CLAUDIA DONNINI

Curriculum Vitae

Education and training

Education
1969. High School Diploma at "*Lyceum Classicum* Romagnosi", Parma.
1973. MD degree *Cum Laude* in Biological Sciences at University of Parma.
1977. Certificate of Complementary Studies in Biophysics at University of Liège (Belgium).

Training
1972 - 1973. Undergraduate trainee. Institute of Genetics, University of Parma
Under the supervision of Prof. Carlo Rossi learnt basic principles of genetics, as well as experimental genetic analysis and cytotoxicity. She partecipated in studies on chromosome maps to diagnosis of genetic diseases and genetic harmfulness of chlorpromazine in human cells lines and of ionizing radiation in humans.
1974 – 1980. Research fellowship. Institute of Genetics, University of Parma
Under the supervision of Prof. Pier Paolo Puglisi, she undertook the study of dependence of the nucleus-mitochondrial relationships in different cellular processes in yeast. In particular, she has been analysed the role that alterations of mitochondrial enzymatic and/or biosynthetic functions have on the maintenance of the mitochondrial information, on the control of compartment-specific RNAs and proteins during nutritional shift-down, and on enzymatic induction, highlighting as most salient result the different regulation of cytoplasmic and mitochondrial RNA and proteins and the genetic control of this regulatory process.

Employment and research experience
Employment:
1980/1992 - Researcher in Genetics at University of Parma
1992/2005 - Associate Professor of Genetics at University of Parma
2005/currently - Full Professor of Genetics at University of Parma
2002-2004 – Counsellor of the Italian Association of Genetics (AGI)
2009-2011 – Director of the Department of Genetics, Biology of microorganism, Anthropology, Evolution at University of Parma.

Research experience:
She has more than thirty years experience in physiology, genetics and genetic manipulation of yeasts. The study of nucleo-mitochondrial interactions was the major field of interest. The research has been developed in the petite positive species *Saccharomyces cerevisiae* as well as in the petite negative species *Kluyveromyces lactis* due to the different role played by the mitochondria in the two species. In particular, in *Saccharomyces cerevisiae*, she has been analysed the role that alterations of mitochondrial enzymatic and/or biosynthetic functions have on the maintenance of the mitochondrial information. She also isolated and characterized a number of nuclear genes involved in the nucleo-mitochondrial control. Among them, nuclear genes necessary in the absence of mitochondrial protein synthesis (IMP genes, Independent of Mitochondrial Particle). In *Kluyveromyces lactis*, the main subjects of research has been glucose repression, with the identification of genes that control the major regulatory system in the energy and carbon metabolism, and comprehension of the mechanisms involved in "Kluyver effect", i.e. on the seeming respiration-dependent assimilation of several fermentable carbon sources.
On the basis of knowledge on the genetics of mitochondrial–core systems in yeast, she has undertaken research aimed at the establishment of yeast as a model system of human mitochondrial disease (MD). To date several models have been studied in yeast: ANT1, the ADP/ATP carrier; EFTu and EFG1, elongation factors of mitochondrial protein synthesis; MPV17, a mitochondrial inner membrane protein of unknown function; MTO1, encoding the mitochondrial-tRNA modifier 1; LYRM7/MZM1L, encoding a recently identified new assembly factor for cIII respiratory complex; VARS2, encoding the mitochondrial valyl-tRNA-synthetase;

TRIT1, encoding the human tRNA iso-pentenyl-transferase, which is responsible for i6A37 modification of the anticodon loops of a small subset of cytosolic and mitochondrial tRNAs; POLG, the mitochondrial DNA polymerase; YARS2 the mitochondrial tyrosyl-tRNA synthetase; TRMT5, the mitochondrial tRNA methyltransferase 5. Aim of the researche is validation in yeast of the genetic causes of MD, investigation of the pathogenesis of human mutations, understanding of the role of unknown functions, identification of molecules able to suppress mitochondrial defects in yeast.
More recently she entered the field of behavioral genetics, studying the relation between human polymorphism and behavior, with regard to substance abuse disorder. The research has allowed to identify susceptibility polymorphisms that can increase the risk of developing drug addiction also in relation to environmental factors such as, in particular, parental relationships, childhood trauma and abuse and to correlate genotypes with response to drug treatment and with neuroendocrine context.

