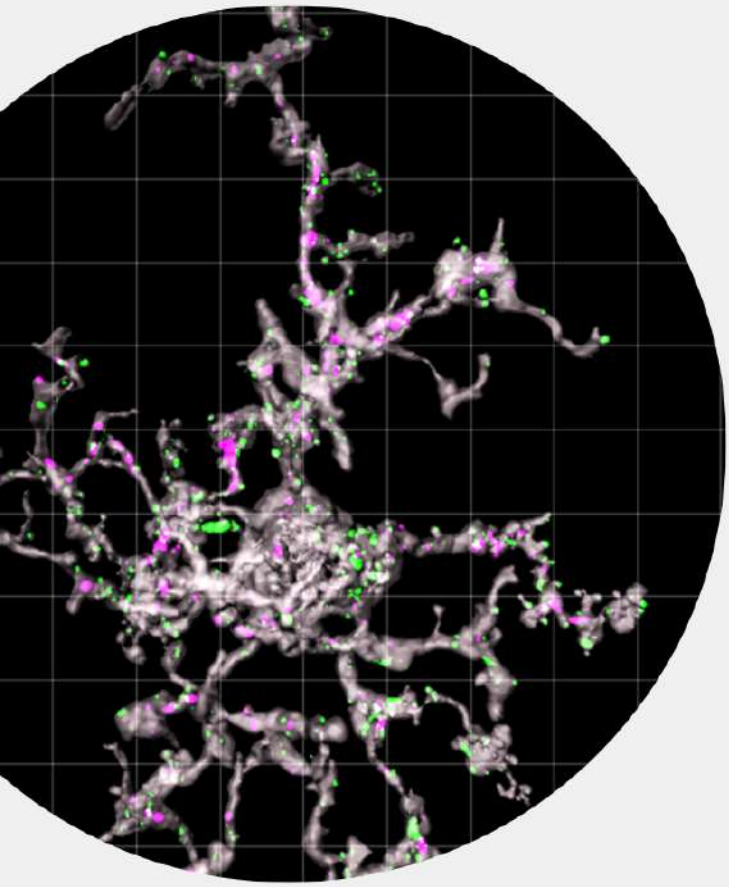
BORDEAUX SCHOOL OF NEUROSCIENCE

ADVANCED NEUROSCIENCE TRAINING — CAJAL —

19 JUNE TO
7 JULY 2022



THE CAJAL ADVANCED NEUROSCIENCE TRAINING PROGRAMME

Glial cells in health and disease

INTERNATIONAL BRAIN IBRO RESEARCH ORGANIZATION

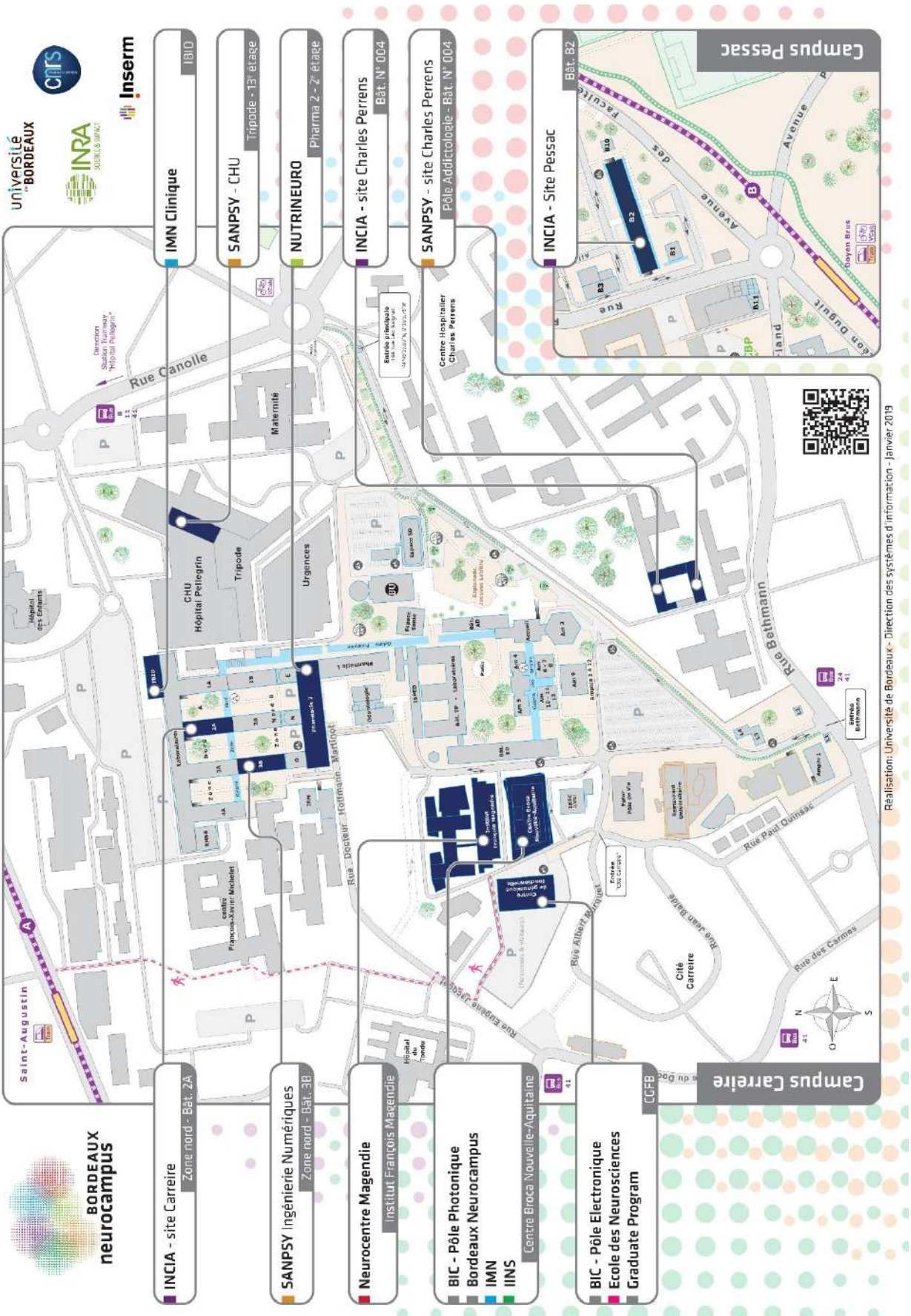
FENS Federation of European Neuroscience Societies

GATSBY

BORDEAUX neurocampus

SUMMARY

LOCATION OF THE FACILITIES



SCHEDULE

Block 1

	Monday 19	Tuesday 20	Wednesday 21	Thursday 22	Friday 23	Saturday 24	Sunday 25	Monday 26	Tuesday 27	Wednesday 28
9.00 -9.45	Welcome - Students presentations	Experiment 1	Experiment 1	**Wiebke Moebius**	**Thomas Papouin**	**Caroline Smith**	Day off - free time	**Kelly Monk**	Students presentations preparation	Free time
9.45 -10.30				**3Brain**		**Giampaolo Milior**				
10.30 -11.00	Coffee break			Coffee break				Coffee break		
11.00 -11.45	**Course directors talk**			**Amit Agarwal**	**Mikael Simons** virtual			**Maarten Kole**	Panel discussion - publications	
11.45 -12.30										
12.30 -14.00	Lunch with speakers and instructors							Lunch with speakers and		
14.00 -19.00	Experiment 1							Experiment 1	Students presentations	Social event
19.00 -20.00	Dinner with speakers and instructors					Free time		Dinner with s/i	Free time	
20.00 -21.00	poster session									

Block 2

	Thursday 29	Friday 30	Saturday 1	Sunday 2	Monday 3	Tuesday 4	Wednesday 5	Thusday 6	Friday 7	Saturday 8
9.00 -9.45	**Addgene**	**Sthephane Oliet**	**Bart Eggen**	Day off - free time	**Sonia Garel**	Experiment 2	Experiment 2	**Soyon Hong**	Students presentations	Departures
9.45 -10.30	**Zeiss**									
10.30 -11.00	Coffee break				Coffee break			Coffee break		
11.00 -11.45	Experiment 2	**Nathalie Rouach**	Experiment 2		**Eric Boué-Grabot**			Panel discussion - publications		
11.45 -12.30										
12.30 -14.00	Lunch with speakers and instructors				Lunch with speakers and instructors					
14.00 -19.00	Experiment 2	Experiment 2			Experiment 2	Experiment 2		**David Belin**	Free	
								TDT		
	David Rowitch (17:45)virtual				**Paola Arlotta** (17:30)virtual			Student presentations preparation		
19.00 -20.00	Dinner with speakers and		Free time		Dinner with s/i				Farewell dinner	
20.00 -21.00	poster session									

COURSE ORGANISATION BOARD & LOCAL CONTACTS

Directors

Ragnhildur Thora Karadottir (Cambridge University, UK)
Cagla Eroglu (Duke University, USA)
Staci Bilbo (Duke University, USA)

Local Director

Jean-Christophe Delpech (Bordeaux University, France)

BSN (Bordeaux School of Neurosciences) team

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ANTI-COVID 19 GUIDELINES

The current health situation allows the laboratories of Bordeaux Neurocampus to work in normal conditions, according to the University of Bordeaux and the French Government regulations.

General guidelines:

- In the campus, use of mask is no more compulsory at the moment.
- The "barrier actions" must be respected everywhere and as much as possible.

Guidelines Bordeaux School of Neuroscience:

- Every room has a dispenser of hydro alcoholic gel.
- We ask you to respect the following procedures in the resting/coffee room, during breaks and meals:
    - o Always wash your hands before using the stuff in the kitchen and before / after meals
    - o Mark your glass and cup with your name on a tape and use them throughout the course, please wash them after each use.
    - o After meals, please rinse your plate and cutlery and put them into the dishwasher.

Guidelines Conference Room:

- A dispenser of hydro alcoholic gel is installed at the entrance of the room.
- No food and drinks are allowed in the conference room.

We ask you to keep vigilant also during the time spent outside the course. Having a correct behaviour towards others and oneself is a sign of civility and mutual respect ☺

WIFI

SSID wifi : Ubx-invites

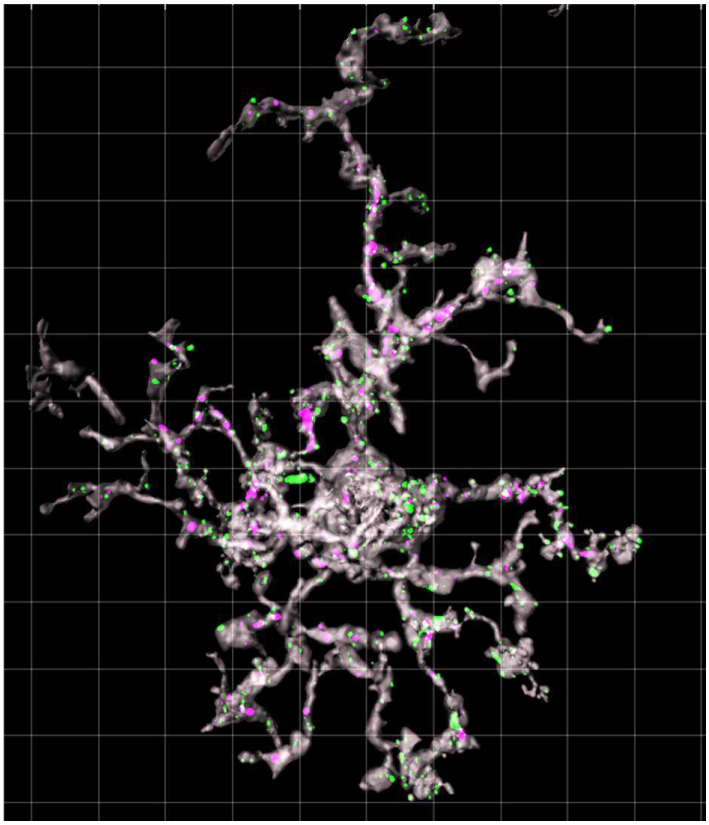
login : GCHD

Password : 32YsDg+?

THE COURSE

For over a century, the main focus of neuroscience research has been on neurons. It is however, becoming ever more clear that **brain functions** such as conceptual reasoning, memory, and processing speed depend on **glial cells** (microglia, astrocytes and oligodendrocytes).

The lack of understanding of the role of glia in normal brain development, function and disease is mainly due to lack of tools and methods to accurately study these cells. In recent years, neuroscience has seen a methodological revolution. The **function of glial cells** in neuronal circuit development, and neurodegenerative disease has become evident. The study of **glial biology** and the understanding on how glial cells impact on circuit function are key to understanding how the brain works and what goes wrong in brain disease. Advanced training of a new generation of neuroscientists with strong focus on glial function is crucial to make these studies a success in the coming decades.



DIRECTORS

Ragnhildur Thora Karadottir | Cambridge University (UK)

Ragnhildur Thóra Káradóttir is currently the director of the MS Society Cambridge Centre for Myelin Repair, a professor of cellular Neuroscience at the Department of veterinary Medicine, and a group leader at the Wellcome -MRC Cambridge Stem Cell Institute. Her research interests are to determine the changes in myelin and myelin repair throughout the lifespan and to understand how neuronal activity can regulate oligodendrocyte precursor cells (OPCs) differentiation and myelin plasticity in health and disease.
Since establishing her lab she has been awarded a number of awards, including the Lister Institute Research Prize (one of 5 in the UK), the Allen Distinguished Investigator Award (one of 5 worldwide, first time given outside of USA) and an ERC consolidator award. In 2015 she was elected to the FENS-Kavli Network of Excellence (one of 20 in Europe) and in 2017 awarded the Fabiane Carvalho Miranda International Prize for the best paper published in the years 2015-2017 in myelin biology and MS related research.

Selected publications :

- *De Faria Jr, Pivonkova H, Varga B, Timmler S, Evans KA &* ***Káradóttir RT****. (2021) Periods of synchronised myelin changes shape brain function and plasticity.* ***Nature Neuroscience*** *24, 1508-1521*
- *Bonetto G, Belin D,* ***Káradóttir RT****. (2021) Myelin: A gatekeeper of activity-dependent circuit plasticity?* ***Science*** *2;374(6569) Spitzer S, Sitnikov S, Kamen Y, Evans KA, Kronenberg-Versteeg D, Dietmann S, de Faria O, Agathou S &* ***Káradóttir R.*** *(2019) Oligodendrocyte progenitor cells become regionally diverse and heterogeneous with age.* ***Neuron****,101(3):459-47.*
- *Goebbels S, Wieser GL, Pieper A, Spitzer S, Weege B, Yan K, Edgar J, Yagensky O, Wichert S, Rossner M,* ***Káradóttir R*** *& Nave KA. (2017) De novo myelination of cerebellar granule cell axons triggered by PI(3,4,5)P3-dependent neuronal signals.* ***Nature Neuroscience*** *20(1):10-1.*
- *Gautier HO, Evans K, Volbracht K, James R, Sitnikov S, Lundgaard I, James F, Lao-Peregrin C, Franklin RJM &* ***Káradóttir R*** *(2015). Neuronal activity regulates remyelination via glutamate signaling to oligodendrocyte progenitors.* ***Nature Communications*** *6: 8518.*
- ***Káradóttir R*,*** *Hamilton N, Bakiri Y & Attwell D (2008). Spiking and nonspiking classes of oligodendrocyte precursor glia in CNS white matter.* ***Nature Neuroscience*** *11(4): 450-456.* *******corresponding author*
- ***Káradóttir R****, Cavalier P, Bergersen LH & Attwell D (2005). NMDA receptors are expressed in oligodendrocytes and activated in ischaemia.* ***Nature*** *438: 1162-1166.*

Cagla Eroglu | Duke University (USA)

My lab is seeking to elucidate new principles of brain development based on how cells called astrocytes guide the assembly and function of synaptic circuits underlying cognition. Eroglu's team is developing new techniques to visualize astrocytes and study astrocyte-neuron interactions. Currently, they are working to identify novel molecular mechanisms by which astrocyte morphogenesis and maturation are coupled to synapse development and function. The team has revealed that a combined astrocyte-neuron chemo-affinity code regulates synaptic wiring. Eroglu's work has implications for understanding autism and other disorders rooted in brain connectivity.

Selected publications:

- *Lawal O, Ulloa Severino FP, Eroglu C. Glia (2022). The role of astrocyte structural plasticity in regulating neural circuit function and behavior. Aug;70(8):1467-1483. doi: 10.1002/glia.24191.*
- *Baldwin, KT, Tan, CX, Strader, S, Jiang, C, Savage, JS, Estevez, R, Ji, R and Eroglu, C (2021), HepaCAM controls astrocyte self-organization and coupling. Neuron Jun 21:S0896-6273(21)00378-0. doi: 10.1016/j.neuron.2021.05.025. Online ahead of print.*
- *Tan CX, Eroglu C. Cell adhesion molecules regulating astrocyte-neuron interactions. Curr Opin Neurobiol. 2021 May 3;69:170-177.*
- *Takano T, Wallace JT, Baldwin KT, Purkey A, Uezu A, Courtland JL, Soderblom EJ, Shimogori T, Maness PF, Eroglu C, Soderling SH (2020). Chemico-genetic discovery of astrocytic control of inhibition in vivo. Nature, Oct 11; https://doi.org/10.1038/s41586-020-2926-0.*
- *Stogsdill JA, Ramirez J, Liu D, Kim Y-H, Baldwin KT, Enustun E, Ejikeme T, Ji R-R and Eroglu C (2017). Astrocytic Neuroligins Control Astrocyte Morphogenesis and Synaptogenesis. Nature, 551, 192–197.*

Staci Bilbo |Duke University (USA)

Dr. Staci Bilbo is a Professor of Psychology and Neuroscience, Neurobiology, and Cell Biology at Duke University whose research is broadly focused on the mechanisms by which the immune and endocrine systems interact with the brain to impact health and behavior, particularly during critical developmental windows. Her research program is primarily aimed at exploring the mechanisms by which innate central nervous system immune cells - microglia - and signaling molecules such as cytokines and chemokines, influence both normal and abnormal brain development, and the implications for (mal)adaptive behavioral outcomes later in life, including a focus on neurodevelopmental disorders such as autism spectrum disorder, but extending to later life neurodegeneration as well. Dr. Bilbo received her B.A. in Psychology and Biology from the University of Texas at Austin and her PhD in Neuroendocrinology at Johns Hopkins University. She was on the faculty at Duke University from 2007-2015 before she joined the faculty at Harvard where she served as the Lurie Family Associate Professor of Pediatrics and Neuroscience at Harvard Medical School and as the Director of Research for the Lurie Center for Autism at Massachusetts General Hospital for Children. She returned to Duke in 2019 as the Haley Family Professor of Psychology and Neuroscience, and maintains an appointment at MGH to continue her research collaborations in Boston and beyond.

