CAJAL Advanced Neuroscience Training Course on

Advanced Techniques for Synapse Biology

Bordeaux, October 13- 1 November, 2019

Instructors

Camin Dean, PhD (European Neuroscience Institute, Germany)

During my doctoral research on synapse formation at the University of California, Berkeley, I discovered that neurexin is the receptor of neuroligin; the neurexin-neuroligin trans-synaptic link acts as a nucleation site to induce bidirectional synapse formation both pre- and post-synaptically (Dean et al. Nat. Neurosci. 2003). My postdoctoral research focused on synapse function, where I discovered that synaptotagmin-4 is on BDNF (brain-derived neurotrophic factor)-containing vesicles and inhibits BDNF release to limit synaptic function and maintain LTP within a functional range necessary for normal learning and memory (Dean et al. Nat. Neurosci. 2009). I began my own lab at the European Neuroscience Institute in Goettingen, Germany after securing a European Research Council starting grant to fund my group. We have continued to study how memory-related circuits encode information. We combine imaging, electrophysiology, biochemistry, and behavior to identify molecules and distinct cell types (specified by molecular composition) that promote remembering or forgetting.

Selected publications

- Awasthi A, Ramachandran B, Ahmed S, Benito E, Shinoda Y, Nitzan N, Heukamp A, Rannio S, Martens H, Barth J, Burk K, Wang YT, Fischer A, Dean C. Synaptotagmin-3 drives AMPA receptor endocytosis, depression of synapse strength, and forgetting. Science, in press
- Bharat V, Siebrecht M, Burk K, Ahmed S, Reissner C, Kohansal-Nodehi M, Steubler V, Zweckstetter M, Ting JT, Dean C (2017) Capture of dense core vesicles at synapses by JNK-dependent phosphorylation of synaptotagmin-4. Cell Rep Nov 21;21(8):2118-2133.
- Hurtado-Zavala JI, Ramachandran B, Ahmed S, Halder R, Bolleyer C, Awasthi A, Wagener RJ, Anderson K, Drenan RM, Lester HA, Miwa JM, Staiger JF, Fischer A, Dean C (2017) TRPV1 regulates excitatory innervation of OLM neurons in the hippocampus. Nat Commun Jul 19;8: 15878.
- Burk K, Ramachandran B, Ahmed S, Hurtado-Zavala JI, Awasthi A, Benito E, Faram R, Ahmad H, Swaminathan A, McIlhinney J, Fischer A, Perestenko P, Dean C (2017) Regulation of Dendritic Spine Morphology in Hippocampal Neurons by Copine-6. Cereb Cortex Feb 3: 1-18.

Joris De Wit, PhD (VIB-KU Leuven Center for Brain & Disease Research, Belgium)

Joris de Wit is group leader and vice director at the VIB-KU Leuven Center for Brain & Disease Research in Leuven, Belgium. His lab studies the molecular and cellular mechanisms that determine where and when specific synaptic connections form, how these connections change with experience, and how they are affected in disease. The lab focuses on the role of cell surface interactions in these processes. Joris de Wit obtained his Master's degree at Utrecht University, the Netherlands and his PhD degree at VU University, the Netherlands. He performed his postdoctoral work in the labs of Matthijs Verhage (CNCR/VU University, the Netherlands) and Anirvan Ghosh (UCSD, USA). He became group leader at the VIB-KU Leuven Center for Brain & Disease Research in 2013.

Selected Publications:

- Condomitti G, Wierda KD, Schroeder A, Rubio SE, Vennekens KM, Orlandi C, Martemyanov KA, Gounko NV, Savas JN, de Wit J. An input-specific orphan receptor GPR158-HSPG interaction organizes hippocampal mossy fiber-CA3 synapses. Neuron 100:201-215. PMID: 30315127.
- Schroeder A, Vanderlinden J, Vints K, Ribeiro LF, Vennekens KM, Gounko NV, Wierda KD, de Wit J (2018). A modular organization of LRR protein-mediated synaptic adhesion defines synapse identity. Neuron 99:329-344. PMID: 29983322.
- Savas JN, Ribeiro L, Wierda KD, Wright R, DeNardo-Wilke LA, Rice HC, Chamma I, Wang YZ, Zemla R, Lavallée-Adam M, Vennekens KM, O'Sullivan ML, Antonios JK, Hall EA, Thoumine O, Attie AD, Yates III JR*, Ghosh A, de Wit J (2015). The sorting receptor SorCS1 regulates trafficking of neurexin and AMPA receptors. Neuron 87:764-780. PMID: 26291160.
- De Wit J and Ghosh A(2016). Specification of synaptic connectivity by cell surface interactions. Nat Rev Neurosci 17:22-35. PMID: 26656254.

Christophe Leterrier, PhD (Marseille University, France)

Christophe Leterrier has been working on the organization of the axon since his PhD with Zsolt Lenkei in Paris, where he studied the axonal targeting of the CB1 cannabinoid receptor. For his postdoc in Bénédicte Dargent's lab in Marseille, he worked on revealing new cytoskeletal components of the axon initial segment, as well as their nanoscale organization. He started the NeuroCyto lab in 2017, with the aim of deciphering the axonal cytoskeleton architecture using advanced microscopy techniques. The team currently focuses the organization of axonal actin and its partners in order to understand the function of newly discovered axonal actin structures: rings, hotspots and trails.

Selected Publications:

- The functional architecture of axonal actin. Papandréou MJ, Leterrier C. Mol Cell Neurosci. 2018 Sep;91:151-159.
- Quantitative mapping and minimization of super-resolution optical imaging artifacts. Culley S, Albrecht D, Jacobs C, Pereira PM, Leterrier C, Mercer J, Henriques R. Nat Methods. 2018 Apr;15(4):263-266.

- The nano-architecture of the axonal cytoskeleton. Leterrier C, Dubey P, Roy S. Nat Rev Neurosci. 2017 Dec;18(12):713-726.
- A dynamic formin-dependent deep F-actin network in axons. Ganguly A, Tang Y, Wang L, Ladt K, Loi J, Dargent B, Leterrier C, Roy S., J Cell Biol. 2015 Aug 3;210(3):401-17.

