

## IBBE

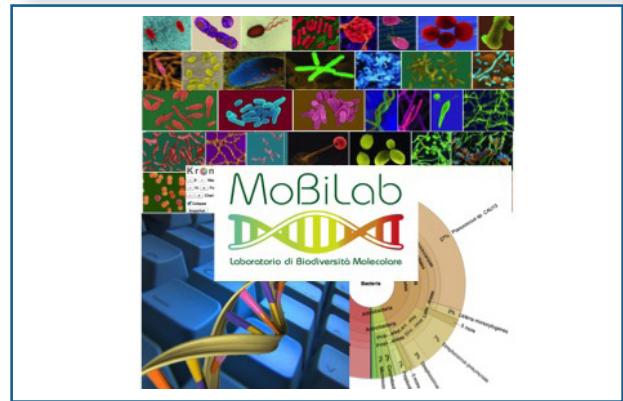
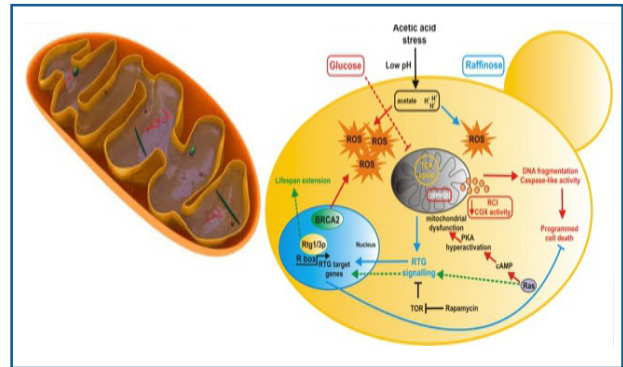
### Institute of Biomembranes and Bioenergetics

The Institute of Biomembranes and Bioenergetics (IBBE) is one of the major research centers in the field of Bioenergetics and Biomembranes at national and international level. The main research activities of the institute include: functional characterization and physiopathology of bioenergetic membrane systems, including mitochondrial carriers and respiratory chain complexes; role of mitochondria in cell differentiation, apoptosis and stress response; structural and functional characterization of known or newly-identified genes and proteins involved in mitochondrial biogenesis and energy metabolism; mitochondrial alterations in hereditary and degenerative diseases and aging. More recently, the IBBE research activity has expanded into the “omic” fields of comparative genomics and transcriptomics by using data generated from new generation sequencing platforms, bioinformatics and molecular biodiversity.

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## Biogenesis of Membranes for Energy Transduction

This research activity is based on different membrane systems.

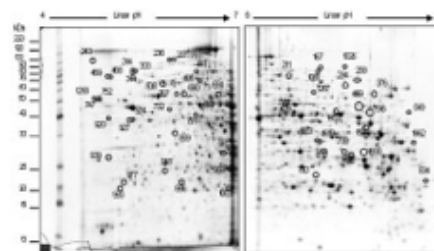
Particular attention is given to the study of mitochondrial biogenesis and its regulation under physiopathological conditions. Indeed, mitochondria, organelles equipped with membranes for energy transduction, have a pivotal role in the cell response to various kind of stress. The following topics are studied in detail: i) molecules of the mitochondrial membrane, such as cardiolipin, ii) aspects of mitochondrial bioenergetics under physiopathological and metabolic conditions; iii) mitochondrial DNA and nuclear factors that regulate its expression; iv) mitochondrial proteome.

The study of membranes for energy transduction has also been extended to other systems, such as the chloroplasts membranes of spinach, as the seat of proteins involved in light capture (light harvesting complex), and photosynthetic bacteria (*Rhodobacter sphaeroides*) for their involvement in environmental bioremediation.

The interest in bacteria and the possibility to exploit them as a source of enzymes of industrial interest, gave the start to new studies based on metagenomic approaches for the identification of enzymes active in extreme and harsh conditions.



Mountains of salt extracted from the Salterns of Margherita di Savoia



2D electrophoresis of mitochondrial proteins from adult rats. Circled spots correspond to proteins whose expression differs with age or after treatment with acetyl-carnitine

**References:** Paradies G. et al (2014) *Antioxid Redox Signal.* 20:1925-53.

Musicco C et al. (2014) *Mol Biosyst.* 10: 1313-19.

Volpicella M. et al. (2014) *FEMS Microbiol Ecol.* 88:345-57.

