

WELCOME

Dear Colleagues,

We are pleased to welcome you at the Black Sea Neurogenesis 2023 international conference. This year's event is the third Neurogenesis meeting taking place at the Black Sea in the last 6 years. We hope that thanks to the excellent speakers, and support from Bulgarian and European Commission funding, we shall be able to keep the conference as a regular event on the neuroscience calendar in the future.

In 2023, the meeting includes topics that cover the process of neurogenesis during the development of the brain, in adulthood, after injury as well as under conditions of tumorigenesis. As in previous meetings, the speakers will address the most recent progress made in understanding how neural stem and progenitor cells generate neurons in the developing and adult brain. Single-cell technologies have revolutionized our understanding of how stem cell division, cell fate decision, and differentiation impact neurodevelopmental disorders and regenerative therapies. This knowledge is rapidly evolving, and new tools are being developed to trace specific cell populations and the various cell lineages.

We hope that the presentations and discussions during the meeting will not only shed new light on this exciting topic in the field of neurosciences, but will also be of help to build new partnerships between the participating researchers.

Yours sincerely,

Anton B. Tonchev, Organizer
Wieland B. Huttner, Programme Advisor

Varna, Bulgaria, June 2023



**Welcome to
BLACK SEA NEUROGENESIS
2023**

WEDNESDAY, MAY 31 – ARRIVAL

17:00 Registration, poster placement

20:00 Speakers' welcome dinner

JUNE 01-03 BLACK SEA NEUROGENESIS

THURSDAY JUNE 1 – GRAND HALL, FLAMINGO GRAND HOTEL (2ND FLOOR)

8:30 Registration, poster placement

9:00 Welcome address and opening

Session on developmental neurogenesis (16:00-17:30)

CHAIR: ANTON TONCHEV

9:30- 10:30 SPECIAL LECTURE: Victor Borrell
Evolution of neurogenesis and cortical complexity

10:30- 11:00 Coffee break

11:00- 11:30 Boyan Bonev
Epigenetic regulation of cortical development and evolution

11:30- 12:00 Michael Heide
Neocortex evolution, development and malformation:
Lessons from primate and patient-derived brain organoids

12:00- 16:00 Lunch and free time

Session on developmental neurogenesis (16:00-17:30)

CHAIR: DENIS JABAUDON

16:00- 16:30 Sven Falk
Molecular control of cellular identity

JUNE 01-03 BLACK SEA NEUROGENESIS

**16:30-
17:00** **Eckart Förster**
Reelin signalling, progenitor cells and migrating neurons

**17:00-
17:30** **Stavros Taraviras**
Distinct responses of neural stem and progenitor
cells to replication stress

**17:30-
18:30** **Coffee break and posters**

Session on developmental neurogenesis (18:30-20:00)
CHAIR: VICTOR BORRELL

**18:30-
19:00** **Pauline Ulmke**
Intermediate progenitor cells in cortical (mal)formation

**19:00-
20:00** **SPECIAL LECTURE: Hiroshi Kawasaki**
Molecular mechanisms underlying the formation
of folds on the mammalian cerebral cortex

20:00 **Opening reception**



JUNE 01-03 BLACK SEA NEUROGENESIS

FRIDAY

JUNE 2 – GRAND HALL, FLAMINGO GRAND HOTEL (2ND FLOOR)

Session on developmental neurogenesis (9:00-12:00)

CHAIR: ZOLTÁN MOLNÁR

- 9:00-10:00** **SPECIAL LECTURE: Denis Jabaudon**
Temporal controls over neuronal diversity in the developing brain
-
- 10:00-10:30** **Simon Hippenmeyer**
Principles of neural stem cell lineage progression
-
- 10:30-11:00** **Coffee break**

Session on adult neurogenesis (11:00-12:00)

CHAIR: FEDERICO CALEGARI

- 11:00-11:30** **Gregor Eichele**
Extracellular vesicles derived from the choroid plexus trigger the differentiation of neural stem cells
-
- 11:30-12:00** **Thorsten Döppner**
Lipid droplet accumulation in residing microglia and its impact on post-stroke neurogenesis
-
- 12:00-16:00** **Lunch and free time**

JUNE 01-03 BLACK SEA NEUROGENESIS

Session on adult neurogenesis (16:00-17:30)

CHAIR: SIMON HIPPENMEYER

16:00-16:30 **Harold Cremer**
Neuronal integration in the postnatal and adult olfactory bulb

16:30-17:00 **Nicolas Toni**
Regulation of adult hippocampal neurogenesis
in the context of anxiety

