

Prof. Dr. Pascal Kienlen-Campard, PhD
Professor in neuroscience and molecular biology
University of Louvain

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E-mail: pascal.kienlen-cmaprd@uclouvain.be
Date of birth : April 20, 1968 **Place of birth**: Rouen
Nationality : French

Education

Bachelor in Biology, University of Strasbourg, France 1988
Master in Biochemistry/Molecular Biology, University of Strasbourg, France 1991
Qualified teacher (aggregation) in Biochemistry/Molecular Biology,
French Ministry for higher Education 1994
Post-graduate (DEA) in Pharmacology/Pharmacochimistry 1995
Ph.D. in Biology, University of Strasbourg, France 1999

Post Graduate Training

- Postdoc Fellow, University of Strasbourg/Biovalley (France/Switzerland) 02/99 - 09/99
- Postdoc Associate, UCLouvain, Department of Physiology, Belgium 10/99 - 09/02
- Research associate, UCLouvain, Department of Physiology, Belgium 10/02 - 08/05

Academic and Institutional Appointments

- Associate Professor, UCLouvain, Experimental Pharmacology Unit, Belgium 01/09/05
- Professor, UCLouvain, Institute of Neuroscience (IoNS), Belgium 01/09/13
- *Group leader* at IoNS, UCLouvain, Belgium 01/09/10 - present
- *Vice-Dean*, Faculty of Pharmacy/Biomed. Sciences, UCLouvain, Belgium 01/09/10 - 31/08/16
- *President of the Institute of Neuroscience*, UCLouvain, Belgium 01/09/201 - present

Postdoc Fellowships and Travel Awards

- Postdoc Fellowship from the Biovalley fund/Société Française des amis des Sciences to conduct research on cell cycle gene regulation in neuronal death (Biovalley/CNRS/University of Strasbourg, France) (01/01/99 – 30/09/99).
- Postdoc Fellowships and Grants of the UCLouvain, UCLouvain Action de recherche concertée (ARC) and BELSPO/Interuniversity Attraction Poles (IAP) for postdoctoral research at UCLouvain. (Belgium) (01/10/99 – 31/08/05 and 01/10/99).

Scientific Awards

- Best Presentation award at the French Society of Experimental Neuropathology, Paris, 4th december 1999.
- King Baudouin Foundation – Aline Prize Fund 2013 (100,000 euro dedicated to a research project).

Peer Reviewing

- Ad hoc for the following journals (~5/year): Journal of Neurochemistry, Journal of Cellular and Molecular Medicine, Cellular and Molecular Life Sciences, PLOS One

Reviewing Grant Applications of: *French National Research Agency (ANR, France); International Alzheimer Research Foundation (USA); SAO/FRA Alzheimer Foundation (Belgium); Ligue Européenne contre la Maladie d'Alzheimer (LECMA) and France Alzheimer (France). Member of the EU Joint Programme – Neurodegenerative Disease Research (JPND) Board (as of April 2017).*

Member of: *UCLouvain Fonds de Développement pédagogique (2010-2014)*

Member of the International Action Council UCLouvain (2010 – 2015)

Member of Health Sector Council UCLouvain (01/09/2010 – present)

Member of the Euron Network Board (as of 2010)

Member of the Louvain4Evolution council (as of September 2016)

Obtained Grants (past 10 years)

- 2007-2009: SAO-FRMA Standard award. “Role of transmembrane motifs in APP dimerization and function”. Promoter: Pascal Kienlen-Campard.

- 2008-2009: FRNRS Crédit aux chercheurs. “Role of GXXXG motifs in APP dimerization”. Promotor: Pascal Kienlen-Campard

- 2011-2012: FNRS Crédit de Recherche CDR 1.5076.12F “New tools to analyze APP dimerization and its impact on APP function”. Promotor: Pascal Kienlen-Campard.

- 2011-2012: SAO-FRMA Standard award. “Transmembrane helix association in APP processing and gamma-secretase activity”. Promotor: Pascal Kienlen-Campard.

- 2013-2014: SAO-FRA Standard award. “Peptidic tools targeting the transmembrane domain to modulate APP dimerization and Amyloid pathology”. Promoter: Pascal Kienlen-Campard.