Ruud Toonen, PhD (CNCR, Netherlands)

Ruud Toonen did his PhD with Matthijs Verhage in Utrecht on the presynaptic gene, Munc18-1 and subsequently worked with Jurgen Klingauf in Göttingen, Germany. Ruud is now a group leader at CNCR in Amsterdam, The Netherlands working on the presynaptic mechanisms of synaptic plasticity and secretory vesicle dynamics and fusion using mammalian neurons and optical and physiological approaches. During the course, Ruud will instruct neuropeptide trafficking and fusion studies in cultured mouse neurons.

Selected Publications:

- Pool size estimations for dense-core vesicles in mammalian CNS neurons. Persoon CM, Moro A, Nassal JP, Farina M, Broeke JH, Arora S, Dominguez N, van Weering JR, Toonen RF, Verhage M. EMBO J. 2018 Oct 15;37(20). pii: e99672.
- Munc18-1 redistributes in nerve terminals in an activity- and PKC-dependent manner. Cijsouw T, Weber JP, Broeke JH, Broek JA, Schut D, Kroon T, Saarloos I, Verhage M, Toonen RF. J Cell Biol. 2014 Mar 3;204(5):759-75.
- Munc18-1 expression levels control synapse recovery by regulating readily releasable pool size. Toonen RF, Wierda K, Sons MS, de Wit H, Cornelisse LN, Brussaard A, Plomp JJ, Verhage M. Proc Natl Acad Sci U S A. 2006 Nov 28;103(48):18332-7. Epub 2006 Nov 16.
- Dissecting docking and tethering of secretory vesicles at the target membrane. Toonen RF, Kochubey O, de Wit H, Gulyas-Kovacs A, Konijnenburg B, Sørensen JB, Klingauf J, Verhage M. EMBO J. 2006 Aug 23;25(16):3725-37. Epub 2006 Aug 10.

Julien Dupuis, PhD (University of Bordeaux, France)

Julien Dupuis is an Inserm investigator in the Development and Adaptation of Neuronal Circuits laboratory (http://www.iins.u-bordeaux.fr/research-teams-laurent-groc) at the Interdisciplinary Institute for Neuroscience (Bordeaux, France). Based on a combination of cell / molecular biology, electrophysiology and high resolution imaging approaches, his work is focused on deciphering the contribution of neurotransmitter receptor surface trafficking and interactions to synaptic transmission, cognitive functions and neuropsychiatric diseases. He discovered that quick lateral diffusion-based modifications in the distribution and nano-organization of NMDA glutamate receptors (NMDAR) play a central role in the initiating steps of synaptic plasticity and memory formation, and that these redistribution processes are dynamically regulated by physical interactions between NMDAR and other neurotransmitter receptors such as dopamine receptors. He also contributed to dissect the mechanisms through which NMDA receptor surface

redistribution and synaptic stabilization processes are impaired in autoimmunity-related neuropsychiatric diseases

Selected Publications:

- Dynamic disorganization of synaptic NMDA receptors triggered by autoantibodies from psychotic patients. Jézéquel J, Johansson EM, Dupuis JP, Rogemond V, Gréa H, Kellermayer B, Hamdani N, Le Guen E, Rabu C, Lepleux M, Spatola M, Mathias E, Bouchet D, Ramsey AJ, Yolken RH, Tamouza R, Dalmau J, Honnorat J, Leboyer M, Groc L. Nat Commun. 2017 Nov 27;8(1):1791.
- Differential Nanoscale Topography and Functional Role of GluN2-NMDA Receptor Subtypes at Glutamatergic Synapses. Kellermayer B[1], Ferreira JS, Dupuis J, Levet F, Grillo-Bosch D, Bard L, Linarès-Loyez J, Bouchet D, Choquet D, Rusakov DA, Bon P, Sibarita JB, Cognet L, Sainlos M, Carvalho AL, Groc L. Neuron. 2018 Oct 10;100(1):106-119.e7. doi: 10.1016/j.neuron.2018.09.012. Epub 2018 Sep 27.
- Surface dynamics of GluN2B-NMDA receptors controls plasticity of maturing glutamate synapses. Dupuis JP, Ladépêche L, Seth H, Bard L, Varela J, Mikasova L, Bouchet D, Rogemond V, Honnorat J, Hanse E, Groc L. EMBO J. 2014 Apr 16;33(8):842-61.
- Dopamine-dependent long-term depression at subthalamo-nigral synapses is lost in experimental parkinsonism. Dupuis JP, Feyder M, Miguelez C, Garcia L, Morin S, Choquet D, Hosy E, Bezard E, Fisone G, Bioulac BH, Baufreton J. J Neurosci. 2013 Sep 4;33(36):14331-41.

Alexandre Favereaux, PhD (University of Bordeaux, France)

Alexandre Favereaux is an associate professor in the team central mechanisms of pain sensitization (http://www.iins.u-bordeaux.fr/research-teams-marc-landry) at the Interdisciplinary Institute for Neuroscience (Bordeaux, France). Based on the combination of cellular and molecular biology approaches is work is dedicated to understand how gene regulation can modulate neuronal function. He focused is work on the role of non-coding RNAs (such as miRNAs) in the regulation of neuronal plasticity in physiological (LTP, homeostatic scaling) and pathological conditions (chronic & cancer pain, Alzheimer's disease). In collaboration with Yves Le Feuvre is now developing single cell RNA-Seq methods to correlate gene expression and electrophysiological properties at the single neuron level.

Selected Publications:

- Soula A, Valere M, Lopez-Gonzalez MJ, Ury-Thiery V, Groppi A, Landry M, Nikolski M, Favereaux A. (2018) Small RNA-Seq reveals novel miRNAs shaping the transcriptomic identity of rat brain structures. Life Sci Alliance. 1(5):e201800018.
- Letellier M, Elramah S, Mondin M, Soula A, Penn A, Choquet D, Landry M, Thoumine O, Favereaux A. (2014) miR-92a regulates expression of synaptic GluA1-containing AMPA receptors during homeostatic scaling. Nat Neurosci. 17(8):1040-1042.
- Favereaux A, Thoumine O, Bouali-Benazzouz R, Roques V, Papon A, Abdel Salam S, Drutel G, Léger C, Calas A, Nagy F, Landry M. (2011) Bidirectional integrative regulation of Cav1.2 calcium channel by microRNA miR-103: role in pain. EMBO J. 30(18):3830-41.