17:00-17:30 **Tommaso Mazza**
Network biology, bioinformatics and computational
biology, multi-omics integration, in-silico variant
pathogenicity assessment

17:30-18:30 **Coffee break and posters**

Session on adult neurogenesis (18:30-20:00)

CHAIR: GREGOR EICHELE

18:30-19:00 **Anton Tonchev**
Transcriptional profiling of adult monkey neurogenic
zones following cerebral ischemia

19:00-20:00 **Special lecture: Zaal Kokaia**
Reconstruction of cortical neuronal networks
with human reprogrammed cells

20:00 **Dinner**

JUNE 01-03 BLACK SEA NEUROGENESIS

SATURDAY JUNE 3 – GRAND HALL, FLAMINGO GRAND HOTEL (2ND FLOOR)

Session on adult neurogenesis (9:00-12:00)

CHAIR: CHAIR: ZAAL KOKAIA

9:00-10:00 **Special Lecture: Federico Calegari**
Improving brain function by expansion of neural stem cells

10:00-10:30 **Noelia Urbán**
Local and systemic regulation of adult neurogenesis

10:30-11:00 **Coffee break**

11:00-11:30 **Pierre Lavenex**
Lesion-induced plasticity in the primate medial temporal lobe

11:30-12:00 **Bogdan Draganski**
The curious case of modulating human hippocampal neurogenesis

12:00-16:00 **Lunch and free time**

Session on neural stem cells and glioblastoma (16:00-17:00)

CHAIR: BOGDAN DRAGANSKI

16:00-16:30 **Nadejda Tsankova**
The right place at the right time: Multi-omics resolves the transience and diversity during human gliogenesis and provides clues to diseased states

JUNE 01-03 BLACK SEA NEUROGENESIS

16:30-17:00 **Manlio Vinciguerra**
Liquid biopsies and diffuse intrinsic pontine glioma (DIPG)

17:00-18:00 **Coffee break and posters**

Session "Neurogenesis – further aspects" (18:00-20:00)

CHAIR: HIROSHI KAWASAKI

18:00-18:30 **Dimitre Staykov**
Art, music, and the ill and recovering brain

18:30-19:00 **Wieland B. Huttner**
Neocortex expansion in development
and human evolution – the role of metabolism

19:00-20:00 **Special Lecture: Zoltán Molnár**
Evolution of thalamocortical development

CONFERENCE CLOSING

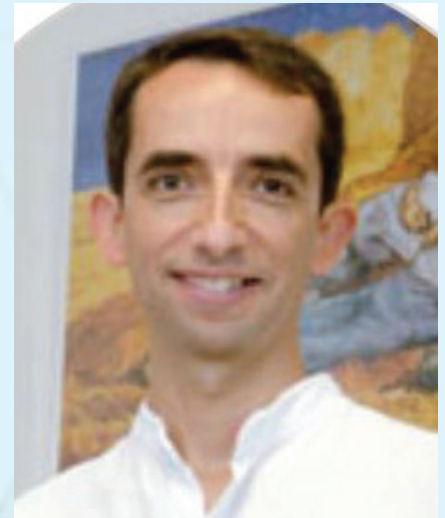
Speakers' farewell dinner

*Lametrus
2022*

Víctor Borrell

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Evolution of neurogenesis and cortical complexity

In the field of ***neocortical neurogenesis in development and evolution***, I will report the following:

- Neocortical expansion during evolution involved extensive folding.
- Patterns of cortical folding are defined transcriptomically.
- Transcriptional maps of cortex folding are established by early epigenetic regulation.
 - Specific epigenetic modifications favor basal progenitor amplification and cortex folding.
 - Distinct subclasses of apical Radial Glia Cells (aRGCs) are specifically enriched in prospective gyrus or sulcus in ferret.
 - Subclasses of aRGCs and IPCs are specifically involved in distinct parallel cell trajectories and lineages.
 - Parallel progenitor cell trajectories are repeated in VZ and OSVZ, and converge onto a single class of newborn neuron.
 - Multiple parallel cell trajectories exist in human as in ferret, but not mouse.
 - Parallel diversification of progenitor cell types and their lineages characterizes cortical expansion and folding during development.





Boyan Bonev

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Joint epigenome profiling reveals cell-type-specific gene regulatory programs in human cortical organoids

Gene expression is regulated by multiple epigenetic mechanisms, which are often coordinated in development and disease. However, current multiomic methods are frequently limited to one or two modalities at a time, making it challenging to obtain a comprehensive gene regulatory signature.