Responsibility of recent research projects

- Generisk 2009, Presidenza del Consiglio dei Ministri – Dipartimento Politiche Antidroga *"Valutazione di vulnerabilità genetica: individuazione di fattori di rischio relativi all'abuso di cannabinoidi e di disordini psichiatrici correlati*).
- PRIN 2009 MIUR "*Il lievito come organismo modello per lo studio della biogenesi mitocondriale*",
- Generisk 2 2011, Presidenza del Consiglio dei Ministri – Dipartimento Politiche Antidroga "*Valutazione di vulnerabilità genetica: individuazione di fattori di rischio relativi all'abuso di cannabinoidi e di disordini psichiatrici correlati.*
- Ministero della Salute - Ricerca Finalizzata e Giovani ricercatori 2010 *"New nuclear genes responsible for mitochondrial disorders: identification by high-throughput exome sequencing and functional characterization of the corresponding proteins"*, (2012-14)
- Fondazione Cariplo - Cariplo 2011 *"Definition and characterization of disease genes in mitochondrial disorders".*
- Telethon 2011. "*MitMed: a multicenter consortium for the identification and characterization of nuclear genes responsible for human mitochondrial disorders*.
- Telethon 2015. "*MitMed consortium: from the identification and characterization of nuclear genes responsible for human mitochondrial disorders towards potential therapeutic approaches in experimental models*".

Collaboration in recent research projects

- Telethon 2008 "*Identification and characterization of nuclear genes responsible for human mitochondrial disorders",* (2009-11)
- Farmagen 2011 Presidenza del Consiglio dei Ministri – Dipartimento Politiche Antidroga *"Caratteristiche farmaco genetiche e psicobiologiche e risposta ai trattamenti farmacologici con metadone e bufrenorfina,* (2012-13)

Most recent peer–reviewed publications

1. Sommerville EW, Ng YS, Alston CL, Dallabona C, Gilberti M, He L, Knowles C, Chin SL, Schaefer AM, Falkous G, Murdoch D, Longman C, de Visser M, Bindoff LA, Rawles JM, Dean JC, Petty RK, Farrugia ME, Haack TB, Prokisch H, McFarland R, Turnbull DM, **Donnini C**, Taylor RW, Gorman GS. 2017. Clinical Features, Molecular Heterogeneity, and Prognostic Implications in YARS2-Related Mitochondrial Myopathy. JAMA Neurol. 74:686-694.

