



LIFELONG LEARNING PROGRAMME



School of Pharmacy

**PLACEMENTS IN ITALY
FOR INCOMING ERASMUS STUDENTS**

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SAPIENZA UNIVERSITY LABORATORIES, ROME (WWW.UNIROMA1.IT)

Fabio Altieri's Lab

Selected publications:

Chichiarelli S, Gaucci E, Ferraro A, Grillo C, **Altieri** F, Cocchiola R, Arcangeli V, Turano C, Eufemi M. Role of ERp57 in the signaling and transcriptional activity of STAT3 in a melanoma cell line. Arch Biochem Biophys. 2010 Feb 15;494(2):178-83. Epub 2009 Dec 6. PubMed PMID: 19995546.

Piacentini L, Fanti L, Negri R, Del Vescovo V, Fatica A, **Altieri** F, Pimpinelli S. Heterochromatin protein 1 (HP1a) positively regulates euchromatic gene expression through RNA transcript association and interaction with hnRNPs in Drosophila. PLoS Genet. 2009 Oct;5(10):e1000670. Epub 2009 Oct 2. PubMed PMID: 19798443; PubMed Central PMCID: PMC2743825.

Laneve P, Gioia U, Ragno R, **Altieri** F, Di Franco C, Santini T, Arceci M, Bozzoni I, Caffarelli E. The tumor marker human placental protein 11 is an endoribonuclease. J Biol Chem. 2008 Dec 12;283(50):34712-9. Epub 2008 Oct 20. PubMed PMID: 18936097.

Altieri F, Grillo C, Maceroni M, Chichiarelli S. DNA damage and repair: from molecular mechanisms to health implications. Antioxid Redox Signal. 2008 May;10(5):891-937. Review. PubMed PMID: 18205545.

Croce A, Firuzi O, **Altieri** F, Eufemi M, Agostino R, Priori R, Bombardieri M, Alessandri C, Valesini G, Saso L. Effect of infliximab on the glycosylation of IgG of patients with rheumatoid arthritis. J Clin Lab Anal. 2007;21(5):303-14. PubMed PMID: 17847113.

Di Matteo A, Gianni S, Schininà ME, Giorgi A, **Altieri** F, Calosci N, Brunori M, Travaglini-Allocatelli C. A strategic protein in cytochrome c maturation: three-dimensional structure of CcmH and binding to apocytochrome c. J Biol Chem. 2007 Sep 14;282(37):27012-9. Epub 2007 Jul 10. PubMed PMID: 17623665.

Grillo C, D'Ambrosio C, Consalvi V, Chiaraluce R, Scaloni A, Maceroni M, Eufemi M, **Altieri** F. DNA-binding activity of the ERp57 C-terminal domain is related to a redox-dependent conformational change. J Biol Chem. 2007 Apr 6;282(14):10299-310. Epub 2007 Feb 5. PubMed PMID: 17283067.

Chichiarelli S, Ferraro A, **Altieri** F, Eufemi M, Coppari S, Grillo C, Arcangeli V, Turano C. The stress protein ERp57/GRP58 binds specific DNA sequences in HeLa cells. J Cell Physiol. 2007 Feb;210(2):343-51. PubMed PMID: 17061245.

Grillo C, D'Ambrosio C, Scaloni A, Maceroni M, Merluzzi S, Turano C, **Altieri** F. Cooperative activity of Ref-1/APE and ERp57 in reductive activation of transcription factors. Free Radic Biol Med. 2006 Oct 1;41(7):1113-23. Epub 2006

Jul 4. PubMed PMID: 16962936.

Cervoni L, Egistelli L, Eufemi M, d'Abusco AS, **Altieri** F, Lascu I, Turano C, Giartosio A. DNA sequences acting as binding sites for NM23/NDPK proteins in melanoma M14 cells. J Cell Biochem. 2006 May 15;98(2):421-8. PubMed PMID: 16440314.

Mariangela Biava's lab

Our research group is involved in design and synthesis of pyrrole derivatives with possible antimycobacterial or anti-inflammatory activities

The laboratory training will consist of:

- 1) design of the compounds based on molecular modelling suggestions or target structure;
- 2) synthesis, purification and chemical-physical characterization of pyrrole derivatives;
- 3) discussion of the biological data derived from biological and microbiological tests.

Selected publications of the research group:

Biava M, Porretta GC, Cappelli A, Vomero S, Manetti F, Botta M, Sautebin L, Rossi A, Makovec F, Anzini M. 1,5-Diarylpyrrole-3-acetic acids and esters as novel classes of potent and highly selective cyclooxygenase-2 inhibitors. J. Med. Chem. 2005; 48: 3428.

Biava M, Porretta GC, Poce G, Supino S, Deidda D, Pompei R, Mollicotti P, Manetti F, Botta M. Antimycobacterial agents. Novel diarylpyrrole derivatives of BM 212 endowed with high activity toward Mycobacterium tuberculosis and low cytotoxicity. J. Med. Chem. 2006; 49: 4946.

Biava M, Porretta GC, Manetti F. New derivatives of BM 212: a class of antimycobacterial compounds based on the pyrrole ring as a scaffold. M.R.M.C. 2007; 7: 65.

Biava M, Cirilli R, Fares V, Ferretti R, Gallinella B, La Torre F, Poce G, Porretta GC, Supino S, Villani C. HPLC enantioseparation and absolute configuration of novel anti-inflammatory pyrrole derivatives. Chirality 2008;

Bruno Botta's lab

Natural products chemistry: structure elucidation, synthesis and biotransformation studies

- Synthesis and application of resorcarenes
- Molecular recognition studies
- Supramolecular chemistry of gases

Selected publications of the research group:

1. Botta, Bruno; D'Acquarica, Ilaria; Laura Nevola, Fabiola Sacco, Zara Valbuena Lopez, Giovanni Zappia, Caterina Frascchetti, Maurizio Speranza, Andrea Tafi, Fabiana Caporuscio, Matthias C. Letzel, Jochen Mattay. Bis(diamido)-Bridged Basket Resorcin[4]arenes as Enantioselective Receptors for Amino Acids and Amines. European Journal of Organic Chemistry 2007, 5995-6002.

2. Botta, Bruno; D'Acquarica, Ilaria; Delle Monache, Giuliano; Subissati, Deborah; Uccello-Barretta, Gloria; Mastrini, Massimo; Nazzi, Samuele; Speranza, Maurizio. Synthesis and Host-Guest Studies of Chiral N-Linked Peptidoresorc[4]arenes. Journal of Organic Chemistry 2007, 72(24), 9283-9290.

