## The CAJAL Advanced Neuroscience Training Programme

## NUTRITION AND BRAIN FUNCTIONS (NBF) 2016

### Speakers

**21/09/2016**

*What the brain uptake rate of fatty acids tells us about their dietary requirements: Implications for food sources and the environment*

**Richard BAZINET (Toronto, Canada) _ Also Instructor on an NBF school project!**

What Dr. Bazinet received his BSc from the University of Western Ontario and completed his PhD under the supervision of Dr. Stephen Cunnane at the University of Toronto in 2003. Dr. Bazinet then completed a postdoctoral fellowship in Dr. Stanley Rapoport's Brain Physiology and Metabolism Section at the National Institute on Aging, National Institutes of Health. Dr. Bazinet joined the University of Toronto in 2006, where he is currently an Associate Professor and Canada Research Chair in Brain Lipid Metabolism. Dr. Bazinet is the recipient of several awards, including the Early Career Award from the International Society for the Study of Fatty Acids and Lipids; the Jordi-Folch-Pi Memorial Award from the American Society for Neurochemistry; the Future Leaders Award from the International Life Sciences Institute and the Young Scientist Award for the American Oil Chemists'Society. Dr. Bazinet sits on several editorial boards and is currently Editor-in-Chief of Prostaglandins, Leukotrienes and Essential Fatty Acidsas well as a Senior Associate Editor of Lipids.
The overall goal of Dr. Bazinet's research program is to identify the mechanisms that regulate brain lipid metabolism (signaling) and to identify the role of brain lipid metabolism in the pathogenesis of neurodegenerative diseases and neuropsychiatric disorders.

Dr. Bazinet has published over 90 papers, largely in the field of brain fatty acid metabolism and is co-author of the joint WHO/FAO joint expert consultation on dietary fats and the central nervous system during aging and disease.

*Food for thoughts*

**Olivier MANZONI (Marseille, France) _ Also Instructor on an NBF school project!**

Olivier Manzoni: "Early on, my group discovered how naturally released endogenous cannabinoids participate to long-term synaptic plasticity. Endocannabinoid-mediated long-term depression (eCB-LTD) has since proven to be one of the most widely expressed forms of synaptic plasticity in the CNS. Our work revealed that eCB-LTD is a common synaptic correlate of neuropsychiatric diseases. Thus, eCB-LTD is altered in mice models of malnutrition, Fragile X, Down syndrome and drug abuse. Our multiple scale approach (from individual spine to behavior) aims at discovering new endophenotypes of neuropsychiatric diseases and suggests new therapeutic strategies."


- Jung KM, et al. 2012 Nature Commun. 3:1080.
- Puente N et al. 2011 Nature Neurosci. 14(12):1542-7.
- Lafourcade M et al. 2011 Nature Neurosci. 14(3):345-50.

**22/09/2016**

*Comparing dietary interventions in animal models of neurodegenerative diseases: cognitive enhancement or disease modification*

**Frédéric CALON (Québec, Canada, Laval University)**

Comparing dietary interventions in animal models of neurodegenerative diseases: cognitive enhancement or disease modification Dr Frédéric Calon is a biochemist-pharmacist focusing his research program on the development of treatments for neurodegenerative diseases. His PhD studies on he neurochemical basis of levodopa-induced dyskinesias were recognized with the Gold Medal from the Governor General of Canada in 2001. Since the start-up of his laboratory in 2003, his research team has gathered significant support fromthe Canadian Institutes of Health Research (CIHR), the Alzheimer Society Canada (ASC), the Parkinson Society Canada, the Natural Sciences and Engineering Research Council of Canada (NSERC) the Canadian Foundation for Innovation and other private or public organisms. Dr Calon has published over 100 papers, which have been cited more than 4500 times. He and his team at Laval University, Quebec city, mainly carry on preclinical assays in animal models of brain diseases or neuropathology studies on human brain samples.
Besides his expertise on Alzheimer's disease and movement disorders, his group has developed an unique research platform to investigate quantitatively and qualitatively the capacity of drugs to cross the blood-brain barrier. Dr Calon is mostly known for his contribution to the discovery of a neuroprotective effect of omega-3 fatty acids in animal models of Alzheimer's disease, Parkinson's disease and ischemic stroke. The ultimate goal of Dr Calon's work is to accelerate the transfer of knowledge from basic neuroscience to clinical applications for CNS diseases.

- Neurodegenerative diseases, Nutrition, blood-brain barrier, neuropharmacology. Calon, F, Lim, GP, Yang, F, Morihara, T, Teter, B, Ubeda, O, Rostaing, P, Triller, A, Salem, NJ, Ashe, KH, Frautschy, SA, Cole, GM (2004)
- Docosahexaenoic acid protects from dendritic pathology in an Alzheimer's disease mouse model. Neuron, 43:633–645.Paris-Robidas, S, Brochu, E, Sintes, M, Emond, V, Bousquet, M, V and al, M, Pilote, M

*How does dietary fatty acids influence brain function*

**Sophie LAYE (Bordeaux, France, INRA), Head of the Laboratory NutriNeuro**

Dr Layé is a neurobiologist who has developed researches on the effect of nutrition on brain functions. In particular, her team is interested in understanding the role of dietary lipids, obesity and diabetes in mood and cognitive disorders. They identified the mechanisms underlying the protective effect of n-3 PUFAs on depression, through the identification of their interaction with endocannabinoid-dependant neuronal plasticity and neuroinflammatory pathways. In addition, her team discovered in animal models and humans that inflammation is the pathophysiological mechanisms involved in mood and cognitive disorders associated to obesity. She has authored more than 120 publications, review articles and book chapters on the mechanisms underlying the effect of nutrition on brain functions and behavior and has been invited to more of 90 conferences and congresses. Dr Layé is a research fellow at Institut National de la Recherche Agronomique, and is the recipient of the prestigious Laurier INRA Scientific Breakthrough Award, the INRA Award for Excellence in Research, the faculty mentor Award from Bordeaux University.

