IBCN
Institute of Cell Biology and Neurobiology

The Institute of Cell Biology and Neurobiology (IBCN) of the National Research Council (CNR) was established in December 2010 building on a partnership among CNR scientists with complementary expertise, backgrounds and interests, from the Institute of Neurobiology and Molecular Medicine, the Institute of Cell Biology (both founded by the Nobel Laureate Rita Levi Montalcini) and the Rome Section of the Institute of Neuroscience. The Institute is part of the International Scientific Campus “Adriano Buzzati-Traverso” and coordinates the European Mouse Mutant Archive (EMMA) animal facility and the Monterotondo Mouse Clinic for the production, phenotypic analysis, cryo-preservation and distribution of mutant mouse strains as models of human pathologies. The Institute also hosts the Monterotondo outlet of the European Molecular Biology Laboratory (EMBL) and a Research Unit of the International Centre for Genetic Engineering and Biotechnology (ICGEB). The idea of this multi-task joint venture is mainly to remove traditional barriers among disciplines, bringing together different expertise and develop a shared, more innovative ground for intellectual, experimental and technological exchange among scientists. The task force of the Institute comprises about 100 members of staff (scientists, technicians and administrative personnel) plus a cohort of post-doctoral scientists, PhD students and associated members, working together within a campus of about 16 acres and located in the northern outskirts of Rome.

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Mouse models of human diseases: production, archiving and phenotyping

The laboratory mouse is the crucial living model for studying human diseases and exploiting the potential benefits to human health presented by the most advanced research in mammalian genetics.

The Italian National Research Council established and coordinates the Core Structure of the European Mouse Mutant Archive (EMMA) Network and the new Mouse Clinic facility, at the “A. Buzzati-Traverso” International Campus in Monterotondo. The EMMA network ensures the pathogen-free archiving, world-wide distribution and data resourcing of more than 600 new mutant strains per year (ca. 7000 strains currently available), as new in vivo models of human diseases. The EMMA Core Structure and Monterotondo Mouse Clinic participate in the International Consortia IMPC, IKMC, IMSR and are key components of the INFRAFRONTIER project, which is specifically organizing the complementary and integrated networks for large-scale and comprehensive production, primary phenotyping, archiving and dissemination of mouse models, serving the European genetics and biomedical research community for the benefit of human health.

INFRAFRONTIER has been selected as an highest-priority distributed infrastructure by the European Strategy Forum for Research Infrastructures (ESFRI) Roadmap, the Italian

Keywords: mutant phenotypes, disease models.
External links: https://www.infrafrontier.eu/
http://strains.emmanet.org/
http://www.mousephenotype.org/

Functional scheme of the Infrafrontier organization.

Roadmap for Pan-European Research Infrastructures and related national roadmaps.
Neuroscience

Neuroscience research at IBCN focuses on studying neuronal and glial responses to physiological and pathological conditions, and in particular on:

- providing contributions to the understanding of purinergic signaling in amyotrophic lateral sclerosis and multiple sclerosis, by pioneering the use of P2 receptor antagonists for preventing these diseases;
- analyzing mechanisms underlying acute and chronic pain through functional responses and changes in the expression of specific markers at peripheral and central levels, for the identification of new therapies;
- dissecting gene-environment interactions affecting behavioral development, with focus on early physical, nutritional and social manipulations as tools for functional recovery from neurodevelopmental disorders;
- identifying neural circuits and cellular mechanisms critical for normal and pathological memory in neurodegenerative diseases, by combining behavioral protocols with functional anatomy and molecular biology techniques;
- discovering new cellular and molecular strategies to reactivate adult neural stem cells, for delaying neuron depletion in brain region involved in learning and memory during aging and brain injuries.

Keywords: aging, learning and memory, neurodegeneration, neurodevelopmental disorders, neurogenesis, neuroinflammation, pain, animal models.