- 2013-2016: FRME Queen Elizabeth Medical Research Foundation research grant. “Alteration of cholesterol turnover in Alzheimer disease”. Promotor: Jean-Noël Octave. Co-promoters: Pascal Kienlen-Campard, Ilse Dewachter.

- 2013-2017: IAP P7-16 ‘An integrated approach towards understanding the pathogenesis of neurodegeneration (NeuroBrainNet)’. Coord: C. Van Broeckhoven; co-PI of Partner 5 Jean-Noël Octave.

-2013: FNRS Equipment # 19540444. “Acquisition and update of fluorescence microscope systems for the development of the imaging platform of the Cellular and Molecular Neuroscience division of the Institute of Neuroscience”. Promotor: Frédéric Clotman. Co-promoters: Ilse Dewachter, Emmanuel Hermans, Pascal Kienlen-Campard.

- 2015-2019: ARC (Action de Recherche Concertée) EPIMODIS Epigenetic mechanisms of disease. Spokesperson: Charles Desmet. Promoters: Charles Desmet, Olivier Debaeker, Anabelle Decottignies.

- 2015-2017: SAO-FRA Standard award. “Control of GDNF expression by Amyloid Precursor Protein & Presenilins and implications in neurodegenerative and neuromuscular diseases”. Promotor/ Pascal Kienlen-Campard.

(Co-)Promotorship of doctorates

- Naouel Ben Khalifa - *Mechanisms regulating the dimerization of the Amyloid Precursor Protein and their role in its trafficking and processing*. October 22nd, 2010. (promotor)
- Salim Hage - *Etude de l'action d'extraits tirés de plantes africaines traditionnellement utilisées en cas de démence, sur le métabolisme du peptide β -amyloïde*. January 15th, 2013. (co-promotor)
- Claudia Marinangeli - *Role of presenilin transmembrane domain interactions in γ -secretase activity and characterization of natural inhibitors*. December 15th, 2014. (promotor)
- Marie Decock - *Role of transmembrane GXXXG motifs in APP dimerization and beta-amyloid peptide oligomerization in Alzheimer's disease*. January 14th, 2016.(promotor)

Currently ongoing

- Remi Opsomer - *AICD-dependent transcriptional regulation in neurons*. Promotor
- Sabrina Contino – *Role of the Presenilins in mitochondrial morphology and function*. Promotor
- Florian Perrin – *Dimeric orientations of APP and pathological functions*. (Copromoter)
- Celine Vranckx – *Pathological properties of A β oligomers*. 2011.(promotor)

Invited Lectures.

- “Folding APP Membrane regions: the shape of Alzheimer’s disease to come”
IPBMC Lecture, Nice Sophia-Antipolis, December 16th 2016
- “Structural features of the extracellular and juxta/transmembrane domains controlling APP dimerization, trafficking, processing”.
Alzheimer’s Association International Conference, Vancouver, July 15-20, 2012
- “Structural requirements for APP processing by gamma-secretase and Abeta oligomerization”.
BIT’s 3rd Annual Protein and Peptide Conference (PepCon 2010)-Lecture. Beijing, March 23rd, 2010
- “APP in Alzheimer’s disease: structure resolves function”.
Conference of the Federative Institute of Neuroscience. Strasbourg, May 11th, 2008
- “Les domaines GXXXG juxtamembranaires et transmembranaires de l’APP contrôlent sa maturation amyloïdogénique ».
9^e Réunion Francophone sur la Maladie d’Alzheimer et les syndromes apparentés. Nice, November 20th-22nd 2007.

Prof. Pascal Kienlen-Campard

Publications in international Peer-reviewed journals

1994

Schimschowitsch S, Plante M, Kienlen P, Felix JM, Stoeckel ME. Glucocorticoids, but not dopamine, negatively regulate the melanotrophic activity of the rabbit pituitary intermediate lobe. *J. Neuroendocrinology*. 1994;6:385-390

1996

Laurent-Huck FM, Egles C, Kienlen P, Stoeckel ME, Felix JM. Expression of the c-ets1 gene in the hypothalamus and pituitary during rat development. *Dev. Brain Res*. 1996;97:107-117.

