HAP1-KIF5 trafficking complex essential for GABA-A receptor transport and inhibitory synaptic transmission. *Neuron*, 65, 53-65.
28. Pardo R, Molina-Calavita M, Poizat G, Keryer G, **Humbert S** and Saudou F (2010). pARIS-htt: an optimised expression platform to study huntingtin reveals functional domains required for vesicular trafficking. *Mol Brain*, 3, 1-17.
29. Godin JD, Poizat G, Hickey MA, Maschat F and **Humbert S** (2010). Mutant huntingtin-impaired degradation of beta-catenin causes neurotoxicity in Huntington's disease. *EMBO J*, 29, 2433-2445.
30. Godin JD, Colombo K, Molina-Calavita M, Keryer G, Zala D, Charrin BC, Dietrich P, Volvert ML, Guillemot F, Dragatsis I, Bellaïche Y, Saudou F, Nguyen L and **Humbert S** (2010). Huntingtin is required for mitotic spindle orientation and mammalian neurogenesis. *Neuron*, 67, 392-406.
31. Del Toro D, Xifró X, Pol A, **Humbert S**, Saudou F, Canals JM and Alberch J (2010). Altered cholesterol homeostasis contributes to enhanced excitotoxicity in Huntington's Disease. *J Neurochem*, 115, 153-67.
32. Mochel F, Durant B, Meng X, O'Callaghan J, Yu H, Brouillet E, Wheeler VC, **Humbert S**, Schiffmann R and Durr A (2012). Early alterations of brain cellular energy homeostasis in Huntington disease models. *J Biol Chem*, 287, 1361-70.
33. Moreira Sousa C, McGuire JR, Thion MS, Gentien D, de la Grange P, Tezenas du Montcel S., Vincent-Salomon A, Durr A and **Humbert S** (2013). The Huntington disease protein accelerates breast tumor development and metastasis through ErbB2/HER2 signaling. *EMBO Mol. Med.*, 5, 309-325.
34. Ben M'Barek K, Pla P, Orvoen S, Benstaali, Godin JD, Gardier AM, Saudou F, David DJ and **Humbert S** (2013). Huntingtin Mediates Anxiety/Depression-related Behaviors and Hippocampal Neurogenesis. *J Neurosci*, 33, 8608-8620.
35. Berger F, Vaslin L, Belin L, Asselain B, Forlani S, **Humbert S**, Durr A and Hall J (2013). The impact of single-nucleotide polymorphisms (SNPs) in OGG1 and XPC on the age at onset of Huntington disease. *Mutat Res*, 15, 115-119.
36. Pla P, Orvoen S, Benstaali C, Dodier S, Gardier AM, David DJ, **Humbert S**, Saudou F (2013). Huntingtin acts non cell-autonomously on hippocampal neurogenesis and controls anxiety-related behaviors in adult

mouse. *PLoS One*, 8, e73902.