Yves Le Feuvre, PhD (University of Bordeaux, France)

Yves Le Feuvre is a CNRS investigator in the central mechanisms of pain sensitization (http://www.iins.u-bordeaux.fr/research-teams-marc-landry) at the Interdisciplinary Institute for Neuroscience (Bordeaux, France). Based on a combination of electrophysiology and molecular biology approaches, his work is focused on deciphering the organization of neuronal networks that process noxious and non noxious sensory inputs within the spinal cord, and the impairment of these networks in pathologic pain context. He developed new methods to investigate sensory-nociceptive integration within spinal cord (Mourot et al., 2012). He discovered several novel mechanisms regarding the role of low threshold sensory inputs in the modulation of synaptic transmission between noxious receptors and spinal interneurons (Delfini et al., 2013; Gaillard et al., 2014). Part of his work has emphasized the role of microglial cells in this regulation, shedding new lights on the interaction between microglial cells, presynaptic and post synaptic neurons (Kambrun et al., 2018). He is now developing combined single cell transcriptomic, morphologic and transcriptomic approaches to unravel the diversity of dorsal horn spinal neurons.

Selected Publications:

- Delfini, M.-C., Mantilleri, A., Gaillard, S., Hao, J., Reynders, A., Malapert, P., Alonso, S., François, A., Barrere, C., Seal, R., Landry, M., Eschallier, A., Alloui, A., Bourinet, E., Delmas, P., Le Feuvre, Y., Moqrich, A., 2013. TAFA4, a chemokine-like protein, modulates injury-induced mechanical and chemical pain hypersensitivity in mice. Cell Rep 5, 378–388. https://doi.org/10.1016/j.celrep.2013.09.013
- Gaillard, S., Lo Re, L., Mantilleri, A., Hepp, R., Urien, L., Malapert, P., Alonso, S., Deage, M., Kambrun, C., Landry, M., Low, S.A., Alloui, A., Lambolez, B., Scherrer, G., Le Feuvre, Y., Bourinet, E., Moqrich, A., 2014. GINIP, a Gαi-interacting protein, functions as a key modulator of peripheral GABAB receptor-mediated analgesia. Neuron 84, 123–136. https://doi.org/10.1016/j.neuron.2014.08.056
- Kambrun, C., Roca-Lapirot, O., Salio, C., Landry, M., Moqrich, A., Feuvre, Y.L., 2018. TAFA4 Reverses Mechanical Allodynia through Activation of GABAergic Transmission and Microglial Process Retraction. Cell Reports 22, 2886–2897. https://doi.org/10.1016/j.celrep.2018.02.068
- Mourot, A., Fehrentz, T., Le Feuvre, Y., Smith, C.M., Herold, C., Dalkara, D., Nagy, F., Trauner, D., Kramer, R.H., 2012. Rapid optical control of nociception with an ion-channel photoswitch. Nat. Methods 9, 396–402. https://doi.org/10.1038/nmeth.1897

Tara Spires Jones, PhD (University of Edinburgh, United Kingdom)

Tara Spires-Jones is Professor of Neurodegeneration, Deputy Director of the Centre for Brain Sciences, and a UK Dementia Research Institute Programme Lead at the University of Edinburgh. Her research focuses on the mechanisms and reversibility of neurodegeneration in Alzheimer's disease, other degenerative brain diseases, and ageing. Her work has shown that soluble forms of both of the proteins involved in the neuropathological lesions in Alzheimer's (amyloid beta and tau) contribute to synapse degeneration, and further that reducing the levels of these can prevent and even reverse degeneration. In addition to her research, Prof Spires-Jones is passionate about communicating scientific findings to the public and policy makers in order to share the joy of our ever-expanding understanding of the brain and to facilitate a productive conversation about the role of science in society. She also advises the Scottish Government on science policy as a member of the Scottish Science Advisory Council.

Selected Publications:

- Henstridge, C.M., Sideris, D.I., Carroll, E., Rotariu, S., Salomonsson, S., Tzioras, M., McKenzie, C.A., Smith, C., von Arnim, C.A.F., Ludolph, A.C., *et al.* (2018). Synapse loss in the prefrontal cortex is associated with cognitive decline in amyotrophic lateral sclerosis. Acta Neuropathol 135, 213-226.
- Pickett, E.K., Koffie, R.M., Wegmann, S., Henstridge, C.M., Herrmann, A.G., Colom-Cadena, M., Lleo, A., Kay, K.R., Vaught, M., Soberman, R., *et al.* (2016). Non-Fibrillar Oligomeric Amyloid-beta within Synapses. J Alzheimers Dis 53, 787-800.
- Kay, K.R., Smith, C., Wright, A.K., Serrano-Pozo, A., Pooler, A.M., Koffie, R., Bastin, M.E., Bak, T.H., Abrahams, S., Kopeikina, K.J., *et al.* (2013). Studying synapses in human brain with array tomography and electron microscopy. Nat Protoc 8, 1366-1380.
- Koffie, R.M., Hashimoto, T., Tai, H.C., Kay, K.R., Serrano-Pozo, A., Joyner, D., Hou, S., Kopeikina, K.J., Frosch, M.P., Lee, V.M., *et al.* (2012). Apolipoprotein E4 effects in Alzheimer's disease are mediated by synaptotoxic oligomeric amyloid-beta. Brain 135, 2155-2168.

