UNIVERSITÀ DEGLI STUDI DI GENOVA

ISTITUTO ITALIANO DI TECNOLOGIA

Università degli Studi di Genova – Istituto Italiano di Tecnologia

Corso di Dottorato "Neuroscienze"
Curriculum"Neuroscienze e Neurotecnologie"

Anno Accademico 2017-2018
Ciclo XXXIII

Research Themes

10 positions available with scholarship

INTRODUCTION TO RESEARCH THEMES

Candidates are asked to prepare a research project of their choice related to one or more topics of the themes listed below. The soundness and originality of the project will be part of the evaluation process.

Title: Role of receptor diffusion in short-term inhibitory postsynaptic plasticity

Tutor: Andrea Barberis andrea.barberis@iit.it

The project aims at understanding the post-synaptic mechanisms of short-term plasticity at GABAergic synapses. The project will specifically investigate the lateral diffusion of GABAA receptors at the dendritic level with particular focus on the receptor transition between different nano and micro domains at the neuronal surface. This subject will be investigated by exploiting an array of techniques including electrophysiology, single particle tracking, superresolution and optogenetics. The successful candidate will be familiar with the post-synaptic molecular organization of GABAergic synapses and with synaptic physiology.

Title: Physiological characterization of epileptogenic mutants of the mTOR pathway

Tutor: Fabio Benfenati fabio.benfenati@iit.it

The research project will focus on the characterization of epileptogenic mutants belonging to the mammalian target of rapamycin (mTOR) pathway. Primary neurons will be infected with viruses encoding mutant proteins identified in epileptic patients, and the effect(s) of these proteins on neuronal physiology will be evaluated by electrophysiological techniques such as patch-clamp, as well as by standard cell biology and biochemical approaches. The successful candidate will hold a Master degree in Biosciences (Medicine, Biology, Pharmacy, Biotechnology and similar) and have a good background in neurophysiology. Some experience in electrophysiology techniques will be an advantage.

Title: Early cellular and network dysfunctions induced by disease-relevant neurotoxicity

Tutor: Luca Berdondini luca.berdondini@iit.it

The primary goal of this project is the study of early neurotoxicity dysfunctions at cellular level within neuronal networks, prior to cell-death. High-resolution electrical recording devices and read-outs developed in our laboratory allow monitoring in-vitro the early cellular and network-wide activity changes induced by disease-relevant neurotoxic insults. Here we aim at developing and applying an experimental framework enabling to induce neurotoxicity within single cells and to characterize rules of cellular susceptibility and of cell-to-cell transmission of degeneration. Electrical read-outs will be combined with optical and bimolecular quantifications and the experimental models will include the study of astrocytes-neurons co-cultures of human-derived cells. In addition to contribute in clarifying mechanisms of early cellular neurotoxocity in neuronal networks, an important potential outcome of this project is the development of cell culture models of human-derived cells for preclinical studies on neurodegenerative diseases.

Title: Cellular determinants of brain circuit development and wiring in health and disease

Two positions are available.

Tutor: Laura Cancedda laura.cancedda@iit.it

The goal of the laboratory is to understand the molecular determinants of brain circuit development. In particular, we are interested in how extracellular factors and especially GABAergic signaling modulate events such cell proliferation, polarization, migration, morphological maturation and network wiring in health and disease. This fellowship is funded by the European Research Council (ERC) and the candidate will investigate the molecular basis of Down syndrome with a particular focus on new therapeutic approaches. To achieve these goals, the laboratory uses a combination of in vivo and in vitro approaches (in vitro electrophysiology, biochemistry, confocal microscopy, molecular biology and behavioral testing). We are also developing technology to achieve DNA transfection of specific brain areas for genetic manipulations during development. The ideal is a highly motivated and creative person that should hold a Master degree in Biosciences (Medicine, Biology, Pharmacy, Biotechnology and similar) and have a good background in bioinformatics, cellular and molecular neurobiology, behavioral neuroscience or electrophysiology.

Title: Molecular mechanism of gliogenesis and relevance for glioblastoma in the postnatal mammalian brain

Tutor: Davide De Pietri Tonelli davide.depietri@iit.it

In the mammalian brain gliogenesis mostly occurs early postnatal and in the adult brain in the subventricular zone (SVZ) of the lateral ventricle and in the subgranular zone (SGZ) of the hippocampal dentate gyrus (DG). Gliogenesis is regulated by both intrinsic and extrinsic mechanisms that control neural stem cells (NSCs) maintenance, activation, fate choice, differentiation and survival. Understanding of these mechanisms holds great potential for regenerative and cancer therapies, especially gliomas.