3. Botta, Bruno; Delle Monache, Giuliano; Frascchetti, Caterina; Nevola, Laura; Subissati, Deborah; Speranza, Maurizio. Gaseous- versus solution-phase recognition of some aromatic amino esters by 2,8,14,20-tetrakis(L-valinamido)[4]resorcinarene. *International Journal of Mass Spectrometry* (2007), 267(1-3), 24-29.
4. Botta, Bruno; D'Acquarica, Ilaria; Delle Monache, Giuliano; Nevola, Laura; Tullo, Danila; Ugozzoli, Franco; Pierini, Marco. Nitrosonium (NO⁺) Complexes of Resorc[4]arenes: Spectral, Kinetic, and Theoretical Studies. *Journal of American Chemical Society* (2007), 129(36), 11202-11212.
5. Zappia, G.; Cancelliere, G.; Gacs-Baitz, E.; Delle Monache, G.; Misiti, D.; Nevola, L.; Botta, Bruno. Oxazolidin-2-one ring, a popular framework in synthetic organic chemistry part 2]. Applications and modifications. *Current Organic Synthesis* (2007), 4(3), 238-307.
6. Zappia, Giovanni; Menendez, Pilar; Delle Monache, Giuliano; Misiti, Domenico; Nevola, Laura; Botta, Bruno. The contribution of oxazolidinone frame to the biological activity of pharmaceutical drugs and natural products. *Mini-Reviews in Medicinal Chemistry* 2007, 7(4), 389-409.
7. Zappia, Giovanni; Gacs-Baitz, Eszter; Delle Monache, Giuliano; Misiti, Domenico; Nevola, Laura; Botta, Bruno. Oxazolidin-2-one ring, a popular framework in synthetic organic chemistry: part 1. The construction of the oxazolidin-2-one ring. *Current Organic Synthesis* (2007), 4(1), 81-135.
8. Sampaio de Andrade Lima, Cláudia; Zappia, Giovanni; Delle Monache, Giuliano; Botta, Bruno. Uncommon 5-Methoxyisoflavans from *Desmodium canum*. *European Journal of Organic Chemistry* 2006, 5445-5448.
9. D'Acquarica, Ilaria; Nevola, Laura; Delle Monache, Giuliano; Gacs-Baitz, Eszter; Massera, Chiara; Ugozzoli, Franco; Zappia, Giovanni; Botta, Bruno. Cyano-resorc[5]arenes: Isolation, Conformation and Crystal Structure. *European Journal of Organic Chemistry* 2006, 3652-3660.
10. Botta, Bruno; Caporuscio Fabiana, D'Acquarica Ilaria, Subissati, Deborah; Delle Monache Giuliano, Tafi, Andrea; Botta Maurizio; Filippi, Antonello; Speranza, Maurizio. Gas-Phase Enantioselectivity of Chiral Amido[4]resorcinarene Receptors. *Chemistry--A European Journal* 2006, 12, 8096-8105.
11. Botta, Bruno; Caporuscio, Fabiana; Subissati, Deborah; Tafi, Andrea; Botta Maurizio; Filippi, Antonello; Speranza, Maurizio. Flattened cone 2,8,14,20-tetrakis (L-valinoamido)[4]resorcinarene: The first example of enantioselective allosteric receptors in the gas phase. *Angewandte Chemie, International Edition* 2006, 45, 2717-2720.

Maria Antonietta Casadei's lab

The research activity of the group deals with the multidisciplinary field of pharmaceutical science and is especially focused on various aspects of modified (sustained, modulated and/or site-specific) release of the drug. In particular we have acquired a good expertise on the synthesis of new polymeric materials to be employed for the development of new drug delivery systems. Therefore, the first step of our research regards the modification of natural polysaccharides (dextran and scleroglucan) and their physicochemical characterization by NMR and FT-IR techniques among others. These polymers are then used for the preparation of chemical and/or physical biodegradable hydrogels, which have found wide application as drug delivery systems, because they combine a good tissue biocompatibility with the possibility to manipulate the permeability for solutes. After the complete characterization of the matrices, they are employed for the preparation of oral or topical formulations. The release of the drug from these systems is followed by spectrophotometric or HPLC analysis. Chemical and enzymatic stability tests are also performed together with in-vivo experiments. Further information on the work carried on in this laboratory can be found in the following research papers.

Selected publications of the research group:

- 1) M. A. Casadei, F. Cerreto, S. Cesa, M. Giannuzzo, M. Feeney, C. Marianecchi, P. Paolicelli, "Solid lipid nanoparticles incorporated in dextran hydrogels: a new drug delivery system for oral formulations", *Int. J. Pharm.*, 2006, 325, 140-146.
- 2) M. A. Casadei, P. Matricardi, G. Fabrizi, M. Feeney, P. Paolicelli, "Physical gels of a carboxymethyl derivative of scleroglucan: synthesis and characterization", *Eur. J. Pharm. Biopharm.*, 2007, 67, 682-689.
- 3) G. Pitarresi, M. A. Casadei, D. Mandracchia, P. Paolicelli, F. S. Palombo, G. Giammona, "Photocrosslinking of dextran and polyaspartamide derivatives: a combination suitable for colon-specific drug delivery", *J. Control. Rel.*, 2007, 119, 328-338.
- 4) M. A. Casadei, G. Pitarresi, R. Calabrese, P. Paolicelli, G. Giammona, "Photocrosslinking of biodegradable and pH-sensitive dextran and polyaspartamide derivatives for colon-specific drug delivery", *Biomacromolecules*, 2008, 9, 43-49.

Previous experiences with foreign students:

Maria Gerasimova (Sofia): alexmay@abv.bg

Paola Casolini's Lab

The present proposition should be addressed to Erasmus Students having basic knowledge of brain anatomy and physiology and neuropharmacology. Students will be introduced in the research field of how perinatal environment could influence brain development.

Students will participate at laboratory activities and will be encouraged to interact with all the laboratory staff. They will acquire scientific methods and the ability to be engaged in critical thinking. They will be also trained in learning experimental designs and data analysis.

Students will be trained in learning the follow techniques:

- Rat and/or mouse manipulation (including enteral and parenteral injections)
- Behavioural Animal Tests
- Brain structures dissection
- Immunohistochemistry
- Enzyme Immunoassay (EIA, ELISA), RadioImmunoAssay (RIA)
- Western Blotting

Selected publications of the research group:

- 1: Casolini P, Domenici MR, Cinque C, Alema GS, Chiodi V, Galluzzo M, Musumeci M, Mairesse J, Zuena AR, Matteucci P, Marano G, Maccari S, Nicoletti F, Catalani A. Maternal exposure to low levels of corticosterone during lactation protects the adult offspring against ischemic brain damage. *J Neurosci.* 2007 27(26):7041-6.
- 2: Casolini P, Zuena AR, Cinque C, Matteucci P, Alema GS, Adriani W, Carpinelli G, Santoro F, Alleva E, Bosco P, Nicoletti F, Laviola G, Catalani A. Sub-neurotoxic neonatal anoxia induces subtle behavioural changes and specific abnormalities in brain group-I metabotropic glutamate receptors in rats. *J Neurochem.* 2005 95(1):137-45.
- 3: Morley-Fletcher S, Darnaudery M, Mocaer E, Froger N, Lanfumey L, Laviola G, Casolini P, Zuena AR, Marzano L, Hamon M, Maccari S. Chronic treatment with imipramine reverses immobility behaviour, hippocampal corticosteroid receptors and cortical 5-HT(1A) receptor mRNA in prenatally stressed rats. *Neuropharmacology.* 2004 47(6):841-7.