Vanessa Morais, PhD (Instituto de Medicina Molecular, Portugal)

My research is focused on the understanding of mitochondria and how they go astray in neurodegeneration. I am a biochemist in training and throughout my career I have specialized in cell biology, in particular in mitochondrial biology. The link between neurodegeneration and mitochondria function is a subject that I find fascinating. Mitochondria homeostasis requires an intimate crosstalk between energy production and intrinsic quality control. At the synapse, mitochondria have a pivotal role in synapse maintenance and neurotransmitter release. Therefore, mitochondrial function is crucial for the maintenance of a healthy brain. Over the years I have pursued this passion by unravelling how synaptic mitochondria have learnt to adapt to their environmental demands and deciphering the mechanisms involved in mitochondrial quality control and bioenergetic adaptation at synapse. In the long run, the overarching goal is to reveal how the disruption of these acquired mechanisms contributes to mitochondrial dysfunction and ultimately to neuronal loss.

Selected Publications:

- Morais, V.A., Haddad, D., Craessaerts, K., De Bock, P., Swerts, J., Vilain, S., Aerts, L., Overbergh, L., Grünewald, A., Seibler, P., Klein, C., Gevaert, K., Verstreken, P., De Strooper, B.(2014). PINK1 Loss of Function Mutations Affect Mitochondrial Complex I Activity via NdufA10 Ubiquinone Uncoupling, Science, 344 (6180), 203-207.
- Haddad, D., Vilain, S., Vos, M., Esposito, G., Matta, S., Kalscheuer, V., Craessaerts, K., Leyssen, M., Nascimento, R., Vianna-Morgante, A., De Strooper, B., Van Esch, H., Morais, V.A., Verstreken, P. (2013). Mutations in the Intellectual Disability Gene Ube2a Cause Neuronal Dysfunction and Impair Parkin-Dependent Mitophagy, Molecular cell, 50 (6), 831-43.
- Vos, M., Esposito, G., Edirisinghe, J., Vilain, S., Haddad, D., Slabbaert, J., Van Meensel, S., Schaap, O., De Strooper, B., Meganathan, R., Morais, V.A., Verstreken, P. (2012). Vitamin K2 is a mitochondrial electron carrier that rescues pink1 deficiency, Science, 336 (6086), 1306-10.
- Vilain, S., Esposito, G., Haddad, D., Schaap, O., Dobreva, M., Vos, M., Van Meensel, S., Morais, V.A., De Strooper, B., Verstreken, P. (2012). The yeast complex I equivalent NADH dehydrogenase rescues pink1 mutants, PLoS Genetics, 8 (1), e1002456.

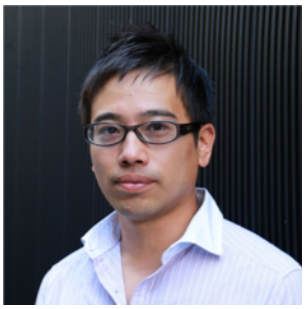
Sandra Soukup, PhD (University of Bordeaux, France)

In many neurogenerative diseases like Parkinson's and Alzheimer, synaptic decay precedes neuronal loss. Therefore, synaptic decay is one of the earliest steps in these pathologies. Thus, understanding molecular mechanisms leading to synaptic decay is critical to fully understand neurodegenerative diseases and will serve to identify novel therapies to stop the progression of these diseases before pathological symptoms appear. My research makes use of Drosophila to identify key players having a role in synaptic homeostasis and dysfunction to understand the root of neurodegenerative processes. My current research focus is to decipher the molecular basis of synaptic autophagy, a self-degrading process required to turnover synaptic material, and its implication in Parkinson's disease.

Selected publications:

- A LRRK2-Dependent EndophilinA Phosphoswitch Is Critical for Macroautophagy at Presynaptic Terminals. Soukup *et al.*, Neuron. 2016
- The SAC1 domain in Synaptojanin is required for autophagosome maturation at presynaptic terminals. Vanhauwaert *et al.*, EMBO J. 2017
- DLin-7 is required in postsynaptic lamina neurons to prevent light-induced photoreceptor degeneration in Drosophila. Soukup *et al.*, Curr Biol. 2013

Shigeki Watanabe, PhD (Johns Hopkins University, USA)



Shigeki Watanabe studies cellular and molecular mechanisms underlying synaptic transmission and plasticity at the Johns Hopkins University. He has established two novel approaches in electron microscopy. One technique localizes proteins to the subcellular structures by coupling super-resolution imaging with electron microscopy. Another technique, flash-and-freeze, visualizes membrane dynamics in electron micrographs with millisecond temporal resolution by coupling optogenetics with high-pressure freezing. He has discovered that synaptic vesicles are recycled via a two-step process: ultrafast endocytosis followed by clathrin-dependent endosomal sorting. Using the combination of these techniques, his lab is characterizing the cellular and molecular basis of the rapid changes that are essential to synaptic functions.

Selected publication:

- Watanabe, S., Mamer, L.E., Raychaudhuri, S., Luvsanjav, D., Eisen, J., Trimbuch, T., Söhl-Kielczynski, B., Fenske, P., Milosevic, I., Rosenmund, C., and Jorgensen, E.M. (2018) Synaptojanin and endophilin mediate neck formation during ultrafast endocytosis. Neuron 98, 1184-1197.
- Watanabe S, Trimbuch T, Camacho-Perez M, Rost BR, Brokowski B, Söhl-Kielczynski B, Felies A, Rosenmund C, Jorgensen EM. (2014) Clathrin regenerates synaptic vesicles from endosomes, Nature 515, 228-33.
- Watanabe S, Rost BR, Camacho-Perez M, Davis MW, Söhl-Kielczynski B, Rosenmund C, Jorgesen EM. Ultrafast endocytosis at mouse hippocampal synapses, Nature 2013:504; 242-247.
- Watanabe S, Punge A, Hollopeter G, Willig KI, Hobson RJ, Davis MW, Hell SW, Jorgensen EM. Protein localization in electron micrographs using fluorescence nanoscopy. Nat. Methods 2011;8:80–84

Sha Liu, PhD (Leuven Center for Brain & Disease Research, Belgium)

Sha Liu is a group leader in VIB-KU Leuven, Center for Brain & Disease Research. His lab studies the synaptic and circuit mechanisms underlying sleep homeostasis and the roles of sleep in synaptic plasticity by using multi-disciplinary approaches, including Drosophila genetics, quantitative behavior analysis, electrophysiology, and in vivo functional imaging. Before he started his lab in Belgium, he identified a central sleep homeostatic circuit in the fruit fly brain and demonstrated that synaptic plasticity of this circuit underlies generation and persistence of sleep drive.