**Keywords:** Mitochondrial Biogenesis, Oxidative stress, Bacterial Genomics

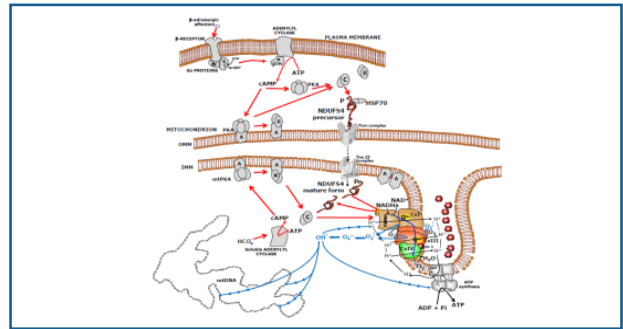
**Contacts:** Luigi Ruggero Ceci, Clara Musicco, Giuseppe Petrosillo, Bruno Gattulli.

## Biomembrane bioenergetics system: functional mechanism and pathophysiology

This research activity includes the following research lines:  
1. Regulation of expression, structure and assembly of membrane energy transducing systems of both eukaryotes and prokaryotes.

In this context, the signal transduction and second messengers, in particular cAMP, play an important role in regulating the biogenesis and functional capacity of membrane energy transducing systems and oxygen free radical balance in physiological and pathological conditions. Another area involves the study of energy transducing systems in microorganisms of industrial interest. Particularly significant results have been obtained concerning structure and functional mechanisms of mitochondrial and bacterial cytochrome c oxidase and ATP synthase.

2. Many genetic diseases, including some forms of cancer, are caused by nonsense mutations that generate in-frame premature termination codons (PTC). PTCs cause a premature arrest of translation and activate nonsense-mediated mRNA decay (NMD), a process that specifically recognizes and degrades PTCs-containing mRNA, with consequent loss of protein function. To date there is no genetic therapy available for these disorders. One approach, called "suppression therapy" is based on chemical-induction of suppression at PTCs (read-through), but not at the natural stop codon. Searching for small compounds able to suppress PTCs and/or modulate NMD to restore the synthesis of a



Mitochondrial section, with surrounding cytosol, showing a crista with complex I (NADH-ubiquinone oxidoreductase, CxI), complex III (bc1, ubiquinone-cytochrome c oxidoreductase, CxIII) and complex IV (cytochrome c oxidase, CxIV) assembled in the respiratory chain, cytochrome c molecules and ATP synthase dimer (CxV, FoF1) at the crista curvature.

functional full-length protein is highly demanded and requires development of efficient screening systems suitable for a high-throughput scale.

**References:** Altamura et al. (2013) *Journal of Cystic Fibrosis* 12:806-811.

Papa S. et al. (2013) *Trend Mol Med.* 19:61-69.

Palorini R. et al. (2013) *Oncogene* 32:352-62.

De Rasmio D. et al. (2012) *Free Radic Biol Med.* 52:757-64.

**Keywords:** Mitochondrial signaling; neurodegenerative and proliferative diseases

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## Mitochondrial carriers: structure and functional mechanisms

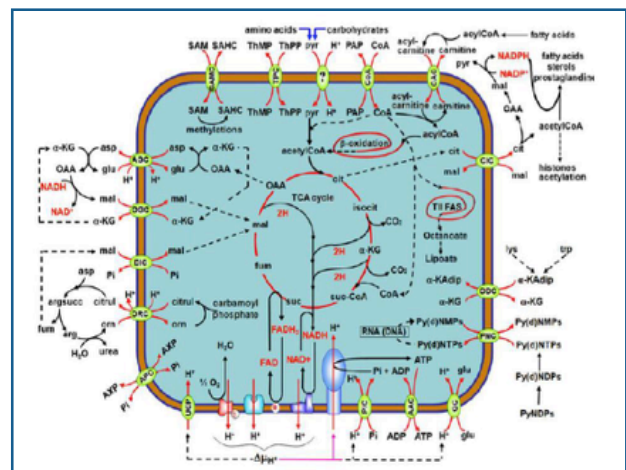
This research activity is involved in the identification and in the functional and structural characterization of mitochondrial membrane transporters belonging to the family SLC25 known as "mitochondrial carrier family (MCF)".

Main research topics are:

- study of the relationship between structure and function of mitochondrial carriers;
- effects of either endogenous and xenobiotic molecules on the transport activity, mediated by mitochondrial carriers;
- identification of the catalytic activity of members of the mitochondrial carrier family with still unknown function and study of their physiological role in cellular models as well as in vitro;
- identification of mutations of genes encoding members of the MCF in patients suffering diseases associated with dysfunction of mitochondrial carriers and study of pathogenetic mechanisms in cell models.

**References:** Poduri A. et al. (2013) *Annals of Neurology* 74:873-82.

Rimessi A. et al. (2013) *Autophagy* 9:1-10.



Metabolic role of mitochondrial carrier

Indiveri C. et al. (2011) *Mol Aspects Med.* 32:223-233.