- 4: Cinque C, Zuena AR, Casolini P, Ngomba RT, Melchiorri D, Maccari S, Nicoletti F, DiGiorgi Gerevini, Catalani A. Reduced activity of hippocampal group-I metabotropic glutamate receptors in learning-prone rats. *Neuroscience*. 2003;122(1):277-84.
- 5: Catalani A, Casolini P, Cigliana G, Scaccianoce S, Consoli C, Cinque C, Zuena AR, Angelucci L. Maternal corticosterone influences behavior, stress response and corticosteroid receptors in the female rat. *Pharmacol Biochem Behav*. 2002 73(1):105-14

Roberto Di Santo's Lab

The group is coordinated by Prof. R. Di Santo and is engaged in medicinal chemistry. The research fields are heterocyclic chemistry (heterocyclic systems, pyrrole annulate system with benzoazepine, benzodiazepine, and benzothiadiazepines; use of TosMIC in medicinal chemistry); chemotherapeutics: antiviral, antifungal, antitumor agents. Antifungal agents with potent activity against *Candida albicans* and *Candida* spp. were designed and synthesized, which were more potent than reference drugs. A number of novel reverse transcriptase and protease inhibitors were designed and produced as anti-HIV agents. The resistance to the drugs currently used in clinical practice as anti-AIDS agents led to focus the attention of the researchers against a third enzyme of HIV-1, namely integrase. Various polyhydroxylated derivatives were found as inhibitors of HIV-1 IN. Moreover, potent aryldiketoacids were designed and synthesized, which were endowed of both selective anti-IN and antiviral activities. Further, novel antitumor agents were designed targeting to specific enzymes, according to the most modern approach in the anticancer therapy.

The students are required to develop the synthesis of the designed agents, possibly cooperating also in the design of the biologically active compounds and participating in the resolution of the problems that arise during the development of the synthetic pathways.

The laboratory has the following facilities: HPLC, LC-MS, FT-IR, NMR for analytical purposes. Moreover, Syncore reactor for parallel synthesis and CEM Discovery reactor for non-conventional heating performed with microwaves, are available and currently used to synthesize the designed compounds.

Selected publications of the research group:

- R. Di Santo, A. Tafi, R. Costi, M. Botta, M. Artico, F. Corelli, M. Forte, F. Caporuscio, L. Angiolella, A. T. Palamara. Antifungal Agents. 11. N-Substituted Derivatives of 1-[(Aryl)(4-aryl-1H-pyrrol-3-yl)methyl]-1H-imidazole, Synthesis, Anti-Candida Activity and QSAR Studies. *J. Med. Chem.* 2005, 48, 5140-5153.
- R. Di Santo, G. Maga. Human Terminal Deoxynucleotidyl Transferase as Novel Targets for Anticancer Chemotherapy. *Curr. Med. Chem.* 2006, 13, 2353-2368.
- R. Di Santo, R. Costi, A. Roux, M. Artico, A. Lavecchia, L. Marinelli, E. Novellino, L. Palmisano, M. Andreotti, R. Amici, C. M. Galluzzo, L. Nencioni, A. T. Palamara, Y. Pommier, C. Marchand. Novel Bifunctional Quinolonyl Diketo Acid Derivatives as HIV-1 Integrase Inhibitors: Design, Synthesis, Biological Activities and Mechanism of Action *J. Med. Chem.* 2006, 49, 1939-1945.
- R. Costi, R. Di Santo, M. Artico, G. Miele, P. Valentini, E. Novellino, A. Cereseto. Cynamoyl compounds as simple molecules that inhibit p300 histone acetyltransferase. *J. Med. Chem.* 2007, 50, 1973-1977.

Previous experiences with foreign students:

Aude Carton (Besançon): Audecarton84@aol.com

Delphine Noirmain (Amiens): delphinenoirmain@hotmail.fr

Pietro Matricardi's Lab

Synthesis by means of different procedures (chemical and physical crosslinkings) and characterization (including mechanical and rheological studies) of new hydrogels for the preparation of modified delivery dosage forms. Particular attention is devoted to polysaccharides and their derivatives as starting materials.

- Synthesis and characterization of new chemical and physical hydrogels suitable as scaffolds for cell culture
- Novel Interpenetrating Polymer Networks (IPN) and semi-IPN: preparation and characterization.
- Preparation of model dosage forms (tablets, micro and nano spheres, implantable matrices etc.) for modified release of drugs. Tests in vitro.
- Formulation and characterization of new vesicles (liposomes, non-ionic surfactant vesicles, ethosomes) for sustained drug delivery and targeting to specific sites.

Recent publications:

- COVIELLO T., ALHAIQUE F., PARISI C., MATRICARDI P., BOCCHINFUSO G., GRASSI M. (2005). A new polysaccharidic gel matrix for drug delivery: preparation and mechanical properties. *J. Control. Release*, vol. 102, pp. 643-656.
- COVIELLO T., PALLESCHI A., GRASSI M., MATRICARDI P., BOCCHINFUSO G., ALHAIQUE F. (2005). Scleroglucan: a versatile polysaccharide for modified drug delivery. *Molecules*. vol. 10, pp. 6-13.
- MATRICARDI P., ONORATI I., COVIELLO T., ALHAIQUE F. (2006). Drug delivery matrices based on scleroglucan/alginate/borax gels. *Int. J. Pharm.* vol. 316, pp. 21-28.
- COVIELLO T., MATRICARDI P., ALHAIQUE F. (2006). Drug delivery strategies using polysaccharidic gels. *Expert Op. Drug Del.* vol. 3, pp. 395-404.
- COVIELLO T., MATRICARDI P., MARIANECCI C., ALHAIQUE F. (2007). Polysaccharide hydrogels for modified release formulations. *J. Control. Release*, 119, pp. 5-24.
- COVIELLO T., ALHAIQUE F., DORIGO A., MATRICARDI P., GRASSI M. (2007). Two galactomannans and scleroglucan as matrices for drug delivery: Preparation and release studies. *Eur. J. Pharm. Biopharm.*, vol. 66, pp. 200-209.
- SANDOLO C., COVIELLO T., MATRICARDI P., ALHAIQUE F. (2007). Characterization of polysaccharide hydrogels for modified drug delivery. *Eur. Biophys. J.*, doi: 10.1007/s00249-007-0158-y.
- CASADEI M.A., MATRICARDI P., FABRIZI G., FEENEY M., PAOLICELLI P. (2007). Physical gels of a carboxymethyl derivative of scleroglucan: synthesis and characterization. *Eur. J. Pharm. Biopharm.*, doi: 10.1016/j.ejpb.
- MATRICARDI P., ONORATI I., MASCI G., COVIELLO T., ALHAIQUE F. (2007). Semi-IPN hydrogel based on scleroglucan and alginate: drug delivery behaviour and mechanical characterization. *J. Drug Del. Sci. Tech.*, 17(3), 193-197.

- SALMASO S., SEMENZATO A., BERSANI S., MATRICARDI P., ROSSI F., CALICETI P. (2007). Cyclodextrin/PEG based hydrogels for multi-drug delivery, *Int. J. Pharm.*, doi: 10.1016/j.ijpharm.2007.05.035.
- SANDOLO C., MATRICARDI P., ALHAIQUE F., COVIELLO T. (2007). Dynamo-mechanical and rheological characterization of guar gum hydrogels. *Eur. Polym. J.*, doi: 10.1016/j.eurpolymj.2007.04.051.

Previous experiences with foreign students:

Ana Figueiredo (Porto) isanapf@hotmail.com

Anna Teresa Palamara's Lab

The main objective of our research group is the study of new antiviral strategies aimed at inhibiting host cell functions, rather than viral functions, that are essential for replication of different viruses, to avoid the emergence of drug-resistance. For this reason, the main research lines are the following:

- *Study of virus/host cell interaction: i) role of different intracellular factors (survival/death proteins, MAPK pathways, caspases activity) in the control of viral replication; ii) study of molecular processes involved in virus life-cycle regulation and host cell fate; iii) role of the autophagic process in the control of viral infection.*
- *Study of relationship between intra/extracellular redox state and viral infection: i) effects of viral infection on intracellular redox state; ii) role of intracellular redox state in controlling replication of different viruses; iii) evaluation of antiviral effect of compounds with antioxidant activity in in vitro ed in vivo models.*
- *Identification and characterization of new antiviral drugs.*

The laboratory of Virology is part of the Department of Public Health and Infectious Diseases “G. Sanarelli”, Pharmaceutical Microbiology Section. It is equipped with all facilities for:

- virus propagation and in vitro viral infection;
- the study and characterization of new antiviral drugs in several models;
- the biochemical equipment for the definition of intracellular pathways that are activated during viral infection.