Selected publications :

- *Smith C.J., Rendina D.N., Kingsbury, M.A., Malacon K.E., Nguyen D.N., Tran J., Burgett L., Zhang J., Devlin B., Tran S., Bilbo S.D. Microbial modulation via cross-fostering prevents the effects of pervasive environmental stressors on microglia and social behavior. Molecular Psychiatry, in press.*
- *Ceasrine, A.M., Devlin, B.A., Bolton, J.L., Green, L.A., Jo ,Y.C., Huynh, C., , Patrick, B., Washington, K., Sanchez, C.L., Joo, F., Campos-Salazar, A.B., Lockshin, E.R., Kuhn, C., Murphy, S.K., Simmons, L.A., Bilbo, S.D. (2022) Maternal diet disrupts the placenta-brain axis in a sex-specific manner. Nature Metabolism, 4(12):1732-1745*
- *Block, C.L., Eroglu, O., Mague, S.D., Smith, C.J., Ceasrine, A.M., Sriworarat, C., Blount, C., Beben, K.A., Malacon, K.E., Ndubuizu, N., Talbot, A., Gallagher, N.M., Jo, Y.C., Nyangacha, T., Carlson, D.E., Dzirasa, K., Eroglu, C., Bilbo, S.D. (2022) Prenatal Environmental Stressors Impair Postnatal Microglia Function and Adult Behavior in Male Mice. Cell Reports, 40(5):111161.*
- *Kopec, AM, Smith, CJ, Ayre, NR, Sweat, SC, Bilbo, SD. (2018) Microglial elimination of dopamine D1 receptors defines sex-specific changes in nucleus accumbens development and social play behavior during adolescence. Nature Communications, 9(1):3769.*
- *Hanamsagar, R, Alter, MD, Block, CS, Sullivan, H, Bolton, JL, Bilbo, SD. (2017) Generation of a microglial developmental index in mice and in humans reveals a sex difference in maturation and immune reactivity. GLIA, 65:1504-1520.*

Jean-Christophe Delpech| INRAE Bordeaux University (France)

Jean Christophe Delpech is an INRAE Researcher at the laboratory NutriNeuro in Bordeaux. He is leading a group focusing on the cognitive trajectories during aging. He obtained his PhD from the University of Bordeaux and performed post-doctoral training at Yale University, Harvard University and Boston University (USA). He developed a very strong knowledge of the central immune system and microglia, the primary effectors of innate immune system in the brain. He has always been interested in understanding pathological conditions by applying an integrated approach based on top-bottom analysis starting from behavior to molecular mechanism. He studied various conditions, all connected to the concept of developmental cognitive reserve, that is the key for optimal functioning during the lifetime of individuals. In addition, he studied in Dr Ikezu's laboratory, the physiopathology of extracellular vesicles that may be the source of biomarkers during aging and also actors of the cognitive aging. Currently the group aim at providing a new era of intervention to slow down and better target relevant pathways to cognitive aging.

Selected publications :

- *Herron S, Delpech JC, Madore C, Ikezu T. Using mechanical homogenization to isolate microglia from mouse brain tissue to preserve transcriptomic integrity. STAR Protoc. 2022 Dec 16;3(4):101670. doi: 10.1016/j.xpro.2022.101670. PMID: 36107747.*
- *Delpech JC, Pathak D, Venkatesan Kalavai1 S, Varghese M, Hof P, Hays E, Ikezu S, Medalla M, Luebke J, Ikezu T. Entorhinal Cortex Wolframin-1-expressing neurons propagate tau to CA1 neurons and impair hippocampal memory. Sciences Translational Medicine,. 2021 Sep 15;13(611):eabe8455. doi: 10.1126/scitranslmed.abe8455. PMID: 34524859.*
- *Ikezu S[1]., Yeh H[1]., Delpech J.C[1]., Woodbury E.M[1]., Van Enoo A.A., Sivakumaran S., Ruan Z., Holland C., Guillamon-Vivancos T., Yoshii-Kitahara A., You Y., Madore C., Botros B.M., Chao P-h., Desani A., Manimaran S., Johnson E.W., Butovsky O., Medalla L., Luebke I.J., Ikezu T. (2019), Repopulation of microglia corrects maternal inflammation-induced microglial and synaptic dysfunction and behavioral abnormalities., (1equal contribution) Mol. Psychiatry, 2020 Feb 18:10.1038/s41380-020-0671-2. doi: 10.1038/s41380-020-0671-2.PubMed PMID: 32071385*
- *Delpech JC, Herron S, Botros MB, Ikezu T. Neuroimmune Crosstalk through Extracellular Vesicles in Health and Disease. Trends Neurosci. 2019 May;42(5):361-372. Doi: 10.1016/j.tins.2019.02.007. Epub 2019 Mar 26. Review. PubMed PMID: 30926143; PubMed Central PMCID: PMC6486849*
- *Delpech JC, Wei L, Hao J, Yu X, Madore C, Butovsky O, Kaffman A. Early life stress perturbs the maturation of microglia in the developing hippocampus. Brain Behav Immun. 2016 Oct;57:79-93. Doi: 10.1016/j.bbi.2016.06.006. Epub 2016 Jun 11. PubMed PMID: 27301858; PubMed Central PMCID: PMC5010940*

SPEAKERS

Amit Agarwal | Heidelberg University (Germany)

Amit Agarwal is the Chica and Heinz Schaller Research Group Leader at the Institute for Anatomy and Cell Biology, Heidelberg University, Germany. He received his Ph.D. in neurosciences, at the Max-Planck Institute of Experimental Medicine, Göttingen, Germany with Dr. Klaus-Armin Nave. He performed his post-doctoral training from 2010 to 2017, in the Department of Neuroscience at the Johns Hopkins University, USA with Dr. Dwight Bergles. The Agarwal laboratory uses optical and electron microscopic techniques, single-cell genetics, mouse transgenics, multi-omics approaches and computational methodologies to decipher cellular connectivity and molecular pathways by which neurons and glia (astrocytes and oligodendrocytes) interact, interconnect and integrate into the neural networks. The focal aim of his laboratory is to understand the functional significance of neuron-glia and glia-glia connectivity in the neural circuits function and neurometabolism, and study how disturbances in these fine cell-cell interactions contribute to pathophysiology of neurodegenerative and psychiatric disorders ranging from multiple sclerosis to autism.

Selected publications:

- *Fiore F, Dereddi RR, Alhalaseh K, Coban I, Harb A,* ***Agarwal A****. (2022) Norepinephrine regulates Ca^{2+} signals and fate of oligodendrocyte progenitor cells in the cortex* ***bioRxiv*** *doi: https://doi.org/10.1101/2022.08.31.505555*
- *Streich L, Boffi JC, Wang L, Alhalaseh K, Barbieri M, Rehm R, Deivasigamani S, Gross CT,* ***Agarwal A****, Prevedel R. (2021) High-resolution structural and functional deep brain imaging using adaptive optics three-photon microscopy.* ***Nature Methods****. 2021 Oct;18(10):1253-1258.*
- *Semyanov A., Henneberger C., and* ***Agarwal A.*** *(2020) Making sense of astrocytic calcium signals — from acquisition to interpretation.* ***Nature Reviews Neuroscience*** *Oct;21(10):551-564*
- ***Agarwal, A.****, Wu., P.H., Hughes, E.G., Fukaya, M. Tischfield, M.A., Langseth, A.J., Wirtz, D., Bergles, D.E. (2017) Transient opening of the mitochondrial permeability transition pore induces microdomain calcium transients in astrocyte processes.* ***Neuron*** *93(3): 587-605*
- *Paukert, M*.,* ***Agarwal, A****., Cha, J., Doze, V.A., Kang, J.U., Bergles D.E. (2014) Norepinephrine controls astroglial responsiveness to local circuit activity.* ***Neuron****. 82(6): 1263-70.*

Paola Arlotta | Harvard University (USA)

Dr. Paola Arlotta is the Golub Family Professor of Stem Cell and Regenerative Biology and chair of the Harvard Department of Stem Cell and Regenerative Biology (HSCRB) at Harvard University. She is a principal investigator at the Harvard Stem Cell Institute, and an associate member of the Stanley Center for Psychiatric Research at the Broad Institute of MIT and Harvard. She received her M.S. in biochemistry from the University of Trieste, Italy, and her Ph.D. in molecular biology from the University of Portsmouth in the UK, and subsequently completed her postdoctoral training in neuroscience at Harvard Medical School.

Dr. Arlotta's work focuses on understanding the molecular laws that govern the birth, differentiation, and assembly of the brain's cerebral cortex. Her lab integrates developmental and genomic approaches to elucidate the formation of cortical cellular diversity and the mechanistic underpinnings of neurodevelopmental disease. She has developed *in vitro* models of human cortical development, stem-cell derived brain organoids, and applies this model to understanding human cortical development and disease.

Selected publications:

- *Stogsdill JA, Kim K, Binan L, Farhi SL, Levin JZ, and Arlotta P. Pyramidal neuron subtype diversity governs microglia states in the neocortex.* ***Nature****, 2022 608(7924):750-756. doi: 10.1038/s41586-022-05056-7.*
- *Paulsen B, Velasco S, Kedaigle AJ, Pigoni M, Quadrato G, Deo AJ, Adiconis X, Uzquiano A, Sartore R, Yang SM, Simmons SK, Symvoulidis P, Kim K, Tsafou K, Podury A, Abbate C, Tucewicz A, Smith SN, Albanese A, Barrett L, Sanjana NE, Shi X, Chung K, Lage K, Boyden ES, Regev A, Levin JZ, and Arlotta P. Autism genes converge on asynchronous development of shared neuron classes.* ***Nature****, 2022. 602(7896):268-273. doi: 10.1038/s41586-021-04358-6.*
- *Di Bella DJ, Habibi E, Stickels RR, Scalia G, Brown J, Yadollahpour P, Yang SM, Abbate C, Biancalani T, Macosko EZ, Chen F, Regev A, and Arlotta P. Molecular logic of cellular diversification in the mouse cerebral cortex****.*** ***Nature,*** *2021.595(7868):554-559. doi: 10.1038/s41586-021-03670-5.*
- *Yang SM, Michel K, Jokhi V, Nedivi E, and Arlotta P. Neuron class-specific responses govern adaptive myelin remodeling in the neocortex.* ***Science,*** *2020. 370(6523):eabd2109. doi: 10.1126/science.abd2109.*
- *Velasco S, Kedaigle AJ, Simmons SK, Nash A, Rocha M, Quadrato G, Paulsen B, Nguyen L, Adiconis X, Regev A, Levin JZ, Arlotta P. Individual brain organoids reproducibly form cell diversity of the human cerebral cortex.* ***Nature****, 2019.570(7762):523-527. doi: 10.1038/s41586-019-1289-x.*

David Belin | Cambridge University (UK)

David Belin is Professor of Behavioural Neuroscience at the Department of Psychology of the University of Cambridge and the Director of Studies in Psychological and Behavioural Sciences at Homerton College. After a Licence and Maîtrise in Cellular and Molecular Physiology, David graduated in 2005 in Neuroscience and Neuropharmacology at the University of Bordeaux 2. During his PhD he developed the first preclinical model of cocaine addiction based in the operationalization of multiple clinical criteria of the pathology as defined in humans.

David then moved to the laboratory of Professor Barry Everitt at the Department of Experimental Psychology of the University of Cambridge in January 2006. With his mentor he investigated the corticostriatal mechanisms of cocaine seeking habits and the relationships between impulsivity and compulsive cocaine self-administration, leading to a breakthrough in our understanding of the neurological and psychological mechanisms subserving individual vulnerability to cocaine addiction.

In 2009 David tenured at the INSERM and established his INSERM team in Poitiers (France) which focused on the psychological, neural and cellular mechanisms of the individual vulnerability to develop compulsive disorders and their modulation by the environment. Soon it became apparent that this decision was a mistake and Cambridge is where he wanted to carry out his research and he came back in October 2013, being appointed Lecturer at the Department of Pharmacology. He moved back to the Department of Psychology in October 2016, as the head of the CLIC Cambridge Laboratory for research Impulsive & Compulsive disorders.

Professor Belin has authored over 85 publications. He has received the Mémain-Pelletier Award from the French Academy of Science and the Young Investigator Award from the European Behavioural Pharmacology Society. He is an adjunct professor at Mount Sinai (New York, USA), an alumnus of the FENS/Kavli Network of Excellence, a former International Fellow of the Chinese Academy of Science and a former visiting scientist at NIDA.

Selected publications :

- *Fouyssac M, Pena-Oliver Y, Puaud M, Lim N, Giuliano C, Everitt BJ & **Belin D** (2022) Negative urgency exacerbates relapse to cocaine seeking following abstinence, Biological Psychiatry 91(12) 1051-1060, doi: 10.1016/j.biopsych.2021.10.009*
- *Bonetto G, **Belin D*** and Karadottir R.T.* (2021), Myelin: A gatekeeper of activity-dependent circuit plasticity?, Science, doi: 10.1126/science.aba6905, *:co-last authors.*
- *Fouyssac M, Puaud M, Ducret E, Marti-Prats L, Vanhille N, Ansquer S, Zhang X, Belin-Rauscent A, Giuliano C, Houeto JL, Everitt BJ, **Belin D** (2020) Environment-dependent behavioral traits and experiential factors shape addiction vulnerability. European Journal of Neuroscience, 53(6) 1794-1808, doi: 10.1111/ejn.15087.*
- *Puaud M, Higuera-Matas A, Brunault P, Everitt BJ, **Belin D** (2020) The Basolateral amygdala--> Nucleus Accumbens core circuit mediates the conditioned reinforcing effects of cocaine-paired cues on cocaine seeking, Biological Psychiatry, 89 (4) 356-365.*
- *Fouyssac M & **Belin D**, (2019) Beyond drug-induced alteration of glutamate homeostasis. Astrocytes may contribute to the dopamine-dependent instrastriatal functional shifts that underlie the development of addiction: a working hypothesis. European Journal of Neuroscience 50 (6), 3014-3027.*

Eric Boué-Grabot | Neurodegenerative Disease Institute (IMN), Bordeaux University (France)

Eric Boué-Grabot, Research Director DR1 at CNRS, is a neurobiologist who is investigating the regulation and function of purinergic receptors in the healthy and diseased brain.

After graduating in biochemistry and genetics, he received his PhD in Neurosciences at the university of Bordeaux (France) and was trained as postdoctoral fellow at McGill university (Canada). He was recruited at the French CNRS as a permanent scientist in 2000; He is currently leader of the team "purinergic-mediated inflammation and brain disorders » (co-leader Marc Landry) and is serving as deputy director of the institute for neurodegenerative disease of Bordeaux affiliated to CNRS and university of Bordeaux. In particular, his work characterized molecular properties of ATP P2X receptors and identified interaction between synaptic receptor-channels modulating synaptic activity and novel form of synaptic plasticity By combining electrophysiology, cellular and biochemical and behavioral approaches on rodent models, his current research interests include the study of P2X receptor regulation and develop new transgenic knockin mice to better understand how neuronal versus microglial P2X receptors affect neuronal activity/plasticity, neuroinflammation and contribute to several brain diseases such as neurodegenerative and neuropsychiatric disorders.

Selected publications:

- *Bertin E, Martinez A, Fayoux A, Carvalho K, Carracedo S, Fernagut PO, Koch-Nolte F, Blum D, Bertrand SS and Boué-Grabot E (**2022)** Increased surface P2X4 receptors by mutant SOD1 proteins contribute to ALS pathogenesis in SOD1-G93A mice. **Mol Cell Life Sci** 79:431 doi : 10.1007/s00018-022-04461-5*
- *Bertin E, Deluc T, Pilch KS, Audrey Martinez A, Pougnet JT, Doudnikoff E, Allain AE, Bergmann P, Russeau M, Toulmé E, Bezard E, Koch-Nolte F, Séguéla P, Lévi S, Bontempi B, Georges F, Bertrand S, Nicole O and Boué-Grabot E. **(2021)** Increased surface P2X4 receptor regulates anxiety and memory in P2X4 internalization-defective knock-in mice **Mol Psy** 26, 629–644 DOI: 10.1038/s41380-019-0641-8*
- *Duveau A, Bertin E and Boué-Grabot E **(2020)** Implication of neuronal versus microglial P2X4 receptors in central nervous system disorders. **Neurosci Bull.** 36 (11),1327-1343 doi:10.1007/s12264-020-00570-y*
- *Boué-Grabot E and Pankratov Y **(2017)** Modulation of central synapses by astrocyte-released ATP and postsynaptic P2X receptors. **Neural Plasticity** 2017:9454275. doi: 10.1155/2017/9454275. PMID: 28845311*
- *Pougnet J-T, Toulmé E, Martinez A, Choquet D, Hosy E, and Boué-Grabot E. **(2014)** ATP P2X receptors down-regulate AMPA receptor trafficking and postsynaptic efficacy in hippocampal neurons. **Neuron** 83(2):417-430. doi: 10.1016/j.neuron.2014.06.005. PMID: 2503318*

Bart Eggen | UMCG/RUG (The Netherlands)

Bart Eggen received his MSc (1989) and PhD (1995) from the University of Utrecht in The Netherlands. As a graduate student, he worked on the regulation of B-50/GAP-43 gene expression in the Department of Physiological Chemistry and the Rudolf Magnus Institute, Utrecht, with Prof. Loes Schrama and Prof. Willem Hendrik Gispen.
He obtained a Human Frontiers Science Program fellowship to work with Prof. Gail Mandel at the State University of New York and later with Prof. Ali Hemmati Brivanlou at the Rockefeller University in New York on the characterization of the transcriptional repressor protein REST/NRSF that controls neuron-specific gene expression. In 2000, he joined the Department of Developmental Genetics at the University of Groningen to work on the epigenetic regulation of embryonic stem cell pluripotency.
In 2010, he moved to the Department of Biomedical Scieces of Cells and Systems where he is appointed as professor of Molecular Neurobiology. There his main research focus is on the (epi)genetic regulation of microglia identity and function in the context of the normal brain, during aging and under neuroinflammatory or neurodegenerative conditions such as multiple sclerosis, frontotemporal dementia and Alzheimer's disease. He uses a range of -omics approaches on human brain tissue to delineate developmental and pathological processes. With this approach, genes and molecular pathways altered in affected CNS cell types, are identified which are then investigated in a range of model systems to understand their role in CNS development or CNS pathology.

Selected publications:

- *Gerrits E, Giannini LAA, Brouwer N, Melhem S, Seilhean D, Le Ber I, The Brainbank Neuro-CEB Neuropathology Network, Kamermans A, Kooij G, de Vries HE, Boddeke EGWM, Seelaar H, van Swieten JC and* ***Eggen BJL*** *(2022) Neurovascular unit disruption underlies GRN-associated frontotemporal dementia,* ***Nature Neuroscience****, 25(8):1034-1048.*
- *Puvogel S, Alsema A, Kracht L, Webster MJ, Weickert CS, Sommer IEC,* ***Eggen BJL****. (2022) Single-nucleus RNA sequencing of midbrain blood-brain barrier cells in schizophrenia reveals subtle transcriptional changes with overall preservation of cellular proportions and phenotypes.* ***Molecular Psychiatry****, 27(11):4731-4740.*
- *Gerrits E, Brouwer N, Kooistra SM, Woodbury ME, Vermeiren Y, Mirjam Lambourne M, Mulder J, Kummer M, Möller T, Biber KP, den Dunnen WFA, de DeynPP,* ***Eggen BJL,*** *EWG Boddeke. (2021) Distinct amyloid-beta and tau-associated microglia profiles in Alzheimer's disease* ***Acta Neuropathologica****, 41(5):681-696.*
- *Kracht L, Borggrewe M, Eskandar S, Brouwer N, Chuva de Sousa Lopes SM, Laman JD, Scherjon SA, Prins JR, Kooistra SM,* ***Eggen BJL****. (2020) Human fetal microglia acquire homeostatic immune-sensing properties early in development.* ***Science****, 369(6503):530-537.*
- *Galatro TF, Holtman IR, Lerario AM, Vainchtein ID, Brouwer N, Sola PR, Veras MM, Pereira TF, Leite REP, Möller T, Wes PD, Sogayar MC, Laman JD, den Dunnen W, Pasqualucci CA, Oba-Shinjo SM, Boddeke EWGM, Marie SKN,* ***Eggen BJL*** *(2017) Transcriptomic analysis of purified human cortical microglia reveals age-associated changes* ***Nature Neuroscience****, 20(8):1162-1171.*

Sonia Garel | PSL University (Paris)

Sonia Garel is a developmental neurobiologist. She currently heads a team at the Institut of Biology of the Ecole Normale Superieure (IBENS) in Paris and is a Professor at the College de France. Her research focuses on the mechanisms that control the assembly of cortical circuits during development, with a particular interest on the roles of microglia, interactions with the immune system and environmental signals, such as the microbiota. After obtaining a PhD in developmental biology in Paris, she did a postdoctoral stay at UCSF and joined the IBENS, where she has headed the "Brain Development and Plasticity" team since 2008. Her work has been rewarded by several awards and recognitions including the European Young Investigator Award (EURYI), the ERC consolidation program, the Antoine Lacassagne Prize, the Grand Prize of the NRJ-Institut de France Foundation, and she is a member of the EMBO. In 2020, Sonia Garel was elected professor at the College de France on the "Neurobiology and Immunity" chair.