Selected Publications:

- *Branch-specific plasticity of a bifunctional dopamine circuit encodes protein hunger*Liu Q, Tabuchi M, Liu S, Kodama L, Horiuchi W, Daniels J, Chiu L, Baldoni D, Wu MSCIENCE, 356, 534-539, 2017

- *Sleep Drive Is Encoded by Neural Plastic Changes in a Dedicated Circuit*Liu S, Liu Q, Tabuchi M, Wu MCELL, 165, 1347-1360, 2016
- *Improved and expanded Q-system reagents for genetic manipulations*Riabinina O, Luginbuhl D, Marr E, Liu S, Wu M, Luo L, Potter CNATURE METHODS, 12, 219-22, 5 p following 222, 2015
- *Sleep interacts with abeta to modulate intrinsic neuronal excitability*Tabuchi M, Lone S, Liu S, Liu Q, Zhang J, Spira A, Wu MCURRENT BIOLOGY, 25, 702-12, 2015

Xavi Altafaj, PhD(Bellvitge Biomedical Research Institute, Spain)

Team Leader "Neurobiology of ionotropic Glutamate receptors in health and disease" Group, at Bellvitge Biomedical Research Institute (IDIBELL), Barcelona, Spain.
After obtaining his degree in Molecular Biology (University of Barcelona, 1997) he developed a Functional Genomics study of Down syndrome (PhD degree Univ. Barcelona, 2002), and moved to the "Calcium channels: Functions and Pathology"lab (CEA, France, 2002-2006), where he studied the crosstalk between the plasma membrane DHPR and the ER-spanning Ryanodine receptor (RyR). Afterwards, he joined Dr. Fillat lab (2006-2011, Center for Genomic Research, Barcelona) and developed gene therapy strategies for Down syndrome models, while starting to study ionotropic glutamate receptors (iGluRs) in neurological conditions. His laboratory is currently focused to study the physiology of NMDA-type iGluRs and to unveil the molecular and cellular mechanisms bridging the gap between glutamate receptor dysfunction and neurological diseases. In particular, his main reseach interest is the functional evaluation, stratification and development of precision therapies for pediatric encephalopathies resulting from *de novo* mutations affecting the NMDA receptor.

Selected Publications:

- Gómez de Salazar M., *et al*. "Phosphoproteomic Alterations of Ionotropic Glutamate Receptors in the Hippocampus of the Ts65Dn Mouse Model of Down Syndrome". Front Mol Neurosci. 2018 Jul 25;11:226.
- Grau C. *et al*. DYRK1A-mediated phosphorylation of GluN2A at Ser(1048) regulates the surface expression and channel activity of GluN1/GluN2A receptors. Front Cell Neurosci. 2014; 8: 331.
- Altafaj, X., *et al*. "Normalization of Dyrk1A expression by AAV2/1-shDyrk1A attenuates hippocampal-dependent deficits in the Ts65Dn mouse model of Down syndrome". Neurobiol Dis. 2013; 52: 117-27.
- Altafaj X., *et al*. Increased NR2A expression and prolonged decay of NMDA-induced calcium transient in cerebellum of TgDyrk1A mice, a mouse model of Down syndrome. Neurobiol Dis. 2008 Dec; 32 (3): 377-84

Keimpe Weirda, PhD (Leuven Center for Brain & Disease Research, Belgium)

Keimpe Wierda is currently head of the electrophysiology expertise unit at VIB, KU Leuven in Belgium. His interest in electrophysiology started during his master's (medical biology) at the University of Utrecht and he continued exploring this field in a PhD project at the Vrije Universiteit (VU) in Amsterdam where he developed electrophysiology on single, cultured neurons to study the role of Munc18 in presynaptic function. Together with his family, he moved to Germany for a postdoc at the Max Planck Institute for Biophysical Chemistry in the lab of Prof. Dr. Erwin Neher. Here he studied the role of neuronal interactions on synaptic function in minimal networks. After two years, Keimpe accompanied his direct supervisor (Prof. Dr. Jakob Sørensen) to start up his lab in Copenhagen, Denmark. In Copenhagen Keimpe was responsible for neuronal electrophysiology and was involved and/or supervised several projects in the lab. After five years, he was looking for another challenge and found this within VIB, KU Leuven where they were looking for an expert to establish an electrophysiology expertise unit. For the next four years, he has been building up this unit, presently including six setups (acute slice, primary cell culture, multi electrode array and combined two-photon/electrophysiology). Keimpe now collaborates with VIB research groups in projects that require electrophysiology or supervises and/or supports researchers to conduct experiments within the electrophysiology expertise unit.

Selected publications:

- *Secreted amyloid-β precursor protein functions as a GABABR1a ligand to modulate synaptic transmission.,* Science 2019 Rice HC, de Malmazet D, Schreurs A, Frere S, Van Molle I, Volkov AN, Creemers E, Vertkin I, Nys J, Ranaivoson FM, Comoletti D, Savas JN, Remaut H, Balschun D, Wierda KD, Slutsky I, Farrow K, De Strooper B, de Wit J.
- *An Input-Specific Orphan Receptor GPR158-HSPG Interaction Organizes Hippocampal Mossy Fiber-CA3 Synapses.,* Neuron 2018 Condomitti G, Wierda KD, Schroeder A, Rubio S, Vennekens K, Orlandi C, Martemyanov K, Gounko N, Savas J, de Wit J
- *A Modular Organization of LRR Protein-Mediated Synaptic Adhesion Defines Synapse Identity.,* Neuron, 2018 Schroeder A, Vanderlinden J, Vints K, Ribeiro LF, Vennekens KM, Gounko NV, Wierda KD, de Wit J
- *Synaptogyrin-3 Mediates Presynaptic Dysfunction Induced by Tau*., Neuron, 2018 McInnes J, Wierda K, Snellinx A, Bounti L, Wang YC, Stancu IC, Apóstolo N, Gevaert K, Dewachter I, Spires-Jones TL, De Strooper B, De Wit J, Zhou L, Verstreken P
- *Tau association with synaptic vesicles causes presynaptic dysfunction.,* Nat Commun. 2017 Zhou L, McInnes J, Wierda K, Holt M, Herrmann AG, Jackson RJ, Wang YC, Swerts J, Beyens J, Miskiewicz K, Vilain S, Dewachter I, Moechars D, De Strooper B, Spires-Jones TL, De Wit J, Verstreken P.

