PROGRAM FOR THE CONFERENCE

Developing Brains

Biomedicum, Karolinska Institutet, Sweden
September 5th, 2019

Karolinska Institutet

FOREWORD

How can a single cell give rise to complex structures such as the central (brain/spinal cord) and peripheral (including the brain in the gut) nervous systems? This is the overarching question in neural development; knowing how such intricate structures are assembled gives not only crucial knowledge about these nervous systems, but also important insight to the etiology of some of our most common diseases.

The 6th edition of the KI Conference "Developing Brains" gathers some of the leading scientists working on critical questions ranging from transcriptional and functional heterogeneity of neural cell types, patterning during their specification, emerging roles of glia and creation of mature neural circuits.

Gonçalo Castelo-Branco, Jens Hjerling-Leffler,
Ulrika Marklund and Francois Lallemend

PROGRAM

5TH SEPTEMBER 2019, BIOMEDICUM 1

ORGANIZERS

Gonçalo Castelo-Branco
Jens Hjerling-Leffler
Ulrika Marklund
Francois Lallemend

08.30-09.00	**Registration**
9.00-9.10	**Welcoming address**

SESSION I: PRINCIPLES OF DEVELOPMENT I

CHAIR: Francois Lallemend, Karolinska Institutet, Stockholm, Sweden

9.10-10.00	**Specification of spinal cord pattern by opposing morphogen gradients.** *Anna Kicheva, IST, Austria*
10.00-10.20	**COFFEE BREAK**
10.20-11.10	**Genetic aspects of the temporal patterning of cortical neurogenesis** *Ludovic Telley, University of Lausanne, Switzerland*

SESSION II: PRINCIPLES OF DEVELOPMENT II

CHAIR: Ulrika Marklund, Karolinska Institutet, Stockholm, Sweden

11.10-12.00	**Mechanisms of synaptic specificity underlying interneuronal circuit formation** *Julia Kaltschmidt, Stanford University School of Medicine, USA*
12.00-12.50	**A revised anatomy of the autonomic nervous system** *Jean-François Brunet, IBENS, Paris, France*
12.50-13.50	**LUNCH BREAK**

SESSION III: GLIA IN THE CENTRAL NERVOUS SYSTEM

CHAIR: Gonçalo Castelo-Branco, Karolinska Institutet, Stockholm, Sweden

13.50-14.40 **What do reactive astrocytes (really) do?**
Shane Liddelow, NYU Langone Medical Center, USA

14.40-15.30 **How do glia sculpt synaptic circuits?**
Çağla Eroğlu, Duke University Medical Center, USA

15.30-15.50 **COFFEE BREAK**

SESSION IV: NEURONAL NETWORKS IN THE CENTRAL NERVOUS SYSTEM

CHAIR: Jens Hjerling-Leffler, Karolinska Institutet, Stockholm, Sweden

15.50-16.40 **Post-translational palmitoylation and the regulation of synaptic plasticity**
Shernaz X. Bamji, University of British Columbia, Canada

16.40-17.30 **Mechanisms of experience-dependent plasticity in GABAergic microcircuits in the cortex**
Ivo Spiegel, Weizmann Institute of Science, Israel

17.30-17.40 **CLOSING REMARKS**

“Specification of spinal cord pattern by opposing morphogen gradients.”

ANNA KICHEVA
IST, Austria

Anna Kicheva is an Assistant Professor at IST Austria since November 2015. She studies the control of tissue growth and pattern formation during development. The research aim of her group is to unravel the feedbacks between cell fate specification, tissue growth and morphogen signaling in the developing spinal cord. Their approach combines biophysics, mouse genetics, and ex vivo assays.

Anna started working on spinal cord development during her postdoc with James Briscoe at the NIMR (currently Francis Crick) in London. Before that she did her PhD with Marcos Gonzalez-Gaitan at the MPI-CBG in Dresden and the University of Geneva, studying morphogen gradient formation in the Drosophila wing disc.

Selected publications

Guerrero P, Perez-Carrasco R, Zagorski M, Page D, Kicheva A*, Briscoe J*, Page K*. Neuronal differentiation affects tissue mechanics and progenitor arrangement in the vertebrate neuroepithelium.
bioRxiv 536342; doi: 10.1101/536342

Zagorski M, Brandenberg N, Tabata Y, Tkacik G, Lutolf MP, Bollenbach T*, Briscoe J*, Kicheva A* (2017) Specification of spinal cord pattern by opposing morphogen gradients. ***Science*** 356 (6345): 1379-1383.