2. Gerra G, Manfredini M, Somaini L, Milano G., Ciccocioppo R, **Donnini C.** 2016. Perceived parental care during childhood, ACTH, cortisol and nicotine dependence in the adult. Psychiatry Research 245:458-465
3. Gerra G, Manfredini M, Somaini L, Maremmani I, Leonardi C, **Donnini C**. 2016. Sexual Dysfunction in Men Receiving Methadone Maintenance Treatment: Clinical History and Psychobiological Correlates. Eur Addict Res. 22:163-75.
4. Baruffini E, Ferrari J, Dallabona C, **Donnini C**, Lodi T. 2015. Polymorphisms in DNA polymerase γ affect the mtDNA stability and the NRTI-induced mitochondrial toxicity in Saccharomyces cerevisiae. Mitochondrion 20:52-63.
5. Ardissone A, Lamantea E, Quartararo J, Dallabona C, Carrara F, Moroni I, **Donnini C**, Garavaglia B, Zeviani M, Uziel G. 2015. A novel homozygous YARS2 mutation in two Italian siblings and a review of literature. has been accepted for publication in "JIMD Reports". JIMD Rep. 20:95-101.
6. Lodi T, Dallabona C, Nolli C, Goffrini P, **Donnini C**, Baruffini E. 2015. DNA polymerase γ and disease: what we have learned from yeast. Front Genet. 2015 6:106.
7. Powell CA, Kopajtich R, D'Souza AR, Rorbach J, Kremer LS, Husain RA, Dallabona C, **Donnini C**, Alston CL, Griffin H, Pyle A, Chinnery PF, Strom TM, Meitinger T, Rodenburg RJ, Schottmann G, Schuelke M, Romain N, Haller RG, Ferrero I, Haack TB, Taylor RW, Prokisch H, Minczuk M. 2015. TRMT5 Mutations Cause a Defect in Post-transcriptional Modification of Mitochondrial tRNA Associated with Multiple Respiratory-Chain Deficiencies. Am J Hum Genet. doi: 10.1016/j.ajhg.2015.06.011.
8. Tigano M, Ruotolo R, Dallabona C, Fontanesi F, Barrientos A, **Donnini C**, Ottonello S. 2015. Elongator-dependent modification of cytoplasmic tRNALysUUU is required for mitochondrial function under stress conditions. Nucleic Acids Res. PMID: 26240381
9. Gerra G, Somaini L, Manfredini M, Raggi MA, Saracino MA, Amore M, Leonardi C, Cortese E, **Donnini C.** 2014. Dysregulated responses to emotions among abstinent heroin users: Correlation with childhood neglect and addiction severity. *Prog Neuropsychopharmacol Biol Psychiatry.* 48:220-228
10. Gerra G, Somaini L, Leonardi C, Cortese E, Maremmani I, Manfredini M, **Donnini C**. 2014. Association between gene variants and response to buprenorphine maintenance treatment. Psychiatry Res. 215:202-207.
11. Diodato D, Melchionda L, Haack T, Dallabona C, Baruffini E, **Donnini C**, Granata T, Ragona F, Balestri P, Margollicci M, Lamantea E, Nasca A, Powell CA, Minczuk M, Strom TM, Meitinger T, Prokisch H, Lamperti C, Zeviani M, Ghezzi D. 2014. VARS2 and TARS2 Mutations in Patients with Mitochondrial Encephalomyopathies. Hum Mutat. 35:983-989.
12. Baruffini E, Dallabona C, Invernizzi F, Yarham JW, Melchionda L, Blakely EL, Lamantea E, **Donnini C**, Santra S, Vijayaraghavan S, Roper HP, Burlina A, Kopajtich R, Walther A, Strom TM, Haack TB, Prokisch H, Taylor RW, Ferrero I, Zeviani M, Ghezzi D. 2013. MTO1 mutations are associated with hypertrophic cardiomyopathy and lactic acidosis and cause respiratory chain deficiency in humans and yeast. *Hum Mutat.* 34:1501-1509.
13. Invernizzi F, Tigano M, Dallabona C, **Donnini C**, Ferrero I, Cremonte M, Ghezzi D, Lamperti C, Zeviani M. 2013. A Homozygous Mutation in LYRM7/MZM1L Associated with Early Onset Encephalopathy, Lactic Acidosis, and Severe Reduction of Mitochondrial Complex III Activity. *Hum Mutat.* 2013. 34:1619-1622
14. Somaini L, Manfredini M, Amore M, Zaimovic A, Raggi MA, Leonardi C**,** Gerra ML, **Donnini C**., Gerra G. 2012. Psycobiological responses to unpleasant emotions in cannabis users. *Eur Arch Psychiatry Clin Neurosci*. 262:47-57
15. Somaini L, **Donnini C**., Manfredini M, Raggi MA,. Saracino MA, Gerra ML, Amore M, Serpelloni G, Gerra G. 2011. Adverse childhood experiences (aces), genetic polymorphisms and neurochemical correlates in experimentation with psychotropic drugs among adolescents**.** *Neuroscience and Biobehavioral Reviews* 35:1771-1778
16. Gerra G, Saenz E, Busse A , Maremmani I, Ciccocioppo R, Zaimovic A, Gerra ML, Amore M, Manfredini M, **Donnini C**, Somaini L. 2011. Supervised daily consumption, contingent take-home