Pierre Trifilieff, PhD (University of Bordeaux, France)

Pierre Trifilieff was a postdoc in Eric Kandel's lab at Columbia University (New York), where he studied the implication of local protein synthesis in long-term plasticity and memory consolidation. In 2010 he became a Research scientist at the New York State Psychiatric Institute and focused on the implication of dopamine D2 receptor-dependent signalling in reward processing and motivation.

His work unravelled a central role of the striatal dopamine D2 receptor in the pathophysiology of motivation. In 2013 he obtained a faculty position in Bordeaux where he works on the implication of membrane lipid composition on the modulation of dopaminergic signalling and associated behaviors. Pierre Trifilieff will instruct on the Impact of membrane lipid composition on D2-dependent recruitment of arrestin signalling.

Selected Publications:

- The Persistence of Hippocampal-Based Memory Requires Protein Synthesis Mediated by the Prion-like Protein CPEB3. Fioriti L, Myers C, Huang YY, Li X, Stephan JS, Trifilieff P, Colnaghi L, Kosmidis S, Drisaldi B, Pavlopoulos E, Kandel ER. Neuron. 2015 Jun 17;86(6):1433-48
- Evidence against dopamine D1/D2 receptor heteromers. Frederick AL, Yano H, Trifilieff P, Vishwasrao HD, Biezonski D, Mészáros J, Urizar E, Sibley DR, Kellendonk C, Sonntag KC, Graham DL, Colbran RJ, Stanwood GD, Javitch JA. Mol Psychiatry. 2015 Nov;20(11):1373-85
- Imaging addiction: D2 receptors and dopamine signaling in the striatum as biomarkers for impulsivity. Trifilieff P, Martinez D. Neuropharmacology. 2014 Jan;76 Pt B:498-509.
- Increasing dopamine D2 receptor expression in the adult nucleus accumbens enhances motivation. Trifilieff P, Feng B, Urizar E, Winiger V, Ward RD, Taylor KM, Martinez D, Moore H, Balsam PD, Simpson EH, Javitch JA. Mol Psychiatry. 2013 Sep;18(9):1025-33

Etienne Herzog, PhD (University of Bordeaux, France)

With an initial training in molecular genetics and biotechnology, I focus my research on the molecular characterization of neurotransmitter systems in the rodent brain. I first contributed to the characterization of the 3 vesicular glutamate transporters and used VGLUTs as markers of synapses and synaptic vesicles of glutamatergic neurons. Our more recent work built on the VGLUT1^{venus} knock-in mice I generated as a fellow with Prof Nils Brose (MPIEM, Goettingen). Through fluorescence imaging on VGLUT1^{venus} mouse model samples we characterized several features of synaptic vesicle trafficking at glutamatergic synapses and axons. More recently, we established the purification of synaptosomes from adult brain tissue using fluorescence activated sorting, a method we named FASS. We now explore the local molecular composition of synapses using highly purified populations of synaptosomes. We aim at unravelling the molecular diversity of synapses required to build functional neuron circuits.

Selected publications:

- Purification of Synaptosome Populations Using Fluorescence-Activated Synaptosome Sorting. Luquet E, Biesemann C, Munier A, Herzog E. Methods Mol Biol. 2017;1538:121-134.
- Synapse biology in the 'circuit-age'-paths toward molecular connectomics. Schreiner D, Savas JN, Herzog E, Brose N, de Wit J. Curr Opin Neurobiol. 2017 Feb;42:102-110
- Physical determinants of vesicle mobility and supply at a central synapse. Rothman JS, Kocsis L, Herzog E, Nusser Z, Silver RA. Elife. 2016 Aug 19;5. pii: e15133.
- Proteomic screening of glutamatergic mouse brain synaptosomes isolated by fluorescence activated sorting. Biesemann C, Grønborg M, Luquet E, Wichert SP, Bernard V, Bungers SR, Cooper B, Varoqueaux F, Li L, Byrne JA, Urlaub H, Jahn O, Brose N, Herzog E. EMBO J. 2014 Jan 13;33(2):157-70.

Véronique De Smedt-Peyrusse, PhD (University of Bordeaux, France)

Véronique De Smedt-Peyrusse joined the Nutrineuro lab (Bordeaux) in 2003 as an engineer (INRA). Her previous work and PhD project performed in C. Jessus and R. Ozon's lab (UPMC, Paris) was the study of the regulation of Cdc2, a protein kinase playing a pivotal role in the achievement of cell cycle M phase (Xenopus laevis model).
This expertise in cell signaling allowed her to develop *in vitro* and *in vivo* studies to investigate the impact of polyunsaturated fatty acid (PUFAs) on neuroinflammation processes. More recently, her activity has been focused on the impact of PUFAs on dopaminergic signalling with P. Trifilieff. To investigate the modulation of Dopamine 2 Receptor (D2R) activity by membrane PUFA composition, she has developed various biophysical, pharmacological and biochemical approaches that specifically allow thorough characterization of lipid-protein interaction. Together with the other instructors, she has also optimized biochemical approaches for isolation of synaptosomes from brain structures. V. De Smedt-Peyrusse will instruct the following assays : BRET (beta Arrestin recruitment), cAMP measurement, and synaptosomes preparation.