Barthel F, Kienlen-Campard P, Demeneix BA, Feltz P, Loeffler JP. GABAB receptors negatively regulate transcription in cerebellar granule neurons through cyclic AMP responsive element binding protein-dependent mechanisms. *Neuroscience*. 1996;70:417-427.

1997

Kienlen-Campard P, Crochemore C, René F, Monnier D, Koch B, Loeffler JP. PACAP type I receptor promotes cerebellar neuron survival through the cAMP/PKA signaling pathway. *DNA and Cell Biol*. 1997;16:323-333.

1998

Muller A, Lutz-Bucher B., Kienlen-Campard P, Koch B, Loeffler JP. Continuous activation of Pituitary Adenyl Cyclase-Activating Polypeptide Receptors elicits antipodal effects on cyclic AMP and Inositol Phospholipid signaling pathways in CATH.a cells: role of protein synthesis and protein kinases. *J. Neurochem*. 1998;70:1431-1440

Simonneaux V, Kienlen-Campard P, Loeffler JP, Basille M, Gonzalez BJ, Vaudry H, Robberecht P, Pevet P. Pharmacological, molecular and functional characterization of Vasoactive Intestinal Polypeptide/Pituitary Adenylate Cyclase-Activating Polypeptide receptors in the rat pineal gland. *Neuroscience*. 1998;85:887-896.

1999

Boutillier AL, Kienlen-Campard P, & Loeffler JP. Depolarization regulates cyclin D1 degradation and neuronal apoptosis: a hypothesis about the role of the ubiquitin/proteasome signaling pathway. *Eur. J. Neurosci*. 1999;11:441-448.

Kienlen-Campard P, Boutillier AL & Loeffler JP. Le neurone: un condamné à mort en sursis permanent. *Médecine/Sciences*. 1999;15:77-81.

González de Aguilar JL, Gordon JW, René F, Lutz-Bucher B, Kienlen-Campard P, Loeffler JP. Amyotrophic lateral sclerosis in mice expressing a mutant super oxide dismutase 1 is associated with neurodegeneration of the hypothalamo-neurohypophysial axis. *Eur. J. Neurosci*. 1999;11:1-9.

2000

Kienlen-Campard P, Tasiaux B, Octave JN. The processing and biological function of human amyloid precursor protein (APP): lessons from different cellular models. *Exp Gerontology*. 2000;35:843-850.

Toussaint O, Baret PV, Brion JP, Cras P, Collette F, De Deyn PP, Geenen V, Kienlen-Campard P, Labeur C, Legros JJ, Neve J, Octave JN, Pierard GE, Salmon E, Van Den Bosch de Aguilar P, Van Der Linden M, Van Leuven F, Vanfleteren J. Experimental Gerontology in Belgium : from model organisms to age-related pathologies. *Exp Gerontology*. 2000;35:901-916.

2002

Kienlen-Campard P, Octave JN. Correlation between beta-amyloid peptide production and human APP-induced neuronal death. *Peptides*. 2002;23:1199-1204.

Kienlen-Campard P, Miolet S, Tasiaux B, Octave JN. Intracellular Amyloid- β 1-42, but not extracellular soluble Amyloid- β peptides, induces neuronal apoptosis. *J Biol Chem*. 2002;277:15666-15670.

Pitsi D, Kienlen-Campard P, Octave JN. Failure of the interaction between presenilin 1 and the substrate of γ -secretase to produce A β in insect cells. *J Neurochem*. 2002;83:390-399.

2004

Race V, Marie S, Kienlen-Campard P, Hermans E, Octave JN, Van Den Bergh G, Vincent MF. Adenylosuccinate lyase deficiency: study of physiopathologic mechanism(s). *Nucleosides, nucleotides, and nucleic acids*. 2004;8-9:1227-1229.

2005

Feyt C, Kienlen-Campard P, Leroy K, Brion JP, Octave JN. Lithium chloride increases the production of amyloid- β peptide independently from its inhibition of GSK3. *J Biol Chem*. 2005;280:33220-33227.