- Thomazeau A, Bosch-Bouju C, Manzoni O, Layé S. Nutritional n-3 PUFA Deficiency Abolishes Endocannabinoid Gating of Hippocampal Long-Term Potentiation. Cereb Cortex. 2016 Mar 5
- Delpech JC, Thomazeau A, Madore C, Bosch-Bouju C, Larrieu T, Lacabanne C, Remus-Borel J, Aubert A, Joffre C, Nadjar A, Layé S. Dietary n-3 PUFAs Deficiency Increases Vulnerability to Inflammation-Induced Spatial Memory Impairment. Neuropsychopharmacology. 2015 Nov;40(12):2774-87
- Bazinet RP, Layé S. Polyunsaturated fatty acids and their metabolites in brain function and disease. Nat Rev Neurosci. 2014 Dec;15(12):771-85
- Lafourcade M, Larrieu T, Mato S, Duffaud A, Sepers M, Matias I, De Smedt-Peyrusse V, Labrousse VF, Bretillon L, Matute C, Rodríguez-Puertas R, Layé S, Manzoni OJ. Nutritional omega-3 deficiency abolishes endocannabinoid-mediated neuronal functions. Nat Neurosci. 2011 Mar;14(3):345-50.

**23/09/2016**

*The interaction between nutrition and the brain; studies in rodents and men*

**SUSANNE LAFLEUR (The Netherlands) _ Also Instructor on an NBF school project!**

Susanne la Fleur was a postdoc with Mary Dallman at UCSF in San Francisco (UAS) and pioneered the idea to provide animals with choice to consume fat and sugar separate from pelleted chow as a new obesogenic animal model and showed with this the importance of frequent snacking in obesity development1 and stress reducing properties of palatable intake2. She is currently group leader at the Academic Medical Center in Amsterdam studying the role of classic neuropeptides3 and novel neuroinflammatory markers in the hyperphagia occurring with snacking. During the course, Susanne will instruct imaging, brain infusion and behavioral studies in this novel obesogenic diet.

Int J Obes (Lond). 2014 May;38(5):643-9
Prog Neurobiol. 2006 Aug;79(5-6):247-340.
Biol Psychiatry. 2015 Apr 1;77(7):633-41

*When a calorie is not a calorie: Unravelling the signals driving sugar reward*

**Dana SMALL (USA)**

Deputy Director for Research and Fellow, The John B. Pierce Laboratory _ Professor of Psychiatry at Yale School of Medicine ; Professor of Psychology at Yale University

Dr. Small is a clinical neuropsychologist who has used neuroimaging to study taste, flavor and feeding in humans since the mid 90s. She performed the first neuroimaging studies of feeding showing that responses in dopamine source and target regions decrease as a function of satiety while response in lateral prefrontal regions increase, and was awarded the Allan Epstein Award by the Society for the Study of Ingestive Behavior for this work in 2015. More recently, her laboratory focuses on understanding the mechanisms by which the modern food environment challenges physiology to promote obesity. Towards this aim she has recently established the Modern Diet and Physiology Research Center and was recently appointed to the National Academy of Sciences Board on Behavioral, Cognitive and Sensory Sciences (BBCSS) where she is leading a task force to understand the intersection between diet, metabolism and cognitive dysfunction.

* 2015: Allan Epstein Award for award honors an individual for a specific research discovery that has advanced the understanding of ingestive behavior, Awarded by the Society for the Study of Ingestive Behavior
* 2014: Elected to the National Academy of Sciences Board on Behavioral, Cognitive and Sensory Sciences (BBCSS)
* 2010: Ruth Pike Award for Contributions to Research in Nutrition, Pennsylvania State University, Department of Nutrition
* 2007: Firmenich Young Investigator Award for Research in Fragrance and Flavors, presented by Firmenich, Geneva Switzerland 2006: Invitee National Academy of Sciences'Eighteenth Annual Kavli Frontiers of Science Symposium for Young Investigators 2005: Moskowitz-Jacobs Award for Research Excellence in the Psychophysics of Taste and Smell presented by the Association for Chemoreception Sciences
* 2003: Ajinomoto Young Investigator Award for Research in Gustation
presented by the Association for Chemoreception Sciences
* 2002: Election to the International Neuropsychology Symposium

- de Araujo, T. Lin, M. Veldhuizen, D. M. Small "Metabolic regulation of brain response to food cues. Current Biology, 2013, 23: 878-883. E. Stice, S. Spoor, C. Bohon, D. M. Small
- "Relation between obesity and blunted striatal response to food is moderated by Taq1A1 DRDE Gene"Science 2008, 322: 449-452. D. M. Small, R. J. Zatorre, A. Dagher, Alan C. Evans, M. Jones-Gotman,
- "Brain activity related to eating chocolate: From pleasure to aversion", Brain, 2001, 124(10): 1720-1733.

**26/09/2016**

*Targeting the gut microbiome to combat obesity-linked diseases*

**André Marette (Québec, Canada)**

Dr. Marette is Professor of Medicine at the Heart and Lung Institute and Scientific Director of the Institute of Nutrition and Functional Foods at Laval University. He also holds a research Chair on the pathogenesis of insulin resistance and cardiovascular diseases. Dr. Marette isan international renowned expert on the pathogenesis of insulin resistance and his research has advanced the understanding of the cellular/molecular mechanisms ofinflammation, and opened new possibilities for prevention and treatment of metabolic syndrome through modulation of the gut microbiota by prebiotics.
He recently discovered that omega3-PUFA-derived protectin DX can protect against insulin resistance and type 2 diabetes through a novel myokine-liver glucoregulatory axis (Nat Med 2014). Dr. Marette has received several awards for his work including the prestigious Young Scientist Award of the Canadian Diabetes Association, and the Charles Best Award from the University of Toronto for his overall contribution to the advancement of scientific knowledge in the field of diabetes.