Kicheva A* and Briscoe J*. (2015) Developmental pattern formation in phases. ***Trends Cell Biol.*** 25(10):579-91.

Kicheva A, Bollenbach T, Ribeiro A,Valle HP, Rovell-Badge R, Episkopou V, Briscoe J. (2014) Coordination of progenitor specification and growth in mouse and chick spinal cord. ***Science*** 345 (6204):1254927.

Kicheva A, Cohen M, Briscoe J. (2012) Developmental pattern formation: insights from physics and biology. ***Science*** 338, 210.

Homepage:
https://ist.ac.at/en/research/life-sciences/kicheva-group/

“Genetic aspects of the temporal patterning of cortical neurogenesis”

LUDOVIC TELLEY
University of Lausanne, Switzerland

Ludovic Telley obtained his PhD in Neurosciences at the University of Montpellier (France), where he studied the cerebellar development in the laboratory of Dr Fabrice Ango at the Institut de Génomique Fonctionnelle (IGF). After his graduation, he started a postdoctoral fellowship at the University of Geneva in the laboratory of Prof. Denis Jabaudon. In the following years, he developed a solid dual expertise in single cells transcriptomics and bioinformatics, including state-of-the-art machine learning approaches. He recently started his research group (February 2018) at the University of Lausanne with the support of an ERC Starting Grant. His research is focused on cerebellar development, particularly in understanding the molecular programs that control cerebellar neuron differentiation, interaction and assembly into functional circuits which serve as a basis for the cerebellar various functions. To address these questions, he is combining single-cells technologies, bioinformatics tools and in vitro/in vivo gain- and loss-of-function strategies.

Selected publications

Sequential transcriptional waves direct the differentiation of newborn neurons in the mouse neocortex. Telley L, Govindan S, Prados J, Stevant I, Nef S, Dermitzakis E, Dayer A, Jabaudon D
Science, *2016, Volume 35, Issue 6280, 1143-1446.*

A mixed model of neuronal diversity
Telley L, Jabaudon D
Nature, *2018, Volume 555, 452-454, News and Views.*

Progenitor Hyperpolarization Regulates the Sequential Generation of Neuronal Subtypes in the Developing Neocortex.
Vitali I, Fièvre S, Telley L, Oberst P, Bariselli S, Frangeul L, Baumann N, McMahon JJ, Klingler E, Bocchi R, Kiss JZ, Bellone C, Silver DL, Jabaudon D. ***Cell,*** *2018, Volume 174, 2018, 1264-1276.*

A cross-modal genetic framework for the organization and plasticity of sensory pathways.,
Frangeul L, Pouchelon G, Telley L, Lefort S, Lüscher C, Jabaudon D.
Nature, *2016, Volume 538, Issue 7623, 96-98.*

Dual Function of NRP1 in Axon Guidance and Subcellular Target Recognition in Cerebellum. Telley L, Cadilhac C, Cioni JM, Saywell V, Huettl R, Sarrailh-Faivre C, Dayer A, Huber A, Ango F.
Neuron, *2016, Volume 91, Issue 6, 1276-1291.*

Homepage:

https://wwwfbm.unil.ch/dnf/group/molecular-mechanisms-of-cerebellar-development/member/telley-ludovic-telley

“Mechanisms of synaptic specificity underlying interneuronal circuit formation”

JULIA KALTSCHMIDT

Stanford University School of Medicine, USA

Julia Kaltschmidt is a Wu Tsai Neurosciences Institute Faculty Scholar and an Associate Professor in the Department of Neurosurgery at Stanford Medical School. Originally from Germany, she received my undergraduate degree in Molecular Biology and Biochemistry from the University of Madison, Wisconsin. Julia then completed her PhD at the University of Cambridge in the UK, where she trained as a developmental biologist and studied the cellular mechanisms underlying early Drosophila nervous system development. During her postdoc at Columbia University, she began working with mouse as a model system, and became interested in mechanisms that underlie sensory-motor circuit connectivity in the spinal cord. She continued to explore the development and molecular regulation of spinal circuity as an Assistant Professor at the Sloan Kettering Institute in New York City. During this time, the focus of Julia's laboratory further expanded to include neuronal circuits that underlie sexual function and gut motility.