2006

Sato T, Kienlen-Campard P, Ahmed M, Liu W, Li H, Elliott J, Aimoto S, Constantinescu SN., Octave JN, Smith SO. Inhibitors of amyloid toxicity based on beta-sheet packing of Abeta40 and Abeta42. *Biochemistry*. 2006;45:5503-5516.

Kienlen-Campard P, Feyt C, Huysseune S, Octave JN. Lactacystin decreases amyloid- β peptide production by inhibiting γ -secretase activity. *J. Neurosci Research*. 2006;84:1311-1322.

2007

Feyt C, Pierrot N, Tasiaux B, Van Hees J, Kienlen-Campard P, Courtoy PJ, Octave JN. Phosphorylation of APP695 at Thr668 decreases gamma-cleavage and extracellular Abeta. *Biochem Biophys Res Commun*. 2007;357:1004-1010.

Huysseune S, Kienlen-Campard P. & Octave J.N. Fe65 does not stabilize AICD during activation of transcription in a luciferase assay. *Biochem Biophys Res Commun*. 2007;361:317-22.

2008

Kienlen-Campard P, Tasiaux B, Van Hees J, Li M., Huysseune S, Sato T, Fei JZ, Aimoto S, Courtoy PJ, Smith SO, Constantinescu SN, Octave JN. Amyloidogenic processing but not AICD production requires a precisely orientated APP dimer assembled by GxxxG motifs. *J Biol Chem*. 2008;283:7733-7744.

2009

Sato T, Tang TZ, Reubins G, Fei JZ, Fujimoto T, Kienlen-Campard P, Constantinescu SN, Octave JN, Aimoto S, Smith SO. A Helix-to-Coil Transition in the Transmembrane Dimer of the Amyloid Precursor Protein is Required for Proteolysis by γ -secretase. *Proc. Nat. Acad. Sci. US*, 2009;106:1421-6.

Huysseune S, Kienlen-Campard P, Hébert S, Tasiaux B, Leroy K, Devuyst O, Brion JP, de Strooper B, Octave JN. Epigenetic control of Aquaporin 1 expression by the Amyloid Precursor Protein. *FASEB J*. 2009 12:4158-67.

2010

Ben Khalifa N, Van Hees J, Tasiaux B, Huysseune S, Smith SO, Constantinescu SN, Octave JN, Kienlen-Campard P. What is the role of Amyloid Precursor Protein Dimerization? *Cell Adhesion Migration* 2010;4:1-5

Hage S, Muccioli G, Kienlen-Campard P, Octave JN, Quetin-Leclercq J. In vitro screening on β -amyloid peptide production of plants used in Beninese popular medicine for cognitive disorders. *J Ethnopharmacol.* 2010 Oct 5;131(3):585-91.

2011

Ben Khalifa N, Tyteca D, Depuydt M, Collet JF, Courtoy PJ, Renauld JC, Constantinescu SN, Octave JN, Kienlen-Campard P. Structural features of the KPI domain control APP dimerization, trafficking and processing. *FASEB J.* 2012 Feb;26(2):855-6727.

Ben Khalifa N, Tyteca D, Courtoy PJ, Renauld JC, Constantinescu SN, Octave JN, Kienlen-Campard P. Contribution of Kunitz Protease Inhibitor and transmembrane domains to Amyloid Precursor Protein homodimerization. *Neurodegener Dis.* 2012;10(1-4):92-5

2013

Pierrot N, Tyteca D, D'auria L, Dewachter I, Muls N, Gailly P, Hendrickx A, El Haylani L, Tasiaux B, N'Kuli F, Laquerrière A, Demoulin JB, Campion D, Brion JP, Courtoy PJ, Kienlen-Campard P, Octave JN. Amyloid Precursor Protein Controls Neuronal Cholesterol Turnover Needed For Synaptic Activity *EMBO Mol Med.* 2013 Apr;5(4):608-25

Hendrickx A, Pierrot N, Tasiaux B, Schakman O, Brion JP, Kienlen-Campard P, De Smet C, Octave JN. Epigenetic induction of EGR-1 expression by the Amyloid Precursor Protein during exposure to novelty. *PLoS One.* 2013 Sep 16;8(9):e74305. doi: 10.1371/journal.pone.0074305. eCollection 2013.