incentive and non-contingent take-home in methadone maintenance. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*. 35:483-489.
17. Somaini L, **Donnini C**, Raggi MA, Amore M, Ciccocioppo R, Saracino MA, Kalluppi M, Malagoli M, Gerra ML, Gerra G. 2011. Promising medications for cocaine dependence treatment. *Recent Pat CNS Drug Discov.* 6:146-160
18. Gerra G, Zaimovic A, Castaldini L, Garofano L, Manfredini M, Somaini L, Leonardi C, Gerra ML, and **Donnini C.** 2010. Relevance of perceived childhood neglect, 5-HTT gene variants and hypothalamus-pituitary-adrenal axis dysregulation to substance abuse susceptibility *Am. J. Med. Genet*. (Neuropsychiatric Genetics) 153B:715-722
19. Dallabona C, Marsano RM, Arzuffi P, Ghezzi D, Mancini P, Zeviani M, Ferrero I, **Donnini C**. 2010. Sym1, the yeast ortholog of the MPV17 human disease protein, is a stress-induced bionergetic and morphogenetic mitochondrial modulator *Hum Mol Genet* 19:1098-1107
20. Gerra G, Leonardi C; Cortese E. Zaimovic A, Dell'Agnello G, Manfredini M, Somaini L, Petracca F, Caretti V, Raggi MA, **Donnini C.** 2009. Childhood neglet and parental care perception in cocaine addicts: Relation with psychiatric symptoms and biological correlates. *Neuroscience and Biobehavioral Reviews* 33:601-610
21. Gerra G, Leonardi C; Cortese E. Zaimovic A, Dell'Agnello G, Manfredini M, Somaini L, Petracca F, Caretti V, Baroni C., Raggi MA, **Donnini C.** 2008. Adrenocorticotropic hormone and cortisol plasma levels directly correlate with childhood neglect and depression measures in addicted patiens. *Addict Biol* **13**:95-104.
22. Bao WG, Guiard B, Fang ZA, **Donnini C**, Gervais M, Passos FM, Ferrero I, Fukuhara H, Bolotin-Fukuhara M. 2008. Oxygen-dependent transcriptional regulator Hap1p limits glucose uptake by repressing the expression of the major glucose transporter gene RAG1 in Kluyveromyces lactis. *Eukaryot Cell* 7:1895-1905
23. Gerra G., Zaimovic A, Garofano L., Ciusa F., Moi G., Avanzini P., Talarico E., Gardini F., Brambilla F., Manfredini M., **Donnini C.** (2007) Perceived parenting behaviour in the childhood of cocaine users: relationship with genotype and personality traits. *Am. J. Med. Genet. (Neuropsychiatric Genetics)* 144B:52-57
24. Valente L, Tiranti V, Marsano R M, Malfatti E, Fernandez-Vizarra E, **Donnini C,** , Mereghetti P, De Gioia L, Burlina A, Castellan C, Comi G.P, e Savasta S, Ferrero I, Zeviani M (2007) Infantile encephalopathy and defective mtDNA translation in patients with mutations of mitochondrial elongation factors EFG1 and EF-Tu *Am J Hum Genet.* 80:44-58
25. Gerra G., Leonardi C., Cortese E., D'Amore A, Lucchini A., Strepparola G., Serio G., Farina G., Magnelli F., Zaimovic A., Mancini A., Turci M, , Manfredini M, **Donnini C**. (2007) Human kappa opioid receptor gene (OPRK1) polymorphism is associated with opiate addiction *Am. J. Med. Genet*. (Neuropsychiatric Genetics) 144B:771-775
26. Marchi E., Lodi T., **Donnini C**. 2007. *KNQ1*, a *Kluyveromyces lactis* gene encoding a transmembrane protein may be involved in iron homeostasis. *Fems Yeast Res*. **7**:715-721
27. Gerra G., Leonardi C., Cortese E., Zaimovic A., Dell'Agnello G., Manfredini M., Somaini L., Petracca F., Caretti V., Saracino M.A., Raggi M.A., **Donnini C.** 2007. Homovanillic acid (HVA) plasma levels inversely correlate with attention deficit-hyperactivity and childhood neglect measures in addicted patients. *J Neural Transm.* **114**:1637-1647
28. Spinazzola A, Viscomi C, Fernandez-Vizarra E,Carrara F, D'Adamo P., Calvo S, Marsano RM, **Donnini C**, Weiher H, Strisciuglio P, Parini R, Sarzi E, Chan A, Dimauro S, Rotig A, Gasparini P, Ferrero I, Mootha VK, Tiranti V, Zeviani M (2006) MPV17 encodes an inner mitochondrial membrane protein and is mutated in infantile hepatic mitochondrial DNA depletion. *Nat. Genet*. 38:570-575
29. Baruffini E., Goffrini P., **Donnini C.,** Lodi T. (2006) Galactose transport in *Kluyveromyces lactis:* major role of the glucose permease Hgt1 *FEMS Yeast Res* **6**:1235-1242