Selected publications

Zhang J, Weinrich JAP, Russ JB, Comer JD, Bommareddy PK, CiCasoli RJ, Wright CVE, Li Y, van Roessel PJ, Kaltschmidt JA. A role for Dystonia-Associated Genes in Spinal GABAergic Interneuron Circuitry.
Cell Rep 2017 Oct 17;21(3): 666-678.

Mende M, Fletcher EV, Belluardo JL, Pierce JP, Bommareddy PK, Weinrich JA, Kabir ZD, Schierberl KC, Pagiazitis JG, Mendelsohn AI, Francesconi A, Edwards RH, Milner TA, Rajadhyakscha AM, van Roessel PJ, Mentis GZ, Kaltschmidt JA. Sensory-Derived Glutamate Regulates Presynaptic Inhibitory Terminals in Mouse Spinal Cord.
Neuron 2016 Jun 15;90(6):1189-1202.

Ashrafi S, Betley JN, Comer JD, Brenner-Morton S, Bar V, Shimoda Y Watanabe K, Peles E, Jessell TM, Kaltschmidt JA. Neuronal Ig/Caspr recognition promotes the formation of axoaxonic synapses in mouse spinal cord.
Neuron 2014 Jan 8;81(1):120-9.

Betley JN, Wright CV, Kawagushi Y, Erdelyi F, Szabo G, Jessell TM, Kaltschmidt JA. Stringent specificity in the construction of a GABAergic presynaptic inhibitory circuit.
Cell 2009 Oct 2;139(1):161-74.

Homepage:

http://med.stanford.edu/kaltschmidt-lab.html

“A revised anatomy of the autonomic nervous system”

JEAN-FRANÇOIS BRUNET
IBENS, Paris, France

Jean-François Brunet completed an MD (1984) and a PhD in immunology (1987), started working on the nervous system during a post-doc at Columbia University (1988-1990), joined the Centre National de la Recherche Scientifique, leading a group of developmental neuroscience first at the Developmental Biology Institute of Marseillle (1993-2001), then at the École Nomale Supérieure in Paris (2002-Present). He studies the neural control of vital functions (breathing, digestion and blood circulation) in an effort to integrate its developmental, evolutionary and physiological dimensions.

Selected publications

Espinosa-Medina I, Outin E, Picard CA, Chettouh Z, Dymecki S, Consalez GG, Coppola E, Brunet JF. (2014) Parasympathetic ganglia derive from Schwann cell precursors. ***Science*** *345:87-90*

Espinosa-Medina I, Saha O, Boismoreau F, Chettouh Z, Rossi F, Richardson WD, Brunet JF. (2016)
The sacral autonomic outflow is sympathetic. ***Science*** *354:893-897*

Espinosa-Medina I, Jevans B, Boismoreau, Chettouh Z, Enomoto H, Müller T, Birchmeier C, Burns, A.J., and Brunet JF. (2017) Dual origin of enteric neurons in vagal Schwann cell precursors and the sympathetic neural crest
Proc Natl Acad Sci U S A. 114:11980-11985

Espinosa-Medina I, Saha O., Boismoreau, and Brunet JF. (2018) The sacral «parasympathetic»: Ontogeny and anatomy of a myth. ***Clinical Autonomic Research*** 28:13-21.

Homepage:

https://www.ibens.ens.fr/spip.php?rubrique12&lang=en

"What do reactive astrocytes (really) do?"

SHANE LIDDELOW

NYU School of Medicine, USA

Shane Liddelow gained his Bachelors of Science and Biomedical Science from the University of Melbourne, Australia, majoring in Neuroscience and Anatomy & Cell Biology. He received his PhD with Katarzyna Dziegielewska and Norman Saunders in Pharmacology also from the University of Melbourne. His graduate work focused on the protective barriers of the brain during early development. As a postdoctoral fellow in the lab of Ben Barres at Stanford University he discovered a close association between astrocytes, microglia, and abnormal neuron function. His most recent research showed that one form of reactive astrocyte is induced by factors released by microglia. These reactive astrocytes release a toxic factor that kills specific subtypes of neurons and are present in brains of patients with multiple neurodegenerative diseases like Alzheimer's and amyotrophic lateral sclerosis.His lab at NYU School of Medicine in New York City continues to investigate the functions of glial cells and how they change between normal physiological and pathological states.Shane was a recipient of the NHMRC (Australia) CJ Martin Training Award (2012-2016), the Glenn Foundation award for Aging in 2016, and The Inge Grundke-Iqbal Award for Alzheimer's Research in 2019 as author of the most impactful study published in Alzheimer's research over the preceding two years.