37. Lopes C, Ribeiro M, Duarte AI, **Humbert S**, Saudou F, Pereira de Almeida L, Hayden M, Rego AC. (2013). IGF-1 Intranasal Administration Rescues Huntington's Disease Phenotypes in YAC128 Mice. *Mol Neurobiol*, 49, 1126-1142.
38. Elias S, Thion MS, Yu H, Moreira Sousa C, Lasgi C, Morin X and **Humbert S** (2014). Huntingtin Regulates Mammary Stem Cell Division and Differentiation. *Stem Cell Reports*, 2, 491-506.
39. Naia L, Ferreira IL, Cunha-Oliveira T, Duarte AI, Ribeiro M, Rosenstock TR, Laço MN, Ribeiro MJ, Oliveira CR, Saudou F, **Humbert S** and Rego AC (2014). Activation of IGF-1 and Insulin Signaling Pathways Ameliorate Mitochondrial Function and Energy Metabolism in Huntington's Disease Human Lymphoblasts. *Mol Neurobiol*, 51, 331-348.
40. Forget A, Bihannic L, Cigna SM, Lefevre C, Remke M, Barnat M, Dodier S, Shirvani H, Mercier A, Mensah A, Garcia M, **Humbert S**, Taylor MD, Lasorella A, Ayrault O (2014). Shh signaling protects atoh1 from degradation mediated by the e3 ubiquitin ligase huwe1 in neural precursors. *Dev Cell*, 29, 649-661.
41. Molina-Calavita M, Barnat M, Elias S, Aparicio E, Piel M and **Humbert S** (2014). Mutant huntingtin affects cortical progenitor cell division and development of the mouse neocortex. *J Neurosci*, 34, 10034-10040.
42. Prundean A, Youssov K, **Humbert S**, Bonneau D, Verny C (2014). A phase II, open-label evaluation of cysteamine tolerability in patients with Huntington's disease. *Mov Disord*, 30, 288-289.
43. Ochaba J, Lukacsovich T, Csikos G, Zheng S, Margulis J, Salazar L, Mao K, Lau AL, Yeung SY, **Humbert S**, Saudou F, Klionsky DJ, Finkbeiner S, Zeitlin SO, Marsh JL, Housman DE, Thompson LM, Steffan JS (2014). Potential function for the Huntingtin protein as a scaffold for selective autophagy. *Proc Natl Acad Sci USA*, 25, 16889-94.
44. Elias S, McGuire JR, Yu H and **Humbert S** (2015). Huntingtin is required for epithelial polarity through RAB11A mediated apical trafficking of PAR3-aPKC. *Plos Biol*, 13:e1002142.
45. El Daher MT, Hangen E, Bruyère J, Poizat G, Al-Ramahi I, Pardo R, Bourg N, Souquere S, Mayet C, Pierron G, Lévêque-Fort S, Botas J, **Humbert S** and Saudou F (2015). Huntingtin proteolysis releases non-polyQ fragments that cause toxicity through dynamin 1 dysregulation. *EMBO J*, 34, 2255-2271.
46. Thion MS, McGuire JR, Sousa CM, Fuhrmann L, Fitamant J, Leboucher S, Vacher S, Tezenas du Montcel S, Bièche I, Bernet A, Patrick Mehlen P, Anne Vincent-Salomon A, and **Humbert S** (2015). Unravelling the role of huntingtin in breast cancer metastasis. *JNCI*, 107. doi: 10.1093/jnci/djv208.
47. Lopes C, Aubert S, Bourgois-Rocha F, Barnat M, Rego AC, Déglon N, Perrier AL and **Humbert S** (2016). Dominant-negative effects of adult-onset huntingtin mutations alter the division of human embryonic stem cells-derived neural cells. *PLoS ONE* 11(2): e0148680. doi:10.1371/journal.pone.0148680.
48. Thion MS, Tézenas du Montcel S, Golmard JL, Vacher S, Barjhoux L, Sornin V, Cazeneuve C, Bièche I, Sinilnikova O and Stoppa-Lyonnet D for GEMO, Durr A and **Humbert S**. CAG repeat size in Huntingtin alleles predicts cancer prognosis. *EJHG*, doi:10.1038/ejhg.2016.13.

REVIEWS, BOOK CHAPTERS

1. **Humbert S** and Saudou F (2001). Neuronal death in Huntington's disease: Multiple pathways for one issue? In *Neuronal death by accident or by design*, Editors: C. E. Henderson, D. Green, J. Mariani, and Y. Christen, Berlin Heidelberg, Springer-Verlag, 137-152.
2. **Humbert S** and Saudou F (2002). Toward cell specificity in SCA1. *Neuron*, 34, 701-713.
3. **Humbert S** and Saudou F (2003). Huntingtin phosphorylation and signaling pathways that regulates toxicity in Huntington's disease. *Clin. Neurosci. Res.*, 3, 149-155.
4. Rangone H, **Humbert S** and Saudou F (2004). Huntington's disease: how does huntingtin, an anti-apoptotic protein, become toxic? *Pathologie Biologie*, 52, 338-342.
5. **Humbert S** and Saudou F (2004). Stimulation of BDNF transport by huntingtin. *Médecine/Science*, 20, 952-054.
6. Charrin BC, Saudou F and **Humbert S** (2005). Axonal transport failure in neurodegenerative disorders: the case of Huntington's disease. *Pathologie Biologie*, 53, 189-192.
7. **Humbert S** and Saudou F (2005). Huntington's disease: intracellular signaling pathways and neuronal death. *J. Soc. Biol.*, 199, 247-251.
8. **Humbert S** and **Saudou F** (2006). The ataxia-ome: Connecting disease proteins of the cerebellum. *Cell*. 125, 645-647.
9. **Humbert S** and **Saudou F** (2006). Cysteamine restores intracellular dynamics and BDNF secretion in Huntington's disease. *Médecine/Science*, 22, 906-908.
10. Borrell-Pages M, Zala D, **Humbert S** and Saudou F (2006). Huntington's disease: from huntingtin function and dysfunction to therapeutic strategies. *Cell. Mol. Life Sci.*, 63, 2642-60.
11. Saudou F and **Humbert S** (2008). The biology of Huntington's disease. In *Handbook of Clinical Neurology, Dementias*, Editors C. Duyckaerts, I. Litvan, Elsevier BV, 89, 619-629.
12. Saudou F and **Humbert S** (2008). Axonal transport and Huntington's disease. In *Encyclopedia of Neuroscience*, Editor-in-Chief Larry R. Squire, Academic Press, Oxford.