Epigenetics

Alteration of epigenetic mechanisms, fundamental to respond to numerous biological stimuli, such as development and differentiation, are involved in the pathogenesis and progression of some muscular dystrophies such as Emery Dreifuss, Duchenne and Facioscapulohumeral Muscular Dystrophies (EDMD, DMD, FSHD). For this reason, elucidation of the mechanisms behind global and focal changes in chromatin structure and function represent one of the main focus at IBCN. Epigenetic regulation relies on multiple mechanisms including histone modifications, non-coding RNA and changes in the three-dimensional structure of chromatin. Chromatin localization at the nuclear periphery, where it interacts with lamins and nuclear pore complexes, or in the nucleoplasm has been described to be associated with inactive or transcribed domains, respectively. Indeed, lamins mutations are associated to the development of EDMD, whereas alteration of nuclear pore proteins regulates pathological gene expression in dystrophic cardiomyopathy. Another important activity is devoted to the investigation of DNA methylation patterns, histone modifying enzymes and histone marks toward development of novel diagnostic and therapeutics tools with relevant implications in stem-cell-based strategies and adult tissue functional improvement in neuromuscular diseases.

Keywords: chromatin higher order structures, histone deacetylases, lysine methyltransferases, muscle progenitor cells, [Duchenne, Emery Dreifuss, facioscapulohumeral] muscular dystrophy, nuclear lamina, nitric oxide, nuclear pore proteins, polycomb.
Muscle physiology, pathology and regenerative medicine

Muscular tissue represents the vast majority of the body, and many severe diseases, of both genetic and traumatic origin, involve cardiac and skeletal muscles. Research from different groups focuses on mechanisms regulating myo/pathogenesis at transcriptional and post-transcriptional levels, aiming at developing new therapeutic strategies. These approaches include: generation of human models of cardiac and skeletal muscle pathologies through cell reprogramming (iPS) technology and murine models of ischemic events to develop cell therapy supported by innovative biomaterials; studying the effect of HDAC inhibitors and the contribution of macrophages in cardiac regeneration/remodelling and in muscular dystrophies; refining the role of the tyrosin-kinase receptor c-Kit in cardiac repair after injury; defining mechanisms regulating skeletal muscle stem cell function; validating zinc-finger based artificial transcription factors targeting utrophin gene promoter for treatment of Duchenne Muscular Dystrophy; identification of potentially pathogenetic microRNAs and target genes through analyses of microRNA-target interactions in muscle tissues from patients affected by Myotonic Dystrophy.

Keywords: iPS cells, muscular dystrophies, heart, cardiomyocytes, cardiac regeneration, cardiac repair, PEG-fibrinogen scaffold, skeletal muscle, HDAC inhibitors, macrophages, zinc-finger-based artificial transcription factors, microRNAs, tyrosin-kinase receptor.

Molecular oncology and immunity

Tumor cells utilize highly versatile strategies to grow, escape the immune system and invade into surrounding tissues.

At the IBCN-CNR we aim to characterize mechanisms leading to cancer development and progression by the integration of multidisciplinary experimental approaches ranging from gene expression profile-based screening and bioinformatics analysis to phenotypical and biochemical characterization of genetically modified cellular and murine models of human epithelial (prostate, breast, NSCLC, thyroid, melanoma), brain and nervous system tumors. Multiple cancer-associated deregulated processes are investigated, including gene expression (mRNA, IncRNA and miRNA), cell growth, apoptosis, hormone-dependency, differentiation, angiogenesis, cell invasion, DNA damage response, cell-cell signaling and tumor innate immunity.

A better understanding of the mechanisms regulating the activation of selected oncogenes (i.e. EGFR) and tumor suppressors genes (i.e. p53 family members, Tis21/BTG2), signaling pathways (i.e. Receptor tyrosin kinases, hypoxia and nuclear lamina proteins) and mediators (i.e. calcium, eNOS) are instrumental to identify mechanisms of resistance to target therapies, valuable targets (i.e anticancer peptides) and biomarkers for unmet research and medical needs.

Keywords: Cancer development and progression, mechanisms, cell signaling, targets, biomarkers

2015 selected highlight: Anticancer peptide able to impair the inhibiting activity of MDM2/MDM4 towards p53 – EU Patent: 1408/2639240, supported by Project CNR-FaReBio di Qualità, Ministry of Economy and Finance and AIRC; fabiola.moretti@cnr.it.