Here, we describe a novel approach, 3DRAM-seq, which simultaneously interrogates spatial genome organization, chromatin accessibility, DNA methylation genome-wide and at high resolution. We demonstrate that 3DRAM-seq outperforms other multiomic approaches and can be used to map cis-regulatory regions and chromatin loops and determine their epigenetic status. To further enable the profiling of specific cell types, we combine 3DRAM-seq with immunoFACS in human cortical organoids and map the epigenome landscape in neural stem cells and intermediate progenitors, identifying TFs associated with a widespread epigenetic remodeling across multiple layers. Finally, we develop a new variant of the massively parallel reporter assay (MPRA) to profile cell type-specific enhancer activity in organoids and employ it to functionally assess the role of key transcription factors for human enhancer activation and function. Using this assay we identify and characterize a novel human-specific enhancer for *FBXO32*, a marker for ventricular radial glia cells which is expressed in the human but not the mouse brain.

Overall, 3DRAM-seq uncovers coordinated epigenome remodeling across multiple regulatory layers, enables paired single-molecule footprinting to study TF cooperativity and can be used to functionally dissect the molecular logic of human brain enhancers.



Michael Heide

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Neocortex development, evolution and malformation: Lessons from primate and patient-derived brain organoids

In the field of *neocortical neurogenesis in development and evolution*, I will report the following:

- A unified protocol for the generation of brain organoids of different primate species.
- The genetic modification of these organoids by electroporation.
- Expression of the human-specific gene ARHGAP11B increases the abundance of basal progenitors in chimpanzee brain organoids.
- Inhibition of ARHGAP11B's function in human brain organoids reduces basal progenitor abundance to the level of chimpanzee.
- ARHGAP11A or ARHGAP11B rescue experiments in ARHGAP11A plus ARHGAP11B double-knockout human brain organoids indicate a role of ARHGAP11B in maintaining basal radial glia levels.
- Brain organoids generated from Baraitser-Winter-CerebroFrontoFacial syndrome (BWCF-S) patient-derived induced pluripotent stem cells recapitulate patients' microcephaly.
 - BWCF-S brain organoids have reduced apical progenitor (AP) levels.
 - Mitotic APs in BWCF-S organoids show horizontal rather than vertical cleavage planes, providing a likely underlying mechanism for the reduction in the size of the AP pool of these organoids.

<https://www.dpz.eu/en/unit/nwg-brain-development-and-evolution/about-us.html>





Sven Falk

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Forced neurogenesis, direct lineage reprogramming, neural stem cells, mechanical forces, mechanics instructing lineage decisions

In the field of ***forced neurogenesis***:

- Human adult brain pericytes can be reprogrammed into induced neurons (iNs).
- The change of cellular identity happens in the absence of proliferation.
- We identified an identity safe-guarding mechanism in the pericyte starter population. that is induced upon induction of identity change.
- Along their trajectory toward iNs cells pass through a state that is transcriptionally similar to neural stem cells during development.
- This neural stem cell like state can be modulated and allows navigation of the reprogramming trajectory.
- Along the reprogramming trajectory mechano-sensors show an intriguing dynamic expression pattern.
- To test the impact of mechanics on developmental neurogenesis we use human brain organoids in conjunction with rheometer-based manipulations.
- We show that mechanics influence neural stem cell lineage decisions and influence patterning processes.



<https://www.falklab.info>

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Role of the ECM glycoprotein Reelin for the development and maintenance of the dentate granule cell layer

In the field of ***dentate granule cell layer formation and maintenance of granule cell layering***, I will report on following:

- From attempts to rescue dentate granule cell layer formation in the reelin deficient dentate gyrus by reelin supplementation to work in progress:
- Attempts to disrupt the properly formed dentate granule cell layer by conditionally induced reelin deficiency.
- The observed effects, in particular on dentate granule cells and on dentate radial glia (like) cells will be presented and discussed.





Stavros Taraviras

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Distinct responses of neural stem and progenitor cells to replication stress

The importance of genome integrity maintenance during embryonic development has been pointed out given the number of developmental syndromes induced by the presence of genomic instability during the prenatal or early infant life. DNA replication represents one of the main intrinsic factors of genomic instability and therefore is subject to strict regulation to ensure the accurate transmission of genetic information. Aberrant DNA replication, generally described as replication stress, has been associated with developmental defects including microcephaly due to incomplete cortical development. Eventhough impaired replication has been previously linked with growth retardation and microcephaly, why the brain is critically affected compared to other organs remains elusive.