This laboratory collaborates with the Animal Housing in the Istituto Superiore di Sanità, in which there is a room dedicated for viral infection, equipped with a vertical flow laminar cabinet used for viral infection and for isolation of organs, and with all instruments needed for following the infection (such as temperature cabinet for housing infected animals, balance for measuring body weight and infrared rays thermometer for measuring the body temperature). The laboratory for in vitro experiments is equipped with four vertical flow laminar cabinets, four incubators, a Real Time PCR, and all the instruments for biochemical studies including electrophoretic assays, molecular imaging, and spectrophotometric tests.

Selected publications of the research group:

Raffaele Saladino, Maurizio Barontini, Marcello Crucianelli, Lucia Nencioni, Rossella Sgarbanti, and Anna Teresa Palamara. *Current Advances in Anti-influenza Therapy. Curr. Med. Chem.* 2010: 17, 2101-2140.

Lucia Nencioni, Giovanna De Chiara, Maria E. Marcocci, Rossella Sgarbanti, Donatella Amatore, Annalucia Serafino, Maria Torcia, Federico Cozzolino, Katia Aquilano, Maria R. Ciriolo, Enrico Garaci, and Anna T. Palamara. Bcl-2 does not prevent influenza A virus-induced apoptosis: role of activated p38 MAPK. *J. Biol. Chem.* 2009: 284 (23), 16004-16015.

- Fraternale A, Paoletti MF, Casabianca A, Nencioni L, Garaci E, Palamara AT, Magnani M. GSH and analogs in antiviral therapy. *Mol. Aspects Med.* 2009; 30 (1-2), 99-110.
- Giorgio Conti, Walter Magliani, Stefania Conti, Lucia Nencioni, Rossella Sgarbanti, Anna Teresa Palamara, and Luciano Polonelli. Therapeutic Activity of an Anti-Idiotypic Antibody-Derived Killer Peptide against Influenza A Virus Experimental Infection. *Antimicrob. Agents Chemother.* 2008; 52, 4331–4337.
- Anna T. Palamara, Lucia Nencioni, Katia Aquilano, Giovanna De Chiara, Leyanis Hernandez, Federico Cozzolino, Maria R. Ciriolo, and Enrico Garaci. Resveratrol inhibits Influenza A virus replication in vitro and in vivo. *J. Infect. Dis.* 2005; 191, 1719-1729.
- Nencioni L., Iuvara A., Aquilano K., Ciriolo M.R., Cozzolino F., Rotilio G., Palamara A.T., Garaci E. Influenza A virus replication is dependent on an antioxidant pathway that involves GSH and Bcl-2. *Faseb J.* 2003; 17, (6), 758-760.
- Torcia M., De Chiara G., Nencioni L., Ammendola S., Labardi D., Lucibello M., Rosini P., Marlier L., Bonini P., Dello Sbarba P., Palamara A.T., Zambrano N., Russo T., Garaci E., Cozzolino F. Nerve growth factor inhibits apoptosis in memory B lymphocytes via inactivation of p38 MAPK, prevention of Bcl-2 phosphorylation, and cytochrome c release. *J. Biol. Chem.* 2001; 276, 39027-39036.
- Nucci C., Palamara A.T., Ciriolo M.R., Nencioni L., Savini P., D'Agostini C., Rotilio G., Cerulli L., Garaci E. Imbalance in corneal redox state during Herpes Simplex virus 1-induced keratitis in rabbits. Effectiveness of exogenous glutathione supply. *Experimental Eye Research* 2000; 70, 215-220.
- Torcia M., Bracci-Laudiero L., Lucibello M., Nencioni L., Labardi D., Rubartelli A., Cozzolino F., Aloe L., Garaci E. Nerve growth factor is an autocrine survival factor for memory B lymphocytes. *Cell* 1996; 85 (3), 345-56.

Claudio Passariello's Lab

The activity of this training will be devoted to the use of in vitro models to study coinfections involving respiratory viruses and bacterial or fungal opportunists.

In particular the pathogenesis of different opportunistic infections during infection by the Influenza A virus is at present studied, including pneumonia caused by *Staphylococcus aureus* and by *Candida albicans* and acute otitis media and pneumonia caused by *Moraxella catarrhalis*. The student will have the opportunity to learn how to set up cultures of human epithelial cells, how to infect these cells with viruses, how to study within these infectious models bacterial and fungal adhesivity and invasivity. We are moreover interested at characterizing the influence of the intracellular environment generated by the virus on gene expression of opportunist.

The training will consequently include also the procedures to study the expression of selected genes within these complex biologic systems, using both transcriptional and translational approaches.

Selected publications of the research group:

Selan L., Passariello C., Rizzo L., et al. Diagnosis of vascular graft infections with antibodies against staphylococcal slime antigens. *Lancet*, 359: 2166-68, 2002.

Passariello C., Schippa S., Conti C., et al. Rhinoviruses promote internalization of *Staphylococcus aureus* into scarcely permissive cultured pneumocytes. *Microbes and Infection* 8(3):758-66, 2006.

Mai A., Rotili D., Massa S., Somonetti G., Passariello C., Palamara AT. Discovery of uracil-based histone deacetylase inhibitors able to reduce acquired antifungal resistance and trailing growth in *Candida albicans*. *Biorganic and Medicinal Chemistry Letters* 17(5):1221-25, 2007.

Simonetti G., Passariello C., Rotili D., et al. Histone deacetylase inhibitors may reduce pathogenicity and virulence in *Candida albicans*. *FEMS Yeast Research* 7(8):1371-80, 2007.

Rino Ragno's lab

In our lab the student is trained to learn computational methodologies applied to the medicinal chemistry. In particular molecular docking, molecular alignment and three-dimensional quantitative structure-activity relationships are the main fields that are used to carry out theoretical models are to design new drugs.

Selected publications of the research group:

1. Ragno, R., et al., Class II-selective histone deacetylase inhibitors. Part 2: Alignment-independent GRIND 3-D QSAR, homology and docking studies. *Eur. J. Med. Chem.*, 2008. 43(3): p. 621-632.
2. Ragno, R., et al., Small Molecule Inhibitors of Histone Arginine Methyltransferases: Homology Modeling, Molecular Docking, Binding Mode Analysis, and Biological Evaluations. *J. Med. Chem.*, 2007. 50(6): p. 1241-1253.
3. Mai, A., et al., Synthesis and Biological Properties of Novel 2-Aminopyrimidin-4(3H)-ones Highly Potent against HIV-1 Mutant Strains. *J. Med. Chem.*, 2007. 50(22): p. 5412-5424.
4. Ragno, R., et al., Design, Molecular Modeling, Synthesis, and Anti-HIV-1 Activity of New Indolyl Aryl Sulfones. Novel Derivatives of the Indole-2-carboxamide. *J. Med. Chem.*, 2006. 49(11): p. 3172-3184.
5. Mai, A., et al., Synthesis and biological properties of novel, uracil-containing histone deacetylase inhibitors. *J. Med. Chem.*, 2006. 49(20): p. 6046-6056.
6. Ragno, R., et al., HIV-Reverse Transcriptase Inhibition: Inclusion of Ligand-Induced Fit by Cross-Docking Studies. *J. Med. Chem.*, 2005. 48(1): p. 200-212.
7. Ragno, R., et al., Docking and 3-D QSAR Studies on Indolyl Aryl Sulfones. Binding Mode Exploration at the HIV-1 Reverse Transcriptase Non-Nucleoside Binding Site and Design of Highly Active N-(2-Hydroxyethyl)carboxamide and N-(2-Hydroxyethyl)carbohydrazide Derivatives. *J. Med. Chem.*, 2005. 48(1): p. 213-223.
8. Mai, A., et al., Design, Synthesis, and Biological Evaluation of Sirtinol Analogues as Class III Histone/Protein Deacetylase (Sirtuin) Inhibitors. *J. Med. Chem.*, 2005. 48(24): p. 7789-7795.
9. De Martino, G., et al., Novel 1-[2-(Diarylmethoxy)ethyl]-2-methyl-5-nitroimidazoles as HIV-1 Non-Nucleoside Reverse Transcriptase Inhibitors. A Structure-Activity Relationship Investigation. *J. Med. Chem.*, 2005. 48(13): p. 4378-4388.
10. Ragno, R., et al., Computer-aided design, synthesis, and anti-HIV-1 activity in vitro of 2-alkylamino-6-[1-(2,6-difluorophenyl)alkyl]-3,4-dihydro-5-alkylpyrimidin-4(3H)-ones as novel potent non-nucleoside reverse transcriptase inhibitors, also active against the Y181C variant. *J. Med. Chem.*, 2004. 47(4): p. 928-934.
11. Ragno, R., et al., 3-(4-Aroyl-1-methyl-1H-pyrrol-2-yl)-N-hydroxy-2-propenamides as a New Class of Synthetic Histone Deacetylase Inhibitors. 3. Discovery of Novel Lead Compounds through Structure-Based Drug Design and Docking Studies. *J. Med. Chem.*, 2004. 47(6): p. 1351-1359.

Daniela Secci's Lab

The Laboratory of Pharmaceutical Chemistry of the Faculty of Pharmacy at Sapienza University of Rome has easy access to all the facilities required for the synthesis of organic compounds. The main equipments include NMR spectrometer (400 MHz), FT/IR, UV and gas/mass spectrometer for analytical purposes. For synthetic purposes, apart from the equipment of an usual organic chemistry laboratory, there is a microwave reactor, very useful for decreasing organic reaction times and

increasing yields of products. The enantioseparation of chiral molecules with enantioselective HPLC are also performed.

The research projects of this Laboratory are focused on the synthesis of new molecules active as antifungals, antiprotozoarians, antibacterials, anti-Parkinson and anticancer. In the period we are developing new pyrazoline, hydrazothiazole, and coumarin derivatives with classical and microwave methods. The new structures are then tested in our affiliate biological laboratories, especially on *Candida albicans*, *Toxoplasma gondii*, *Helicobacter pylori*, Monoamine Oxidases (MAO) and Hystone Acetyltransferases (HAT).

Selected publications of the research group

- Chimenti, Franco; Bizzarri, Bruna; Bolasco, Adriana; Secci, Daniela; Chimenti, Paola; Carradori, Simone; Granese, Arianna; Rivanera, Daniela; Frishberg, Nathan; Bordon, Claudia; Jones-Brando, Lorraine. Synthesis and Evaluation of 4-Acyl-2-thiazolylhydrazone Derivatives for Anti-Toxoplasma Efficacy in Vitro. *Journal of Medicinal Chemistry* (2009), 52(15), 4574-4577.
- Chimenti, Franco; Carradori, Simone; Secci, Daniela; Bolasco, Adriana; Chimenti, Paola; Granese, Arianna; Bizzarri, Bruna. Synthesis and biological evaluation of novel conjugated coumarin-thiazole systems. *Journal of Heterocyclic Chemistry* (2009), 46(3), 575-578.
- Chimenti, Franco; Fioravanti, Rossella; Bolasco, Adriana; Chimenti, Paola; Secci, Daniela; Rossi, Francesca; Yanez, Matilde; Orallo, Francisco; Ortuso, Francesco; Alcaro, Stefano. Chalcones: A Valid Scaffold for Monoamine Oxidases Inhibitors. *Journal of Medicinal Chemistry* (2009), 52(9), 2818-2824.
- Chimenti, Franco; Secci, Daniela; Bolasco, Adriana; Chimenti, Paola; Bizzarri, Bruna; Granese, Arianna; Carradori, Simone; Yanez, Matilde; Orallo, Francisco; Ortuso, Francesco; Alcaro, Stefano. Synthesis, Molecular Modeling, and Selective Inhibitory Activity against Human Monoamine Oxidases of 3-Carboxamido-7-Substituted Coumarins. *Journal of Medicinal Chemistry* (2009), 52(7), 1935-1942.
- Chimenti, Franco; Bizzarri, Bruna; Maccioni, Elias; Secci, Daniela; Bolasco, Adriana; Chimenti, Paola; Fioravanti, Rossella; Granese, Arianna; Carradori, Simone; Tosi, Federica; Ballario, Paola; Vernarecci, Stefano; Filetici, Patrizia. A Novel Histone Acetyltransferase Inhibitor Modulating Gcn5 Network: Cyclopentylidene-[4-(4'-chlorophenyl)thiazol-2-yl]hydrazone. *Journal of Medicinal Chemistry* (2009), 52(2), 530-536.
- Chimenti, Franco; Fioravanti, Rossella; Bolasco, Adriana; Manna, Fedele; Chimenti, Paola; Secci, Daniela; Rossi, Francesca; Turini, Paola; Ortuso, Francesco; Alcaro, Stefano; Cardia, Maria Cristina. Synthesis, molecular modeling studies and selective inhibitory activity against MAO of N1-propanoyl-3,5-diphenyl-4,5-dihydro-(1H)-pyrazole derivatives. *European Journal of Medicinal Chemistry* (2008), 43(10), 2262-2267.
- Chimenti, Franco; Maccioni, Elias; Secci, Daniela; Bolasco, Adriana; Chimenti, Paola; Granese, Arianna; Carradori, Simone; Alcaro, Stefano; Ortuso, Francesco; Yanez, Matilde; Orallo, Francisco; Cirilli, Roberto; Ferretti, Rosella; La Torre, Francesco. Synthesis, Stereochemical Identification, and Selective Inhibitory Activity against Human Monoamine Oxidase-B of 2-Methylcyclohexylidene-(4-arylthiazol-2-yl)hydrazones. *Journal of Medicinal Chemistry* (2008), 51(16), 4874-4880.
- Chimenti, Franco; Bizzarri, Bruna; Maccioni, Elias; Secci, Daniela; Bolasco, Adriana; Fioravanti, Rossella; Chimenti, Paola; Granese, Arianna; Carradori, Simone; Rivanera, Daniela; Lilli, Daniela; Zicari, Alessandra; Distinto, Simona. Synthesis and in vitro activity of 2-thiazolylhydrazone derivatives compared with the activity of clotrimazole against clinical isolates of *Candida* spp. *Bioorganic & Medicinal Chemistry Letters* (2007), 17(16), 4635-4640.
- Chimenti, Franco; Bizzarri, Bruna; Bolasco, Adriana; Secci, Daniela; Chimenti, Paola; Carradori, Simone; Granese, Arianna; Rivanera, Daniela; Lilli, Daniela; Zicari, Alessandra; Scaltrito, M. Maddalena; Sisto, Francesca. A novel class of selective anti-*Helicobacter pylori* agents 2-oxo-2H-chromene-3-carboxamide derivatives. *Bioorganic & Medicinal Chemistry Letters* (2007), 17(11), 3065-3071.
- Cirilli, R.; Ferretti, R.; La Torre, F.; Secci, D.; Bolasco, A.; Carradori S.; Pierini, M. [High-performance liquid chromatographic separation of enantiomers and diastereomers of 2-methylcyclohexanone thiosemicarbazone, and determination of absolute configuration and configurational stability](#). *Journal of Chromatography, A* (2007), 1172(2), 160-169.