Selected publications:

- *Thion MS, Ginhoux F and Garel S (2018). Microglia and early brain development: an intimate journey.* ***Science****, 362: 185-189. DOI: 10.1126/science.aat0474*
- *Thion* MS, Low* D, Silvin A, Chen J, Grisel P, Schulte-Schrepping J, Blecher R, Ulas T, Squarzoni P, Hoeffel G, Coulpier F, Siopi E, David FS, Scholz C, Shihui F, Lum J, Amoyo AA, Larbi A, Poidinger M, Buttgereit A, Lledo PM, Greter M, Chan JKY, Amit I, Beyer M, Schultze JL, Schlitzer A, Pettersson S, Ginhoux* F, Garel* S. Microbiome influences prenatal and adult microglia in a sex-specific manner. 2018.* ***Cell****, 172: 500-516. DOI: 10.1242/dev.153692*
- *Thion° MS, Mosser° CA, Ferezou I, Grisel P, Baptista S, Low, D, Ginhoux F, Garel* S and Audinat* E Biphasic impact of prenatal inflammation and macrophage depletion on the wiring of neocortical inhibitory circuits. 2019.* ***Cell Reports****, 28:1119-1126. DOI: 10.1016/j.celrep.2019.06.086*
- *Riva° M, Genescu° I, Habermacher° C, Orduz D, Ledonne F, Rijli FM, Lopez-Bendito G, Coppola E, Garel* S, Angulo* MC and Pierani* A (2019) Activity-dependent death of transient Cajal-Retzius neurons is required for functional cortical wiring. 2019.* ***eLife****, 8:e50503. DOI: 10.7554/eLife.50503*
- *Genescu I, Anibal-Martinez M, Kouskoff V, Chenouard N, Mailhes-Hamon C, Cartonnet H, Lokmane L, Rijli F, Lopez-Bendito G, Gambino F and Garel S. Dynamic interplay between thalamic activity and Cajal-Retzius cells regulates the wiring of cortical layer1. 2022.* ***Cell Reports****,28:1119-1126. DOI: 10.1016/j.celrep.2022.110667*

Soyon Hong | Dementia Research Institute, University College London (UK)

Dr Soyon Hong is a Group Leader at the UK Dementia Research Institute at University College London. Soyon studies how neuroimmune interactions contribute to synapse function, health, and degeneration. Specifically, she is interested in understanding how brain macrophages and glia work together to coordinate synaptic homeostasis, and how this cell-cell crosstalk breaks down in disease, including Alzheimer's and Parkinson's diseases. Soyon received her PhD in Neuroscience in 2012 from Harvard University, after having trained with Dennis Selkoe on amyloid-induced synaptic degeneration. Her post-doctoral work with Beth Stevens at Boston Children's Hospital and Harvard Medical School led to the identification of microglia as cellular mediators of synapse loss in Alzheimer's disease models. Soyon started her independent lab at the UK DRI in UCL in fall 2018. The lab employs cutting-edge spatial and single-cell omics to profile cell-cell interactions in mouse models and human patient tissues as well as hypothesis-driven approaches to address whether, and if so, how, neuroimmune signalling confers region-specific synapse vulnerability, a hallmark of neurodegenerative diseases. To that end, the lab recently discovered a role for perivascular cells in influencing microglia-synapse phagocytosis via SPP1/osteopontin in models of amyloidosis. The lab also utilizes similar approaches to understand intercellular communications between nervous and immune cells along the gut-brain axis in Parkinson's disease.

Selected publications:

- *Rueda-Carrasco J*, Sokolova D*, Lee SE*, Childs T, Jurčáková N, De Schepper S, Ge JZ, Lachica JI, Toomey CE, Freeman OJ, Hardy J, Barnes SJ, Lashley T, Stevens B, Chang S,* ***Hong S****.* ***In Revision at EMBO J*** *Microglia target synapses with externalized phosphatidylserine to ameliorate neuronal hyperactivity. https://doi.org/10.1101/2022.04.04.486424*
- *De Schepper S, Ge JZ, Crowley G, Ferreira LSS, Garceau D, Toomey C, Sokolova D, Rueda-Carrasco J, Shin SH, Kim JS, Childs T, Lashley T, Burden JJ, Sasner M, Sala Frigerio C, Jung S,* ***Hong S.*** *(2023)* ***Nature Neuroscience*** *Perivascular cells induce microglial phagocytic states and synaptic engulfment via SPP1 in mouse models of Alzheimer's disease. doi: 10.1038/s41593-023-01257-z*
- *Bartels T, De Schepper S,* ***Hong S****. (2020)* ***Science*** *Microglia modulate neurodegeneration in Alzheimer's and Parkinson's diseases. doi: 10.1126/science.abb8587*
- ***Hong S****, Nfonoyim BM, Beja-Glasser VF, Frouin A, Li S, Ramakrishnan S, Merry KM, Shi Q, Rosenthal A, Barres BA, Lemere CA, Selkoe DJ, Stevens B. (2016)* ***Science*** *Complement and microglia mediate early synapse loss in Alzheimer mouse models. doi: 10.1126/science.aad8373*
- *De Schepper S, Crowley G,* ***Hong S****. (2020)* ***Developmental Neurobiology*** *Understanding microglial diversity and implications for neuronal function in health and disease. doi: 10.1002/dneu.22777*

Maarten H.P. Kole | Netherlands Institute for Neuroscience (NL)

Maarten Kole is group leader at the Netherlands Institute for Neuroscience (Amsterdam) and Professor of Biophysics of Complex Cellular Systems at the Utrecht University. As postdoctoral fellow he was trained in cellular neuroscience under supervision of Professor Greg Stuart at the John Curtin School of Medical Research (Australia, 2004–2008), where they established the fundamental electrophysiological basis of the axon initial segment. Since 2011 his group aims to understand how myelin patterns impact the neuronal properties and circuit functions in health and disease, including multiple sclerosis. By employing diverse cellular methods ranging from biophysical modeling to high-speed optical imaging approaches, electron microscopy and in vivo recordings in experimental models they focus on mechanisms of action potential propagation and myelination at the cellular and circuit level in cortical regions of the brain. In 2016 they rediscovered the satellite oligodendrocyte and in 2020, using empirically constrained computational models fed by detailed anatomical, ultrastructural, and voltage-sensitive dye imaging they obtained a direct visualization of the absolute axolemmal potentials under the myelin sheath. Maarten Kole received the A.W. Campbell Award from the Australian Neuroscience Society (2010), was recipient of an ERC Starting Grant (2011) and a VICI-grant from the Dutch Research Organization talent scheme (2018).

Selected publications:

- *Kole MHP, Stuart GJ. 2012. Signal Processing in the Axon Initial Segment. Neuron 73:235–247. https://doi.org/10.1016/j.neuron.2012.01.007*
- *Jamann N, Dannehl D, Lehmann N, Wagener R, Thielemann C, Schultz C, Staiger J, Kole MHP, Engelhardt M. 2021. Sensory input drives rapid homeostatic scaling of the axon initial segment in mouse barrel cortex. Nat Commun 12:23. doi:10.1038/s41467-020-20232-x*
- *Cohen CCH, Popovic MA, Klooster J, Weil M-T, Möbius W, Nave K-A, Kole MHP. 2020. Saltatory Conduction along Myelinated Axons Involves a Periaxonal Nanocircuit. Cell 180:311-322.e15. doi:10.1016/j.cell.2019.11.039*
- *Kole K, Voesenek BJB, Brinia ME, Petersen N, Kole MHP. 2022. Myelination-dependent mitochondria clustering and calcium buffering in parvalbumin interneuron axons. Nat Commun 13, 7598. https://doi.org/10.1038/s41467-022-35350-x*
- *Ramaglia V, Dubey M, Malpede MA, Petersen N, Vries SI de, Ahmed SM, Lee DSW, Schenk GJ, Gold SM, Huitinga I, Gommerman JL, Geurts JJG, Kole MHP. 2021. Complement-associated loss of CA2 inhibitory synapses in the demyelinated hippocampus impairs memory. Acta Neuropathol 142:643–667. doi:10.1007/s00401-021-02338-8*

Giampaolo Milior | Collège de France (France)

Giampaolo Milior obtained a PhD in "Clinical- Experimental Neuroscience and Psychiatry" from the laboratory of Prof. Cristina Limatola at the Department of Physiology and Pharmacology at the Sapienza University of Rome, Italy. He developed a particular interest for the interactions between glia cells and neurons in physiological and pathological conditions.
Specifically, he asked how glial cells are involved in the effects of persistent stress on synaptic transmission. The data pointed to an environmental influence on fractalkine signals (CX3CL1) between neurons and microglia and to how the SSRI antidepressant fluoxetine modifies relations between a chronically stressing environment and microglial activation.
After the thesis, he moved to Paris joining the Richard Miles team at the ICM, in Paris, as a postdoctoral researcher, working on human epileptic tissue. He studied two neurologically defined diseased tissues (mesial temporal lobe epilepsies and cortical glioma), supplemented with slices from mice injected with kainic acid (KA) to mimic focal hippocampal epilepsies.
He fully participated in the development of long-term organotypic cultures of human tissue (temporal lobe epilepsy and peritumoral cortex) for drugs and genetic therapies tests. In the Miles' laboratory, he continued to work on microglia in tissues from patients with neurological syndromes developing a staining technique for selective fluorescent staining of microglial cells, which can be observed under 2-photon microscopy over several hours. This technique helped to understand the differential effects of microglial activation via purinergic stimulation on ramified or amoeboid cells in pathological human tissues.
Since January 2019, he is working as postdoc in the the Dr. Nathalie Rouach's laboratory at the College de France in Paris. His research activity focuses on the role of the astroglia in human epilepsy.
In particular, his project aims at testing whether astrocytes, generated from progenitors obtained from human epileptic tissues can promote or counteract epileptic activity. His work aim to understand if the altered calcium signals and gliotransmission in astrocytes are responsible for the brain hyper-excitability in epileptic and tumoral tissues.

Selected publications:

- ***Milior G,*** *Morin-Brureau M, Pallud J, Miles R, Huberfeld G. Animal models and human tissue compared to better understand and treat the epilepsies. Epilepsia. 2023; 10.*
- ***Milior G****, Morin-Brureau M, Chali F, Le Duigou C, Savary E, Huberfeld G, Rouach N, Pallud J, Capelle L, Navarro V, Mathon B , Clemenceau S & Miles R. Distinct P2Y receptors mediate extension and retraction of microglial processes in epileptic and peri-tumoral human tissue. Journal of Neuroscience. 2020 Jan 2; 0218-19*
- *Morin-Brureau M,* ***Milior G*** *, Royer J , Chali F , Le Duigou C , Savary E , Blugeon C , Jourdren L , Akbar D , Dupont S , Navarro V , Baulac M , Bielle F , Mathon B , Clemenceau S, Miles R. Microglial phenotypes in the human epileptic temporal lobe. Brain. 2018 Dec 1;141(12):3343-3360.*
- *Le Duigou C, Savary E, Morin-Brureau M, Gomez-Dominguez D,* ***Milior G****, Chali F, Sobczyk A, Eugène E, Kraus L, C. Meier J, M. Kullmann D, Mathon B, de la Prida LM, Dorfmuller G, Pallud J, Clemenceau S, & Miles R. Imaging pathological activities of human brain tissue in organotypic culture. J Neurosci Methods. 2018 Mar 15;298:33-44.*
- ***Milior G****, Lecours C, Samson L, Bisht K, Poggini S, Pagani F, Deflorio C , Lauro C, Alboni S, Limatola C, Branchi I, Tremblay ME, Maggi L. Fractalkine receptor deficiency impairs microglial and neuronal responsiveness to chronic stress. Brain Behav and Immun. 2015; 55:114-125*

Kelly Monk | Vollum Institute (USA)

Kelly Monk is a senior scientist and co-director of the Vollum Institute. After earning her B.S. degree in Biochemistry from Elmira College in 2001, Kelly pursued doctoral studies at the University of Cincinnati/Cincinnati Children's Hospital under the mentorship of Nancy Ratner and was awarded her Ph.D. in Cell Biology in 2006. She did postdoctoral training in the lab of William Talbot at Stanford University School of Medicine. In 2011, she was appointed as an assistant professor in the Department of Developmental Biology at Washington University School of Medicine in St. Louis, and was promoted to associate professor with tenure in 2016. Monk joined the Vollum Institute in 2017 and served as director of the Vollum/OHSU Neuroscience Graduate Program from 2017-2022.

Kelly has been instrumental in establishing zebrafish as a model to study glia, and her studies demonstrated that zebrafish and mammalian glia are remarkably similar. Through genetic screens, she discovered that the adhesion G protein-coupled receptor (aGPCR) Gpr126 is essential for myelination. Kelly began her independent career in 2011 and has since gained recognition as a leader in the fields of glial cell biology and neuron-glial interactions. Her work on Gpr126 and other aGPCRs has helped to lay the foundation for the rapidly growing aGPCR field. She and her team have discovered new roles for aGPCRs in the developing nervous system, were the first to delineate aGPCR functions in the adult nervous system during homeostasis and injury, and defined new activation paradigms, ligands, and downstream signaling mechanisms for this previously completely enigmatic receptor class. Beyond aGPCRs, she has leveraged the power of zebrafish genetics coupled with synergistic approaches in mouse, and her group is working to address key outstanding questions in glial cell biology and neuroscience including: glial fate specification and heterogeneity; the cell biology of myelination; mechanisms of glial-neuron and glial-glial interactions; glial support of neurons; and the contribution of glia to circuits and behavior.

Selected publications:

- *Petersen SC, Luo R, Liebscher I, Giera S, Jeong SJ, Mogha A, Ghidinelli M, Feltri ML, Schöneberg T, Piao X*, **Monk KR*** (2015) Neuron **85**:755-69.*
- *Harty BL, Coelho F, Pease-Raissi SE, Mogha A, Ackerman SD, Herbert AL, Gereau RW 4th, Golden JP, Lyons DA, Chan JR, **Monk KR** (2019) Myelinating Schwann cells ensheath multiple axons in the absence of E3 ligase component Fbxw7. Nat Commun **10**:2976.*
- *Chen J, Poskanzer KE, Freeman MR, **Monk KR** (2020) Live-imaging of astrocyte morphogenesis and function in zebrafish neural circuits. Nat Neuro **23**:1297-1306. **DOI:** 10.1038/s41593-020-0703-x*
- *Li J, Miramontes T, Czokpa T, **Monk KR** (2022) Synapses and Ca^{2+} activity in oligodendrocyte precursor cells predict where myelin sheaths form. bioRxiv 2022.03.18.484955.*
- *Chen J, Stork T, Kang Y, Sheehan A, Paton C, **Monk KR***, Freeman MR* (2022) Astrocyte growth during morphogenesis is driven by the Tre1/S1pr1 phospholipid binding G protein-coupled receptor. bioRxiv2022.09.15.508188. **DOI:** https://doi.org/10.1101/2022.09.15.508188*

Wiebke Möbius| Max-Planck Institute of Multidisciplinary Sciences, Göttingen (Germany)

Professor Wiebke Möbius is an electron microscopy specialist studying the biology of myelinating glia. Her special focus is on myelin turnover in the CNS and axon-glia interactions influencing axonal mitochondria and energy homeostasis in conditional mouse mutants. Electron microscopy is also a valuable tool to study myelin characteristics in multiple sclerosis (MS) in samples from human donors. This was recently applied to characterize normal-appearing white matter (NAWM) and investigate its contribution to inflammation. Her lab developed methods for optimized myelin preservation and applies transmission electron microscopy, immunoelectron microscopy according to Tokuyasu as well as volume EM by focused ion beam-scanning electron microscopy (FIB-SEM). Using these methods her lab has shown that myelin internodes are slowly and continuously renewed by the addition of newly synthetized membranes at the inner tongue of the myelin sheath and at paranodes and juxtaparanodes while removal of myelin most likely happens in the form of myelinoid bodies. Currently she focuses her research on the *Plp*-deficient mouse model of spastic paraplegia type 2 (SPG2) to investigate by which mechanism a genetic defect in the myelinating glia, the lack of the major myelin protein PLP, affects axonal function causing axonal swellings and ultimately neurodegeneration.

Wiebke studied Biology in Göttingen and Bonn and obtained her PhD in 1998 by investigating the intracellular transport of glycosphingolipids by electron microscopy in the group of Konrad Sandhoff at the University of Bonn, Germany. She worked as a postdoctoral researcher in Utrecht, The Netherlands, in the group of Hans Geuze and Jan Willem Slot until 2003. During this time, she explored the intracellular distribution of cholesterol by developing methods for lipid localization by immunoelectron microscopy. After another year as postdoctoral researcher at the EMBL (Heidelberg, Germany) she became in 2004 a research associate heading the Electron Microscopy Facility in the department of Klaus-Armin Nave at the Max-Planck-Institute of Experimental Medicine which changed to the Max-Planck-Institute for Multidisciplinary Sciences in 2022. She was a board member of the German Society of Electron Microscopy (DGE) 2013-2019 and 2013-2018 a board member of the A1 Research area of the Cluster of Excellence and DFG Research Center Nanoscale Microscopy and Molecular Physiology of the Brain (CNMPB), Göttingen, Germany. Since 2021 she is the spokesperson of the Max Planck BioImaging Network of Core Units (MaxBI).

Selected publications:

- *Van den Bosch A, Hümmert S, Steyer AM, Ruhwedel T, Hamann J, Smolders J, Nave KA, Stadelmann C, Maarten K, Möbius W, Huitinga I. Ultrastructural axon-myelin unit alterations in MS correlate with inflammation. Annals of Neurology 2023; early view: https://doi.org/10.1002/ana.26585*
- *Meschkat M., Steyer A.M., Weil M.-T., Kusch K., Jahn O., Piepkorn L., Agüi-Gonzalez P., Phan N.T.N., Ruhwedel T., Sadowski B., Rizzoli S.O., Werner H.B., Ehrenreich H., Nave K.A. and Möbius W. (2022). White matter integrity requires continuous myelin synthesis at the inner tongue. Nature Comm. 2022 Mar 4;13(1):1163. doi: 10.1038/s41467-022-28720-y.*
- *Steyer AM, Ruhwedel T, Nardis C, Werner HB, Nave K-A, Möbius W (2020): Pathology of myelinated axons in the PLP-deficient mouse model of spastic paraplegia type 2 revealed by volume imaging using focused ion beam-scanning electron microscopy. J Struc Biol, 2020 May 1;210(2):107492. doi: 10.1016/j.jsb.2020.107492.*
- *Weil MT, Ruhwedel T, Meschkat M, Sadowski B, Möbius W. Transmission Electron Microscopy of Oligodendrocytes and Myelin. Methods Mol Biol, 2019;1936:343-375.doi: 10.1007/978-1-4939-9072-6_20*

Stéphane H. R. Oliet | Neurocentre Magendie, INSERM, Bordeaux University (France)

Stéphane Oliet is a French neurophysiologist who is investigating neuron-glia interactions in the healthy and diseased brain. He received his PhD from McGill University investigating intrinsic properties of neuroendocrine neurons. He then trained as a postodoctoral fellow at UCSF working on hippocampal synaptic plasticity. Back in France, he developped a strong interest in neuron-glia interactions in the context of synaptic transmission and activity-dependent plasticity.