**Keywords:** Mitochondrial transport proteins, protein reconstitution, mitochondrial diseases, structure/function protein characterization

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## Nucleus/cytoplasm/mitochondria crosstalk in cellular homeostasis

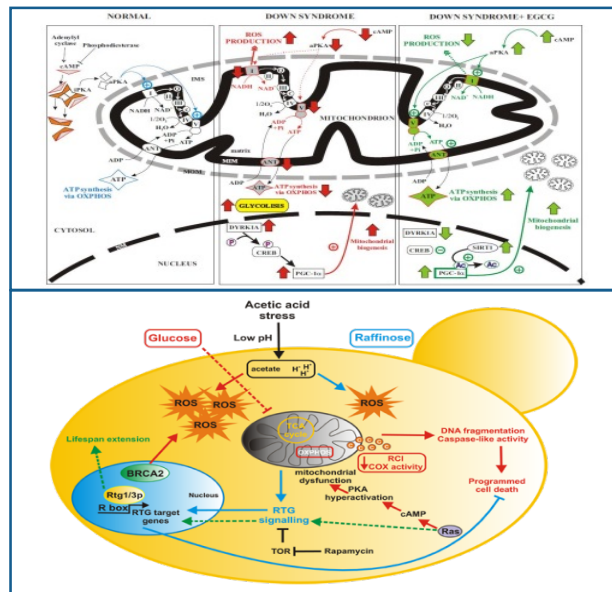
Objective of this research is the study of signaling pathways and mitochondrial metabolism in different models of neurodegenerative/neurodevelopmental diseases and in cancer. The delicate balance between cell death and proliferation is essential to the genesis of various pathologies and the mitochondria are proving to be the key factors in regulating: cell growth and death, intracellular signaling and integration of stress signals. The targets of this research concern: mitochondria-nucleus retrograde communication, modulation of the mitochondrial metabolism in pathophysiological conditions and network of intra and inter-cellular signals in the regulation of proliferation, invasion and cell death. The main scientific objectives are: i) understand how the cell signaling networks regulate decisions of life and death; ii) discover new natural and/or synthetic compounds capable of interfering with the disease for future applications in the pharmacological field.

**References:** Valenti D et al. (2014) *Neurosci Biobehav Rev.* 2:212-217.

Bobba et al. (2014) *Biochim Biophys Acta* 1837:1338-49.

Guaragnella N. et al. (2014) *Apoptosis* 19:1330-41.

Tsai YS et al. (2014) *Oncotarget* 5:6425-36.



**Keywords:** Neurodegeneration, Neurodevelopment, Neoplastic transformation, Programmed cell death, Cell Metabolism, Mitochondrial bioenergetics

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## Study of molecular biodiversity for the development of innovative product and processes

This research activity include the following research topics:

- 1) Development of bioinformatics methodologies and specialized databases for taxonomic analysis and functional characterization of "omics" data.

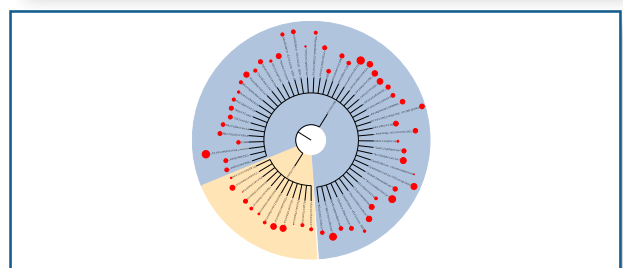
- 2) Structural and functional annotation of the genome and study of the mechanisms of regulation of gene expression in prokaryotic and eukaryotic organisms, viruses and organelles (mitochondria and chloroplasts) through High-Throughput Sequencing (HTS) technology and advanced bioinformatics tools.

- 3) Taxonomic and functional characterization of the microbiome in environmental (including water, soil, sediments), clinical (including faeces, intestinal mucosa, respired air) and food (including intermediate products of fermentation chains) samples, based on metagenomic approaches through HTS technologies and advanced bioinformatics tools.

**References:** Giulietti M. et al. (2013) *Nucleic Acid Res.* 41: D125-31.

Santamaria M. et al. (2012) *Brief Bioinform.* 13:682-95.

Picardi E. and Pesole G. (2012) *Nat Methods* 9:523-4.



RDPII Database

Pesole G. et al. (2012) *EMBO Rep.* 13:473-4.

**Keywords:** Genomics, Metagenomics, High-Throughput Sequencing, Bioinformatics

**Contacts:** Graziano Pesole, Monica Santamaria, Luigi Ceci, Francesca De Leo, Giuseppe Sgaramella, Annarita Armenise, Barbara de Marzo, Laura Marra, Marisa Mirizzi.