Romano Silvestri's lab

The research activity focuses the design and synthesis of new chemical entities in the field of antivirals, antifungals, antitumor agents, antiinflammatory drugs, CNS agents. The research on anti-AIDS agents led to the discovery of potent HIV-1 non-nucleoside reverse transcriptase inhibitors (NNRTIs), such as pyrrolo[1,2-b][1,2,5]benzothiadiazepine 5,5-dioxides (PBTDS), pyrrol aryl sulfones (PASs) and indolyl aryl sulfones (IASs). The hybrid IAS-peptide derivatives bearing one to three glycine or alanine units as elongated 2-carboxamide chains were more active against some clinically relevant mutant strains than the parent indole L-737,126. Recently, a refined molecular modeling study and the application of an updated highly predictive 3-D QSAR model led to design new IASs that were exceptionally potent against both WT and drug resistant mutants, and gave us some insight for the development of a newer IAS generation.

Drugs able to modulate the microtubule assembly either by inhibition of tubulin polymerization or by blocking microtubule disassembly are of great interest in anticancer therapy. Arylthioindoles bearing a 3-(3,4,5-trimethoxyphenyl)thio moiety were found potent tubulin polymerization M range. They also inhibited MCF-7 μ inhibitors, with IC₅₀s in the 2.0 to 4.5 cell growth at nanomolar concentrations, with potencies comparable to those of the reference compounds colchicine and combretastatin A-4. From careful analysis of the biological and in silico data, a basic pharmacophore for this class of compounds was hypothesized.

Our decennial interest in CNS agents, pulsed us to synthesize new 1-phenyl-5-(1H-pyrrol-1-yl)pyrazole-3-carboxamides by bioisosteric replacement of Rimonabant's 5-phenyl ring with a pyrrole nucleus. Several carboxamides were endowed with high receptor affinity. Docking studies and molecular dynamics simulations of the most selective and potent hCB1 ligands were undertaken using an in house built inactive state model of hCB1 receptor. The compounds fitted their N-substituents in a pocket formed by lipophilic residues, and the carboxamide oxygen formed a H-bond with K3.28(192). The H-bond accounted for the high affinity for receptors's inactive state and their inverse agonist activity.

Lab's activity involves synthesis, purification (MPLC, HPLC and chiral HPLC) and characterization (IR, ¹H NMR, ¹³C NMR) of new chemical entities bearing an heterocyclic group. The lab is particularly specialized on pyrrole, indole and imidazole chemistry, and microwave synthesis.

Selected publications of the research group

G. De Martino, M. C. Edler, G. La Regina, A. Coluccia, M. C. Barbera, D. Barrow, R. I. Nicholson, G. Chiosis, A. Brancale, E. Hamel, M. Artico, R. Silvestri. Arythioindoles, potent inhibitors of tubulin polymerization. 2. structure activity relationships and molecular modeling studies. *J. Med. Chem.* 2006, 49, 947-954.

G. De Martino, G. La Regina, R. Ragno, A. Coluccia, A. Bergamini, C. Ciaprini, A. Sinistro, G. Maga, E. Crespan, M. Artico, R. Silvestri. Indolyl aryl sulfones (IASs) as HIV-1 non-nucleoside reverse transcriptase inhibitors. synthesis, biological evaluation and binding mode studies of new derivatives at indole-2-carboxamide. *Antiviral Chem. Chemoth.* 2006, 57, 59-77.

R. Ragno, A. Coluccia, G. La Regina, G. De Martino, F. Piscitelli, A. Lavecchia, E. Novellino, A. Bergamini, C. Ciaprini, A. Sinistro, G. Maga, E. Crespan, M. Artico, and R. Silvestri. Design, molecular modeling, synthesis and anti-HIV-1 activity of new indolyl aryl sulfones. Novel derivatives of the indole-2-carboxamide. *J. Med. Chem.* 2006, 49, 3172-3184.

R. Cirilli, V. Orlando, R. Ferretti, L. Turchetto, R. Silvestri, G. De Martino, F. La Torre. Direct HPLC enantioseparation of chiral aptazepine derivatives on coated and bonded polysaccharide-based chiral stationary phases. *Chirality* 2006, 18, 621-632.

R. Silvestri and G. Maga. Current state-of-the-art in pre-clinical and clinical development of novel non-nucleoside HIV-1 reverse transcriptase inhibitors. *Expert Opinion on Therapeutic Patents* 2006, 16, 939-962.

R. Silvestri, G. Marfè, M. Artico, G. La Regina, G. De Martino, A. Lavecchia, E. Novellino, E. Morgante, C. Di Stefano, G. Catalano, G. Filomeni, E. Abruzzese, M. R. Ciriolo, M. A. Russo, S. Amadori, R. Cirilli, F. La Torre, P. Sinibaldi Salimei. Pyrrolo[1,2-b][1,2,5]benzothiadiazepines (PBTDs): a new class of agents endowed with high apoptotic activity in chronic myelogenous leukemia K562 cells and in cells from patients at onset and imatinib-resistant. *J. Med. Chem.* 2006, 49, 5840-5844.

R. Ragno, A. Coluccia, G. La Regina, R. Silvestri. Indolyl aryl sulphones as HIV-1 reverse transcriptase inhibitors: docking and 3-D QSAR studies. *Expert Opinion on Drug Discovery* 2007, 2, 87-114.

G. La Regina, R. Silvestri, M. Artico, A. Lavecchia, E. Novellino, O. Befani, P. Turini, E. Agostinelli. New pyrrole inhibitors of monoamine oxidase: synthesis, biological evaluation and structural determinants of MAO-A and MAO-B selectivity. *J. Med. Chem.* 2007, 50, 922-931.

A. Brancale, R. Silvestri. Indole, a core nucleus for potent inhibitors of tubulin polymerization. *Medicinal Research Reviews* 2007, 27, 209-238.

G. La Regina, M. C. Edler, A. Brancale, S. Kandil, A. Coluccia, F. Piscitelli, E. Hamel, G. De Martino, R. Matesanz, J. F. Díaz, A. I. Scovassi, E. Prosperi, A. Lavecchia, E. Novellino, M. Artico, R. Silvestri. New arythioindoles inhibitors of tubulin polymerization. 3. Biological evaluation, SAR and molecular modeling studies. *J. Med. Chem.* 2007, 50, 2865-2874.

G. La Regina, A. Coluccia, F. Piscitelli, A. Bergamini, A. Sinistro, A. Cavazza, G. Maga, A. Samuele, S. Zanolì, E. Novellino, M. Artico, R. Silvestri. Indolyl aryl sulfones as HIV-1 non-nucleoside reverse transcriptase inhibitors: role of two halogen atoms at the indole ring in developing new analogues with improved antiviral activity. *J. Med. Chem.* 2007, 50, 5034-5038.