While transcriptional mechanisms regulating adult neurogenesis is being elucidated, little is known about control played on gene expression at the post-transcriptional level. Indeed, multiple classes of regulatory noncoding (ncRNAs) such as miRNAs, circRNAs, piRNAs and lncRNAs are overly represented in the central and peripheral nervous systems, underscoring the possibility that nervous system function and diseases are heavily dependent on ncRNA regulatory networks. Unraveling functions of such regulatory networks in gliogenesis is crucial in order to understand their physiological role and to explore their diagnostic and therapeutic value. Recent work in the "Neurobiology of microRNA lab" has recently identified miRNAs that suppress gliogenesis while sustaining adult neurogenesis (Pons Espinal et al., Stem Cell Reports 2017) and novel functions of astrocytes in brain circadian rhythms (Barca Mayo et al Nature Comm, 2017). Starting from this evidence, the aim of the project is to understand the role of miRNAs and additional ncRNAs in gliogenesis and gliomas, both in vitro and in vivo.

Title: Cellular mechanisms of perception
Tutor: Tommaso Fellin tommaso.fellin@iit.it
The cerebral cortex is an extremely complex network of highly interconnected neurons which mediate fundamental functions of the brain, such as attention, perception and motor coordination. However, how these higher brain functions stem from the coordinated activity of the cortex's individual cellular components is unclear. This project focuses on the cellular mechanisms underlying the coding of sensory information in the mouse cortex. To tackle this question, experimental approaches including two-photon functional imaging, patch-clamp recordings and optogenetic manipulations will be coupled with advanced analytical and computational approaches. Applicants should have strong interest in both physiological approaches to monitor/manipulate cortical microcircuits and mathematical methods to describe and model neural networks.

Title: Genetics determinant of cognitive/social brain circuits
Tutor: Francesco Papaleo francesco.papaleo@iit.it
Cognitive and social impairments represent the earlier, most impairing and incurable symptoms in neuropsychiatric disorders such as schizophrenia, autism and ADHD, disorders characterized by a high genetic component. Despite this, the understanding of genetics and then brain mechanisms underlying these behavioral alterations are still very poor. The aim of this project is to evaluate how variations in candidate genes might alter the development of brain circuits relevant to higher order cognitive abilities and social behaviors. To achieve this goal, using genetically modified mice, we will employ a combined approach strictly linking behavioral outputs (from mice performing complex cognitive and social tasks) with circuit-level manipulations with in vivo pharmaco- and opto-genetics. The candidate should be highly motivated and creative with a completed master in Pharmacology, Mathematics, Statistics, Medicine, Physics or Biology.

Title: Noradrenergic modulation in action control
Tutor: Raffaella Tonini raffaella.tonini@iit.it
Our lab focuses on the behavioral-relevant synaptic and circuit adaptations at cortical and subcortical circuits in response to incentive stimuli and environmental stressors. This is instrumental to gain knowledge in the context of diseases such as such Parkinson's disease, post-traumatic stress disorders, drug addiction and obsessive-compulsive disorders. The project will focus on the functional remodeling of inputs from the prefrontal cortex and amygdala circuits to the Locus Coeruleus (LC), the major source of noradrenaline for the entire forebrain. In particular, the successful candidate will investigate how adaptations at afferent inputs to LC neurons during development and upon experience-dependent plasticity affect action control. To this purpose, she/he will apply a variety of experimental approaches that encompasses neurophysiological techniques (ex-vivo and in-vivo electrophysiology), viral-based approaches to deconstruct and manipulate neural circuits combined with optogenetic/chemogenetic approaches (both ex-vivo and in-vivo), in-vivo pharmacology and behavioral analysis (instrumental behavior and social behavior).

Title: Elucidation of microRNA role during emergence of T-cell exhaustion
Tutor: Velia Siciliano nbtphdcourse@iit.it
T-cell exhaustion is the process whereby "active" T cells become "dysfunctional", compromising the ability of immune system to mount an effective response against a wide range of diseases. The biological mechanisms underlying T-cell exhaustion remain still largely unknown, although RNAseq recently revealed distinct gene-expression signatures for activated vs. dysfunctional T cells. The goal of the project is to integrate system and synthetic biology approaches to study microRNAs (miRNAs) role in the emergence of T-cell dysfunction, and will be conducted in collaboration with the University of Edinburgh and UCLA. The successful candidate will hold a Master degree in Biosciences (Biology, Biotechnology, Medicine, or equivalent) and have experience in cell culture manipulation, and molecular biology. Experience with microRNA biology, RNA-seq techniques and T-cell manipulation is a plus.