His work has contributed to the emerging concept of the tripartite synapse that considers astrocytes as active players of cerebral communication. In particular, he showed that the astrocytic environment of neurons and synapses plays a key role in shaping excitation through glutamate uptake. He also characterized glia-derived D-serine as an essential component of NMDA receptor activation, a mechanism by which astrocytes regulate synaptic plasticity and memory.

Awards : Prix La Recherche 2006, Prix Rachel Azjen et Léon Iagolnitzer 2014; Member of Academia Europaea.

Key findings: Cellular basis of osmoreception ; Postsynaptic expression of synaptic plasticity ; Different forms of hippocampal LTD ; Role of astrocytes in shaping excitation through glutamate uptake; Astroglial release of D-serine is mandatory for synaptic NMDA receptor activity.

Selected publications:

- *Panatier A, Theodosis DT, Mothet JP, Touquet B, Pollegioni L, Poulain DA and Oliet SHR (2006) Glia-derived D-serine controls NMDA receptor activity and regulates synaptic memory. Cell 125, 775-784.*
- *Henneberger C, Papouin T, Oliet SHR* and Rusakov DA* (2010) Long term potentiation depends on release of D-serine from astrocytes. Nature 463: 232-236 (*corresponding authors)*
- *Papouin T, Ladépêche L, Ruel J, Sacchi S, Labasque M, Hanini M, Groc L, Pollegioni L, Mothet JP, Oliet SH. Synaptic and extrasynaptic NMDA receptors are gated by different endogenous coagonists. Cell. 2012 Aug 3;150(3):633-46.*
- *Murphy-Royal C, Dupuis JP, Varela JA, Panatier A, Pinson B, Baufreton J, Groc L, Oliet SHR. Surface diffusion of astrocytic glutamate transporters shapes synaptic transmission. Nat Neurosci. 2015 Feb;18(2):219-26.*
- *Robin LM, Oliveira da Cruz JF, Langlais VC,…Oliet SHR*, Marsicano G*. Astroglial CB1 Receptors Determine Synaptic D-Serine Availability to Enable Recognition Memory. Neuron. 2018 Jun 6;98(5):935-944*

Thomas Papouin | Washington University, School of Medicine (USA)

Dr. Thomas Papouin is an Assistant Professor in the Department of Neuroscience at Washington University, School of Medicine (St Louis, MO, USA) whose research seeks to obtain a comprehensive understanding of how astrocytes contribute to brain function at the synaptic, circuit and behavioral levels. He completed his PhD in the field of synaptic physiology at the University of Bordeaux, where he elucidated some of the molecular determinants of NMDA receptors activation, and then trained as an HFSP postdoctoral fellow in the lab of Dr. Philip Haydon, a pioneer of neuron-glia interactions, where he studied the effect of vigilance states on astrocyte functions. In doing so, he contributed seminal work at the junction of molecular neuroscience (Papouin et al., Cell 2012), astrocyte biology (Henneberger, Nature 2010) and systems neuroscience (Papouin et al., Neuron 2017). Research in his lab currently explores the mechanisms, importance and biomedical opportunities of the interplay between neuromodulation and astrocytes. Specifically, his group seeks to 1) understand the role of astrocytes in neuromodulatory signaling in the brain and how astrocyte-based neuromodulation contributes to the state-dependent tuning of synaptic properties; 2) elucidate general operating principles of astrocyte-based neuromodulation and the molecular determinants that permit input-output fidelity in astrocytes; 3) define tractable relationships between astrocyte signaling and cognitive behavior, and build better conceptual frameworks to advance the field in this direction; 4) transpose available knowledge on astroglia interactions in silico, to build more holistic and robust artificial neural network models of brain computation that could better inform biological investigations; and 5) fuel an astroglial perspective to the study and treatment of neuropsychiatric disorders and cognitive disabilities.

Selected publications :

- *Murphy-Royal C., Ching S., Papouin T. (under review) Contextual guidance: A framework for astrocytes' function in brain circuits and behavior. Nature Neuroscience. NN-P80739. https://arxiv.org/abs/2211.09906*
- *Nagai J., Yu X., Papouin T., Cheong E., Freeman MR., Monk KR., Hastings MH., Haydon PG., Rowitch D., Shaham S., Khakh BS. Behaviorally consequential astrocytic regulation of neural circuits (2020). Neuron. 109(4):576-596.*
- *Papouin T., Dunphy J., Tolman M., Dineley K, and Haydon, P.G. (2017). Septal cholinergic neuromodulation tunes the astrocyte-dependent gating of hippocampal NMDA receptors to wakefulness. Neuron. 94, 1-15.*
- *Henneberger, C., Papouin, T., Oliet, S.H.R., and Rusakov, D.A. (2010). Long-term potentiation depends on the release of D-serine from astrocytes. Nature. 463, 232-236.*
- *Papouin, T., Ladépêche, L., Ruel, J., Sacchi, S., Labasque, M., Hanini, M., Groc, L., Pollegioni, L., Mothet, L-P., and Oliet, S.H.R. (2012). Synaptic and extrasynaptic NMDA receptors are gated by different endogenous co-agonists. Cell. 150, 633-646.*

Nathalie Rouach| Collège de France (France)

Nathalie Rouach is a neurobiologist developing research on the role of glial cells in brain physiology and pathologies. She is an Inserm Research Director at Collège de France, Paris. She received her Ph.D. in Neuroscience, performed jointly at University Pierre and Marie Curie and the Weizmann Institute, where she studied the contribution of astrocytic gap junctional communication to neuroglial network interactions. She then joined the laboratory of Roger Nicoll at University of California San Francisco as a postdoc, where she worked on glutamate receptors trafficking and synaptic plasticity. She now runs the laboratory « Neuroglial Interactions in Cerebral Physiopathology and Pathologies » within the Interdisciplinary Center for Research in Biology at the Collège de France. Her research aims at determining whether and how astrocytes play a direct role in information processing. In particular, her team explores the molecular modalities and functional consequences of neuron-glia interactions in various physiological and pathological contexts, such as memory, social interactions, epilepsy or intellectual disability, with ex vivo and in vivo studies of neuronal excitability, synaptic transmission and plasticity, synchronization of neuronal networks, and cognitive functions in mouse models or human tissues. N. Rouach is a French Government Oversea Fellow of Churchill College (Cambridge, UK) and has received several awards including the Human Frontier Career Development award (2006), the Emergence award and Silver Medal of the City of Paris (2012), the Rachel Ajzen and Leon Iagolnitzer prize (2022) and is a Laureate of ERC Consolidator (2016) and Proof of Concept (2022) grants.

Selected publications:

- *Physiological synaptic activity and recognition memory require astroglial glutamine. G. Cheung, D. Bataveljic, J. Visser, N. Kumar, J. Moulard, G. Dallérac, D. Mozheiko, A. Rollenhagen, P. Ezan, C. Mongin, O. Chever, A.P. Bemelmans, J. Lübke, I. Leray, N. Rouach. Nature Communications. 2022. 13(1):753.*
- *Astrocytes close the mouse critical period for visual plasticity. J. Ribot, R. Breton, C.F. Calvo, J. Moulard, P. Ezan, J. Zapata, K. Samama, M. Moreau, A.P. Bemelmans, V. Sabatet, F. Dingli, D. Loew, C. Milleret, P. Billuart, G. Dallérac, N. Rouach. Science. 2021. 373(6550):77-81*
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- *Astroglial metabolic networks sustain hippocampal synaptic transmission. N. Rouach, A. Koulakoff, P. Ezan, K. Willecke, C. Giaume. Science. 2008. 322:1551-5.*

David Rowitch| Cambridge University (UK)

Professor David Rowitch MD PhD ScD FMedSci FRS is a developmental neuroscientist and Head of Department of Paediatrics at the University of Cambridge. Originally from California, he obtained his MD from UCLA and PhD from the University of Cambridge. His laboratory in the Wellcome-MRC Cambridge Stem Cell Institute investigates genetic factors that determine diversity of glia, which comprise 90% of cells in the human brain. He has applied a developmental neuroscience perspective to better understand white matter injury in premature infants and in multiple sclerosis, and he uses genomic technologies to better diagnose and treat serious neurogenetic disorders in children. Professor Rowitch was awarded Doctor of Science (ScD), the highest degree of the University of Cambridge for distinguished research in science, in 2016. He was appointed to the National Advisory Council for Child Health and Development (USA) in 2020, elected a Fellow of the Academy of Medical Sciences in 2018 and Fellow of the Royal Society in 2021.

Selected publications:

- *Nguyen V, Chavali M, Larpthaveesarp A, Kodali S, Gonzalez G, Franklin RJM, **Rowitch DH**, Gonzalez F. Neuroprotective effects of Sonic hedgehog agonist SAG in a rat model of neonatal stroke. Pediatr Res. 2021 Mar 2. doi: 10.1038/s41390-021-01408-7. Epub ahead of print. PMID: 33654279.*
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- *Ben Haim L, Schirmer L, Zulji A, Sabeur K, Tiret B, Ribon M, Chang S, Lamers WH, Boillée S, Chaumeil MM, **Rowitch DH**. Evidence for glutamine synthetase function in mouse spinal cord oligodendrocytes. Glia. 2021 Dec;69(12):2812-2827. doi: 10.1002/glia.24071. Epub 2021 Aug 15. PMID: 34396578; PMCID: PMC8502205.*

Mikael Simons|TU Munich & German Center for Neurodegenerative Diseases (DZNE) (Germany)

Mikael Simons is a Professor for Molecular Neurobiology at the TU Munich and at the Center for Neurodegenerative Diseases (DZNE) in Munich. He is board-certified clinical neurologist with specialized expertise in neuroimmunological diseases including multiple sclerosis. The main focus is on myelin biology, an insulating membrane sheath produces by specialized glial cells. Destruction of myelin leads to several neurological diseases such as multiple sclerosis, and is also associated with psychiatric and neurodegenerative disorders. His lab combines molecular, biochemical and advanced light and electron microscopy techniques in mice and zebrafish to study how myelin is formed, maintained, and broken down in diseases. In addition, the lab works on the mechanisms of CNS regeneration and on the question of how new myelin sheaths are reformed in demyelinating diseases. The overall aim is to come up with new strategies of how to promote repair of the damaged CNS in diseases such as multiple sclerosis.

Selected publications:

- *Kaya T*, Mattugini N*, Liu L*, Ji H, Cantuti-Castelvetri L, Wu J, Schifferer M, Groh J, Martini R, Besson-Girard S, Kaji S, Liesz A, Gokce O*, Simons M* (2022). CD8+ T cells induce interferon-responsive oligodendrocytes and microglia in white matter aging.* ***Nat Neurosci.*** *2022 Nov;25(11):1446-1457*
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- *Trajkovic K*, Hsu C*, Chiantia S, Rajendran L, Wenzel D, Wieland F, Schwille P, Brügger B, Simons M (2008) Ceramide triggers budding of exosome vesicles into multivesicular endosomes.* ***Science*** *319(5867):1244-7.*

Caroline Smith | Boston College (USA)

Dr. Smith began her academic career as an undergraduate student at the University of Massachusetts Amherst in the lab of Dr. Nancy Forger studying the epigenetic mechanisms underlying sex differences in the brain. She then completed her PhD in the lab of Dr. Alexa Veenema at Boston College. Her graduate research aimed to elucidate sex differences in the roles of neuropeptides (such as oxytocin and vasopressin) and endogenous opioids in the regulation of adolescent social behavior. She completed her postdoctoral fellowship in the lab of Dr. Staci Bilbo at Duke University where her work focused on understanding how neuroimmune interactions during development influence the organization of social circuits in the brain and how this process is disrupted by a variety of perinatal immune challenges (such as environmental toxicants, stress, opioids, and bacterial mimetics). She was (and remains) particularly interested in the role of microglial synaptic pruning in the developmental organization of social circuits in the brain. She is now an Assistant Professor of Psychology and Neuroscience at Boston College where her lab combines systems level circuit-based approaches and molecular/sequencing technologies to investigate the ways in which microglia and the gutbrain-axis sculpt the social brain in both males and females. Her lab also studies the ways in which exposure to environmental toxicants and psychosocial stressors alter these developmental interactions.

Selected publications:

- ***Smith CJ,*** *Rendina DN, Kingsbury, MA, Malacon KE, Nguyen DN, Tran JJ, Devlin BA, Clark MJ, Raju RM, Burgett L, Zhang JH, Cetinbas M, Sadreyev RI, Chen K, Iyer M., Bilbo SD (2022) Social deficits induced by pervasive environmental stressors are prevented by microbial or dopaminergic modulation. BioRxiv 2202.02.28.482288*
- ***Smith CJ****, Lintz T, Clark MJ, Malacon KE, Abiad A, Constantino NJ, Kim VJ, Jo YC, Alonso-Caraballo Y, Bilbo SD, Chartoff EC (2022) Prenatal opioid exposure induces microglial sculpting of the dopamine system selectively in adolescent male offspring.*
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- ***Smith CJ*** *(2021) Emerging roles for microglia and microbiota in the development of social circuits, Brain, Behavior, and Immunity – Health 16:100296.*
- ***Smith CJ*****, Kingsbury MA*, Dziabis JE, Hanamsagar R, Malacon KE, Tran JN, Norris HA, Gulino M, Bilbo SD (2020) Neonatal immune challenge induces female-specific changes in social behavior and somatostatin cell number, Brain, Behavior, and Immunity, 90:332-345.*
- ***Smith CJ****, Bilbo SD (2021) Sickness and the Social Brain: Love in the time of COVID,Frontiers in Psychiatry, 12:633664.*

PROJECTS

BLOCK 1

Project 1: Effects of Neural and Glial Manipulations on Rodent Behavior

Instructor: Caroline Smith (Boston College, USA)

Background:

Understanding how functional changes in glial cells impact the overall behavior of the organism is the ultimate goal of many glial research programs. However, rodent behavioral testing relies on a very brief window of observation to make inferences about the behavior of the animal more broadly. Therefore, it is critically important to conduct behavioral testing as rigorously as possible. Exposure to bacterial mimetics such as lipopolysaccharide (LPS) has been shown to activate microglia and to induce a suite of behavioral changes collectively referred to as "sickness behaviors" including social withdrawal, lethargy, and decreased appetite in rodents. Tools that directly activate or inhibit relevant neural populations – such as chemogenetics – can also be used to modulate many of the same behaviors.

Aim:

The aim of this project is to analyze and compare the effects of either an in-vivo glial manipulation (LPS administration) or an in-vivo neural manipulation (chemogenetic stimulation of dopamine neurons) on rodent behavior.

Methods:

To study behavioral outcomes following either an LPS challenge or chemogenetic neural activation, we will use a combination of techniques. First, an adeno-associated virus (AAV) will be used to express an excitatory chemogenetic virus in neurons within the ventral tegmental area of the brain. Second, intraperitoneal injections will be used to expose a separate cohort of mice to LPS. Following each of these manipulations, we will conduct several commonly used behavioral assays to test whether these manipulations alter behavioral endpoints. The main objectives of this course will be to learn how to conduct rigorous, reliable, controlled behavioral testing, to understand the myriad factors which can influence testing outcomes, and to cover study design, conduction, and behavioral data analysis/interpretation.

Project 2: Astrocytic local calcium signals in epileptiform activity: from humans to mice

Instructor: Giampaolo Milior (College de France, Paris, France)

Background:

Astrocytes are instrumental regulators of brain physiology from synapse to behavior. They listen and talk to synapses by exerting both excitatory and inhibitory actions on neurons. Astrocytes play important roles in physiology, but these cells also emerge as crucial actors in epilepsy. An increasing body of evidence has documented a dysregulation of astrocyte-specific functions in human and experimental epilepsy. However, the precise mechanisms for astrocytic dysfunction and the outcome in neuronal transmission are still unclear.

Dynamic sensing of the synaptic microenvironment translates into astroglial intracellular calcium signals that mediate the astrocyte's gliotransmission.

An alteration of astroglial intracellular calcium signalling can be a cause for the generation of epileptiform activity.

Most epileptic models have been based on rodents; however, epilepsy itself is a peculiar human brain condition that is difficult to reproduce in animals with the same features as in the human pathological brain. There is an increasing need to cross-verify findings from animal models and from living human tissue to avoid the assumption that the mechanisms are identical and to improve our knowledge about human brain physiology and pathologies. To date, the possible astroglial mechanism underlying the human epilepsy onset is unknown due to the lack of suitable models.

Aim:

The aim of the project is to dissect the role of human astroglial calcium activity as a possible mediator for the aberrant neuronal activity in epilepsy.

Methods:
To study the human astrocytic calcium activities, human astrocytes from control and from epileptic patients will be cultivated and infected with viral constructs to express the GCamp 6f calcium sensor. Alternatively, calcium dyes, such as Fluo-4AM, will be used to visualize the astrocytic intracellular calcium oscillations.
Multiphoton or confocal imaging will be performed in order to characterize the live calcium activities in astrocytic human cells. Immunohistochemical or RNA analysis of Inositol Triphosphate receptor 2 (IP3R2), a receptor mediating calcium signalling at the soma and proximal processes of rodents astrocytes, will be performed in order to assess its presence in human astrocytes.
Organotypic hippocampal slices will be prepared from C57BL6 mice and, after 3 days in vitro, human astrocytes will be engrafted on them. Multiwell Multi Electrodes Arrays will be used to analyze the electrical activities after the engraftment of human astrocytes in mice brain slices.
Students will learn:
1) The protocol for the dissociation of human astrocytes (simulation in situ from the mouse hippocampus);
2) The preparation of mouse organotypic hippocampal slices and how to engraft cells on them;
3) How to use Multiwell Multi Electrode Arrays in order to study neuronal network activities;
4) How to interpret the data and compare them with the existing literature about astrocytic functions in rodents.

Project 3: Investigating contact-dependent astrocyte morphogenesis, in vitro

Instructor: Kristina Sakers Hays (Duke University Medical Center, USA)

Background:
Astrocytes exhibit a highly branched morphology in the adult mouse and human cortex. This morphology is critical for astrocyte function at the synapse, including forming and maintaining cortical synapses, regulating neuronal firing, and providing trophic support for neurons. Astrocytes are born from radial glia stem cells around postnatal day 0 in the mouse brain as relatively simple cells with few branches. Through the first three postnatal weeks, astrocytes undergo extensive morphological growth with increases in both branch number and length. This morphological growth is at least in part due to cell-cell contact. Cell adhesion molecules in astrocytes, such as Neuroligin-2, HepaCAM, and NrCAM, regulate astrocyte cell size through neuronal and astrocyte contacts. The changes in astrocyte cell size due to the loss of either Neuroligin-2, HepaCAM, or NrCAM are accompanied by distinct changes in synapse number and/or synapse function, suggesting that specific cell-adhesion molecules play defined roles in astrocyte growth, and astrocytic control of synapse development and function. Contact-dependent astrocyte morphogenesis can be modelled in vitro, providing an excellent screening platform for molecules that control astrocyte morphological development.
Aim:
The aims of this project are to 1) learn to culture rat primary astrocytes and 2) Image co-cultured astrocytes and neurons and quantify astrocyte complexity between control and Neuroligin knockdown astrocytes.
Methods:
We will dissect Postnatal day 1 (P1) rat cortices and then isolate astrocytes. Students will learn to stain astrocytes and image and analyze astrocyte morphology. The instructor will bring co-cultured astrocytes and neurons to teach students how to image astrocyte morphology, quantify the astrocyte complexity via Sholl Analysis, and then analyze the subsequent results using R programming.