Selected publications

Liddelow SA, Guttenplan KA, Clarke LE, Bennett FC, Bohlen CJ, Schirmer L, Bennett ML, Münch AE, Chung W-S, Peterson TC, Wilton DK, Frouin A, Napier BA, Panicker N, Kumar M, Dawson VL, Dawson TM, Buckwalter MS, Rowitch DH, Stevens B, Barres BA (2017) Neurotoxic reactive astrocytes are induced by activated microglia. ***Nature*** 541:481-487. PMID: 28099414.

Shi Y, Yamada K, Liddelow SA, Smith ST, Zhao L, Luo W, Tsai R, Spina S, Grinberg L, Rojas J, Gallardo G, Wang K, Roh J, Robinson G, Finn MB, Jiang H, Sullivan P, Wood M, Baufeld C, Wood M, Sutphen C, McCue L, Xiong C, Del-Aguila J, Morris J, Cruchaga C, Fagan A, Miller B, Boxer B, Seeley W, Butovsky O, Barres B, Paul S, Holtzman D (2017) ApoE4 markedly exacerbates tau-mediated neurodegeneration in a mouse model of tauopathy. ***Nature*** 549:523-527. PMID: 28959956.

Clarke LE, Liddelow SA, Chakraborty C, Münch AE, Heiman M, Barres BA (2018) Normal aging induces A1-like astrocyte reactivity. ***Proc Natl Acad Sci USA*** 115(8):E1896-E1905. PMID: 29437957.

Gibson EM, Nagaraja S, Ocampo A, Tam LT, Wood LS, Pallegar PN, Greene JJ, Geraghty AC, Goldstein AK, Ni L, Woo PJ, Barres BA, Liddelow S, Vogel H, Monje M (2018) Methotrexate chemotherapy induces persistent tri-glial dysregulation that underlies chemotherapy-related cognitive impairment. ***Cell*** 176(1-2):43-55. PMID: 30528430.

Guttenplan KA, Liddelow SA (2018) Astrocytes and microglia: Models and tools. ***J Exp Med*** 216(1):71-83. PMID: 30541903.

Homepage:

https://www.liddelowlab.com/

"How do glia sculpt synaptic circuits?"

ÇAĞLA EROĞLU
Duke University Medical Center, USA

Cagla Eroglu, Ph.D. is Associate Professor of Cell Biology and Neurobiology, Director of Graduate Studies in Cell and Molecular Biology and Co-Director, Regeneration Next Initiative, Duke University.

Dr. Eroglu's laboratory investigates the cellular and molecular underpinnings of how synaptic circuits are established and remodeled in the mammalian brain by the bidirectional signaling between neurons and glia and how disruption of these mechanisms contributes to the pathogenesis of neurological disorders.

Selected publications

Risher WC*, Kim N, Koh S, Choi J-E, Mitev P, Spence EF, Pilaz L-J, Wang D, Feng G, Silver DL, Soderling SH, Yin HH and Eroglu C* (2018). Thrombospondin receptor α2δ-1 promotes synaptogenesis and spinogenesis via postsynaptic Rac1. ***J Cell Biol.,*** Oct 1; 217(10):3747-3765. PMCID: PMC6168259.

Koh S, Chen WJ, Dejneka NS, Harris IR, Lu B, Girman S, Saylor J, Wang S and Eroglu C* (2018). Subretinal Human Umbilical Tissue-Derived Cell Transplantation Preserves Retinal Synaptic Connectivity and Attenuates Müller Glial Reactivity. ***J. Neuroscience,*** Feb 5, 1532-17.

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,*** Nov 9;551, 192–197. PMCID: PMC5796651.