Our findings show:

- differential response between NSCs and fate committed apical radial glia cells (aRG) to replication defects.
- aRG can tolerate altered expression of replication factors, while NSCs undergo excessive replication stress, identified by impaired replication, increased DNA damage and defective cell cycle progression leading eventually to NSCs attrition and microcephaly.
- NSCs, possessing a short G1, license and activate more origins than aRG, by acquiring higher levels of DNA-bound MCMs.
- In vivo G1 shortening in aRG can induced DNA damage upon impaired licensing, suggesting that G1 length correlates with replication stress hypersensitivity.

NSCs possess distinct cell cycle characteristics to ensure fast proliferation albeit these inherent features render them susceptible to genotoxic stress, providing a mechanistic insight into the pathogenetic mechanisms of microcephaly.



<http://stemcellslab.upatras.gr/>

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Species cell-type specific transcriptome analysis identifies novel conserved and human intermediate progenitor-enriched genes in cortical development

In the field of *developmental neurogenesis*, I will report the following:

- Identification of molecular characteristics of intermediate progenitor cells (IPCs) in the developing mouse and human cortex.
- Identification of more than 1000 novel conserved and human IPC-enriched genes, in which the SVZ expression of more than 350 IPC genes was confirmed.
- IPCs express key factors involved in chromatid segregation, cell-cycle regulation, transcriptional regulation, and cell signaling.
- Mutation of the conserved IPC-specific genes is involved in cortical malformations.
- The conserved IPC-specific gene ESCO2 is critical for IPC maintenance.
- Unique factors define human IPCs versus mouse IPCs.
- Human IPC-specific genes link to brain tumor.
- Human IPC-specific gene, CDKN3 positively regulate IPC proliferation and cortical neurogenesis.





Hiroshi Kawasaki

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Molecular mechanisms underlying the formation of folds on the mammalian cerebral cortex

In the field of the ***development and evolution of the cerebral cortex***, I will report the following:

- In utero electroporation is useful for genetic manipulation in the ferret cerebral cortex.
- Gene expression not only in neurons but also in astrocytes and oligodendrocytes can be manipulated by combining in utero electroporation and the piggyBac system.
- Genes can be knocked-out in the ferret cerebral cortex by combining in utero electroporation and the CRISPR/Cas9 system.
- FGF signaling mediates the proliferation of oRG cells, the increase in upper layer neurons and cortical folding.
- Sonic hedgehog (shh) signaling mediates the self-renewal of oRG cells, the increase in upper layer neurons and cortical folding.
- Shh signaling is more activated in the ferret cortex than in the mouse cortex.
- FGF1 is more expressed in ferret astrocytes than in mouse astrocytes.
- Positive feedback loop of FGF signaling mediates the proliferation of astrocytes and cortical folding.
- Subcortical U-fibers are present in the ferret cerebrum.
- Subcortical U-fibers are derived from the outer fiber layer (OFL) in the developing brain.

<http://square.umin.ac.jp/top/kawasaki-lab/e-top.html>



Denis Jabaudon

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Temporal controls over neuronal diversity in the developing brain

The developing brain exhibits a remarkable diversity of neuronal cell types, each with specialized functions that contribute to the proper function of the mature brain. The mechanisms underlying the generation and specification of neuronal diversity during development are complex and incompletely understood. Here, we investigate temporal controls over this process by analyzing the developmental diversity of neuronal progenitors across multiple brain regions and developmental timepoints. Our results demonstrate that distinct spatial and temporal transcriptional programs control the timing and pattern of neuronal differentiation and specification during brain development. Our findings provide new insights into the mechanisms underlying neuronal diversity in the developing brain and suggest novel strategies for manipulating these processes to direct neuronal identity and connectivity.





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Principles of neural stem cell lineage progression

In the field of *developmental neurogenesis*, I will report the following:

- Ontogeny of the superior colliculus at single cell level.
- Clonal analysis using MADM (Mosaic Analysis with Double Markers) technology.
- Emergence of cell-type diversity in developing superior colliculus.
- Lineage progression of neural progenitors in superior colliculus.
- Determination of progenitor potential by MADM-CloneSeq.
- Assessment of molecular determinants in generating neuronal diversity in superior colliculus.