Dr. Marette has published over 170 papers and reviews in peer-reviewed journals including four in Nature Medicine. He sis the upcoming Editor-in-Chief of the American Journal of Physiology : Endocrinology & Metabolism (July 2016).

*Glucocorticoids and Brain : from early life to senescence*

**Ron de Kloet (The Netherlands, Leiden)**

Academy professor of the Royal Netherlands Academy of Arts and Sciences, (em) professor of Medical Pharmacology LACDR / LUMC, Leiden University

For half a century I am fascinated by the question how stress hormones, that are critical for life, can change their action in the brain from protective to harmful, while enhancing vulnerability to stress-related disorders. We demonstrated that this switch from a resilient to a vulnerable brain depends on the balance between activation and suppression of stress reactions which is under control of one single hormone: cortisol. This discovery has provided leads towards biomarkers and a novel treatment strategy of stress-related mental disorders aimed to promote a mechanism of resilience still present in the diseased brain.
The results have been published in more than 600 scientific articles. My research received international recognition by the Geoffrey Harris Award of the European Federation of Endocrine Societies (2005), the European College of Neuropsychopharmacology Award (2007), and the Lifetime Achievement Award of the International Society of Psychoneuroendocrinology (2008) and the Golden Emil Kraepelin Medal (2014) for the impact of our basic research on the diagnosis and treatment of depression.  August 25, 2010 the Queen of The Netherlands has been pleased to appoint me Knight of the Order of the Dutch Lion.
From 1990 I was professor of Medical Pharmacology at Leiden University/Medical  Centern, reaching recently the emeritus status. The Department of Medical Pharmacology at the Leiden Academic Center for Drug Research with an outstanding research group )*  skilled in experiments from gene to behaviour with a translational perspective for application in drug development and medicine . From 2004 I am appointed Academy Professor of the Royal Netherlands Academy of Arts and Sciences at the LACDR, Leiden University and the Department of Endocrinology & Metabolism, LUMC.


- De Kloet ER (2014) From Receptor Balance to Rational Glucocorticoid Therapy. *Endocrinology* 155: 2754-2769.
- De Kloet ER; Joëls M; Holsboer F (2005) Stress and the brain: From adaptation to disease *Nature Reviews Neuroscience* 6: 6, 463-475.
- De Kloet ER, Oitzl MS; Joëls M  (1999) Stress and cognition: are corticosteroids good or bad guys?  *Trends in Neurosciences* 22: 10, 422-426.

**27/09/2016**

*Hypothalamic nutrient sensing in the regulation of energy balance*

**Daniela COTA (Bordeaux, France)**

Research Team Leader, Team "Energy Balance and Obesity", INSERM U1215 Neurocentre Magendie, Bordeaux, France

Daniela Cota is a neuroscientist with a clinical endocrinology background, focusing on the study of neuronal circuits and intracellular signaling cascades that are involved in the regulation of food intake and body weight. She also studies the impact of these circuits and neural systems on peripheral metabolism.
Her work on the endocannabinoid system, which started with a postdoc at the Max-Planck of Psychiatry in Munich in 2001, has critically determined the role of this system and of the cannabinoid type 1 (CB1) receptor in the regulation of energy balance andin obesity. At the same time, herstudies on the mTOR (mechanistic Target Of Rapamycin) pathway were the first to demonstrate that this intracellular signaling cascade is a critical integrator of the effects of hormones and nutrients at the level of the hypothalamus, a brain structure controlling energy balance.

* 2005 Ethan Sims Young Investigator award of the Obesity Society
* 2007 INSERM Avenir grant prize

***Key findings*** :
Discovery of functional CB1 receptors in peripheral organs (adipose tissue);
Discovery of ability of nutrients (amino acids) to modulate food intake through hypothalamic intracellular pathways


- Cota D, Marsicano G, Tschöp M, Grübler Y, Flachskamm C, Schubert M, Auer D, Yassouridis A, Thöne-Reineke C, Ortmann S, Tomassoni F, Cervino C, NisoliE, Linthorst AC, Pasquali R, Lutz B, Stalla GK, Pagotto U. The endogenous cannabinoid system affects energy balance via central orexigenic drive and peripheral lipogenesis. J Clin Invest. 2003 Aug;112(3):423-31.
- Cota D, Proulx K, Smith KA, Kozma SC, Thomas G, Woods SC, Seeley RJ. Hypothalamic mTOR signaling regulates food intake. Science. 2006 May 12;312(5775):927-30.
- Bellocchio L, Soria-Gómez E, Quarta C, Metna-Laurent M, Cardinal P, Binder E, Cannich A, Delamarre A, Häring M, Martín-Fontecha M, Vega D, Leste-Lasserre T, Bartsch D, Monory K, Lutz B, Chaouloff F, Pagotto U, Guzman M*, Cota D*, Marsicano G*. Activation of the sympathetic nervous system mediates hypophagic and anxiety-like effects of $CB_1$receptor blockade. Proc Natl Acad Sci U S A. 2013 Mar 19;110(12):4786-91. *share last authorship


*Of ghost neurons and ravenous microglia: coupling between apoptosis and microglial phagocytosis in health and disease*

**Amanda SIERRA (Bilbao, Spain) _ Also Instructor on an NBF school project!**

Ikerbasque Research Professor

Amanda Sierra leads the Glial Cell Biology Lab at the Achucarro Basque Center for Neuroscience in Bizkaia, Spain. She originally implemented the ex vivo analysis of microglial function based on FACS-sorting1,2 discovered that microglia are very efficient phagocytes in the hippocampal neurogenic cascade in physiological conditions, where they remove the excess of new born cells3. More recently, she has described that neuronal hyperactivity during seizures exhausts neural stem cells4 and impairs microglial phagocytosis5.