Singh SK*, Stogsdill JA, Pulimood NS, Dingsdale H, Kim YH, Pilaz LJ, Kim IH, Manhaes AC, Rodriguez-Junior WS, Pamukcu A, Enustun E, Ertuz Z, Scheiffele P, Soderling S, Silver DS, Ji R-R, Medina AE, Eroglu C* (2016). Astrocytes assemble thalamocortical synapses by bridging neurexin1-alpha and neuroligin-1 via hevin. ***Cell,*** Jan 14:164(1-2):183-196. PMCID: PMC4715262

Eroglu C*, Allen NJ, Susman MW, O'Rourke NA, Park CY, Ozkan E, Chakraborty C, Mulinyawe SB, Annis DS, Huberman AD, Green EM, Lawler J, Dolmetsch R, Garcia KC, Smith SJ, Luo ZD, Rosenthal A, Mosher DF, Barres BA (2009). Gabapentin receptor alpha2delta-1 is a neuronal thrombospondin receptor responsible for excitatory CNS synaptogenesis. ***Cell*** 139: 380-392. PMCID: PMC2791798.

Homepage:

https://sites.duke.edu/eroglulab/

"Post-translational palmitoylation and the regulation of synaptic plasticity"

SHERNAZ BAMJI
University of British Columbia, Canada

Shernaz Bamji received her Ph.D. at McGill University and did her postdoctoral training at the University of California, San Francisco. Dr. Bamji is currently a full professor in the Department of Cellular and Physiological Sciences at the University of British Columbia and is Vice-President elect of the Canadian Association for Neurosciences. Dr. Bamji has a long-standing interest in understanding the molecular and cellular mechanisms underlying neural connectivity and synaptic plasticity. Her work has provided valuable information about fundamental mechanisms underlying learning and memory, as well as how these processes are perturbed in diseased states.

Selected publications

Brigidi GS, Sun Y, Beccano-Kelly D, Pitman K, Mobasser M, Borgland SL, Milnerwood AJ, Bamji SX.
Palmitoylation of δ-catenin by DHHC5 mediates activity-induced synapse plasticity.
Nat Neurosci. 2014 Apr;17(4):522-32. doi: 10.1038/nn.3657. Epub 2014 Feb 23.

Brigidi GS, Santyr B, Shimell J, Jovellar B, Bamji SX.
Activity-regulated trafficking of the palmitoyl-acyl transferase DHHC5.
Nat Commun. 2015 Sep 3;6:8200. doi: 10.1038/ncomms9200.

Mills F, Globa AK, Liu S, Cowan CM, Mobasser M, Phillips AG, Borgland SL, Bamji SX. Cadherins mediate cocaine-induced synaptic plasticity and behavioral conditioning.
Nat Neurosci. 2017 Apr;20(4):540-549. doi: 10.1038/nn.4503. Epub 2017 Feb 13.

Globa AK, Bamji SX.
Protein palmitoylation in the development and plasticity of neuronal connections. ***Curr Opin Neurobiol.*** 2017 Aug;45:210-220. doi: 10.1016/j.conb.2017.02.016. Epub 2017 Mar 30. Review.

Homepage:
https://www.bamjilab.com/

"Mechanisms of experience-dependent plasticity in GABAergic microcircuits in the cortex"

IVO SPIEGEL

Weizmann Institute of Science, Israel

Ivo Spiegel received his B.Sc. in Biology from the Tel-Aviv University and his M.Sc. in Life Sciences from the Weizmann Institute of Science in Rehovot, Israel. He then conducted his Ph.D.-research with Prof. Elior Peles at the Weizmann Institute of Science where he identified the molecular cues that initiate myelin-wrapping during myelination of the peripheral nervous system. During his postdoctoral research with Dr. Michael E. Greenberg at Harvard Medical School, Dr. Spiegel analyzed the structure and function of experience-induced gene networks in excitatory and inhibitory neurons in the cortex. In his own lab in the Department of Neurobiology at the Weizmann Institute of Science, Dr. Spiegel and his team focus on how different types of cortical GABAergic neurons – via their subtype-specific genetic programs – control experience-dependent functions of the cortex, including sensory processing and memory formation. To this end, the Spiegel-lab takes a comprehensive Molecular Systems Neuroscience approach that combines intersectional mouse genetics, genomic analyses, various molecular trickeries, electrophysiology and in vivo calcium imaging in awake behaving mice.

Selected publications

Gray J.M., Spiegel I. (2018). Cell-type-specific programs for activity-regulated gene expression. ***Curr Opin Neurobiol,*** 56:33-39.