*Asymmetry
2022*



<https://ist.ac.at/en/research/hippenmeyer-group/>

Gregor Eichele

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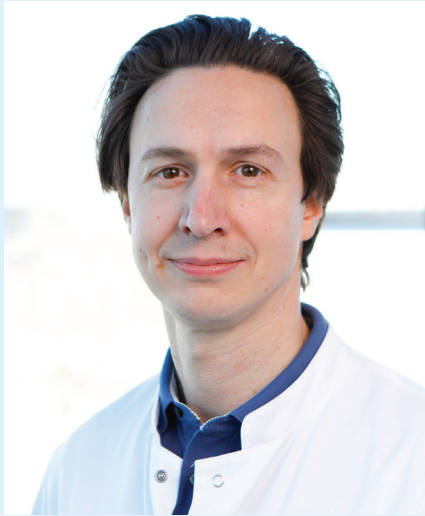


Fluid Flow in the Mammalian Brain Ventricles

Cerebrospinal fluid (CSF) flows through the four brain ventricles. Fresh CSF and its constituents is continuously produced by (or translocated across) the secretory epithelium of the choroid plexi that reach into the ventricular cavities. CSF transport is driven by changes in blood pressure and, along the ventricular walls, by beating cilia that protrude from the interior wall of ventricles. We discovered that in the narrow hypothalamic ventricle, CSF flow patterns display sharp curves, turns, divergences and convergences that reach a velocity in the range of 0.5 mm per second and are in many cases only a few micrometers wide. We show that CSF flows reproducibly move nanometer-size particles. We discuss how such network of flows arise as a result of cell-polarity-mediated ciliary beating. Initial experiments suggest that extracellular vesicles (EVs) are physiologically relevant cargo that is transported by the ventricular flows. These EVs arise in the choroid plexus and the flows carry them to the NSCs during postnatal development and also in the adult brain.



<https://www.mpinat.mpg.de/eichele>



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Lipid droplet (LD) accumulation in residing microglia and its impact on post-stroke neuroregeneration

In the field of **translational stroke research**, I will report the following:

- Distinct lipid profiles lead to lipid droplet (LD) formation in microglia which promote microglial activation and inflammation and various conditions.
- Under in vitro conditions, oxygen-glucose-deprivation (OGD) and LPS induce LD formation in primary microglia.
- Middle cerebral artery occlusion (MCAO) induces the formation of LD in microglia under in vivo stroke conditions.
- Such microglia enriched with LD may play a double-edged role in neuronal ischemic injury via regulating lipid metabolism.
- Altered lipid metabolism affects phenotype polarization and inflammatory characteristics in microglia.
- Ischemia-induced accumulation of LDs triggers the activation of the pro-inflammatory NF-κB pathway.
- Definition of differences in lipid classes by lipidomic analysis indicates that the infarct core exhibits a unique lipid profile.
- Defined lipid profiles correlate with both post-stroke neuroregeneration and neurological recovery.



https://www.ukgm.de/ugm_2/deu/ugi_neu/index.html

Harold Cremer

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Neuronal integration in the postnatal and adult olfactory bulb

In the field of **adult neurogenesis**, I will report on:

- Long-term in vivo imaging of olfactory bulb neurogenesis.
- Neurons are added to the existing circuitry.
- Cell death in the olfactory bulb is rare.
- Thymidine analogues are toxic in long term experiments.
- The olfactory bulb grows throughout life.
- Activity during migration predicts neuronal integration.

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Nicolas Toni

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Regulation of adult hippocampal neurogenesis in the context of anxiety

In the field of **adult neurogenesis**, I will report the following:

- Adult hippocampal stem cells establish perivascular processes at sites of decreased blood-brain barrier permeability.
- In vitro, stem cell proliferation is regulated by blood-circulating molecules.
- Spontaneously anxious mice show decreased neurogenesis.
- The serum from spontaneously anxious mice inhibits neurogenesis in vitro.
- The serum from human anxious psychiatry patients inhibits neurogenesis in vitro.
- Anxious humans and mice share similarities in their serum molecular signatures.
- Targeting blood-circulating molecules increases stress resilience and adult neurogenesis.
- Our results suggest that blood circulating molecules in anxious individuals decrease neurogenesis, leading to decreased stress resilience.

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Network biology, bioinformatics and computational biology, multi-omics integration, in-silico variant pathogenicity assessment

In the field of *multi-omics methods for neurogenesis studies*, I will report the following:

- Most neurogenesis studies have focused on the analysis of single-omics data for years.
- Multi-omics approaches are still relatively new in this field: what's there behind?
- Traditional strategies of data integration: conceptual integration, statistical integration, model-based integration, and pathway data integration.
- Machine-learning-based multi-omics data integration: networks analysis and neural networks.





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Transcriptional profiling of adult monkey neurogenic zones following cerebral ischemia

In the field of **adult primate neurogenesis**, I will report the following:

- The adult monkey subventricular zone (SVZ) can be subdivided into anterior (SVZa) and inferior (SVZi) subdomains.
- Brain ischemia activates progenitors in both domains.
- The SVZa and the SVZi show differential neurogenic potential after ischemia.
- Transcriptomic analyzes demonstrate that global brain ischemia elicits differential gene expression response in SVZa and SVZi.
- Novel gene markers for primate SVZ including the apelin receptor are strongly expressed in the primate SVZa niche upon ischemic insult.