- Sierra A, et al., 2007. Glia 55(4):412-24.
- Sierra A, et al. 2008. Glia 56(6):659-674.
- Sierra A, et al. 2010. Cell Stem Cell 7(4):483-95.
- Sierra A, et al. 2015. Cell Stem Cell 16:488-503.
- Abiega O et al. (under review, PLoS Biology)

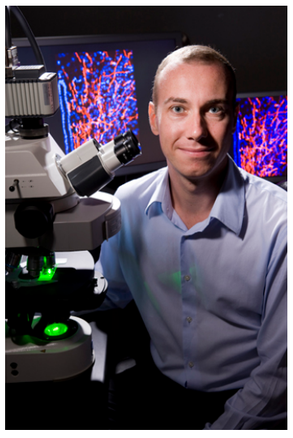
**28/09/2016**

*Neural Control of Energy Balance: Translating Circuits to Therapies*

**Laurent GAUTRON (Houston, USA ; Internal Medicine at UTSouthwestern Medical Center) _ Also Instructor on an NBF school project !**

Laurent Gautron (PhD) was trained at the University of Bordeaux, Harvard Medical school, and the University of Texas Southwestern Medical Center (UTSW) performing work related to the neural circuits involved in regulating energy balance and appetite. Since 2012, he is Assistant Professor at UTSW where is laboratory focuses on the role of C-fibers in metabolism, feeding and immunity. Dr. Gautron will instruct pharmacogenetic techniques allowing the manipulation of hypothalamic neurons regulating appetite in the mouse.


- Gautron et al., Cell. 2015;161(1):133-45.
- Udit and Gautron. Front Neurosci. 2013;7:134.
- Gautron et al., J Comp Neurol. 2011 ;519(15):3085-101.

*Developmental programming of appetite*

**Sébastien BOURET (Los Angeles, USA)**

Associate Professor of Pediatrics , The Saban Research Institute , Developmental Neuroscience Program , University of Southern California ,Research Director CNRS

Dr. Bouret has a broad background in the field of metabolic programming and the neurobiology of obesity. His research has directly led to several breakthroughs in the understanding of the complex hormonal signals and neurodevelopmental substrates responsible for appetite regulation. Most notably, he discovered that metabolic hormones (such as leptin and ghrelin) play a crucial role in hypothalamic development and in the nutritional programming of metabolism. More recently, his lab has reported an unanticipated role for prenatal leptin in the development of the parasympathetic innervation of pancreatic islets.

He has authored more than 65 articles, reviews, and book chapters in the field of developmental programming and the neurobiology of obesity. In addition, Dr. Bouret has served on numerous journal editorial boards, organizing committees and grant review panels (including the NIH) and has been invited to lecture internationally.

* Bronze medal CNRS (2014), French Society for Neuroendocrinology prize (2003)

***Key findings*** : Metabolic hormones exert a developmental action on brain feeding circuits


- Bouret S, Levin BE, Ozanne SE. Gene-environment interactions controlling energy and glucose homeostasis and the developmental origins of obesity. *Physiological Reviews*, 95(1):47-82, 2015
- Steculorum SM, Collden G, Coupe B, Croizier S, Lockie S, Andrews Z, Jarosch F, Klussmann S, Bouret SG. Ghrelin programs development of hypothalamic feeding circuits. *The Journal of Clinical Investigation*, 125(2), 846-858, 2015 (also *J Clin Invest* (commentary), 490-492, 2015)
- Bouret SG, Draper SJ, Simerly RB. Trophic action of leptin on hypothalamic neurons that regulate feeding. *Science*, 2004; 304(5667):108-110. (News & Views, p. 63-64; Science Editor's Choice; also Nature Medicine, 12(1):52-53, 2006; and NIH 2004 Strategic Plan for NIH Obesity Research)

**03/10/ 2016**

*Neuroendocrine polypharmacy targeting obesity and diabetes*

**Mathias TSCHÖP (Munich, Germany)**
Research Director, Helmholtz Pioneer Campus & Helmholtz Diabetes Center,, Helmholtz Zentrum Muenchen, Alexander von Humboldt Professor/Chair, Division of Metabolic Diseases, Technische Universitaet Muenchen

Early in his career, Prof. Tschöp discovered the orexigenic, adipogenic, and metabolic effects of ghrelin, coining it „the hunger hormone“. The corresponding first author publication in *Nature* has to date been cited more than 3170 times (*Nature*, 2000). This groundbreaking discovery added a fundamental pathway to the model of body weight and glucose control and established a novel set of drug targets for the treatment of the metabolic syndrome (*Nature Medicine*, 2009; *Science*, 2010). Prof. Tschöp went on to dissect gut-brain communication pathways, based on GI-hormone signaling and lessons from unraveling the molecular underpinnings of gastric bypass surgery. His series of reports showing efficacy of novel gut hormone co-agonist peptides targeting several neuroendocrine receptors, that in turn reduce body weight and improve glucose tolerance at an unprecedented level, broke new ground and offered novel clinical approaches for the treatment of diabetes and obesity (*Nature Chemical Biology*, 2009; *Science Translational Medicine*, 2013, *Nature Medicine,* 2015). Together with his long-term collaborator, chemist Richard DiMarchi (Indiana University), he recently discovered yet another class of novel drug candidates by engineering peptide based steroid/small molecule delivery to selected cell populations (*Nature Medicine*, 2012). Several of these gut hormone-based single molecule combinatorial therapeutics, are now in clinical development for the treatment of diabetes and obesity. After reporting on a new pathophysiological process of the metabolic syndrome involving hypothalamic astrocytosis and microgliosis (PNAS, 2010, J Clin Invest 2012) Matthias Tschöp is utilizing these novel pharmaceutical tools to specifically target inflammatory processes in metabolically relevant brain control circuits.

