Allegato 2 – Temi di Ricerca

Research Topics for Spoke n. 3
Neuronal Homeostasis and brain-environment interaction

From the final Work Plan: General description and Work Packages

S6.1 Description of the overall aim of the spoke

The conception of homeostasis, embodied by Claude Bernard's aphorism "The steadiness of the internal environment is the condition for a free and independent life", is nowadays declined in cybernetic terms as an equilibrium state controlled by negative feedback regulatory mechanisms. In the brain, homeostasis is maintained at each level (from single molecules to complex behaviors) *via* interdependent networks of interoceptive (brain-body) and exteroceptive (brain-environment) interactions. S3 will investigate some regulatory mechanisms contributing to fundamental homeostatic responses, identify how maladaptive responses trigger or maintain brain disease states, and develop innovative neuropharmacological tools to counteract disease-causing dis-homeostatic responses. Four broad areas will be tackled to achieve such goals: adaptive and maladaptive responses in coordinated transport of ions and water (WP1), organelle homeostatic and dis-homeostatic mechanisms (WP2), genetic and epigenetic signatures of neural cell growth mechanisms (WP3), and sensory and autonomic interface for brain-environment interactions (WP4). The multidisciplinary and complementary research teams participating to S3 will contribute with state-of-the-art technologies in neural cell biology, structural and functional investigation, cellular and animal models development and phenotypization, genomic, epigenomic and transcriptomic analyses, as well as digital technologies ranging from bioinformatics to neural network analysis and control. Experts in drug design, synthesis, and delivery methods participate to ensure that the project overall aims to provide novel neuropharmacological tools based on the investigated processes are met.

WP1 - Adaptive and maladaptive responses in coordinated transport of ions and water as targets for neuropharmacological interventions for brain diseases

WP2 - Organelle homeostasis in brain pathophysiology and innovative molecular interventions to correct organelle dysfunction

WP3 - Genetic and epigenetic signatures of neural cell growth mechanisms and novel treatment strategies for brain diseases

WP4 - Sensory and autonomic interface for brain-environment interaction: tools, models, and neuropharmacological interventions

	Linea d'intervento A – Attività di Ricerca realizzata e/o ascritta nella/alla unità locale dell'Ente localizzata su tutto il territorio nazionale	**Proponente**	**Dimensione massima del contributo**
	Temi di Ricerca		
A1	Multiorgan-on-a-chip engineered platforms for the personalized study of physiopathological molecular patterns in the developing brain	**Soggetti Pubblici**	200.000,00 €
A2	Novel animal models and innovative diamond-based multiarray sensors to elucidate the neuronal basis of behavioral disturbance in autism spectrum disorders	**Soggetti Pubblici**	200.000,00 €
A3	Integrated oligodendrocyte-based platforms for disease modelling and early drug screening in inflammatory and demyelinating brain disorders	**Soggetti Pubblici**	200.000,00 €
A4	Mitochondrial biomarkers and targeted therapeutical approaches for neurodevelopmental disorders	**Soggetti Pubblici**	200.000,00 €
A5	Analysis of the dynamic function of single ion channel proteins in human glioblastoma by electrophysiology using perforated patch-clamp recordings of membrane currents and outside-out experiments to isolate the single (tmCLIC1) channels	**Soggetti Pubblici**	200.000,00 €
A6	Novel optical methods and innovative sensors for functional analysis of neuro-cardiac co-cultures	**Soggetti Pubblici**	200.000,00 €
A7	Disease Model Factory: development of patient-derived iPS, organoids and CRISPR-based cellular and animal models of neurological diseases, and related metabolic imaging and drug screening	**Soggetti Privati**	350.000,00 €
A8	Development of knock-in and knock-out cellular models using gene editing technologies	**Soggetti Privati**	800.000,00 €
A9	Advanced softwares for signal analysis from high-density MEA recordings	**Soggetti Privati**	150.000,00 €

	Linea d'intervento B – "Sud" - Attività di Ricerca realizzata e/o ascritta nella/alla unità locale dell'Ente localizzata nel Mezzogiorno (Abruzzo, Basilicata, Calabria, Campania, Molise, Puglia, Sardegna e Sicilia)	**Proponente**	**Dimensione massima del contributo**
	Temi di Ricerca		
B1	Assessing the role of Gut Microbiota in brain-environment interactions by metaproteomic approaches	**Soggetti Pubblici**	230.000,00 €
B2	A multidisciplinary platform for the identification of novel therapeutic targets and tools involved in neuronal and glial homeostasis, circuits and plasticity, using cellular and animal models (from C. elegans-invertebrates to vertebrates), advanced materials, atomic-resolution cryo-electron microscopy, wide-screen epigenomics, closed-loop optogenetics, electrophysiology, calcium imaging, and novel synthetic and extractive technologies.	**Soggetti Pubblici**	1.150.000,00 €
B3	Homeostatic mechanisms controlling brain zinc distribution: pathophysiological implications revealed by molecular and cellular models	**Soggetti Pubblici**	230.000,00 €
B4	*In silico* and *in vitro* characterization of small molecules targeting potassium channels for the treatment of brain pathologies	**Soggetti Pubblici**	230.000,00 €
B5	Functional and pharmacological characterization of pathogenic variants in voltage- and non-voltage-gated potassium channel genes	**Soggetti Pubblici**	230.000,00 €
B6	Synthesis, optimization, brain distribution and metabolic profiles of novel drugs for the treatment of hyperexcitability disorders involving voltage- and non-voltage-gated channel	**Soggetti Pubblici**	230.000,00 €
B7	Advanced characterization of brain structure and function via 3D printed neurochips, implantable spectroscopic devices, and electrophysiological recordings in mouse models of neurodegeneration	**Soggetti Pubblici**	600.000,00 €
B8	Autophagic targets for the development of new pharmacological approaches for the mitigation of hypoxic/ischemic retinal and optic nerve damage	**Soggetti Pubblici**	230.000,00 €
B9	Homeostatic plasticity of central dopaminergic and glutamatergic pathways elicited by amphetamine-like drugs in rodents during exposure to acute or repeated stress	**Soggetti Pubblici**	230.000,00 €
B10	Interplay between the dopaminergic system and the immune response in the pathogenesis of Alzheimer disease	**Soggetti Pubblici**	230.000,00 €
B11	Long-read technologies to dissect molecular pathomechanisms of rare neurological disorders and brain tumors	**Soggetti Pubblici**	230.000,00 €

B12	HTS cellular models for the selection of small molecules against ion channels and transporters using targeted, focused libraries	**Soggetti Privati**	180.000,00 €