Selected Publications:

- De Smedt-Peyrusse V et al. « Subcellular fractionation of brain tissue from small tissue explants. Synaptosomes pp75-84. The Neuromethods book series (NM, volume 141) 2018.
- Lafourcade M et al. « Nutritional omega-3 deficiency abolishes endocannabinoid-mediated neuronal functions ». Nat Neurosci. 2011
- De Smedt-Peyrusse V et al. « Docosahexaenoic acid prevents lipopolysaccharide-induced cytokine production in microglial cells by inhibiting lipopolysaccharide receptor presentation but not its membrane subdomain localization ». J Neurochem. 2008 Apr;105 (2):296-307.
- De Smedt V, et al. « Thr-161 phosphorylation of monomeric Cdc2. Regulation by protein phosphatase 2C in Xenopus oocytes. » J Biol Chem. 2002 Aug 9;277(32)

Maria Florencia Angelo, PhD (University of Bordeaux, France)

Florencia Angelo studied Biology and did her PhD in neuroscience at the University of Buenos Aires in Argentina. During her doctoral research, she combined molecular biology, biochesmistry and microscopy to study how neuron-glia cross-talk play a crucial role in different phatological models as sleep apnea, brain schemia and epilepsy. After getting her degree, she worked at the Argentinian Ministery of Science, where she performed management, audit and evaluation of research and start-up projects. In 2015, she joined the Interdisciplinary Institut for Neurosciences in Bordeaux to continue doing research in *academia*. There, she works as a research engineer with Dr. Etienne Herzog combining fluorescence activated sorting of synaptosomes (FASS), microscopy and biochemistry to reveal the molecular composition of glutamatergic and dopaminergic synapses in normal and pathological conditions.

Selected Publications:

- The proinflammatory RAGE/NF-κB pathway is involved in neuronal damage and reactive gliosis in a model of sleep apnea by intermittent hypoxia. Angelo MF, Aguirre A, Avilés Reyes

RX, Villarreal A, Lukin J, Melendez M, Vanasco V, Barker P, Alvarez S, Epstein A, Jerusalinsky D, Ramos AJ. PLoS One. 2014 Sep 29;9(9):e107901

- Gabapentin administration reduces reactive gliosis and neurodegeneration after pilocarpine-induced status epilepticus. Rossi AR, Angelo MF, Villarreal A, Lukin J, Ramos AJ. PLoS One. 2013 Nov 8;8(11):e78516
- Intermittent hypoxia during sleep induces reactive gliosis and limited neuronal death in rats: implications for sleep apnea. Aviles-Reyes RX, Angelo MF, Villarreal A, Rios H, Lazarowski A, Ramos AJ. J Neurochem. 2010 Feb;112(4):854-69.
- p75 NTR expression is induced in isolated neurons of the penumbra after ischemia by cortical devascularization. Angelo MF, Aviles-Reyes RX, Villarreal A, Barker P, Reines AG, Ramos AJ. J Neurosci Res. 2009 Jun;87(8):1892-903.

Emilie Pacary, PhD (Neurocentre Magendie, France)

Emilie Pacary is researcher in the group of Dr DN Abrous "Neurogenesis and Physiopathology" in the Neurocentre Magendie (Bordeaux) since 2012. Since her PhD, she has focused her studies on the cellular and molecular mechanisms regulating neurogenesis with a particular interest in actin cytoskeleton regulators. During her postdoc in the lab of Dr François Guillemot, she provided mechanistic insights into the regulation of neuronal migration during the development of the cerebral cortex. Her research aims now at further understanding the regulation of neuronal development by cytoskeleton regulators not only during embryonic and early postnatal periods but also during adulthood. She is also particularly interested in the development of the different population of granular neurons in the dentate gyrus. To study neuronal development, she has extensively used the technique of in utero electroporation (cerebral cortex, hippocampus, ganglionic eminences).

Selected publications:

- Kerloch T, Clavreul S, Goron A, Abrous DN, Pacary E. Dentate granule neurons generated during perinatal life display distinct morphological features compared to later-born neurons in the mouse hippocampus *Cereb Cortex*. 2018 Sep 12. doi: 10.1093/cercor/bhy224.
- Nicole O, Bell DM, Leste-Lasserre T, Doat H, Guillemot F, Pacary E. A novel role for CAMKIIβ in the regulation of cortical neuron migration: implications for neurodevelopmental disorders. *Mol Psychiatry*. 2018 Apr 30. doi: 10.1038/s41380-018-0046-0.
- Pacary E, Haas MA, Wildner H, Azzarelli R, Bell DM, Abrous DN, Guillemot F. (2012) Visualization and genetic manipulation of dendrites and spines in the mouse cerebral cortex and hippocampus using in utero electroporation. *J Vis Exp*. (65). pii: 4163. doi: 10.3791/4163.
- Pacary E, Azzarelli R, Guillemot F. (2013) Rnd3 coordinates early steps of cortical neurogenesis through actin-dependent and -independent mechanisms. *Nat Commun*. 4:1635. doi: 10.1038/ncomms2614.

Sabine Levi, PhD (Fer à Moulin Institute, France)

Sabine Lévi co-heads a laboratory at the Fer à Moulin Institute (Inserm UMR839, Paris) - Team "Plasticity in cortical networks and epilepsy". She has an expertise in synaptic inhibition focusing on molecular aspects of the regulation of synaptic transmission by studying KCC2 and $GABA_AR$ using state-of-the-art imaging techniques such as quantum-dot based single particle tracking approaches, a technique she developed in A. Triller's lab. She received the *Integrative Physiology* price of the *French Academy of Science* in 2009.

Selected Publications:

- Battaglia S, Renner M, Russeau M, Côme E, Tyagarajan S, Lévi S. (2018) Gephyrin phosphorylation conditions GABAAR membrane dynamics and homeostatic plasticity. eNeuro 2018 Jan 18;5(1). pii: ENEURO.0203-17.2017. doi: 10.1523/ENEURO.0203-17.2017. eCollection 2018 Jan-Feb.
- Heubl M, Zhang J, Pressey J, Al Awabdh S, Renner M, Gomez Castro F, Moutkine I, Eugene E, Russeau M, Kahle KT, Poncer JC, Levi S. (2017) GABAA receptor dependent synaptic inhibition rapidly tunes KCC2 activity via the Cl--sensitive WNK1 kinase. Nat Commun. 8, 1776.
- Lévi S, Le Roux N, Eugène E, Poncer JC. (2015) Benzodiazepine ligands rapidly influence GABAA receptor diffusion and clustering at hippocampal inhibitory synapses. Neuropharmacology 88:199-208
- M. Dahan, S. Lévi, C. Luccardini, P. Rostaing, B. Riveau, A. Triller. Diffusion dynamics of glycine receptors revealed by single-quantum dot tracking. (2003) Science 302:442-445.