G. Marfè, C. Di Stefano, R. Silvestri, E. Abruzzese, G. Catalano, L. Di Renzo, G. Filomeni, E. Giorda, G. La Regina, E. Morgante, M. R. Ciriolo, M. A. Russo, S. Amadori, P. Sinibaldi Salimei. Pyrrolo[1,2-b][1,2,5]benzothiadiazepines (PBTDs) induce apoptosis in chronic myelogenous leukemic K562 cells. *BMC Cancer* 2007, 7, 207.

R. Silvestri, M. G. Cascio, G. La Regina, F. Piscitelli, A. Lavecchia, A. Brizzi, S. Pasquini, M. Botta, E. Novellino, V. Di Marzo, F. Corelli. Synthesis, cannabinoid receptor affinity and molecular modeling studies of substituted 1-aryl-5-(1H-pyrrol-1-yl)-1H-pyrazole-3-carboxamides. *J. Med. Chem.* 2008, 51, 1560-1576.

F. Piscitelli, G. La Regina, R. Silvestri. An improved synthesis of ethyl 5-chloro-4-fluoro-1H-indole-2-carboxylate. *Organic Prep. and Proc. Internat. (OPPI)* 2008, 40, 216-220.

G. La Regina, F. Diodata D'Auria, A. Tafi, F. Piscitelli, S. Olla, F. Caporuscio, L. Nencioni, R. Cirilli, F. La Torre, M. Artico, M. Botta, A. T. Palamara, R. Silvestri. 1-(3-Aryloxy-3-arylpropyl)-1H-imidazoles, a new class of antifungal agents with potent activity against *Candida albicans* and dermatophytes. synthesis, structure-activity relationship and molecular modeling studies. *J. Med. Chem.* 2008, 51, 3841-3855

ROMA TRE" UNIVERSITY " LABORATORIES (WWW.UNIROMA3.IT)

Augusto Gambacorta's lab

The study and obtainment of natural antioxidants has been greatly developed in the last few years. A new trend is the modification of natural compounds of well known activity in order to enhance their antioxidant properties or change their stability and solubility in food, cosmetic or pharmaceutical environment.

The research aim is the modification of existing natural antioxidants to obtain both stabilized molecules to be used as pro-drug and conjugation of different antioxidants with potential synergic activity.

The starting materials are commercial compounds from the natural pool or products derived from the recovery of industrial or agricultural waste. The new compounds are synthesized by chemical and enzymatic reactions. Where needed, methodological studies are carried out in order to optimise the procedures and/or the yields.

The syntheses are controlled using TLC and GC-MS or HPLC analysis. Each new product is fully characterized by spectroscopic analysis (NMR, IR and MS).

The antioxidant capacity of each new compound is measured by both in vitro and ex vivo experiments. The in vitro antioxidant capacity is determined by ABTS assays while the ex vivo study are performed using DCF fluorimetric assays on cellular cultures. The experimental data are elaborated using Origin 50 and Excel software in order to obtain statistical errors and the best curves fitting.

Students can choose to work on the synthetic and/or analytical part of the project. The training will permit the student to obtain a high skill in the various chemical reactions and analytical techniques he/she will use.

Selected publications of the research group:

Gambacorta, A.; Tofani, D.; Migliorini, A.: "High yielding synthesis of methyl orthoformate-protected hydroxytyrosol and its use in the preparation of hydroxytyrosyl acetate" *Molecules* 2007, 12, 1762-1770

Gambacorta, A.; Tofani, D.; Bernini, R.; Migliorini, A. "High yielding obtainment of stable hydroxytyrosol by total synthesis and from natural glycoside oleuropein" *J.Agric.Food Chem.* 2007, 55, 3386-3391

Gambacorta, A.; Tofani, D.; Loreto, M.A.; Gasperi, T.; Bernini, R.: "HSAB driven chemoselective N1 alkylation of pyrimidine bases and their 4-methoxy- or 4-acetylamino-derivatives" *Tetrahedron* 2006, 62, 6848-6854

Bernini, R.; Coratti, A.; Provenzano, G.; Fabrizi, G.; Tofani, D.: "Oxidation of aromatic aldehydes and ketones by H₂O₂/CH₃ReO₃ in ionic liquids: a catalytic efficient reaction to achieve dihydric phenols". *Tetrahedron* 2005, 61, 1821-1825

Sandra Incerpi's Lab

1: Pallottini V, Martini C, Pascolini A, Cavallini G, Gori Z, Bergamini E, Incerpi S, Trentalance A. 3-Hydroxy-3-methylglutaryl coenzyme A reductase deregulation and age-related hypercholesterolemia: a new role for ROS. *Mech Ageing Dev.* 2005 Aug;126(8):845-51. Epub 2005 Apr 8.

2: Incerpi S. Thyroid hormones: rapid reply by surface delivery only. *Endocrinology.* 2005 Jul;146(7):2861-3. Review.

3: Incerpi S, Scapin S, D'Arezzo S, Spagnuolo S, Leoni S. Short-term effects of thyroid hormone in prenatal development and cell differentiation. *Steroids.* 2005 May-Jun;70(5-7):434-43.

- 4: D'Arezzo S, Incerpi S, Davis FB, Acconcia F, Marino M, Farias RN, Davis PJ. Rapid nongenomic effects of 3,5,3'-triiodo-L-thyronine on the intracellular pH of L-6 myoblasts are mediated by intracellular calcium mobilization and kinase pathways. *Endocrinology*. 2004 Dec;145(12):5694-703.
- 5: Incerpi S, D'Arezzo S, Marino M, Musanti R, Pallottini V, Pascolini A, Trentalance A. Short-term activation by low 17beta-estradiol concentrations of the Na⁺/H⁺ exchanger in rat aortic smooth muscle cells: physiopathological implications. *Endocrinology*. 2003 Oct;144(10):4315-24.
- 6: Incerpi S, De Vito P, Luly P, Spagnuolo S, Leoni S. Short-term effects of thyroid hormones and 3,5-diiodothyronine on membrane transport systems in chick embryo hepatocytes. *Endocrinology*. 2002 May;143(5):1660-8.
- 7: Barillari G, Albonici L, Incerpi S, Bogetto L, Pistritto G, Volpi A, Ensoli B, Manzari V. Inflammatory cytokines stimulate vascular smooth muscle cells locomotion and growth by enhancing alpha5beta1 integrin expression and function. *Atherosclerosis*. 2001 Feb 1;154(2):377-85.
- 8: Rufini S, de Vito P, Balestro N, Pescatori M, Luly P, Incerpi S. PLA(2) stimulation of Na⁽⁺⁾/H⁽⁺⁾ antiport and proliferation in rat aortic smooth muscle cells. *Am J Physiol*. 1999 Oct;277(4 Pt 1):C814-22.
- 9: Incerpi S, Luly P, De Vito P, Farias RN. Short-term effects of thyroid hormones on the Na/H antiport in L-6 myoblasts: high molecular specificity for 3,3',5-triiodo-L-thyronine. *Endocrinology*. 1999 Feb;140(2):683-9.
- 10: Ricci R, Baldini P, Bogetto L, De Vito P, Luly P, Zannetti A, Incerpi S. Dual modulation of Na/H antiport by atrial natriuretic factor in rat aortic smooth muscle cells. *Am J Physiol*. 1997 Aug;273(2 Pt 1):C643-52.