- 13.** Saudou F and **Humbert S** (2008). Huntington's disease: function and dysfunction of huntingtin in axonal transport. In *Research and Perspectives in Alzheimer disease*, Editors P. St George Hyslop, W. Mobley and Y. Christen, Berlin Heidelberg, Springer-Verlag.
- 14.** **Humbert S** (2010). Is Huntington disease a developmental disorder? *EMBO Rep.*, 11, 899.
- 15.** Godin JD and **Humbert S** (2011). Mitotic spindle: Focus on the function of huntingtin. *Int. J. Biochem. Cell. Biol.*, 43, 852-6.
- 15.** Godin JD and **Humbert S** (2011). Huntingtin, mitosis and cell fate. *Med. Sci.*, 27, 126-8.
- 16.** Sousa CM and **Humbert S** (2013). Huntingtin: Here, There, Everywhere! *Journal of HD*, 2, 395-403.
- 17.** Pla P, Orvoen S, Saudou F, David DJ, **Humbert S** (2014). Mood disorders in Huntington's disease: from behavior to cellular and molecular mechanisms. *Front. Behav. Neurosci.*, 23, 135-150.
- 18.** Saudou F and **Humbert S** (2016). The Biology of Huntingtin. *Neuron*, 89, 910-26.

MAIN LABORATORY FUNDINGS (since 2010)

Agence nationale de la recherche, ANR	09/2009-08/2012 (coordinator)
Subvention libre de l'ARC	06/2009-05/2012 (coordinator)
ANR	10/2012-09/2015 (coordinator)
FRM équipe	10/2012-09/2015 (coordinator)
INCA	01/2014-12/2017 (partner)
COEN	2016-2018 (partner)

SUPERVISION OF GRADUATE STUDENTS AND POSTDOCTORAL FELLOWS

I have supervised 6 PhD and 7 postdocs over the last 8 years. 3 of the PhD students and 1 postdocs are postdocs in highly reputed labs, 1 PhD is working in a scientific consulting office (Alcimed); 1 PhD is working at AstraZeneca (drug discovery department); 1 PhD is now a group leader in Strasbourg (IGBMC; after a post-doc in Belgium); 1 postdoc has a position in a patenting office (USA); 1 postdoc is a teacher; 1 postdoc has a position in my lab as a assistant Prof (Grenoble Alpes University).

TEACHING EXPERIENCE

Lecturer in courses at different well-ranked master degree and doctoral programs of the University Paris Descartes; University Pierre et Marie Curie, Paris; Institut Curie, Paris, University Grenoble Alpes, University of Coimbra, Portugal (approx. 20hrs/yr).

Member of PhD thesis and Research Habilitation committees in France and Europe (3 to 5/yr).

INSTITUTIONAL RESPONSABILITIES and SCIENTIFIC COMMITTEES

Member of the scientific committee for the recruitment of assistant professors (Campagne recrutement MDC 219, Université Paris Diderot, 2013; Campagne recrutement MDC 65, UPMC Paris, 2013.)

Member of the scientific committee of AHF (Association Huntington France, french association of HD families and patients): animation of the annual day of AHF; vulgarization of HD basic science for the AHF journal: organization committee of the french Huntington's disease day (oct 11th, 2013, Institut Curie).

President of the local ethics committee for animal experimentation (registered as number 04 by the Comité National de Réflexion Ethique sur l'Expérimentation Animale).

EDITORIAL BOARD COMMITTEES & REVIEWING

Academic Editor for PLOS One (2013-).

Ad hoc reviewer for Embo Molecular Medicine; HMG; Journal of Neuroscience; Molecular psychiatry; Nature communications; Nature Medicine; Neuron; Neuropharmacology; Traffic.

Grant reviews: fondation pour la recherche sur le cerveau (FRC, France); Telethon (Italie); WellcomeTrust (England); Agence nationale de la recherche (ANR, France); European research council (ERC).

INVITED PRESENTATIONS IN MEETINGS AND SEMINARS

During the last decade, I have been invited to more than 30 conferences as invited speaker (Gordon conference, EMBO meeting, Society for neuroscience meeting, Society of Biological Psychiatry) and gave 25 seminars in France and abroad. I chaired sessions at the 2008 and 2015 meetings of the Society for Neuroscience.