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2022*



<https://www.mu-varna.bg/EN/anton-tonchev>

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Reconstruction of cortical neuronal networks with human reprogrammed cells

In the field of **neurodegeneration and neuroregeneration**, I will report the following:

- The human skin-derived cortical progenitors can differentiate into cortical projection neurons
 - The human skin-derived cortical progenitors functionally integrate (forming afferent and efferent synaptic connections) into stroke-damaged rat cortical networks
 - The human skin-derived cortical progenitors functionally integrate into organotypic cultures of the adult human cortex.
 - The grafted cortical neurons respond to sensory stimulation of in live animals and affect spontaneous behavior when inhibited by optogenetic stimulation.
 - The human skin-derived cortical progenitors can also differentiate into bona fide oligodendrocytes.
 - The generated cells display the structural, molecular, and functional characteristics of human mature oligodendrocytes.
 - The human skin-derived oligodendrocytes can wrap both grafted human cell- and host-derived axons from cortical neurons after xenotransplantation into rat stroke-injured somatosensory cortex and the human adult cortical organotypic system.
 - Our findings raise the possibility that injured neural circuitry might be restored by reprogrammed cell transplantation also in humans with stroke, which would have major clinical implications.





Federico Calegari

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Improving brain function by expansion of neural stem cells

In the field of **adult neurogenesis**, I will report the following:

- Shortening G1 of neural stem cells promotes their expansion.
- Increased olfactory neurogenesis promotes odor discrimination.
- Increased hippocampal neurogenesis promotes learning and memory rescuing age-related cognitive impairment.
- Insights into mechanisms underlying cognitive performance will be presented.

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[https://tu-dresden.de/cmcb/crtd/forschungsgruppen/
crtd-forschungsgruppen/calegari](https://tu-dresden.de/cmcb/crtd/forschungsgruppen/crtd-forschungsgruppen/calegari)



Noelia Urbán

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Local and systemic regulation of adult neurogenesis

In the fields of **adult neurogenesis and neural stem cell quiescence**, I will report and discuss the following:

- Intermittent fasting does not affect adult neural stem cells in the hippocampus, making it a safe intervention to increase life span and healthy ageing.
- In contrast to what was previously accepted, intermittent fasting does not increase the number of new neurons generated in the hippocampus, regardless of strain, sex or experimental set up.
- Heterogeneity is an essential characteristic of adult neural stem cells and is manifested at transcriptomic, proteomic and metabolic levels.
- The transition of adult neural stem cells between active and quiescent states is not linear, with multiple equivalent quiescence “levels” possible.
- Our work puts forward a comprehensive, integrative and dynamic model of aNSC states.
- The model will be of importance for other adult stem cell systems in which quiescence plays a crucial role, such as the muscle or the blood, for reprogramming strategies and for cancer research.





Pierre Lavenex

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Lesion-induced plasticity in the primate medial temporal lobe

Immature neurons expressing the Bcl2 protein are present in various regions of the mammalian brain, including the amygdala and the entorhinal and perirhinal cortices. I will discuss recent studies showing different structural changes in distinct subdivisions of the monkey entorhinal and perirhinal cortices following selective hippocampal lesions, which were further influenced by the time of the lesion.

Bcl2-positive cells were found mainly in areas Eo, Er and Elr of the entorhinal cortex and in layer II of the perirhinal cortex. In neonate-lesioned monkeys, the number of immature neurons in the entorhinal and perirhinal cortices was generally higher than in controls. The number of mature neurons was also higher in layer III of area Er of neonate-lesioned monkeys but no differences were found in layer II of area 36. In adult-lesioned monkeys, the number of immature neurons in the entorhinal cortex was lower than in controls but did not differ from controls in the perirhinal cortex. The number of mature neurons in layer III of area Er did not differ from controls, but the number of small, mature neurons in layer II of area 36 was lower than in controls.

In sum, hippocampal lesions impacted populations of mature and immature neurons in discrete regions and layers of the entorhinal and perirhinal cortices, which are interconnected with the amygdala and provide major cortical inputs to the hippocampus. These structural changes may contribute some functional recovery following hippocampal injury in an age-dependent manner.