* Erwin Schrödinger Prize 2014 *The Erwin Schrödinger Prize recognizes outstanding scientific achievements and technological innovations in medicine, natural sciences and engineering.*
* Elected Member, German National Academy of Science (Leopoldina) 2013

***Key Findings*** : Metabolic regulation and metabolic diseases research _ Development of novel clinical approaches for the treatment of diabetes and obesity _ Treatment of the metabolic syndrome _ Translational research in the fields of diabetes, obesity and metabolism _ Interactions of gastrointestinal hormones with central neuronal networks _ Role of ghrelin in the regulation of food intake and body weight

- Finan, B., Yang, B., Ottaway, N., […], Tschöp M. A rationally designed monomeric peptide triagonist corrects obesity and diabetes in rodents. *Nat Med* Jan;21(1):27-36 (2015).
- Finan, B., Yang, B., Ottaway, N. […], Tschöp, M. Targeted estrogen delivery reverses the metabolic syndrome. *Nat Med* Dec;18(12):1847-56 (2012).
- Day, J.W., Ottaway, N., Patterson, J.T., […], Tschöp, M. A new glucagon and GLP-1 co-agonist eliminates obesity in rodents. *Nat Chem Biol* 5(10):749-57 (2009).
- Tschöp, M., Smiley D., Heiman M.L. Ghrelin induces adiposity in rodents. *Nature* Oct 19;407(6806):908-13 (2000).

*Lean on body neurons*

**Ana DOMINGOS (Lisboa, Portugal)**
Principal Investigator in the Obesity Laboratory, Instituto Gulbenkian de Ciencia ; PhD in Neurobiology, The Rockefeller University

Ana Domingos studies the neural mechanisms acting on fat breakdown. Recently, the research team led by Ana Domingos published an important study in the prestigious journal Cell, establishing for the first time that adipose tissue is innervated. “We determined that activation of sympathetic neurons among adipocytes promotes fat breakdown, and concordant loss of fat mass. This result represents a new strategy for the induction of fat loss and, ultimately, a new anti-obesity therapy that would circumvent the challenges of drug delivery to the brain”. In the newly funded project, Ana Domingos will team up with two other research groups: Paul Cohen (Rockefeller University, USA) and Daniel Razansky (The Helmholtz Institute for Biological and Medical Imaging, University of Munich, Germany) to better understand the anatomy and function of neurons surrounding fat tissue, combining novel techniques of genetics and optoacoustic microscopy. The Portuguese researcher states: "To find a cure to obesity we have to be at the forefront of obesity research, what often requires interdisciplinary and a risk-taking stance ".

- 2013 Rapid regulation of depression-related behaviours by control of midbrain dopamine neurons; D Chaudhury, JJ Walsh, AK Friedman, B Juarez, SM Ku, JW Koo, ..., Nature 493 (7433), 532-536
- 2004 Or83b encodes a broadly expressed odorant receptor essential for Drosophila olfaction; MC Larsson, AI Domingos, WD Jones, ME Chiappe, H Amrein, ..., Neuron 43 (5), 703-714

**04/10/ 2016**

*The impact of stress and anxiety on behavior and brain metabolism*

**Carmen Sandi (Switzerland)**

Professor and Director of the Brain Mind Institute and Laboratory of Behavioral Genetics; EPFL, Lausanne, Switzerland

Research in Carmen Sandi's laboratory aims to understand how stress and personality traits affect brain function and behavior. One of their ultimate goals is the identification of neurobiological mechanisms underlying vulnerability or resilience to psychopathology.
Her lab is currently developing an ambitious research program combining approaches in rodents and humans focusing on the effects of stress on the social brain and the emergence of violence. A special emphasis is placed on the regulation of brain bioenergetics in the long-term programming of behavior and peripheral metabolism by early life stress. Recently, they have identified a key role for mitochondrial function in the nucleus accumbens in the link between anxiety and social competition.

* President of the European Brain and Behavior Society (2009-2011) _ Behavioral Brain Research Prize (2014) _ Valkhof Chair, Radboud University (2015)

***Key findings*** **:** How the social brain and cognition are programmed by stress, including a key role for glucocorticoids and cell adhesion molecules.


- Sandi C. and Haller J. (2015) Stress and the social brain: behavioral effects and neurobiological mechanisms. *Nature Reviews Neuroscience* 16:290-304.
- Hollis F., van der Kooij M.A., Zanoletti O., Lozano L., Cantó C. and Sandi C. (2015) Mitochondrial function in the brain links anxiety with social subordination. Proc Natl Acad Sci USA 112:15486-15491.
- Luksys G., Gerstner W., and Sandi C. (2009) Stress, genotype and norepinephrine in prediction of mouse behavior using reinforcement learning. *Nature Neuroscience* 12: 1180-1186.


*Role of mitochondrial CB1 receptor in energy metabolism*

**Giovanni Marsicano (Bordeaux, France)**

U1215 NeuroCentre Magendie and Université de Bordeaux. DR2 Inserm. Group Leader « Endocannabinoids and Neuroadaptation »

Dr. Giovanni Marsicano is a tenured researcher at Inserm. He leads the group "Endocannabinoids and Neuroadaptation" at the NeuroCentre Magendie, an INSERM and University of Bordeaux Research Center devoted to neuroscience. He is a Veterinary Medicine Doctor as formation. After the Veterinary diploma, he worked on research related to Embryonic Stem Cells from farm animals and to xenotransplantation models in Italy for 4 years. In 1997, he moved to the Max-Planck Institute of Psychiatry in Munich for a PhD student position, where he initiated the work on the role of type-1 cannabinoid receptors (CB1) and of the endocannabinoid system (ECS) in brain physiology, which since has been his main research interest. After PhD graduation in 2001, he made two post-doc periods in Germany and moved to Bordeaux in 2006 (recruited as senior scientist in 2007) to lead his independent research group.
By using conditional mutagenesis in mice and behavioral, biochemical and electrophysiological tools, his work contributed defining the role of CB1 in specific cell populations in learning and memory, food intake and energy balance, anxiety, stress-coping and others. Through a clear bottom-up scientific approach, these studies allowed exploring some general principles of brain functioning, such as the balance between excitation and inhibition, the interactions between the brain and the periphery, the importance of energy metabolism in brain functions and glial-neuron interactions. In particular, the implications of the recent discovery that CB1 receptors are functionally present on brain mitochondria will be the main focus of the presentation.