Project 4: The GABAergic mechanism of microglia activation

Instructor: Mohit Dubey (Netherlands Institute for Neuroscience, The Netherlands)

Background:
Interneurons inhibit brain excitability by releasing the neurotransmitter gamma-aminobutyric acid (GABA). Parvalbumin-positive (PV+) interneurons are the main class of inhibitory interneurons providing powerful and precise control of the peri-somatic domain of pyramidal neurons, controlling neural network oscillations, particularly at the gamma (40 Hz) frequency. Disturbance of PV+ interneuron-mediated inhibition can lead to a change in excitation-inhibition balance and reduced gamma oscillation, which is implicated in neurodegenerative diseases. For example, sensory gamma frequency stimulation activates microglia to clear amyloid plaques and improves cognitive symptoms in mice. These studies have led to clinical trials in which gamma frequency is generated to ameliorate cognitive

symptoms in patients. The molecular mechanisms of microglia-mediated improvement of plaque pathology are not well understood. A recent study of early brain development showed that the PV+ interneuron synapses (Syt2+ terminals) and eliminated by microglia via tagging with complement component 1q (C1q), mediated through GABAB1 receptor activation of microglia. In this project, we will directly test whether GABAB1 receptors on microglia activate complement release during PV+ interneuron-mediated gamma frequency network oscillations.

Aim:

The project aims to determine if 40 Hz network simulation activates microglia via the GABAB1 receptor.

Methods:

To directly answer the research aim, adenovirus injection PV-Cre mice will express channelrhodopsin in neocortical PV+ interneurons. Gamma frequency will be entrained in acute brain slices by optical activation of PV+ interneurons. A pharmacological approach will antagonise the GABAB1 receptor. Electrophysiological whole-cell and field recordings combined with optogenetic activation will be made to validate the efficacy of gamma oscillation.

Post-hoc immunohistochemistry with microglia markers and synaptic proteins, followed by 3D image analysis (IMARIS software), will be used to determine the change in the activation state of microglia. Furthermore, this analysis will measure PV+ interneuron and microglia interaction.

Students will learn to make acute brain slices and perform electrophysiological recordings. They will learn how to perform cell-type specific optogenetics, entrainment of network oscillations and interpret data from extracellular and intracellular recordings. Furthermore, they will be taught how to perform post-hoc immunohistochemistry and image analysis, testing novel pathways of interneuron-microglia interactions.

Project 5: Introduction to sample preparation methods to study differences of myelinating glia in CNS and PNS with the electron microscope

Instructors: Wiebke Möbius and Torben Ruhwedel (Max Planck Institute for Multidisciplinary Sciences, Germany)

Background:

Myelin is a lipid-rich membrane structure produced by Schwann cells in the PNS and oligodendrocytes in the CNS which is tightly wrapped around axons. Although superficially PNS and CNS myelin look alike, there are important differences in structure, protein composition and biology of the myelinating glial cells. By electron microscopy, fine structural details of the myelin sheath and the myelinating glial cells as well as the axon and surrounding cells can be studied. Unfortunately, myelin belongs to the most difficult to preserve cellular structures in the mammalian nervous system. Therefore, in investigating myelin ultrastructure suitable sample preparation methods are required to avoid artefacts that could mask myelin phenotypes.

Aim:

The aim of this project is to prepare PNS and CNS samples and compare the morphology of the myelin sheath using different sample preparation methods.

Methods:

Sciatic and optic nerve samples will be dissected and preserved by chemical fixation using formaldehyde and glutaraldehyde or by high-pressure freezing and freeze substitution. Subsequently, the samples will be processed by conventional embedding after dehydration or by freeze-substitution. Polymerized blocks will be used for semithin and ultrathin sectioning and electron microscopy.

The students will experience the whole workflow from tissue dissection to electron microscopy and learn the pros and cons of the two different sample preparation methods. By interpreting the EM data, they will learn to identify typical features of PNS and CNS myelin.

Data analysis like the determination of myelin thickness by g-ratio measurements will be discussed.

Project 6: Role of astrocyte Ca^{2+} signaling in Learning and Memory

Instructor: Yifan Wu (Washington University School of Medicine in St. Louis, USA)

Background:

A growing body of evidence now suggests that astrocytes are ideally positioned to play a role in the cellular underpinnings, circuit-level correlates, and behavioral manifestations of learning and memory. However, the determinants that drive astrocytes engagement in brain circuits and the signaling mechanisms through which astrocytes may influence neural networks have remained poorly understood or controversial. Hence, whether and how astrocytes actively participate in the cellular underpinnings of learning and memory, and the relevance of such contribution to circuit-level computation remain elusive. This is in large part due to the lack of adequate tools to assess and manipulate astrocytes responsiveness to putative inputs and to block downstream signaling pathways. Interestingly, variations in intracellular free calcium concentration occur in astrocytes, respond to a wide range of stimulations including endogenous signaling molecules, and are thought to trigger downstream astrocyte-derived signaling. Therefore, impeding Ca^{2+} dynamics in astrocyte networks could be a first powerful approach in probing the general role of astrocyte signaling in learning and memory at the cellular, circuit and behavioral levels.

Aim:

The aim of the project is two-fold:

(1) To compare the performance of mice with impaired Ca^{2+} dynamics in hippocampal astrocytes to that of mice with intact astrocytes in a classic learning & memory task,

(2) To validate and quantify the loss of spontaneous and evoked Ca^{2+} activity in astrocytes via two-photon imaging.

Methods:

CalEx (Calcium Extrusion) will be used to inhibit Ca^{2+} dynamics in hippocampal astrocytes. This will consist in the stereotaxic micro-injection of a viral vector (AAV5-GfaABC1D-PMCA2-mCherry) coding for the plasma membrane-bound and constitutively active calcium pump PMCA2, under the control of the astrocyte-specific promoter GfaABC1D. Control animals will be injected with a mCherry-coding viral vector. In addition, animals will receive a co-injection of the genetically encoded calcium indicator GCaMPf6f (AAV5- GfaABC1D-GCaMP6f). Learning and memory performance will be assessed in mice using the contextual fear-conditioning task or the novel object recognition task. Lastly, astrocyte Ca^{2+} dynamics will be assessed via 2-photon recording of GCaMP6f activity in brain slices, under baseline condition (spontaneous) and evoked conditions (norepinephrine applications) from PMCA- and mCherry-injected animals. Analysis of Ca^{2+} recordings will be done using the computational pipeline STARDUST (STreamlined Analysis of Regional calcium Dynamics for Ubiquitous Screening of Transients).

Learning Objectives:

Students will learn how to perform survival micro-injection surgeries, animal behavior practices, 2-photon recordings of astrocyte Ca^{2+} activity and comprehensive STARDUST-assisted analysis.

Project 7: Imaging structural plasticity of mitochondria in astrocytes in vivo

Instructors: Amit Agarwal and Felipe Bodaleo Torres (*Heidelberg University, Germany*)

Background:

The notion that astrocytes are mainly glycolytic cells and do not rely on mitochondrial respiration to obtain energy, has long postponed the study of the mitochondrial structure and function in astrocytes. However, several studies show that mitochondria are multi-faceted organelles, which actively participate in a wide variety of cellular processes such as maintaining calcium homeostasis, producing building blocks for fatty acid synthesis and regulating cellular inflammatory response. Although, in vitro observations indicate that astrocytic mitochondria exhibit complex structural dynamics i.e., fusion-fission events, the long-term mitochondrial dynamics in intact in vivo preparations remain unknown. The ongoing work in our laboratory, using a wide range of optical and electron microscopy techniques, suggests that mitochondria in astrocytes are morphologically complex, form intricate networks and are less dynamic than previously acknowledged. In this project, we will use a wide range of optical microscopy techniques to study astrocytic mitochondrial structure and dynamics in brain slices and in vivo.

Aim:

To study mitochondrial morphology and structural dynamics in cortical astrocytes.

Methods:

To study mitochondrial structure and dynamics we will use a transgenic mouse line that expresses mitochondrial-targeted EGFP (mito-EGFP) in astrocytes. We will implant a cranial window over the mouse somatosensory cortex and perform 2-photon microscopy to track acute and chronic mitochondrial structural changes. To complement our in vivo observations, we will study mitochondrial dynamics ex vivo in acute brain slices and combine them with pharmacological interventions. Finally, we will analyze mitochondrial structure using AI-assisted 'smart' segmentation and tracking methods.

Project 8: Does the morphology of oligodendrocyte lineage cells follow a gradient along the zebrafish spinal cord?

Instructor: Jiaxing Li (Oregon Health & Science University, USA)

Background:

Oligodendrocyte precursor cells (OPCs) and oligodendrocytes (Ols) are born in the spinal cord in early development. The OPCs in the anterior spinal cord are often born earlier than the ones in the posterior spinal cord, and enter differentiation earlier. This is known as a gradient of oligodendrocyte development and myelination. However, it is unclear if the OPCs in anterior spinal cord possess a different morphology than the ones in the posterior spinal cord; it is also unclear if Ols in the anterior spinal cord myelinate more than the ones in the posterior spinal cord.

Aim:

In this project, we will compare the morphology of OPCs and Ols along the anterior-posterior spinal cord and determine if they exhibit differences and/or a gradient.

Methods:

We will use zebrafish to study the morphology of OPCs and Ols. We will conduct embryo injection to deliver plasmid to sparsely label OPCs and Ols. At 3-5 dpf we will identify and image OPCs and Ols and analyze the morphology of OPCs and Ols, such as (OPC: sholl analysis, volume measurement. Ols: sheath length and number measurement). Given the anterior-posterior locations in the spinal cord, we can determine if they exhibit differences and/or a gradient.

BLOCK 2

Project 9: Effect of neuromodulators on intracellular calcium responses in oligodendrocytes

Instructor: Arne Battefeld (IMN, Bordeaux University, France)

Background:

Calcium responses in oligodendrocytes are high during phases of myelin formation and refinement and are reduced during the maintenance of myelin. Not all signalling cascades involved in oligodendrocytic calcium changes have been understood, but neuronal activity has been demonstrated to induce calcium changes in some systems. Recent work has demonstrated the response of oligodendrocyte precursor cells to the neuromodulator norepinephrine and receptors for norepinephrine are also expressed in mature oligodendrocytes. We will test whether noradrenergic receptor activation will lead to calcium changes in mature oligodendrocytes in the neocortical grey matter at two different developmental time points.

Aim:

The aim of this project is to record calcium activity of oligodendrocytes in response to neuromodulators.

Methods:

The proposed experiments will be performed in acute brain slices of the mouse. We will record calcium activity from oligodendrocytes in response to neuromodulator stimulation in young and adult mice. We will use oligodendrocyte specific expression of GCaMPs or perform live filling of oligodendrocytes with a calcium dye via recording pipettes. We will then perform epifluorescence or 2-photon calcium imaging and evaluate the calcium response to neuromodulator agonists. Students will learn how to prepare acute brain slices, perform calcium recordings and analyse and interpret the resulting data.

Project 10: Astrocyte-neuron circuit tracing and synaptic quantification

Instructor: Francesco Ulloa Severino (Duke University, USA)

Background:

Astrocytes, the brain's most abundant glial cell type, play essential roles in neural circuit development and circuits functional and structural adaptations throughout life. A single astrocyte can get in touch with hundreds of thousands of synapses, forming structures defined as tripartite synapses, as well as with neuronal cell bodies. At these points of contact, astrocytes control circuit connectivity by secreting synaptogenic molecules and circuit function through the secretion of gliotransmitters and by controlling the extracellular ionic concentration. Recently, there has been increased attention on how astrocytes control behaviors and cognitive abilities like learning and memory.

Aim:

This project aims to teach how to investigate the interactions between astrocytes and neurons in vivo using stereotactic delivery of Adeno Associated Viruses (AAVs) in adult mice. Students will actively contribute to labeling astrocytes and neurons for their structural analysis. In addition, we will visualize and quantify synaptic connections within astrocytes' territories and perform anatomical studies using immunohistochemistry and confocal imaging.

Methods:

- Stereotactic intracranial injections of AAVs in specific brain regions
- Brain sectioning and free-floating sections collection
- Immunohistochemistry
- Confocal imaging and 3D reconstruction
- Synaptic puncta co-localization analysis
- 3D astrocyte reconstruction and analysis

Project 11: Understanding the impact of n-3 PUFA deficiency on microglia-derived extracellular vesicles

Instructor: Liam Barry-Carroll (IMN, Bordeaux University, France)

Background:

The ratio of n-6 to n-3 polyunsaturated fatty acids (PUFAs) provided in the diet impacts brain function and health in humans. Indeed, several independent studies have shown that increased consumption of n-3 PUFAs may improve cognitive health in aged individuals, which has led to widespread interest in the study of the potential cellular mechanisms involved. Exposure to a diet deficient in n-3 PUFAs during early life is associated with abnormal neuronal connectivity and cognitive alterations in young rodents. Interestingly, the normal function of microglia appears to be impaired in these n-3 deficient mice as indicated by a shift towards an inflammatory phenotype although the mechanisms involved remain unclear. A potential candidate for this microglial dysfunction is extracellular vesicles (EVs), which are membrane bound nanoparticles released by all cell types and participate in short and long-range communication. As such, they contain a variety of cargoes including protein, RNA, DNA and lipids, which can modulate cellular function in recipient cells. Moreover, there has been an increase in the number of studies investigating the role of EVs in neurodegenerative diseases and several studies have reported characteristic changes in the profile of EVs released by microglia during disease that can elicit pro-inflammatory and anti-inflammatory effects.

Aim:

The aim of this project is to compare the phenotype of microglial-derived EVs between n-3 PUFA deficient and sufficient mice.

Methods:

Whole brains have been collected from male and female mice at 3 months old following a gestational deficiency of n-3 PUFAs or supplementation with n-3 PUFAs. EVs will be isolated from whole brain homogenate using either CD11b or CSF1R to target EVs of microglial origin using the MACs separator. The size and concentration of EVs will be analyzed using NanoFCM. The phenotype of microglial EVs will be interrogated using various tetraspanin and inflammatory markers and assessed by nanoscale flow cytometry.

Project 12: Neuronal response to demyelination

Instructor: De Omar Faria Jr. (Stem Cell Institute, University of Cambridge, UK)

Background:

The conventional view that myelin is an inert and immutable structure has been replaced in recent years with the notion that myelin changes in response to experience and that these changes are in turn required for memory formation and learning. However, it is unclear whether and how myelin changes underlie circuit plasticity in the healthy brain and loss of myelin impacts on circuit function in myelin disorders. Tackling these questions will require combining traditional myelin models with cutting-edge techniques to study circuit function.

Aim:

The aim of this project is to investigate the impact of demyelination on circuit activity.

Methods:

We will use fibre photometry to follow in vivo calcium dynamics as a proxy for changes in neuronal activity in an established model of demyelination. Methods will focus on stereotaxic surgery for fibre implantation/induction of demyelination, fibre photometry, toluidine blue staining of lesions and data analysis. Students will learn a method to measure neuronal activity following demyelination in freely-behaving rats.

Project 13: Involvement of surface P2X4 in basal and ATP-induced microglia motility

Instructor: Sara Carracedo Vicente (IMN, Bordeaux University, France)

Background:

P2X receptors are non-selective cationic ATP-gated channels expressed in the central nervous system. They contribute to neuromodulation and neuroglial communication by ATP released either from neurons and/or glial cells. Among the seven P2X receptors, P2X4 is the most abundant receptor in the brain and is found expressed in both neurons and microglia.

In basal conditions, P2X4 is constitutively internalized and is mainly intracellular, limiting its implication in the dialogue between microglia and neurons. Of importance, upregulation of surface P2X4 expression was observed in microglia and/or in neurons in many conditions such as chronic pain, neurodegenerative diseases and neuropsychiatric disorders. If microglial P2X4 play a key role in chronic pain, the role of the surface increase of P2X4 on the microglial properties and its involvement in the disease progression remains unexplored. To address the role of microglial P2X4, we have developed novel conditional knock-in non-internalized P2X4 (P2X4KI) or knock-out (P2X4KO) allowing to increase surface expression or blockage of P2X4 selectively in microglia. These tools will allow us to decipher the role of P2X4 in different pathological contexts but also to unravel the implication of P2X4 on microglia functions such as activation, motility or phagocytosis in various conditions.

Aim:

The aim of the project is to study the contribution of microglial P2X4 on microglia properties such as morphology, basal motility and ATP-induced microglia chemotaxis.

Methods:

To study the role of P2X4 on microglia, we will perform microglia culture from the cerebral cortex of P10-P15 mice from WT, P2X4KO and P2X4KI mice by isolating microglia using the immunomagnetic cell Sorting technology (MACS). Microglia motility and chemotaxis will be recorded using time-lapse in vivo microscopy and analyzed using Kinovea Software. Microglia morphology and expression of P2X4 receptors will be analyzed using confocal microscopy in different experimental conditions by immunostaining. Several morphological parameters will be analyzed using ImageJ software.

Students will learn how to isolate and culture microglia cells, monitor cell motility by video microscopy and reveal the microglial expression of P2X4 by immunostaining. Further, they will learn how to acquire images using confocal microscopy and analyze several parameters of microglia morphology.

Project 14: Identification of the Inflammatory Mechanisms Underlying the Comorbidity between ADHD and Pain

Instructor: Sarah Bou Sader Nehme (IMN, Bordeaux University, France)

Background:

Attention-deficit/hyperactivity disorder (ADHD) is a complex neurodevelopmental disorder characterized by symptoms of inattention, hyperactivity, and impulsivity. It is one of the most common childhood disorders, with 8.4% of children diagnosed worldwide. Clinical evidence suggests that pain hypersensitivity develops in subjects with ADHD. Conversely, pain worsens attentional and cognitive deficits. However, the mechanisms involved in these interactions remain poorly understood. Our team has previously validated a mouse model of ADHD, which is obtained through the injection of 6-hydroxydopamine (6-OHDA) at P5 in the lateral ventricle. The 6-OHDA mice exhibited a marked sensitization to mechanical and thermal stimuli. Moreover, hyperactivity of the anterior cingulate cortex (ACC) as well as deregulation of the ACC-posterior insula pathway were detected. We make the hypothesis that neuroinflammation is at the origin of ACC hyperactivity and the associated pain, under ADHD conditions.

Aim:

The aim of this project is to identify and characterize the altered neuroinflammatory mechanisms underlying the comorbidity between pain sensitization and ADHD.