Abs E., Poorthuis R.B., Apelblat D., Muhammad K., Pardi M.B., Enke L., Kushinsky D., Pu D.L., Eizinger M.F., Conzelmann K.K., Spiegel I., Letzkus J.J. (2018). Learning-Related Plasticity in Dendrite-Targeting Layer 1 Interneurons. ***Neuron,*** 100;684-699

Mardinly A.R., Spiegel I.*, Patrizi A., Centofante E., Bazinet J.E., Tzeng C.P., Mandel-Brehm C., Harmin D.A., Adesnik H.A., Fagiolini M., Greenberg M.E. (2016). Sensory experience regulates cortical inhibition by inducing IGF1 in VIP neurons. ***Nature*** 531(7594):371-375

Spiegel I., Mardinly A.R.*, Gabel H.W., Bazinet J.E., Couch C.H., Tzeng C.P., Harmin D.A., Greenberg M.E. (2014). Npas4 regulates excitatory-inhibitory balance within neural circuits through cell-type specific gene programs. ***Cell*** 157(5):1216-1229.

Homepage:

https://www.weizmann.ac.il/neurobiology/labs/spiegel/welcome

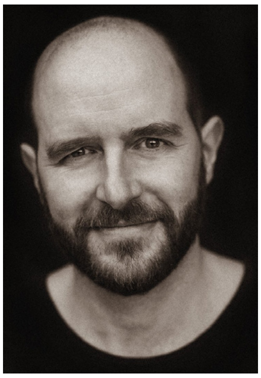
SCIENTIFIC ORGANIZERS

GONÇALO CASTELO-BRANCO

Gonçalo is an associate professor at the Department of Medical Biochemistry and Biophysics, Karolinska Institutet, Stockholm, Sweden. His research group is interested in the molecular mechanisms defining the epigenetic state of cells of the oligodendrocyte lineage, with the long-term goal of designing epigenetic based-therapies to induce regeneration (remyelination) in demyelinating diseases, such as multiple sclerosis. His group focus on how interplay between transcription factors, non-coding RNAs and chromatin modifying enzymes contribute to the transition between epigenetic states within the oligodendrocyte lineage, using technologies such as single cell and population transcriptomics and epigenomics, among others.

https://ki.se/en/mbb/goncalo-castelo-branco-group

JENS HJERLING-LEFFLER



Jens is an associate professor at the Department of Medical Biochemistry and Biophysics, Karolinska Institutet, Stockholm, Sweden. His group's research is focused on how functional neuronal identity is regulated during postnatal and adolescent brain maturation and different brain states from a molecular and network point of view. he laboratory applies methods such as advanced mouse genetics, human genetics, single-cell transcriptomics and electrophysiology to analyze the role of distinct cell classes in normal behavior as well as to increase understanding of genetically complex disorders and traits including Schizophrenia

http://www.hjerling-leffler-lab.org

ULRIKA MARKLUND

Ulrika is an associate professor at the Department of Medical Biochemistry and Biophysics, Karolinska Institutet, Stockholm, Sweden. Her research focuses on neuronal diversity in the enteric nervous system of the gastrointestinal tract. In particular she is interested in understanding the gene regulatory networks and signaling mechanisms that control the diversification of enteric stem cells into the many functionally distinct neuronal subtypes. Her ultimate goal is to recapitulate fate determination and circuitry formation in the purpose of disease modeling and cell-based therapy of bowel neuropathology.

http://ki.se/en/mbb/ulrika-marklund-group

FRANCOIS LALLEMEND

Francois is an associate professor at the Department of Neuroscience, Karolinska Institutet, Stockholm, Sweden. His research group is interested in understanding the molecular principles underlying the neuronal specification and neural circuit formation in the peripheral nervous system. His group particularly focuses on the integration of sensory neurons into functional circuits involved in the control of motor behavior and in hearing process. Research in his lab concentrates both on early development aspects and circuit mapping and function in adult.

https://ki.se/en/neuro/lallemend-laboratory

Karolinska Institutet

This conference is supported by the Ming Wai Lau Center for Reparative Medicine, Strategic Research Area in Stem Cells and Regenerative Medicine, and Frontier Courses in Neuroscience.

http://ki.se/en/research/education-in-neuroscience