* Award Bettencourt-Schueller 2006 _ ERC-Starting Grant 2010 _ Grand Prix Robert Debré 2013

***Key findings*** : Cellular and subcellular specific functions of cannabinoid type-1 CB1 receptors. Role of endocannabinoid regulation of excitatory and inhibitory neurotransmission in food intake, fear, memory and other behaviors. Role of cannabinoid-modulation of neuron-glial interactions in learning and memory. Bioenergetics processes in the brain.


- Marsicano G*, Wotjak C*, Azad SC, Bisogno T, Rammes G, Cascio MG, Hermann H, Tang, J, Hofmann C, Zieglgänsberger W, Di Marzo V and Lutz B (2002) The endogenous cannabinoid system controls extinction of aversive memories. *Nature* 418:530-34.
- Benard G, Massa F, Puente N, Lourenço L, Bellocchio L, Soria-Gómez E, Matias I, Delamarre A, Metna-Laurent M, Cannich A, Hebert-Chatelain E, Mulle C, Ortega-Gutierrez S, Martín-Fontecha M, Klugmann M, Guggenhuber S, Lutz B, Gertsch J, Chaouloff F, López-Rodríguez ML, Grandes P, Rossignol R and Marsicano G (2012) Mitochondrial CB1 receptors regulate neuronal energy metabolism. *Nature Neuroscience* 15(4):558-64.
- Han J, Kesner P, Metna-Laurent M, Duan T, Xu L, Georges F, Koehl M, Abrous DN, Mendizabal-Zubiaga J, Grandes P, Ren W, Marsicano G* and Zhang X* (2012). Astroglial CB1 Receptors Mediate Cannabinoid Alterations of Synaptic Plasticity and Working Memory. *Cell* 148(5):1039-50.

**06/10/ 2016**

*The Gut Microbiome: a Key Regulator of brain Function Across the Lifespan*
**John CRYAN (Cork, Ireland)**

John F. Cryan is Professor & Chair, Dept. of Anatomy & Neuroscience, University College Cork (UCC)., Cork, Ireland He received a B.Sc. (Hons) and PhD from the National University of Ireland, Galway, Ireland. He was a visiting fellow at the Dept Psychiatry, University of Melbourne, Australia, which was followed by postdoctoral fellowships at the University of Pennsylvania, Philadelphia, USA and The Scripps Research Institute, La Jolla, California. He spent four years at the Novartis Institutes for BioMedical Research in Basel Switzerland, as a LabHead, Behavioural Pharmacology prior to joining UCC in 2005. Currently he is also a Principal Investigator in the APC Microbiome Institute.

Prof. Cryan has a H-index of 67 having published over 300 peer-reviewed articles and book chapters. He is a Senior Editor of *Neuropharmacology* and of *Nutritional Neuroscience* and an Editor of *British Journal of Pharmacology*. He is on the editorial board of a further 16 journals. He has edited three books including "*Microbial Endocrinology: The Microbiota-Gut-Brain Axis in Health and Disease"* (Springer Press, 2014). *P*rof. Cryan's current research interests include the neurobiological basis of stress-related neuropsychiatric disorders including depression, anxiety and drug dependence. Moreover, his group is also focused on understanding the interaction between brain, gut & microbiome and how it applies to stress and immune-related disorders, including irritable bowel syndrome and obesity and neurodevelopmental disorders such as autism.

* Elsevier Award, Neurobehavioral Teratology Society, Montreal, 2015
* Alimentary Pharmabiotic Centre, Scientist of the Year Award 2015
* WIRED Health Speaker London 2015
* TEDMED Speaker, Washington DC 2014
* **Thomson Reuters Highly Cited Researcher 2014**
* The World's Most Influential Scientific Minds 2014
* **University of Utrecht Award for Excellence in Pharmaceutical Research 2013**
* University College Cork Researcher of the Year 2012
* European College of Neuropsychopharmacology Fellowship Award, September 2006
* Wyeth Psychopharmacology Award, British Association of Psychopharmacology, July 2006
* Young Scientist Award, Foundation of the European Behavioural Pharmacology Society, September 2005

***Key findings*** :Prof. Cryan is best known for his work on animal models of stress-related disorders and their pharmacological treatment. More recently his team has been instrumental in demonstrating a role for the gut microbiome in regulating brain and behaviour. In particular his research is currently focused on understanding the interaction between brain, gut & microbiome and how it applies to stress, psychiatric and immune-related disorders at key time-windows across the lifespan.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*Programming of brain structure and function by early-life stress: a role for nutrition and opportunities for interventions*
**Aniko KOROSI (The Netherlands) _ Also Instructor on an NBF school project!**

Aniko Korosi was a postdoc at UCI in the lab of dr. Baram where she studied how enriched early life experience rewires the hypothalamus. At the end of 2010 she started her team as Assistant professor at the University of Amsterdam where her research focuses on the programming of cognitive functions by early-life stress and aging and on the role of metabolic signals and nutrients in this context1. Her work encompasses pre-clinical using an established mouse model of chronic early-life stress2 and clinical work and she is interested in developing peripheral (e.g. nutritional) intervention to prevent and/or reverse the lasting consequences of early-life stress.


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## The CAJAL Advanced Neuroscience Training Programme
## NUTRITION AND BRAIN FUNCTIONS (NBF) 2016
### Instructors

**Guillaume Ferreira, NutriNeuro, INRA**

In 2001 Guillaume Ferreira obtained a permanent faculty position at the French National Institute for Agricultural Research (INRA) and he is now Research Director. Since the onset of his career, his main research interest has been the neural basis of cognition. He moved to the lab "Nutrition & Integrative Neurobiology" in Bordeaux in 2009 to develop a project focused on the effect of nutrition at early developmental stages (adolescence) on brain plasticity and cognition. In the course, Guillaume will instruct behavioral and neurobiological experiments on the effect of obesogenic diet on learning and memory processes.