Methods:
Prior to the arrival of the students, ADHD-like mice and their controls will be generated by injecting 6-OHDA and ascorbic acid, respectively, in the right lateral ventricle at P5. The anterior cingulate cortex, the insular cortex, and the amygdala will be extracted from fresh brains and will be utilized for cell sorting using flow cytometry. The samples will then be used to conduct ELISA assays for cytokines whose expressions were previously shown to be altered under ADHD conditions. Indeed, previous RT-qPCR experiments have demonstrated changes in the mRNA levels of inflammatory modulators (IL-6, IL-16, TNF-α, BDNF, APE1, Wnt5a, and MMP9). Moreover, immunofluorescence staining for the transcription factor NF-κB will be performed to detect its subcellular distribution, an indicator of its activation.
Students will learn how to perform cell sorting using flow cytometry, followed by ELISA assays for cytokines highly expressed in ADHD conditions. They will also learn how to do immunofluorescence staining, as well as how to analyze and interpret the results.

Project 15: Polyunsaturated fatty acid-derived Oxylipins on human microglia phagocytosis

Instructor: Charlotte Madore-Delpech (INRAE, Bordeaux University, France)

Background:
Dietary polyunsaturated fatty acids (PUFAs), arachidonic acid (AA, n-6) and docosahexaenoic acid (DHA, n-3), are fundamental to cell signalling via oxylipins, their bioactive metabolites. Microglia are the resident brain macrophages, derived from the yolk sac. During development, they help shape the brain through different functions including elimination of dead cells and synapse refinement. Low n-3 PUFA dietary intake leads to a decreased DHA / increased AA in the brain. During gestation and lactation, it has been associated with impaired neurodevelopmental microglial phagocytic activity mediated by an AA-derived oxylipin, 12HETE and with neuronal network alterations (Madore et al., 2020). However, nothing is known regarding the role of PUFAs-derived oxylipins on human microglia regulation and functions during brain development.

Aim:
The aim of the project is to determine the impact of PUFAs-derived oxylipins on human microglia phagocytosis in 2D- and 3D-brain organoid cultures.

Methods:
2D-culture: Human induced pluripotent stem cells (IPSCs) will be differentiated into hematopoietic stem cells (HSCs). Further, HSC will be differentiated using McQuade et al, 2018 protocol, into microglia cells. At Day 14 of differentiation, microglial phagocytosis will be assessed - (a) TLR4- and (b) TREM2-dependent phagocytosis – after exposure to EPA-/DHA- and AA-derived oxylipins. Microglial phagocytosis will be assessed using time-lapse imaging (Incucyte SX5) and a pHrodo fluorescent labeling of ingested bioparticles.
3D-culture: IPSCs will be differentiated into embroid bodies and further into brain organoids (modified version of Lancaster et al, 2013). After exposure to EPA-/DHA- and AA-derived oxylipins, brain organoids will be fixed. Microglia phagocytic phenotype will be assessed using phagocytic markers and analyzed by microscopy.
Students will learn how to perform different stages of human microglial and brain organoid differentiations, biosafety level 2 cell and molecular biology techniques, immunohistochemistry and epifluorescence microscopy technique, and time-lapse imaging analysis.

INSTRUCTORS

Caroline Smith | Boston College (USA)

Dr. Smith began her academic career as an undergraduate student at the University of Massachusetts Amherst in the lab of Dr. Nancy Forger studying the epigenetic mechanisms underlying sex differences in the brain. She then completed her PhD in the lab of Dr. Alexa Veenema at Boston College. Her graduate research aimed to elucidate sex differences in the roles of neuropeptides (such as oxytocin and vasopressin) and endogenous opioids in the regulation of adolescent social behavior. She completed her postdoctoral fellowship in the lab of Dr. Staci Bilbo at Duke University where her work focused on understanding how neuroimmune interactions during development influence the organization of social circuits in the brain and how this process is disrupted by a variety of perinatal immune challenges (such as environmental toxicants, stress, opioids, and bacterial mimetics). She was (and remains) particularly interested in the role of microglial synaptic pruning in the developmental organization of social circuits in the brain. She is now an Assistant Professor of Psychology and Neuroscience at Boston College where her lab combines systems level circuit-based approaches and molecular/sequencing technologies to investigate the ways in which microglia and the gutbrain-axis sculpt the social brain in both males and females. Her lab also studies the ways in which exposure to environmental toxicants and psychosocial stressors alter these developmental interactions.

Selected publications:

- ***Smith CJ,*** *Rendina DN, Kingsbury, MA, Malacon KE, Nguyen DN, Tran JJ, Devlin BA, Clark MJ, Raju RM, Burgett L, Zhang JH, Cetinbas M, Sadreyev RI, Chen K, Iyer M., Bilbo SD (2022) Social deficits induced by pervasive environmental stressors are prevented by microbial or dopaminergic modulation. BioRxiv 2202.02.28.482288*
- ***Smith CJ****, Lintz T, Clark MJ, Malacon KE, Abiad A, Constantino NJ, Kim VJ, Jo YC, Alonso-Caraballo Y, Bilbo SD, Chartoff EC (2022) Prenatal opioid exposure induces microglial sculpting of the dopamine system selectively in adolescent male offspring.*
  Neuropsychopharmacology, 47(10):1755-1763
- ***Smith CJ*** *(2021) Emerging roles for microglia and microbiota in the development of social circuits, Brain, Behavior, and Immunity – Health 16:100296.*
- ***Smith CJ*****, Kingsbury MA*, Dziabis JE, Hanamsagar R, Malacon KE, Tran JN, Norris HA, Gulino M, Bilbo SD (2020) Neonatal immune challenge induces female-specific changes in social behavior and somatostatin cell number, Brain, Behavior, and Immunity, 90:332-345.*
- ***Smith CJ****, Bilbo SD (2021) Sickness and the Social Brain: Love in the time of COVID,Frontiers in Psychiatry, 12:633664.*

Giampaolo Milior | Collège de France (France)

Giampaolo Milior obtained a PhD in "Clinical- Experimental Neuroscience and Psychiatry" from the laboratory of Prof. Cristina Limatola at the Department of Physiology and Pharmacology at the Sapienza University of Rome, Italy. He developed a particular interest for the interactions between glia cells and neurons in physiological and pathological conditions.
Specifically, he asked how glial cells are involved in the effects of persistent stress on synaptic transmission. The data pointed to an environmental influence on fractalkine signals (CX3CL1) between neurons and microglia and to how the SSRI antidepressant fluoxetine modifies relations between a chronically stressing environment and microglial activation.
After the thesis, he moved to Paris joining the Richard Miles team at the ICM, in Paris, as a postdoctoral researcher, working on human epileptic tissue. He studied two neurologically defined diseased tissues (mesial temporal lobe epilepsies and cortical glioma), supplemented with slices from mice injected with kainic acid (KA) to mimic focal hippocampal epilepsies.
He fully participated in the development of long-term organotypic cultures of human tissue (temporal lobe epilepsy and peritumoral cortex) for drugs and genetic therapies tests. In the Miles' laboratory, he continued to work on microglia in tissues from patients with neurological syndromes developing a staining technique for selective fluorescent staining of microglial cells, which can be observed under 2-photon microscopy over several hours. This technique helped to understand the differential effects of microglial activation via purinergic stimulation on ramified or amoeboid cells in pathological human tissues.
Since January 2019, he is working as postdoc in the the Dr. Nathalie Rouach's laboratory at the College de France in Paris. His research activity focuses on the role of the astroglia in human epilepsy.
In particular, his project aims at testing whether astrocytes, generated from progenitors obtained from human epileptic tissues can promote or counteract epileptic activity. His work aim to understand if the altered calcium signals and gliotransmission in astrocytes are responsible for the brain hyper-excitability in epileptic and tumoral tissues.

Selected publications:

- ***Milior G,*** *Morin-Brureau M, Pallud J, Miles R, Huberfeld G. Animal models and human tissue compared to better understand and treat the epilepsies. Epilepsia. 2023; 10.*
- ***Milior G****, Morin-Brureau M, Chali F, Le Duigou C, Savary E, Huberfeld G, Rouach N, Pallud J, Capelle L, Navarro V, Mathon B , Clemenceau S & Miles R. Distinct P2Y receptors mediate extension and retraction of microglial processes in epileptic and peri-tumoral human tissue. Journal of Neuroscience. 2020 Jan 2; 0218-19*
- *Morin-Brureau M,* ***Milior G*** *, Royer J , Chali F , Le Duigou C , Savary E , Blugeon C , Jourdren L , Akbar D , Dupont S , Navarro V , Baulac M , Bielle F , Mathon B , Clemenceau S, Miles R. Microglial phenotypes in the human epileptic temporal lobe. Brain. 2018 Dec 1;141(12):3343-3360.*
- *Le Duigou C, Savary E, Morin-Brureau M, Gomez-Dominguez D,* ***Milior G****, Chali F, Sobczyk A, Eugène E, Kraus L, C. Meier J, M. Kullmann D, Mathon B, de la Prida LM, Dorfmuller G, Pallud J, Clemenceau S, & Miles R. Imaging pathological activities of human brain tissue in organotypic culture. J Neurosci Methods. 2018 Mar 15;298:33-44.*
- ***Milior G****, Lecours C, Samson L, Bisht K, Poggini S, Pagani F, Deflorio C , Lauro C, Alboni S, Limatola C, Branchi I, Tremblay ME, Maggi L. Fractalkine receptor deficiency impairs microglial and neuronal responsiveness to chronic stress. Brain Behav and Immun. 2015; 55:114-125*

Kristina Sakers Hays | Duke University (USA)

Kristina is broadly interested in astrocyte development and function in the cortex. In her Ph.D. (2013-2018), Kristina worked in the lab of Dr. Joseph Dougherty at Washington University School of Medicine in Saint Louis (Missouri, USA). There, she discovered that astrocytes, like neurons and oligodendrocytes, carry out protein translation in their peripheral processes, which is activity-dependent. In these studies, she found that mRNAs localized in peripheral astrocyte processes (PAPs) have a higher occurrence of the Quaking (QK) RNA binding protein response element, which controls mRNA export, protein abundance, and localization. She also used cross-linking immunoprecipitation and sequencing to identify all QK-bound mRNAs in astrocytes. In her postdoctoral work (2018-current) with Dr. Cagla Eroglu at Duke University (North Carolina, USA), Kristina is investigating how the cell-adhesion molecule Neuroligin-2 controls astrocyte morphogenesis. Further, her interest in genomics approaches and genome regulation led to a project concerning how the astrocyte epigenome changes throughout postnatal astrocyte maturation. Kristina has expertise in primary astrocyte and neuron cell culture, methods to quantify astrocyte cell volume in brain tissue, biochemical techniques, next-generation sequencing and bioinformatics, R programming, and Unix command line tools.

Selected publications:

- *Sapkota, D.*, Kater, M.S.J.*, **Sakers, K.***, Nygaard, K.R., Liu, Y., Koester, S.K., Fass, S.B., Lake, A.M., Khazanchi, R., Khankan, R.R., et al. (2022). Activity-dependent translation dynamically alters the proteome of the perisynaptic astrocyte process. Cell Rep. 41, 111474. 10.1016/j.celrep.2022.111474. *denotes equal contribution*
- ***Sakers, K.**, Liu, Y., Llaci, L., Lee, S.M., Vasek, M.J., Rieger, M.A., Brophy, S., Tycksen, E., Lewis, R., Maloney, S.E., et al. (2021). Loss of Quaking RNA binding protein disrupts the expression of genes associated with astrocyte maturation in mouse brain. Nat. Commun. 12, 1537. 10.1038/s41467-021-21703-5.*
- ***Sakers, K.**, Lake, A.M., Khazanchi, R., Ouwenga, R., Vasek, M.J., Dani, A., and Dougherty, J.D. (2017). Astrocytes locally translate transcripts in their peripheral processes. Proc. Natl. Acad. Sci. U. S. A. 114, E3830–E3838. 10.1073/pnas.1617782114.*

Mohit Dubey | Netherlands Institute for Neurosciences (The Netherlands)

Mohit is a pharmacology graduate from Oxford who studied PhD Neuroscience under Prof. Marjo van der Knaap and Prof. Huib Mansvelder in Amsterdam. During his PhD, Mohit used techniques such as ion-sensitive microelectrode recording and radiotelemetry to investigate the critical role of astrocytes in maintaining ion and water homeostasis in leukodystrophy mouse models. Using these models, he identified impaired extracellular potassium ion buffering by glial syncytium resulting in epilepsy, which is observed in patients. In 2014, he received an outstanding scientific contribution award at the international astrocyte school.

Currently, Mohit is ZonMw Memorable Dementia fellow at Prof Maarten Kole's lab, where he is investigating how myelination consolidates sub-millisecond feed-forward inhibition and synchronises brain oscillations during various brain states and memory. To answer these questions, he employs different techniques, from micro-circuit physiology to multichannel brain network LFP-EEG recordings in combination with optogenetics and pharmacology.

Recently, his research has shown that interneuron myelination is critical for theta-gamma oscillation and that demyelination can trigger microglia-mediated inflammation, which is detrimental to inhibitory synapses and memory.

Selected publications:

- *Dubey M, Pascual-Garcia M, Helmes K, Wever DD, Hamada MS, Kushner SA, Kole MHP (2022) Myelination synchronizes cortical oscillations by consolidating parvalbumin-mediated phasic inhibition. Elife 11.*
- *Ramaglia V, Dubey M, Malpede MA, Petersen N, Vries SI de, Ahmed SM, Lee DSW, Schenk GJ, Gold SM, Huitinga I, Gommerman JL, Geurts JJG, Kole MHP (2021) Complement-associated loss of CA2 inhibitory synapses in the demyelinated hippocampus impairs memory. Acta Neuropathol:1–25.*
- *Dubey M et al. (2014) Mice with megalencephalic leukoencephalopathy with cysts: A developmental angle. Annals of Neurology 77:114–131.*
- *Dubey M, Brouwers E, Hamilton EMC, Stiedl O, Bugiani M, Koch H, Kole MHP, Boschert U, Wykes RC, Mansvelder HD, Knaap MS van der, Min R (2018) Seizures and disturbed brain potassium dynamics in the leukodystrophy megalencephalic leukoencephalopathy with subcortical cysts. Annals of Neurology 83:636–649.*

Wiebke Möbius| Max-Planck Institute of Multidisciplinary Sciences, Göttingen (Germany)

Professor Wiebke Möbius is an electron microscopy specialist studying the biology of myelinating glia. Her special focus is on myelin turnover in the CNS and axon-glia interactions influencing axonal mitochondria and energy homeostasis in conditional mouse mutants. Electron microscopy is also a valuable tool to study myelin characteristics in multiple sclerosis (MS) in samples from human donors. This was recently applied to characterize normal-appearing white matter (NAWM) and investigate its contribution to inflammation. Her lab developed methods for optimized myelin preservation and applies transmission electron microscopy, immunoelectron microscopy according to Tokuyasu as well as volume EM by focused ion beam-scanning electron microscopy (FIB-SEM). Using these methods her lab has shown that myelin internodes are slowly and continuously renewed by the addition of newly synthetized membranes at the inner tongue of the myelin sheath and at paranodes and juxtaparanodes while removal of myelin most likely happens in the form of myelinoid bodies. Currently she focuses her research on the Plp-deficient mouse model of spastic paraplegia type 2 (SPG2) to investigate by which mechanism a genetic defect in the myelinating glia, the lack of the major myelin protein PLP, affects axonal function causing axonal swellings and ultimately neurodegeneration.

Wiebke studied Biology in Göttingen and Bonn and obtained her PhD in 1998 by investigating the intracellular transport of glycosphingolipids by electron microscopy in the group of Konrad Sandhoff at the University of Bonn, Germany. She worked as a postdoctoral researcher in Utrecht, The Netherlands, in the group of Hans Geuze and Jan Willem Slot until 2003. During this time, she explored the intracellular distribution of cholesterol by developing methods for lipid localization by immunoelectron microscopy. After another year as postdoctoral researcher at the EMBL (Heidelberg, Germany) she became in 2004 a research associate heading the Electron Microscopy Facility in the department of Klaus-Armin Nave at the Max-Planck-Institute of Experimental Medicine which changed to the Max-Planck-Institute for Multidisciplinary Sciences in 2022. She was a board member of the German Society of Electron Microscopy (DGE) 2013-2019 and 2013-2018 a board member of the A1 Research area of the Cluster of Excellence and DFG Research Center Nanoscale Microscopy and Molecular Physiology of the Brain (CNMPB), Göttingen, Germany. Since 2021 she is the spokesperson of the Max Planck BioImaging Network of Core Units (MaxBI).

Selected publications:

- *Van den Bosch A, Hümmert S, Steyer AM, Ruhwedel T, Hamann J, Smolders J, Nave KA, Stadelmann C, Maarten K, Möbius W, Huitinga I. Ultrastructural axon-myelin unit alterations in MS correlate with inflammation. Annals of Neurology 2023; early view: https://doi.org/10.1002/ana.26585*
- *Meschkat M., Steyer A.M., Weil M.-T., Kusch K., Jahn O., Piepkorn L., Agüi-Gonzalez P., Phan N.T.N., Ruhwedel T., Sadowski B., Rizzoli S.O., Werner H.B., Ehrenreich H., Nave K.A. and Möbius W. (2022). White matter integrity requires continuous myelin synthesis at the inner tongue. Nature Comm. 2022 Mar 4;13(1):1163. doi: 10.1038/s41467-022-28720-y.*
- *Steyer AM, Ruhwedel T, Nardis C, Werner HB, Nave K-A, Möbius W (2020): Pathology of myelinated axons in the PLP-deficient mouse model of spastic paraplegia type 2 revealed by volume imaging using focused ion beam-scanning electron microscopy. J Struc Biol, 2020 May 1;210(2):107492. doi: 10.1016/j.jsb.2020.107492.*
- *Weil MT, Ruhwedel T, Meschkat M, Sadowski B, Möbius W. Transmission Electron Microscopy of Oligodendrocytes and Myelin. Methods Mol Biol, 2019;1936:343-375.doi: 10.1007/978-1-4939-9072-6_20*

Torben Ruhwedel | Max-Planck Institute of Multidisciplinary Sciences, Göttingen (Germany)

Torben Ruhwedel is a Technician responsible for running facility EM projects at the Electron Microscopy Unit at the Max Planck Institute for Multidisciplinary Sciences-City Campus in Göttingen.
His experience includes various techniques for cell biology and biomaterials like High pressure freezing (HPF), TEM, SEM and 3D volume EM.