Martin Muller, PhD (University of Zurich, Switzerland)

Martin Müller is an Assistant Professor at the Institute of Molecular Life Sciences of the University of Zurich. He was a postdoctoral fellow with Graeme Davis at UC San Francisco, and a graduate student in Ralf Schneggenburger's laboratory at the Max Planck Institute for Biophysical Chemistry in Göttingen, and EPF Lausanne.
His lab studies the mechanisms mediating stable, and yet plastic synaptic transmission. To this end, a major focus is the investigation of presynaptic homeostatic plasticity[1]. The lab recently uncovered a central role for local presynaptic protein degradation in the homeostatic control of neurotransmitter release[2]. Martin also implicated several genes in presynaptic homeostatic plasticity[3,4], and studied the interplay between different forms of synaptic short-term plasticity[5]. To tackle these questions, the lab employs electrophysiology, calcium imaging, confocal/STED microscopy, as well as genetics in *Drosophila*, acute mouse-brain slices and human-derived neurons.
Selected Publications:

- Delvendahl I and Müller M (2019). Homeostatic plasticity—a presynaptic perspective. *Curr Opin Neuobiol*. 54:155–162
- Wenzel C, Delvendahl I, Sydlik S, Georgiev O and Müller M (2018). Dysbindin links presynaptic proteasome function to homeostatic recruitment of low release probability vesicles. *Nature Commun*. Jan 18; 9(1): 267

- Müller M, Genç Õ, and Davis GW (2015). RIM-Binding Protein Links Synaptic Homeostasis to the Stabilization and Replenishment of High Release Probability Vesicles. *Neuron*. Mar 4; 85(5): 1056–1069
- Müller M, Pym EC, Tong A, and Davis GW (2011) Rab3-GAP controls the progression of synaptic homeostasis at a late stage of vesicle release. *Neuron*. Feb 24; 69(4): 749–762

Vassiliki Nikoletopoulou, PhD (Institute of Molecular Biology & biotechnology, Greece)

I established my lab 2 years ago, funded by an ERC starting grant. Our goal is to study the role of autophagy in synaptic function, neural networks and animal behavior. Therefore, a major undertaking is to understand how autophagic degradation contributes to different forms of plasticity. Understanding how autophagy operates in different neuronal populations to shape their synaptic networks and behavioral outcomes can lead to novel interventions for reversing behavioral deficits associated with disorders (such as ASD) implicating autophagy impairment. Moreover, my lab aims to characterize the synaptic cargo of autophagy and understand the molecular mechanisms underlying cargo selectivity. Towards these goals, we have gained expertise in cell and molecular biology tools, confocal and electron microscopy, behavioral tests and mouse genetic models. We have also developed biochemical techniques to purify autophagic vesicles from the mouse brain and cultured neurons and analyze their content by proteomic and other approaches

Selected publications :

- Nikoletopoulou, V., Lickert, H., Frade, J.M., Rencurel, C., Giallonardo, P., Zhang, L., Bibel, M., and Barde, Y.A. (2010). Neurotrophin receptors TrkA and TrkC cause neuronal death whereas TrkB does not. Nature 467, 59-63.
- Kourtis, N., Nikoletopoulou, V., and Tavernarakis, N. (2012). Small heat-shock proteins protect from heat-stroke-associated neurodegeneration. Nature 490, 213-218.
- Nikoletopoulou, V., Sidiropoulou, K., Kallergi, E., Dalezios, Y., and Tavernarakis, N. (2017). Modulation of Autophagy by BDNF Underlies Synaptic Plasticity. Cell metabolism 26, 230-242 e235.
- Nikoletopoulou, V. and Tavernarakis, N.(2018). Autophagy at the synapse. Trends in Cell Biology. PMID: 29731196

Natalia Kononenko, PhD (University of Cologne, Germany)

Natalia Kononenko is a cellular neuroscientist with expertise in analysis of membrane trafficking in neurons. Originally trained in physiology in Russia and in neuroanatomy in Norway, she received an extensive postdoctoral training in the lab of Volker Haucke in Berlin, Germany, where she used a combination of state-of-the-art imaging and genetic approaches to understand the function of endocytic adaptors in the brain. Her work established a novel non-canonical function of endocytic proteins in neurons, where they mediate the survival by regulating the neurotrophin signaling. Since 2016 she is a Research Group Leader in CECAD at the University of Cologne, where she leads a team of 5 researchers. Her lab uses a unique

multidisciplinary approach to study the selective vulnerability of neurons to degeneration at the intersection of neuroscience and cell biology. Natalia Kononenko's lab integrates the state-of-the-art genetic and cell biology approaches with live cell imaging, superresolution microscopy and in-vivo neuroanatomy to understand the role of membrane trafficking in the pathogenesis of neurodegeneration. Currently the group has two focuses, the role of endocytic adaptor AP-2 in regulation of amyloidogenesis in neurons and the autophagy-dependent control of axonal microtubule dynamics.

Selected Publications:

- Kononenko NL*, Claßen GA, Kuijpers M, Puchkov D, Maritzen T, Tempes A, Malik AR, Skalecka A, Bera S, Jaworski J, Haucke V*. Retrograde transport of TrkB-containing autophagosomes via the adaptor AP-2 mediates neuronal complexity and prevents neurodegeneration. Nat. Commun. 2017 Apr 7;8:14819. *equal contributions.
- Kononenko NL. Lysosomes convene to keep the synapse clean. J Cell Biol. 2017 216 (8): 2251.
- Kononenko NL, Haucke V. Molecular Mechanisms of Presynaptic Membrane Retrieval and Synaptic Vesicle Reformation. Neuron. 2015 Feb 4;85(3):484-96.
- Kononenko NL, Puchkov D, Classen GA, Walter AM, Pechstein A, Sawade L, Kaempf N, Trimbuch T, Lorenz D, Rosenmund C, Maritzen T, Haucke V. Clathrin/AP-2 Mediate Synaptic Vesicle Reformation