- Boitard et al. (2015) *The Journal of Neuroscience,* 35(9):4092– 4103.
- Soria-Gomez et al. (2015), *Neuron,* 88(2):306-13.
- Boitard et al. (2014) *Brain, Behavior and Immunity,* 40: 9-17.
- Soria-Gomez et al. (2014), *Nature Neursocience*, 17(3):407-15.
- Boitard et al. (2012) *Hippocampus*, 22:2095 –2100.


**Mariano Ruiz-Gayo, Universidad CEU San Pablo**

Mariano Ruiz-Gayo worked on behavioural effects of cholecystokinin (CCK) with Bernard P. Roques at Université Paris V. He continued studying the relationship between CCK, opioids and cannabinoids at Universidad Complutense (Madrid, Spain). He is currently a professor of Pharmacology at the University San Pablo (Madrid), where he's working on the influence of leptin and CCK on the relationship between feeding behaviour, learning and memory processes. Mariano will instruct behavioural and neurobiological experiments on the effect obesogenic diets on learning and memory processes.


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- Stucchi et al. (2012) Endocrinology 153(2):690-699


**Agnès Nadjar, NutriNeuro, Université de Bordeaux**
Maître de conférence – PhD ; UFR Sciences de la vie ; Université de Bordeaux

Agnès Nadjar is an Associate Professor at the University of Bordeaux and member of the laboratory of Nutrition and Integrated Neurobiology (NutriNeuro, INRA, Bordeaux). She is also the co-director of the Neuroinflammation axis at the Neuroscience Department of Bordeaux and coordinator for bioimaging technologies at NutriNeuro. Mostof her teaching duty is devoted to the coordination of the European Neurasmus Master programme (European Master of excellence in Neurosciences gathering 6 international Universities and students from all over the world). Since 2012, Agnes Nadjar is the scientific director of Scilight® (www.scilight.eu), a company she co-founded and that is dedicated to scientific communication.
Her research falls within the field of psychoneuroimmunology with a particular interest in microglia neuron interactions in physiological and pathological situations. Over the first ten first years of her career, she elucidated some of the cellular and molecular mechanisms underlying the effects of an acute or chronic neuroinflammation on these interactions and subsequent neuropsychiatric disorders. Since she integrated the NutriNeuro lab in 2011, she is leading researches on the impact of nutritional lipid status on microglial function and consequences on neuronal activity. She also developed state-of-the-art techniques, such as high resolution imaging, to unravel microglial function.


Delpech JC et al. 2015 The Journal of Neuroscience, 35(7):3022-33
Delpech JC et al. 2015 Neuropsychopharmacology
Madore C et al. 2013 34:151-8

**Jorge Valero, Universidad Autónoma de Barcelona, Spain**

Jorge Valero did his postdoctoral training at the lab of Dr. Carlos Saura (Universidad Autónoma de Barcelona, Spain) and at the lab of Dr. João Malva (Center for Neursocience and Cell Biology, University of Coimbra, Portugal). He has demonstrated that factors modulating adult neurogenesis, such as environmental stimulation and neuroinflammation, can affect spatial memory and neurogenic reserve in mouse models of Alzheimer's disease1,2. Jorge has developed several tools for automatic image analysis2,3. He is currently an Ikerbasque research fellow at the Achucarro Basque Center for Neuroscience, Bizkaia (Spain). He will instruct on the analysis of adult hippocampal neurogenesis and associated behaviors.


- Valero et al., PLoS ONE. 6, e16832 (2011).
- Valero et al., Front. Neurosci. 8, 83 (2014).
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**Xavier Fioramonti, Centre des Sciences du Gout et de l'Alimentation (CSGA) CNRS, INRA, DIJON**, Equipe: Détection cérébrale des nutriments et homéostasie énergétique

The brain and more particularly the hypothalamus play a critical role in the control of energy homeostasis in controlling feeding behavior and the activity of peripheral organs through humoral and nervous regulation systems. This control relies on neurons that are capable of integrating metabolic signals including hormones (e.g. leptin, insulin and ghrelin) and nutrients (i.e. glucose, fatty and amino acids). Among them, specialized glucose-sensing neurons are able to adapt their electrical activity in response to changes in glucose level. His laboratory uses complementary approaches to study neurons from the electrophysiology on brain slices, calcium imaging on hypothalamic primary cultures, up to the *in vivo* experimentation.


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- Fioramonti X, Contié S, Song Z, Routh VH, Lorsignol A, Pénicaud L. Characterization of glucosensing neuron subpopulations in the arcuate nucleus: integration in neuropeptide Y and pro-opio melanocortin networks? Diabetes. (2007);56(5):1219-27.
- Fioramonti X, Lorsignol A, Taupignon A, Penicaud L. A new $K_{ATP}$ independent mechanism involved in glucose-excited neurons of mouse arcuate nucleus. Diabetes 2004; 53: 2767-75.a


**Clémentine Bosch-Bouju, NutriNeuro, Université de Bordeaux**

Clémentine Bosch-Bouju did her PhD at the lab of Dr. Laurent Venance (Collège de France, Paris, France) and her postdoctoral training at the lab of Dr. Louise Parr-Brownlie (University of Otago, Dunedin, New Zealand). She is an expert in electrophysiology and optogenetics to record and control electrical activity in neuronal networks. She discovered one of the mechanisms of action of deep brain stimulation[1], a powerful therapy used to treat Parkinson's disease. She also demonstrated how the neuronal activity in the motor thalamus is altered in Parkinson's disease[2]. She is currently postdoctoral fellow at NutriNeuro lab (INRA, Bordeaux University, France) to study the impact of dietary omega-3 fatty acids on brain function with a focus on synaptic plasticity and the endocannabinoid system[3].