Selected publications:

- *Three-dimensional virtual histology of the cerebral cortex based on phase-contrast X-ray tomography.*
  *Eckermann M, van der Meer F, Cloetens P, **Ruhwedel T**, Möbius W, Stadelmann C, Salditt T. Biomed Opt Express. 2021 Nov 15;12(12):7582-7598. doi: 10.1364/BOE.434885. eCollection 2021 Dec 1. PMID: 35003854*
- *Pathology of myelinated axons in the PLP-deficient mouse model of spastic paraplegia type 2 revealed by volume imaging using focused ion beam-scanning electron microscopy. Steyer AM, **Ruhwedel T**, Nardis C, Werner HB, Nave KA, Möbius W. J Struct Biol. 2020 May 1;210(2):107492. doi: 10.1016/j.jsb.2020.107492. Epub 2020 Mar 8. PMID: 32156581*
- *Biological Sample Preparation by High-pressure Freezing, Microwave-assisted Contrast Enhancement, and Minimal Resin Embedding for Volume Imaging.*
  *Steyer AM, **Ruhwedel T**, Möbius W. J Vis Exp. 2019 Mar 19;(145). doi: 10.3791/59156. PMID: 30958469*
- *Transmission Electron Microscopy of Oligodendrocytes and Myelin.*
  *Weil MT, **Ruhwedel T**, Meschkat M, Sadowski B, Möbius W. Methods Mol Biol. 2019;1936:343-375. doi: 10.1007/978-1-4939-9072-6_20. PMID: 30820909*
- *Cryo FIB-SEM: volume imaging of cellular ultrastructure in native frozen specimens.*
  *Schertel A, Snaidero N, Han HM, **Ruhwedel T**, Laue M, Grabenbauer M, Möbius W. J Struct Biol. 2013 Nov;184(2):355-60. doi: 10.1016/j.jsb.2013.09.024. Epub 2013 Oct 9. PMID: 24121039*

Yifan Wu | Washington University in St Louis (USA)

Yifan Wu obtained her bachelor degree in biological sciences at Southern University of Science and Technology, China, in 2019. She was awarded several student scholarships and worked at Johns Hopkins University as a visiting scholar. She then moved to the US to pursue her graduate training at Washington University in St Louis. In the Department of Neuroscience at WashU, Yifan explores the role of astrocytes in cholinergic neuromodulation. In particular, she is interested in understanding the contribution of astrocytes to the cognitive effects of cholinergic signaling and to the pro-cognitive benefits of cholinergic therapies employed in schizophrenia. Indeed, in recent years, nicotinic α7 acetylcholine receptors (α7nAChR) have become a major drug target in attempts to alleviate cognitive deficits observed in patients with schizophrenia – accounting for more than a third of all drugs in schizophrenia clinical trials. Yet, the exact cellular and molecular mechanisms by which α7nAChR support cognitive functions remain elusive, in part due to an excessive focus on neuronal α7nAChRs, leaving the role of α7nAChRs on other cell-types unexplored. The Papouin lab showed that astrocytic α7nAChRs control the availability of D-serine, the endogenous co-agonist of synaptic N-methyl D-aspartate receptors (NMDARs), across the 24hrs period. However, the behavioral relevance of this astrocyte-based α7nAChR pathway is still unknown and how α7nAChR-signaling alters astrocytes function is unknown. Yifan's work in the Papouin lab seeks to determine the contribution of neuronal and astrocytic α7nAChRs to cognitive functions (defined by NIMH-MATRICS initiative) and to the behavioral effect of α7nAChRs therapeutics, by leveraging a wide array of commonly used behavior assays and cell-specific, inducible α7nAChR knockout lines she generated. To gain insights into the signaling mechanisms downstream of astrocytic α7nAChRs, Yifan developed a new 2-photon calcium activity analysis pipeline, STARDUST (STreamlined Analysis of Regional calcium Dynamics for Ubiquitous Screening of Transients), which captures spontaneous Ca^{2+} transients occurring anywhere in the cells. Together, Yifan's work provides direct evidence for the involvement of astrocytic α7nAChRs in cognitive behavior and suggests a central role of astrocytes in α7nAChR-based cognitive therapies. While only in her 4^{th} year as a graduate student in the Papouin lab at WashU, Yifan has won numerous awards, including the prestigious Tach Award (2021), the Neuroscience Grant Competition (2022). She is also the 2021 WashU Science writing workshop laureate.

Amit Agarwal | Heidelberg University (Germany)

Amit Agarwal is the Chica and Heinz Schaller Research Group Leader at the Institute for Anatomy and Cell Biology, Heidelberg University, Germany. He received his Ph.D. in neurosciences, at the Max-Planck Institute of Experimental Medicine, Göttingen, Germany with Dr. Klaus-Armin Nave. He performed his post-doctoral training from 2010 to 2017, in the Department of Neuroscience at the Johns Hopkins University, USA with Dr. Dwight Bergles. The Agarwal laboratory uses optical and electron microscopic techniques, single-cell genetics, mouse transgenics, multi-omics approaches and computational methodologies to decipher cellular connectivity and molecular pathways by which neurons and glia (astrocytes and oligodendrocytes) interact, interconnect and integrate into the neural networks. The focal aim of his laboratory is to understand the functional significance of neuron-glia and glia-glia connectivity in the neural circuits function and neurometabolism, and study how disturbances in these fine cell-cell interactions contribute to pathophysiology of neurodegenerative and psychiatric disorders ranging from multiple sclerosis to autism.

- *Fiore F, Dereddi RR, Alhalaseh K, Coban I, Harb A,* ***Agarwal A****. (2022) Norepinephrine regulates Ca^{2+} signals and fate of oligodendrocyte progenitor cells in the cortex* ***bioRxiv*** *doi: https://doi.org/10.1101/2022.08.31.505555*
- *Streich L, Boffi JC, Wang L, Alhalaseh K, Barbieri M, Rehm R, Deivasigamani S, Gross CT,* ***Agarwal A****, Prevedel R. (2021) High-resolution structural and functional deep brain imaging using adaptive optics three-photon microscopy.* ***Nature Methods****. 2021 Oct;18(10):1253-1258.*
- *Semyanov A., Henneberger C., and* ***Agarwal A.*** *(2020) Making sense of astrocytic calcium signals — from acquisition to interpretation.* ***Nature Reviews Neuroscience*** *Oct;21(10):551-564*
- ***Agarwal, A.****, Wu., P.H., Hughes, E.G., Fukaya, M. Tischfield, M.A., Langseth, A.J., Wirtz, D., Bergles, D.E. (2017) Transient opening of the mitochondrial permeability transition pore induces microdomain calcium transients in astrocyte processes.* ***Neuron*** *93(3): 587-605*
- *Paukert, M*.,* ***Agarwal, A****., Cha, J., Doze, V.A., Kang, J.U., Bergles D.E. (2014) Norepinephrine controls astroglial responsiveness to local circuit activity.* ***Neuron****. 82(6): 1263-70.*

Felipe Bodaleo Torres | Heidelberg University (Germany)

Felipe obtained his PhD in Cellular Biology and Neuroscience in the University of Chile. During his PhD (2010-2015), Felipe studied the role of the presynaptic microtubule cytoskeleton in the formation and maintenance of glutamatergic synapses in hippocampal neurons. During his postdoc at the Center for Geroscience and Metabolism, Felipe studied how age-related epigenetic signatures are maintained in directly induced neurons derived from embryonic and adult fibroblasts. Currently, Felipe is a postdoctoral fellow in the Chica and Heinz Schaller Foundation at the Heidelberg University, Germany. His interests are now focused on glial cells in the central nervous system. His main project aims to describe astrocytic mitochondrial structure and dynamics using different microscopy techniques, including FIB-SEM, STED super resolution and multiphoton-based in vivo imaging. To correlate how mitochondrial structure influences astrocyte physiology, Felipe is also interested on understanding and deciphering both cytosolic and mitochondrial calcium dynamics in astrocytes. By combining different microscopy approaches and state of the art analysis tools, he is trying to have a proper and detailed view on how mitochondrial function affects astrocytic calcium homeostasis and astrocyte response to detrimental stimulus.

Selected publications:

- *Wang J, Fröhlich H, Torres FB, Silva RL, Poschet G, Agarwal A, Rappold GA. Mitochondrial dysfunction and oxidative stress contribute to cognitive and motor impairment in FOXP1 syndrome. Proc Natl Acad Sci U S A. 2022 Feb 22;119(8):e2112852119.*
- *Bilches Medinas D, Malik S, Yıldız-Bölükbaşı E, Borgonovo J, Saaranen MJ, Urra H, Pulgar E, Afzal M, Contreras D, Wright MT, Bodaleo F, … , Tolun A. Mutation in protein disulfide isomerase A3 causes neurodevelopmental defects by disturbing endoplasmic reticulum proteostasis. EMBO J. 2022 Dec 17;41(2):e105531. doi: 10.15252/embj.2020105531. Epub 2021 Dec 14. PMID: 34904718; PMCID: PMC8762563.*
- *Pamela J. Urrutia, Felipe Bodaleo, Daniel A. Bórquez, Yuta Homma, Victoria Rozes-Salvador, Cristopher Villablanca, Cecilia Conde, Mitsunori Fukuda, Christian González-Billault. Tuba activates Cdc42 during neuronal polarization downstream of the small GTPase Rab8a. Journal of Neuroscience 21 January 2021, JN-RM-0633-20; DOI: 10.1523/JNEUROSCI.0633-20.2020*
- *Bodaleo F, Tapia-Monsalves C, Cea-Del Rio C, Gonzalez-Billault C, Nunez-Parra A. Structural and Functional Abnormalities in the Olfactory System of Fragile X Syndrome Models. Front Mol Neurosci. 2019 May 28;12:135. doi: 10.3389/fnmol.2019.00135. PMID: 31191246; PMCID: PMC6548058.*
- *Bodaleo, F., Montenegro-Venegas, C., Henríquez, D. et al. Microtubule-associated protein 1B (MAP1B)-deficient neurons show structural presynaptic deficiencies in vitro and altered presynaptic physiology. Sci Rep 6, 30069 (2016). https://doi.org/10.1038/srep30069*

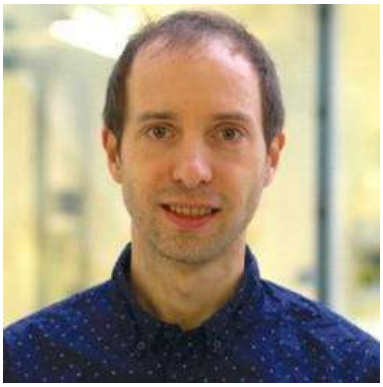
Jiaxing Li | Vollum Institute (USA)

Jiaxing Li is interested in the synapse formation because it is the structural and functional units of the CNS. During his PhD training with Dr. Catherine Collins at University of Michigan, he used Drosophila to study how synapses are assembled at the neural-muscular junctions. He was especially intrigued by the synaptic defects in a Kinesin mutant. Utilizing the genetics and imaging power in Drosophila, he discovered an unexpected mechanism that restrains synapse formation through an injury response signaling that mediates axonal degeneration and regeneration. After his PhD, Jiaxing Li joined Dr. Kelly Monk lab to study the oligodendrocyte development. Oligodendrocyte precursor cells (OPCs) are the only type of glia in the CNS that form synapses with neurons. Since their discovery nearly 20 years ago, the assembly and the function of these synapses still remain largely unclear. Utilizing the unparalleled imaging capability of zebrafish, he uncovered unique synapse assembly mechanisms in OPCs and its contribution to calcium signaling and OPC development.

Selected publications:

- ***Li, J.****, Miramontes, T, Czopka, T, Monk, K. R.* (2022). Synapses in oligodendrocyte precursor cells are dynamic and contribute to Ca^{2+} activity. bioRxiv. doi: https://doi.org/10.1101/2022.03.18.484955. *Co-corresponding author.*
- ***Li, J.*** *and Monk, K. R. (2019). Healthy attachments: Cell adhesion molecules collectively control myelin integrity. J. Cell Biol. 218, 2824–2825*
- ***Li, J.****, Zhang, Y.V.*, Adib, E.A., Stanchev, D.T., Xiong, X., Klinedinst, S., Soppina, P., Jahn, T.R., Hume, R.I., Rasse, T.M., Collins, C.A. (2017). Restraint of presynaptic protein levels by Wnd/DLK signaling mediates synaptic defects associated with the kinesin-3 motor Unc-104. Elife. 6, e24271.*
- ***Li, J.*** *and Collins, C.A. (2017). Mechanisms of axonal degeneration and regeneration: lessons learned from invertebrates. The Oxford handbook of Invertebrate Neurobiology. Oxford University Press.*

Arne Battefeld | Bordeaux University (France)



Dr Arne Battefeld is an assistant professor at the University of Bordeaux and a team leader at the Institute of Neurodegenerative disease (UMR5293) since 2018. He studied biology (Rostock, Germany), performed his PhD studies on lipid-mediated signalling in synaptic transmission and ion channels (sodium and HCN) at the Charité Berlin (Germany) and obtained his PhD in 2011 (Free University Berlin, Germany). Between 2011 and 2018 he was a post-doctoral researcher in the axonal signalling lab headed by Maarten Kole at the Netherlands Institute for Neuroscience. In the group of Maarten Kole, Arne focused on investigating the physiology of the axon (potassium and sodium channels) as well as the interplay of neurons with oligodendrocytes using electrophysiological and imaging approaches (Battefeld et al., 2014, 2016, 2019). In 2016 he was a Grass Fellow at the Marine Biological Laboratory (USA). His team at the University of Bordeaux investigates physiological interactions between oligodendrocyte and neurons and functional differences between oligodendrocytes. The team uses experimental approaches ranging from electrophysiology and live imaging to electron microscopy.

Selected publications:

- *Battefeld A, Klooster J, Kole MHP. 2016. Myelinating satellite oligodendrocytes are integrated in a glial syncytium constraining neuronal high-frequency activity. Nature Communications 7. doi:10.1038/ncomms11298*
- *Battefeld A, Popovic MA, de Vries SI, Kole MHP. 2019. High-Frequency Microdomain Ca2+ Transients and Waves during Early Myelin Internode Remodeling. Cell Reports 26:182-191.e5. doi:10.1016/j.celrep.2018.12.039*
- *Dorrego-Rivas A, Ezan J, Moreau MM, Poirault-Chassac S, Aubailly N, De Neve J, Blanchard C, Castets F, Fréal A, Battefeld A, Sans N, Montcouquiol M. 2022. The core PCP protein Prickle2 regulates axon number and AIS maturation by binding to AnkG and modulating microtubule bundling. Sci Adv 8:eabo6333. doi:10.1126/sciadv.abo6333*
- *Moore S, Meschkat M, Ruhwedel T, Trevisiol A, Tzvetanova ID, Battefeld A, Kusch K, Kole MHP, Strenzke N, Möbius W, de Hoz L, Nave K-A. 2020. A role of oligodendrocytes in information processing. Nature Communications 11. doi:10.1038/s41467-020-19152-7*
- *Palhol JSC, Balia M, Terán FS-R, Labarchède M, Gontier E, Battefeld A. 2022. A population of gray matter oligodendrocytes directly associates with the vasculature (BioRxiv). doi:10.1101/2022.04.11.487873*

Francesco Paolo Ulloa Severino | Cajal Institute CSIC (Spain)

Francesco Paolo Ulloa Severino studied molecular biology at the University of Naples Federico II (2007-2012) and then earned his Ph.D. in neurobiology (2013-2017) at the International School for Advanced Studies (SISSA). During his graduate studies, he acquired skills in brain co-culture and live imaging techniques to study three-dimensional neural network formation and activity on 3D scaffolds fabricated with biocompatible materials (i.e., graphene, collagen, PDMS). After obtaining his Ph.D., Francesco moved to the United States to work as a postdoctoral research associate at Duke University. Co-mentored by Dr. Cagla Eroglu and Dr. Henry Yin, he investigated the behavioral effects of astrocyte-neuron interactions and their synaptogenic pathways. Francesco found that □2□-1, the neuronal receptor for the synaptogenic astrocyte-secreted thrombospondins, is necessary for training-induced and circuit-specific excitatory synaptic formation in the adult brain. Furthermore, through the application of novel viral tools, he generated circuit-specific conditional KO mice to study the behavioral effect of the inhibition of training-induced synaptogenesis. His findings highlighted a novel mechanism the Anterior Cingulate Cortex uses to control the effort exertion during operant behaviors. In those years, he also contributed to the development of live imaging techniques for in vivo experiments, to novel findings about basal ganglia circuits' role in animal movement control and Parkinson's disease, and the astrocytic role in cortical circuit development and experience-dependent remodeling. In 2013 Francesco moved to Spain as Ramon y Cajal research fellow to start his laboratory at the Cajal Institute (CSIC). In his laboratory, Francesco will study the experience-dependent astrocytic structural adaptations and their impact on neural circuits and behaviors. He aims to unveil novel cellular, molecular, and genetic pathways controlling astrocytes' structural remodeling upon learning and performance of operant behaviors.

Selected publications:

- *Ulloa Severino, F. P. et al. The role of dimensionality in neuronal network dynamics. Sci. Rep.* ***6****, 29640 (2016).*
- *Ulloa Severino, F. P. et al. Training-Induced Circuit-Specific Excitatory Synaptogenesis is Required for Effort Control. bioRxiv 2021.04.20.440613 (2022) doi:10.1101/2021.04.20.440613.*
- *Lawal, O., Ulloa Severino, F. P. & Eroglu, C. The role of astrocyte structural plasticity in regulating neural circuit function and behavior. Glia* ***70****, 1467–1483 (2022).*
- *Watson, G. D. R. et al. Thalamic projections to the subthalamic nucleus contribute to movement initiation and rescue of parkinsonian symptoms. Sci. Adv.* ***7****, eabe9192 (2021).*
- *Zhang, J. et al. A one-photon endoscope for simultaneous patterned optogenetic stimulation and calcium imaging in freely behaving mice. Nat. Biomed. Eng. 1–12 (2022) doi:10.1038/s41551-022-00920-3.*

Liam Barry-Carroll | Bordeaux University (France)

L. Barry-Carroll completed a bachelor in Physiology in Trinity College Dublin and completed an internship under the supervision of Professor Marina Lynch investigating the use of monocyte-derived macrophages as blood-based biomarkers of age-related cognitive decline. Between 2017-2021, L. Barry-Carroll undertook their PhD studies at the University of Southampton under the supervision of Professor Diego Gomez-Nicola investigating the developmental dynamics of microglia in the healthy brain. From 2021 until present, L. Barry-Carroll has joined the NutriNeuro laboratory in Bordeaux and is working as part of the ExoMarQuage project under the supervision of Sophie Layé and Jean-Christophe Delpech. This project explores the role of extracellular vesicles in ageing and cognitive decline and the impact of dietary omega-3 polyunsaturated fatty acids on this process.

Selected publications:

- *Barry-Carroll L, Greulich P, Marshall AR, Riecken K, Fehse B, Askew KE, Li K, Garaschuk O, Menassa DA & Gomez-Nicola D. (2022). Microglial colonisation of the developing brain is facilitated by clonal expansion of highly proliferative progenitors and follows an allometric scaling. bioRxiv**,** 2022.2009.2015.507569.*
- *Menassa DA, Muntslag TAO, Martin-Estebané M, Barry-Carroll L, Chapman MA, Adorjan I, Tyler T, Turnbull B, Rose-Zerilli MJJ, Nicoll JAR, Krsnik Z, Kostovic I & Gomez-Nicola D. (2022). The spatiotemporal dynamics of microglia across the human lifespan. Developmental Cell **57,** 2127-2139.e2126.*
- *Wolfe H, Hannigan C, O'Sullivan M, Carroll LB, Brennan S, Lawlor B, Robertson IH & Lynch M. (2018). A shift to glycolysis accompanies the inflammatory changes in PBMCs from individuals with an IQ-discrepant memory. Journal of Neuroimmunology **317,** 24-31.*

Omar de Faria Jr | Cambridge University (UK)

Omar de Faria Jr. has a Bachelor (Biology) and a Master's degree (Biochemistry) from Federal University of Rio de Janeiro, completed under the supervision of Dr. Margaret Magdesian and Prof. Sergio Ferreira. He then moved to the Montreal Neurological Institute of McGill University to pursue his PhD in the laboratories of Dr. Timothy Kennedy and Dr. David Colman, where he investigated mechanisms that regulate myelin development and maintenance. He has uncovered the function of the myelin-specific protein Opalin during oligodendrocyte differentiation and the mechanism by which the netrin receptor UNC5B maintains myelin. He is currently a Research Associate in the laboratory of Prof Thora Karadottir, in the University of Cambridge, where he studies the interplay between neuronal activity and myelin regeneration. Using an *in vivo* model of remyelination and tools to measure and modulate neuronal activity in freely behaving animals, he is investigating whether neurons change their levels of activity in response to demyelination and whether changes in neuronal activity can in turn drive remyelination. To date, Dr. de Faria has mentored 6 students and has been awarded 5 research fellowships.