<https://www.unil.ch/labcd/en/home/menuinst/research/nlm.html>

Bogdan Draganski

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The curious case of modulating human hippocampal neurogenesis

In the field of **adult neurogenesis**, I will review the following topics:

- Epileptic seizures are thought to boost human adult neurogenesis.
- Electro-convulsive treatment (ECT) for pharmaco-resistant depression is associated with > 70% remission.
 - ECT induces a generalised seizure and is administered over 8-10 weeks twice weekly.
 - There is accumulating empirical evidence about ECT-induced structural brain changes.
 - ECT-induced changes are confined to hippocampus.
 - The link between ECT-induced hippocampus changes and mood improvement is unclear.
 - I demonstrate ECT-induced brain-behaviour correlation along the hippocampus longitudinal axis.
 - I argue that ECT-induced changes may represent a proxy for seizure's impact on adult neurogenesis.





Nadejda (Nadia) Tsankova

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The right place at the right time: Multi-omics resolves the transience and diversity during human gliogenesis and provides clues to diseased states

In the fields of *neurodevelopment and neuro-oncology*, I will report the following:

- Transcriptomic and chromatin accessibility atlas of second and third-trimester human neocortical development, capturing the transience and diversity of glial and non-glial cell types, states, and differentiation trajectories in the germinal matrix and cortical plate.
 - ASCL1⁺⁺EGFR⁺OLIG2⁻ multipotent progenitor (mIPC), restricted to the germinal matrix
 - EGFR⁺⁺OLIG2⁺⁺ common glial progenitor cell type (gIPC), present in both the germinal matrix and the cortical plate.
 - PDGFRB⁺⁺EGFR⁻ radial glia / astrocyte (RG-AC) population in the germinal matrix
 - Computational reconstruction of glial lineages identifies astrocyte-restricted (gIPC-A) and oligodendroglial-restricted (gIPC-O) glial intermediates, as well as two distinct pathways of astrogenesis.
 - NOTCH signaling and the ZEB1 transcription factor are putative regulators in gIPC-O biology whereas the FOXO1 transcription factor is a putative regulator of gIPC-A biology.
 - Abundant representation of gIPC developmental states in glioblastoma heterogeneity, across adult and pediatric tumors.



<https://labs.icaohn.mssm.edu/tsankovalab/>

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Circulating histone signature of pediatric Diffuse Intrinsic Pontine Glioma (DIPG)

In the field of **tumors of the brainstem**, I will report the following:

- Pediatric aggressive brain tumors with low survival: focus on diffuse intrinsic pontine glioma (DIPG). Histone H3K27M mutation identifies ~30% of the cases.
- There is a urgent need to improve the survival by targeting biofluids such as cerebrospinal fluids (CSF) and blood plasma for optimizing molecular diagnoses in DIPG.
- A total of 20 healthy children and 25 children diagnosed with DIPG were recruited. Individual histones, histone dimers and nucleosomes were assayed in serum samples by means of advanced multi-channel flow cytometry ImageStream(X).
- We report a significant upregulation of histone dimers and tetramers and a significant downregulation of individual histones, suggesting the involvement of histone chaperones.
- Histones are also detectable with a robust signal in the CSF of DIPG children.
- A new circulating histone signature is able to discriminate the presence DIPG in children, using a non-invasive imaging technology.



<http://transtem.org/en/news/>



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Art, music and the ill and recovering brain

In my presentation I will cover the following topics:

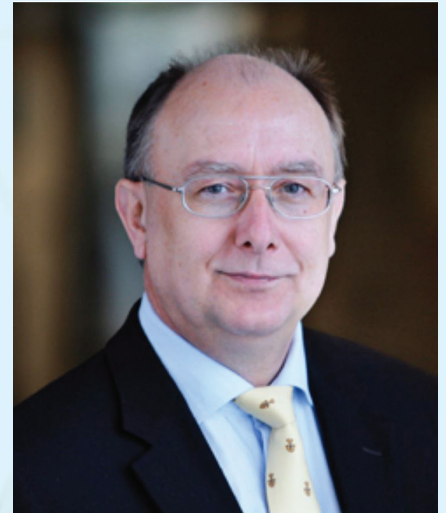
- What is art - art as the product of a creative brain - hemispheric dominance and creativity – neuro-scientific approach to art
- Effect of neurological disease on the creative output of artists and composers
- Neurological disorders associated with creative practice
- Art and music-based interventions – enhancing neuroplasticity in the treatment and rehabilitation of psychiatric and neurological disorders



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Neocortex expansion in development and human evolution – the role of metabolism

In the field of *neocortical neurogenesis in development and evolution*, I will discuss the following topics:

- The human-specific gene ARHGAP11B, which expanded the neocortex during human evolution, gives rise to a protein that is imported into mitochondria and promotes glutaminolysis in basal progenitors.
- Glutaminolysis is a metabolic pathway characteristic of mitotically very active cells, and its increase in basal progenitors leads to their amplification, which in turn underlies neocortex expansion.
- Modern human transketolase-like 1 (TKTL1), but not Neanderthal TKTL1 which differs by just 1 amino acid, specifically amplifies basal radial glia, the basal progenitor type implicated in neocortex expansion, and consequently increases neuron number.
- Modern human TKTL1 acts in the pentose phosphate pathway and causes an increase in fatty acid synthesis, which is required for basal radial glia amplification.