2014

Hage S., Marinangeli C, Stanga S., Octave J.N, Quetin-Leclercq J., Kienlen-Campard P. Gamma-secretase modulator activity of Pterocarpus erinaceus extract. *Neurodegener Dis.* 2014;14(1):39-51.

Hendrickx A, Pierrot N, Tasiaux B, Schakman O, Kienlen-Campard P, De Smet C, Octave JN. Epigenetic regulations of immediate early genes expression involved in memory formation by the amyloid precursor protein of Alzheimer disease. *PLoS One.* 2014 Jun 11;9(6):e99467. doi: 10.1371/journal.pone.0099467. eCollection 2014

Tang TC, Hu Y, Kienlen-Campard P, El Haylani L, Decock M, Van Hees J, Octave JN, Constantinescu SN and Smith SO. Conformational Changes Induced by the A21G Flemish Mutation in the Amyloid Precursor Protein Lead to Increased A β Production *Structure.* 2014 Mar 4;22(3):387-96.

Stancu C, Vasconcelos B., Marinangeli C, Goeminne L, Laporte V, El Haylani L, Couturier J, Schakmann O, Gailly P, Pierrot N, Brion JP, Kienlen-Campard P, Octave JN, Dewachter I. Aggravated Tau-pathology in a model with combined amyloid and Tau-pathology is preceded by dysregulated GSK3beta signaling. *FASEB J.* 2014 Jun;28(6):2620-31.

2015

Hage S, Stanga S, Marinangeli C, Octave JN, Dewachter I, Quetin-Leclercq J, Kienlen-Campard P. Characterization of Pterocarpus erinaceus kino extract and its gamma-secretase inhibitory properties. *J Ethnopharmacol.* 2015 Apr 2;163:192-202

Marinangeli C, Tasiaux B, Opsomer R, Hage S, Sodero AO, Dewachter I, Octave JN, Smith SO, Constantinescu SN, Kienlen-Campard P. Presenilin Transmembrane Domain 8 conserved AxxxAxxxG Motifs Are Required for the Activity of the γ -Secretase Complex. *J Biol Chem.* 2015 Mar 13;290(11):7169-84.

Stancu IC, Vasconcelos B, Ris L, Wang P, Villers A, Peeraer E, Buist A, Terwel D, Baatsen P, Oyelami T, Pierrot N, Casteels C, Bormans G, Kienlen-Campard P, Octave JN, Moechars D, Dewachter I. Templated misfolding of Tau by prion-like seeding along neuronal connections impairs neuronal network function

and associated behavioral outcomes in Tau transgenic mice *Acta Neuropathol.* 2015 Jun;129(6):875-94.

Decock M, El Haylani L, Stanga S, Dewachter I, Octave JN, Smith SO, Constantinescu SN, Kienlen-Campard P. Analysis by a highly sensitive split luciferase assay of the regions involved in APP dimerization and its impact on processing *FEBS Open Bio.* 2015 Sep 6;5:763-73. doi: 10.1016/j.fob.2015.09.002. eCollection 2015.

2016

Stanga S, Zanou N, Audouard E, Tasiaux B, Contino S, Clotman F, Gailly P, Dewachter I, Octave JN, Kienlen-Campard P. APP regulates the Glial cell line-Derived Neurotrophic Factor (GDNF) gene expression driving functional neuromuscular junctions formation *FASEB J.* 2016 May;30(5):1696-711

Couturier J, Stancu IC, Shackman O, Pierrot N, Huaux F, Kienlen-Campard P, Dewachter I, Octave JN. Activation of phagocytic activity in astrocytes by reduced expression of the inflammasome component ASC and its implication in a mouse model of Alzheimer disease. *J Neuroinflammation.* 2016 Jan 27;13:20. doi: 10.1186/s12974-016-0477-y.