Selected publications:

- *Omar de Faria Jr, Helena Pivonkova, Balaz Varga, Sebastian Timmler, Kimberly A Evans, RT Káradóttir. Periods of synchronized myelin changes shape brain function and plasticity. Nature Neuroscience (2021)*
- *Omar de Faria Jr, Ajit S. Dhaunchak, Yasmine Kamen, Alejandro Roth, David R Colman, Tanja Kuhlmann Timothy E Kennedy. TMEM10 Promotes Oligodendrocyte Differentiation and is Expressed by Oligodendrocytes in Human Remyelinating Multiple Sclerosis Plaques. Scientific Reports (2019)*
- *Omar de Faria Jr, Qiao-Ling Cui, Jenea Bin, et al. MicroRNAs 219, 338 and 17-92 cluster expression during human and rodent oligodendrocyte differentiation. Frontiers in Genetics (2012)*
- *Sonia O Spitzer, Serguey Sitnikov, Yasmine Kamen, Kimberly A Evans, Deborah Kronenberg-Versteeg, S Dietmann, Omar de Faria Jr, Silvia Agathou, Ragnhildur T Káradóttir. Oligodendrocyte Progenitor*

Sara Carracedo | Bordeaux University (France)

Sara holds a Bachelor's in Veterinary medicine from the University of Santiago de Compostela (Spain) and a Master's degree on Neurosciences from the University of Bordeaux (France). Currently she is second year PhD student at the Boué-Grabot and Landry team at the Institute des Maladies Neurodégénératives (IMN) from the same University where she is focused on the study of P2X4 receptor in amyotrophic lateral sclerosis (ALS). ALS is a fatal neurodegenerative disease characterized by the motor neuron death which led to motor weakness, paralysis and death within 3-5 years. Growing evidence point ALS to be the result of a complex interplay between the nervous and the immune system. The ATP released by neurons and glial cells may modulates the neuroglial communication via activation of the P2X receptors. Among these, P2X4 receptor, which is a non-selective cationic channel has been recently involved in ALS pathogenesis using SOD1G93A ALS mouse model (SOD1). This receptor is expressed in many cell types such as microglia and neurons in the nervous system and in macrophages at the periphery. Thus, addressing the cell-specific role of P2X4 may give new insights into how the neuroimmune crosstalk modulates ALS progression. To address the neuroglial role of P2X4, we have developed and characterized by biochemical and behavioral approaches novel transgenic mice, expressing conditional either knock-in noninternalized P2X4 (cP2X4KI) or knock-out (cP2X4KO) selectively in macrophage/microglia or neurons. These novel tools will clarify the cell-specific mechanisms of P2X4 receptors in ALS.

Selected publications:

Increased surface P2X4 receptors by mutant SOD1 proteins contribute to ALS pathogenesis in SOD1-G93A mice. Eleonore Bertin, Audrey Martinez, Anne Fayoux, Kevin Carvalho, Sara Carracedo, Pierre Olivier Fernagut, Frederic Koch-Nolte, David Blum, Sandrine Bertrand, Eric Boué-Grabot. Cell Mol Life Sci. 2022 Jul 19;79(8):431.

Sarah Bou Sader Nehme | Bordeaux University (France)

Graduated with a Master in Cellular and Molecular Genetics from the Holy Spirit University of Kaslik, Sarah is currently enrolled in her second year as a joint Ph.D. student between France (Institut of Neurodegenerative Disorders) and Lebanon (Holy spirit University of Kaslik). She aims to understand the inflammatory mechanisms at the origin of attention-deficit/hyperactivity disorder (ADHD) and its comorbid pain. Clinical studies have shown that pain hypersensitivity develops in ADHD patients. Conversely, pain increases attentional and cognitive deficits. However, the mechanisms underlying this concomitance are poorly understood. The purpose of her thesis is to discern whether neuroinflammation underpins the pathophysiology of these two conditions. During her first year as a PhD student, Sarah worked on identifying markers of neuroinflammation in the anterior cingulate cortex, the insular cortex, and the amygdala of ADHD-like mouse model. Using RT-qPCR, she studied over 30 key inflammatory mediators and have found significant differences in the expression of cytokines (IL-6, IL-16, TNF-α) and other proteins (BDNF, APE1, Wnt5a, MMP9) at the mRNA level. Interestingly, alterations in the expression of some of these markers were also detected in ADHD patients. She has also discovered microglial and astrocytic activation under ADHD conditions. Indeed, her preliminary results show a proliferation of both glial populations as well as changes in the morphology of microglia cells. These observations demonstrate the potential implication of neuroinflammation in the pathophysiology of ADHD and its comorbid pain. The experiments were also performed in mice lacking the P2X4 receptor, with the objective of understanding the involvement of this purinergic receptor in inflammation. During her second year, Sarah will focus on identifying signaling pathways that are deregulated under ADHD conditions, using a panel of transcriptomic and proteomic techniques.

Charlotte Madore | INRAE, Bordeaux University (France)

Charlotte Madore's main research is focusing on the role of lipid and lipid derivatives on human microglia regulation and functions during brain development and in neurodevelopmental disorders, at NutriNeuro lab (INRAe/Bordeaux University). She performed her PhD at Bordeaux University studying morphofunctional plasticity of microglia, modulated by immune and dietary cues. She then performed her post-doctoral studies at Harvard Medical School, where she went deeper in the microglial regulatory pathways analysis by identifying specific phenotype of microglia commonly associated with neurodegeneration and neurodegenerative diseases, highlighting a new APOE-TREM2 pathway in disease and during neurodevelopment.

Selected publications **:**

- *Herron S, Delpech JC, Madore C, Ikezu T. Using mechanical homogenization to isolate microglia from mouse brain tissue to preserve transcriptomic integrity. STAR Protoc. 2022 Dec 16;3(4):101670. doi: 10.1016/j.xpro.2022.101670. PMID: 36107747.*
- *Ikezu S1., Yeh H1., Delpech J.C1., Woodbury E.M1., Van Enoo A.A., Sivakumaran S., Ruan Z., Holland C., Guillamon-Vivancos T., Yoshii-Kitahara A., You Y., Madore C., Botros B.M., Chao P-h., Desani A., Manimaran S., Johnson E.W., Butovsky O., Medalla L., Luebke I.J., Ikezu T. (2019), Repopulation of microglia corrects maternal inflammation-induced microglial and synaptic dysfunction and behavioral abnormalities., (1equal contribution) Mol. Psychiatry, 2020 Feb 18:10.1038/s41380-020-0671-2. doi: 10.1038/s41380-020-0671-2.PubMed PMID: 32071385*
- *Madore C*, Leyrolle Q*, Morel L*, Rossitto M*, Greenhalgh AD, Delpech JC, Martinat M, Bosch-Bouju C, Bourel J, Rani B, Lacabanne C, Thomazeau A, Hopperton KE, Beccari S, Sere A, Aubert A, De Smedt-Peyrusse V, Lecours C, Bisht K, Fourgeaud L, Gregoire S, Bretillon L, Acar N, Grant NJ, Badaut J, Gressens P, Sierra A, Butovsky O, Tremblay ME, Bazinet RP, Joffre C, Nadjar A, Layé S. Essential omega-3 fatty acids tune microglial phagocytosis of synaptic elements in the mouse developing brain. Nat Commun. 2020 Nov 30;11(1):6133. doi: 10.1038/s41467-020-19861-z. PMID: 33257673; PMCID: PMC7704669. *Equally contributed*
- *Madore C, Yin Z, Leibowitz J, Butovsky O. Microglia, Lifestyle Stress, and Neurodegeneration. Immunity. 2020 Feb 18;52(2):222-240. doi: 10.1016/j.immuni.2019.12.003. Epub 2020 Jan 7. PMID: 31924476;*
- *Krasemann S*, Madore C*, Cialic R, Baufeld C, Calcagno N, El Fatimy R, Beckers L, O'Loughlin E, Xu Y, Fanek Z, Greco DJ, Smith ST, Tweet G, Humulock Z, Zrzavy T, Conde-Sanroman P, Gacias M, Weng Z, Chen H, Tjon E, Mazaheri F, Hartmann K, Madi A, Ulrich JD, Glatzel M, Worthmann A, Heeren J, Budnik B, Lemere C, Ikezu T, Heppner FL, Litvak V, Holtzman DM, Lassmann H, Weiner HL, Ochando J, Haass C, Butovsky O. The TREM2-APOE Pathway Drives the Transcriptional Phenotype of Dysfunctional Microglia in Neurodegenerative Diseases. Immunity. 2017 Sep 19;47(3):566-581.e9. doi: 10.1016/j.immuni.2017.08.008. PMID: 28930663; PMCID:PMC5719893. *Equally contributed*

STUDENTS

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DELLA GIUSTINA

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DUDEK

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Joana MATEUS

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DE SOUZA

Louisa ZIELKE

Emmy HOEKSEMA

Ben SPIELMAN

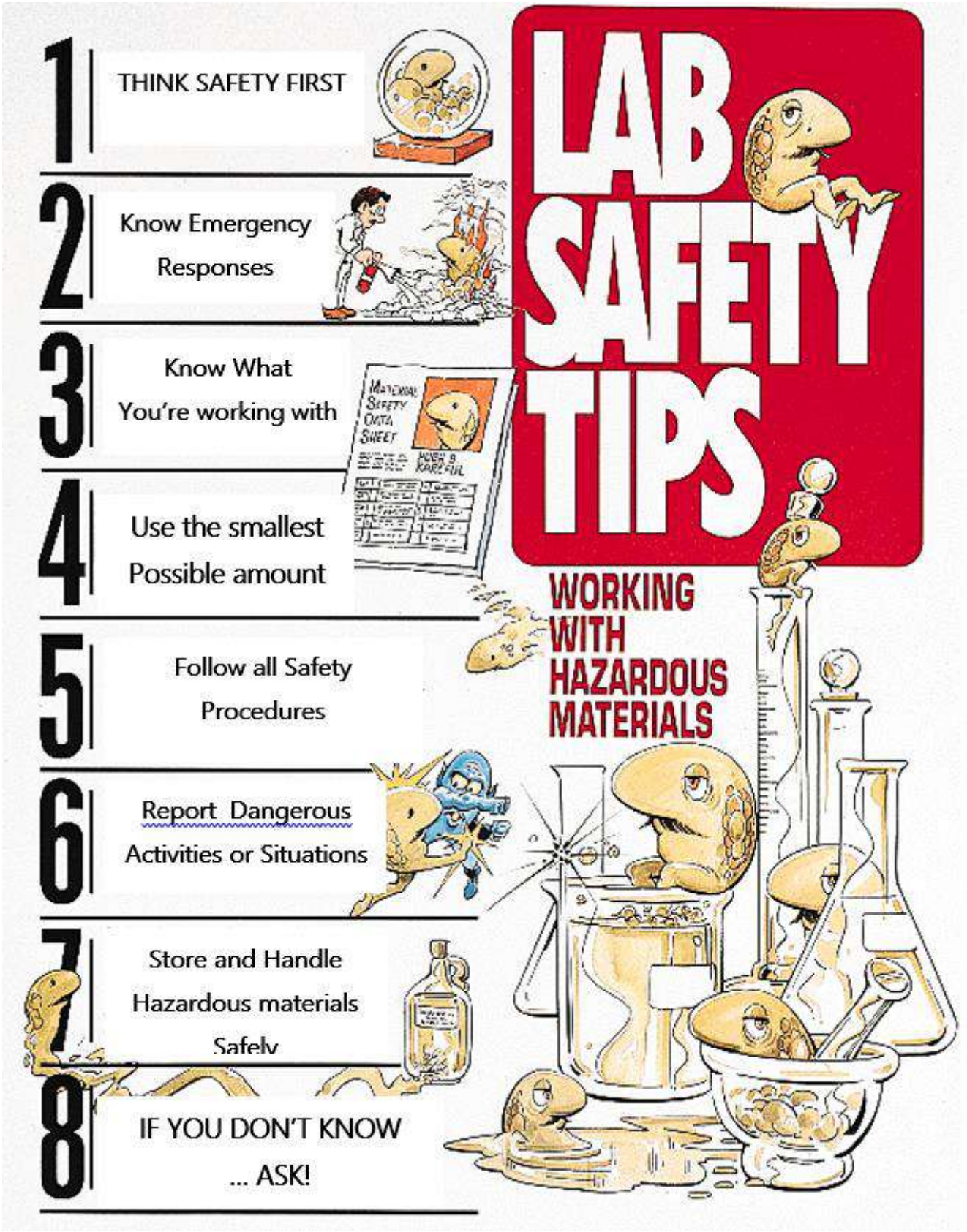
Mariagiovanna
DI CHIANO

Sara SILVA

Clément RIES

Maria Carolina
MACHADO
DASILVA

SAFETY & SECURITY RULES



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WEAR LAB COATS

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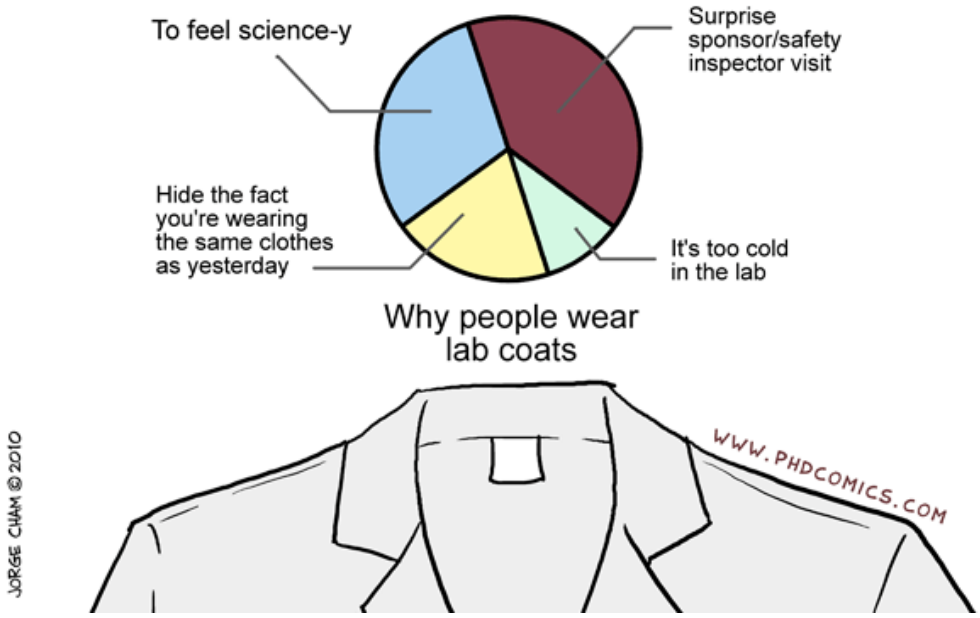
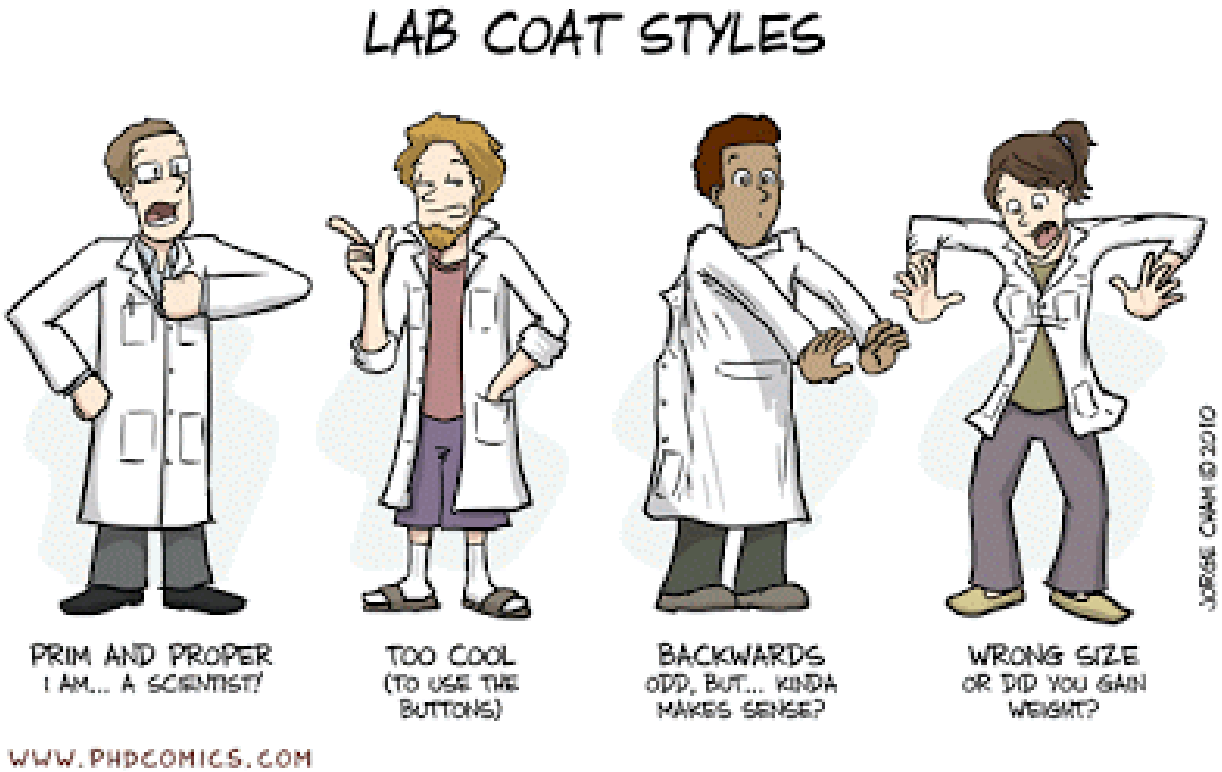
In the school and other premises, you will find disposable lab coats and permanent lab coats





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WEAR

GLOVES

*

Don’t forget to remove your gloves when you are leaving the experimental area !

*

WEAR MASKS and/or GOGGLES (if needed)

*

*

HOW TO DEAL WITH WASTE

*

Doubting ? Just ask !

Biological waste,
Contaminated items
NO LIQUID, NO SHARP items

SHARP items
Small Glass items
NO TIPS, NO LIQUID

Toxic waste,
Contaminated items
NO LIQUID, NO SHARP items

(Chemical Room)

LIQUID waste,
Contaminated liquids

(Chemical Room)

PLEASE, PAY ATTENTION TO

✓ WHAT YOU'RE WORKING WITH
✓ YOUR SAFETY and OTHERS'
✓ YOUR ENVIRONMENT

BE SAFE AND RESPECTFUL

THANK YOU!!!

☺

ANIMAL FACILITY RULES

It is **MANDATORY** to use:

Mask

Cover head

Cover shoes.

Labcoat

Gloves

Please, always respect the well-being of the animals, work properly and quietly

Happy animals make good science ☺

KITCHEN/MEETING ROOM RULES

- **Plates and cutlery**
  Please rinse them by the sink **BEFORE** putting them in the dishwasher

- **Glasses**
  They are **NOT DISPOSABLE**, please label them with your name, don't put it in the washing machine but clean it after use.

- **Coffee cups**
  Please, label them with your name, don't put it in the washing machine but clean it after use.

- You will find **garbage bins** dedicated for:
  - **Regular trash**
  - **Coffee grounds**