<https://www.mpi-cbg.de/research/researchgroups/currentgroups/wieland-huttner/group-leader/>





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Evolution of thalamocortical development

In the field of **neurodevelopment and evolutionary biology**, I will report the following:

- Conscious perception in mammals depends on precise circuit connectivity between the cerebral cortex and thalamus; the evolution and development of these structures are closely linked.
- During the wiring of reciprocal connections between cortex and thalamus, thalamocortical axons (TCAs) first navigate forebrain regions that had undergone substantial evolutionary modifications.
- In particular, the organization of the pallial subpallial boundary (PSPB) diverged significantly between mammals, reptiles, and birds.
- In mammals, transient cell populations in internal capsule and early corticofugal projections from subplate neurons closely interact with TCAs to enable PSPB crossing.
- Prior to TCA arrival, cortical areas are initially patterned by intrinsic genetic factors.
- TCAs then innervate cortex in a sensory modality specific manner to refine cortical arealization and form primary sensory areas.
- Here, we review the mechanisms underlying the guidance of TCAs across forebrain boundaries, the implications of PSPB evolution for TCA pathfinding, and the reciprocal influence between TCAs and cortical areas during development.

Reference: Zoltán Molnár and Kenneth Y. Kwan (2023) Development and evolution of thalamocortical connectivity. "Evolution and Development of Neural Circuits" Cold Spring Harbor Perspectives in Biology, Edited by Laura Andreae, Justus Kebschull, Anthony Zador (invited review in preparation).



POSTERS

Role of Notch Signaling Pathway in Radial Glial Progenitor Lineage Progression

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A cell fate decision map reveals abundant direct neurogenesis in the human developing neocortex

Coquand L, Brunet Avalos C, Macé AS, Farcy S, Di Cicco A, Lampic M, Bessières B, Attie-Bitach T, Fraisier V, Guimiot F, Baffet A.

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Extracellular vesicles of specific composition promote neural stem cells differentiation

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Association between YKL-40 and mitochondrial dysfunction in patients with Autism Spectrum Disorder

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Ultrastructural Study of The Effect of Salicylic Acid in Wistar Rats' Retina and The Role of NMDA Receptor Blockers

Ilaridou I, Liatsos A, Papadopoulou K, Pavlidis P, Tseriotis V, Sardeli C, Kavvadas D, Dombri K, Thimiaki P, Eleftheriadis T, Kapourani V, Fandel G, Kouvelas D, Sioga A, Papamitsou T, Karachrysafti S.

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Anti-obesity compounds reduce obesity and promote adult neurogenesis

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Effects of diet and exercise on adult neurogenesis in the hypothalamic neurogenic niche

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Role of Pten in RGP lineage progression at single-cell resolution using Mosaic Analysis with Double Markers

Miranda OA, Contreras X, Pauler F, Davaatseren M, Amberg N, Hippenmeyer S.

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Immunophenotype of Apelin receptor expressing cells in the adult human subventricular zone

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Joint epigenome profiling reveals cell-type-specific gene regulatory programs in human cortical organoids

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Non-cell-autonomous regulation of interneuron specification mediated by extracellular vesicles

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Self-organizing Principles are Insufficient for Cortical Stem Cell Lineage Progression

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Zbtb20 is required for cortical interneuron development

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Postpartum Depression - Genetic Profiling and Its Correlation with Levels of Oxytocin

Tsokkou S, Katsikidou T, Michail K, Tsiakalos S, Kavvadas D, Georgaki NM, Papamitsou T, Karachrysafti S.

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Expression of the transcription factor ZBTB20 in the subventricular zone of adult macaque monkey under physiological and ischemic conditions-

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Rptor/mTORC1 Function in Radial Glia Progenitor Lineage Progression

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Adult Hippocampal Neurogenesis in Primates

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Interphasic Somal Translocation is a prominent mode of bRG cell dissemination in the human developing neocortex

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BLACK SEA NEUROGENESIS
Varna, Bulgaria, 1-3 June 2023





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