Vasconcelos B, Stancu IC, Buist A, Bird M, Wang P, Vanoosthuyse A, Van Kolen K, Verheyen A, Kienlen-Campard P, Octave JN, Baatsen P, Moechars D, Dewachter I. Heterotypic prion-like seeding of Tau fibrillization by pre-aggregated A β , provides potent seeds for induction and propagation of Tau pathology in vivo: A key-pathogenetic molecular mechanism in AD? *Acta Neuropathol.* 2016 Apr;131(4):549-69. doi: 10.1007/s00401-015-1525-x.

Decock M, Stanga S, Octave JN, Dewachter I, Smith SO, Constantinescu SN, Kienlen-Campard P. Glycines from the APP GXXXG/GXXXA transmembrane motifs promote formation of pathogenic A β oligomers in cells *Frontiers Aging Neurosci,* 2016 May 10;8:107. doi: 10.3389/fnagi.2016.00107. eCollection 2016.

2017

Wang P, Joberty G, Buyst A, Vanoosthuyze A, Stancu IC, Vasconcelos B, Kienlen-Campard P, Octave JN, Bantscheff M, Drewes G, Moechars D, Dewachter I. Tau interactome mapping based identification of OTUB1 as Tau-deubiquitinase, involved in accumulation of pathological Tau forms in vitro and in vivo. *Acta Neuropathol.* 2017 May;133(5):731-749. doi: 10.1007/s00401-016-1663-9.

Doshina A, Gourgue F, Onizuka M, Opsomer R, Wang P, Roussel-Ando K, Tasiaux B, Dewachter I, Kienlen-Campard P, Brion JP, Gailly P, Octave JN, Pierrot N. Cortical cells reveal APP as a new player in the regulation of GABAergic neurotransmission. *Scientific Reports, Vol. 7, no.1, p. 370 (2017).* doi:10.1038/s41598-017-00325-2.

Hu Y, Kienlen-Campard P, Tang TC, Perrin F, Opsomer R, Decock M, Pan X, Van Hees J, Octave JN, Constantinescu SN, Smith SO. β -Sheet Structure within the Extracellular Domain of C99 Regulates Amyloidogenic Processing. *Scientific Reports, Vol. 7, p. 17159 (2017).* doi:10.1038/s41598-017-17144-0.

Contino S, Porporato P; Bird M, Marinangeli C, Opsomer R, Sonveaux P, Bontemps F, Dewachter I, Octave JN, Bertrand L, Stanga S, Kienlen-Campard P. Presenilin 2-Dependent Maintenance of Mitochondrial Oxidative Capacity and Morphology. *Frontiers in Physiology, Vol. 8, p. 796 (2017).* doi:10.3389/fphys.2017.00796.

2018

Stanga S, Vrancx C, Tasiaux B, Marinangeli C, Karlström H, Kienlen-Campard P. Comparative analysis of the presenilin 1 (PS1) and presenilin 2 (PS2)-dependent γ -secretase activity on APP and Notch

processing: effect of mutations and pharmacological inhibitors *J Cell Mol Med.* 2018 Feb;22(2):823-833. doi: 10.1111/jcmm.13364.

Stanga S, Brambilla L, Tasiaux B, Dang HA, Ivanoiu A, Octave JN, Rossi D2, van Pesch V and Kienlen-Campard P. A role for GDNF and soluble APP as biomarkers of Amyotrophic Lateral Sclerosis pathophysiology. *Front in Neurology*, *under revision March 2018*.

Tang TC, Kienlen-Campard P, Dass S, Hu Y, Perrin F, Opsomer R, Van Hees J, Octave JN, Constantinescu SN, Smith1 SO. Influence of the T43I Mutation on the Transmembrane Structure and γ -Secretase Processing of C99. *Submitted*

Opsomer R, Contino S, Perrin F, Tasiaux B, Doyen P, Vergouts M, Vrancx C, Doshina A, Pierrot N, Octave JN, Stanga S, Kienlen-Campard P. Amyloid Precursor Protein (APP) regulates excitatory/inhibitory synaptic inputs by recruiting the Neuronal PAS Domain Protein 4 (NPAS4) transcriptional regulator. *Submitted*