- Bosch, C. et al., *J. Physiol.* **589**, 4189–4207 (2011).
- Bosch-Bouju, C. et al., *J. Neurosci.* **34**, 15836–15850 (2014).
- Thomazeau, A., Bosch-Bouju, et al., *Cereb. Cortex.* **2016** 1-9(2016)

**Marie-Pierre Moisan, NutriNeuro, INRA**

Marie-Pierre Moisan received her PhD from Edinburgh University in the lab of J Seckl, then she did a post-doctoral training in Duke University with KL Parker and finally she got a tenured position at the University of Bordeaux where she used molecular genetics to uncover genes involved in stress response1,2. She is now leading a group focused on the interplay between nutrition, glucocorticoid hormones and memory processes. Marie-Pierre will instruct on the assessment of glucocorticoids regulation and its neurobiological consequences during memory task.


- Moisan MP et al., (1996) Nat Genet. ;14(4):471-3.
- Moisan MP. (2013) Nat Rev Endocrinol. ;9(2):78


**Sylvie Vancassel, NutriNeuro, INRA**

Sylvie Vancassel (PhD) was appointed as a Research Scientist at INRA in 1999, specialized in neurobiology, with a focus on monoaminergic neurotransmission and nutrition. She spent part of his carrer to lead researches on the role of nutritional lipid status on neurotransmission function and consequences on behavior and CNS pathologies. She joined the NutriNeurO lab at Bordeaux in 2012 and her current researches are focused on the role of inflammation in mood disorders. She developed techniques for detection and quantification of neurotransmitter release, using in vivo microdialysis in mice and rats coupled to electrochemical detection.


- *Omega-3 polyunsaturated fatty acids and brain aging*. Denis I, Potier B, Heberden C, Vancassel S. Curr Opin Clin Nutr Metab Care. 2015 Mar;18(2):139-46.
- *Absence of the gut microbiota enhances anxiety-like behavior and neuroendocrine response to acute stress in rats.* Crumeyrolle-Arias M, Jaglin M, Bruneau A, Vancassel S, Cardona A, Daugé V, Naudon L, Rabot S. Psychoneuroendocrinology. 2014.
- *Omega-3 fatty acids deficiency aggravates glutamatergic synapse and astroglial aging in the rat hippocampal CA1.* Latour A, Grintal B, Champeil-Potokar G, Hennebelle M, Lavialle M, Dutar P, Potier B, Billard JM, Vancassel S, Denis I. Aging Cell. 2013 Feb;12(1):76-84.


**Muriel Darnaudéry, NutriNeuro, Université de Bordeaux**

Muriel Darnaudéry did her PhD in the Lab of Michel Le Moal in Bordeaux and was post-doc of Luis Miguel Garcia-Segura in the Cajal Institute of Madrid. She was appointed assistant professor in the Stefania Maccari lab where she started working on early life stress models and neuropsychiatric vulnerability. She is now full professor in the Nutrineuro Lab at the University of Bordeaux studying early life adverse events and neurobiological bases underlying the relationship between stress, mood and nutrition. During the course Muriel will instruct animal models for mood disorders: interest and limitations.


- Barboza Solís C et al., (2015) Proc Natl Acad Sci U S A. 112(7):E738-46
- Lépinay AL et al., (2015) Psychoneuroendocrinology. 53:82-93.
- Laloux C, et al., (2012) Psychoneuroendocrinology. 37(10):1646-58.

**Pierre Trifilieff, NutriNeuro, INRA**

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 mesolimbic dopamine transmission in reward processing and motivation. His work unraveled 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 - and dietary polyunsaturated fatty acids in particular - on the modulation of dopaminergic transmission and associated behaviors. Pierre Trifilieff will instruct on the behavioral and neurobiological bases of food motivation with a focus on mesolimbic dopamine transmission.


- Frederick AL.* et al. (2015) Molecular Psychiatry, PMID: 25560761.
- Trifilieff P. & Martinez D (2013) Neuropharmacology, PMID: 23851257.
- Trifilieff, P et al. (2013) Molecular Psychiatry, PMID: 23711983.


**Cyril Herry, INSERM, Head of the team – « Circuits neuronaux des apprentissages associatifs »**

Cyril Herry: "During my PhD, I showed for the first time electrophysiological evidence of a specific role of prefrontal plasticity in the inhibition of fear responses during consolidation of extinction. I then switched my research during my postdoctoral training in the laboratory of Pr. Andreas Luthï to study the role of the amygdala in the acquisition of extinction. There, I successfully implanted and developed the technique of long lasting single unit recordings in behaving animals and was able to identify distinct amygdala neuronal populations selectively implicated in the behavioral transition between high and low fear states. In 2011 I was awarded a prestigious ERC starting grant that allowed me to set up my laboratory in the Neurocenter Magendie. My laboratory long-term project in this institute is to identify and manipulate the circuits underlying fear behavior to ultimately develop new therapeutic strategies for anxiety-related pathologies."


- Herry, C. et al., (2008). Nature, 454, 600-6.
- Gogolla, N., et al., (2009). Science, 325,1258-61. IF: 33.6.
- Courtin, J. et al., (2014). Nature, 505: 92-96.


**Etienne Coutureau, CNRS/Université de Bordeaux**

Etienne Coutureau was a post-doc with Pr. Simon Killcross at the School of Psychology (Cardiff University, UK) and discovered the subtle interactions of prefrontal regions in the coordination of actions and habits in rodents. He is currently a CNRS Research Director at the Aquitaine Institute for Cognitive and Integrative Neuroscience where he is leading a research group investigating the neural circuit of Decision and Adaptation. Etienne will instruct the neurocognitive bases of food-seeking behavior.


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- Naneix et al. (2012) Journal of Neuroscience, 32:16223-16232.
- Alcaraz et al. (2015) Journal of Neuroscience, 35: 13183–13193