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Francesca D'Amato's Lab

Developmental Psychobiology Laboratory, Behavioral Neuroscience Department, Neuroscience Institute of the National Research Council, Roma , Italy

Studies in developmental psychobiology report that variations in the early environment are associated with changes in gene expression and biological function that persists into adulthood, well beyond the duration of the relevant environmental event. The results of studies in rodents indicate that the behaviour of the mother toward her offspring can “program” stable changes in gene expression that then serve as the basis for individual differences in behavioural and neuroendocrine responses to stress in adulthood. The maternal effects on phenotype are associated with sustained changes in the expression of genes in brain regions that mediate responses to stress and form the basis for stable individual differences in stress reactivity. These findings provide a potential mechanism for the influence of parental care on vulnerability/resistance to stress-induced illness over the lifespan. The analysis of the early environment in developing organism represents a powerful tool to detect and rescue vulnerable genotypes.

The laboratory training consists in learning techniques for the analysis of different aspects of mouse behavioural phenotype. We have developed a series of competences in the field of behavioural models with inbred strains, mutants and knockout mice. Behavioural studies cover the biological bases of learning and memory, the mechanisms of adaptation to the environment, the relationships between emotional and cognitive factors, social and feeding behaviour, as well as pain mechanisms. Moreover, the Institute has developed several techniques to investigate the effects of psychotropic drugs - including substances of abuse- on behaviour.

Selected publications of the research group

- D'Amato FR, Zanettini C, Sgobio C, Sarli C, Carone V, Moles A, Ammassari-Teule M “Intensification of maternal care by double-mothering selectively boosts cognitive function and hippocampal morphology in the adult offspring”. HIPPOCAMPUS in press 2010
- Zanettini C, Carola V, Lo Iacono L, Moles A, Gross C, D'Amato FR. “Postnatal handling reverses social anxiety in serotonin receptor 1A knockout mice”. GENES BRAIN AND BEHAVIOR 9:26-32, 2010.
- Moles A, Sarli C, Bartolomucci A, D'Amato FR: “Interaction with stressed mothers affects corticosterone levels in pups after reunion and impairs the response to dexamethasone in adult mice”. PSYCHONEUROENDOCRINOLOGY, 33: 462-470, 2008. -131.
- D'Amato FR, Barakos E, Ziolkowska B, Obara I, Przewlocka B, Pavone F. “Mild postnatal manipulation reduces proenkephalin mRNA in the striatum in developing mice and increases morphine conditioned place preference in adulthood.” PHARMACOLOGY BIOCHEMISTRY AND BEHAVIOR, 87: 122-129, 2007.
- D'Amato F.R., Scalera E., Sarli C. & Moles A. “Pups call, mothers rush: does maternal responsiveness affects the amount of ultrasonic vocalizations in mouse pups?” BEHAVIOR GENETICS, 35: 103-112, 2005.

Moles A., Kieffer, B. D'Amato F.R. "Deficit in attachment behavior in mice lacking the μ -opioid receptor gene". SCIENCE, 304: 1983-1986, 2004.

Moles A, Rizzi R., D'amato F.R. "Postnatal stress in mice: does "stressing" the mother have the same effects as "stressing" the pups?" DEVELOPMENTAL PSYCHOBIOLOGY, 44: 230-237, 2004.

D'Amato F.R., Moles A. 'Ultrasonic vocalizations as an index of social memory in female mice'. BEHAVIORAL NEUROSCIENCES, 115: 834-840, 2001.

Previous experience with Erasmus Students : Ben Spruit (ben.spruit@gmail.com) Leiden University, The Netherlands

ENEA, NEAR ROME ([HTTP://WWW.CASACCIA.ENEAIT/](http://www.casaccia.enea.it/))**Annamaria Bevivino's Lab*****Laboratory of Microbiology at ENEA Casaccia Research Centre***

The Laboratory of Microbiology of ENEA Casaccia Research Centre is involved in several lines of research. The first one is aimed to investigate the impact of that anthropogenic activity such as land use and management factors and climate change on soil microbial community composition and diversity. The visualization of the biodiversity of a microbial community, also named community fingerprint or profile, can be obtained from a variety of available techniques, such as Denaturing Gradient Gel Electrophoresis (DGGE). This molecular analysis follows a basic protocol which starts with the extraction of DNA from soil samples, followed by PCR (polymerase-chain reaction) of specific DNA fragments. The aims of the research are: assessment of the genetic and functional diversity of soil micro-organisms involved in the C and N cycles in the soil, targeting microbial populations with known functional importance in ecosystem, correlations between the relative abundance of specific microbial populations and environmental variables, managements, etc. The second line of research activity is focused on the investigation of the in vitro dual-species bacterial biofilm formation by *P. aeruginosa* and *B. cenocepacia*, two important opportunistic pathogens affecting patients with cystic fibrosis. The biofilm-forming capability of these microorganisms reduces antibiotic efficacy and makes eradication rarely successful.

Selected publications of the research group

1. Dalmastrì C., Baldwin A., Tabacchioni S., Bevivino A., Mahenthiralingam E., Chiarini L. and Dowson. C. (2007) Investigating *Burkholderia cepacia* complex populations recovered from Italian maize rhizosphere by multilocus sequence typing. *Environmental Microbiology* 9(7): 1632-1639.
2. Pirone L., Bragonzi A., Farcomeni A., Paroni M., Auriche C., Conese M., Chiarini L., Dalmastrì C., Bevivino A* and Ascenzioni A. (2008) *Burkholderia cenocepacia* strains isolated from cystic fibrosis patients are apparently more invasive and more virulent than rhizosphere strains. *Environmental Microbiology* 10: 2773-2784.
3. Tabacchioni S., Ferri L., Manno G., Mentasti M., Cocchi P., Campana S., Ravenni N., Taccetti G., Dalmastrì C., Chiarini L., Bevivino A. and Fani R. (2008) Use of the *gyrB* gene to discriminate among species of the *Burkholderia cepacia* complex. *FEMS Microbiology Letters* 281(2): 175-182.
4. Cesarini S., Bevivino A., Tabacchioni S., Chiarini L. and Dalmastrì C. (2009) *RecA* gene sequence and Multilocus Sequence Typing for species-level resolution of *Burkholderia cepacia* complex isolates. *Letters in Applied Microbiology* 49: 580-586.
5. Ferri L., Perrin E., Campana S., Tabacchioni T., Taccetti G., Cocchi P., Ravenni N., Dalmastrì C., Chiarini L., Bevivino A., Manno G., Mentasti M., Fani R. (2010) Application of multiplex single nucleotide primer extension (mSNuPE) to the identification of bacteria: the *Burkholderia cepacia* complex case. *Journal of Microbiological Methods* (in press). DOI: 10.1016/j.mimet.2010.01.008

Maurizio Calvitti's Lab

Research activities carried out by our laboratory mainly concern biological and genetic control of insect pests and vectors. Within this topic, a biotechnological approach characterizes our methods of study and searching for practical solutions. Laboratory training may involve the acquisition of experiences in: insect rearing; study of insect biology and ethology; application to insects of molecular biology techniques such as, DNA extraction, PCR, agarose gel electrophoresis. At present, the most relevant expertise of our laboratory is the study and application of methods to obtain the sterilization of insect males in order to allow them to be used as genetic control tools against insect vectors such as

mosquitoes. In particular, micromanipulation and microinjection techniques are used to transfer specific symbiotic bacteria, capable to induce useful modifications of insect reproductive biology, from a donor to a target species. Student training may also involve the learning of these techniques in which we are one of the leading group in Europe.

Selected publications of the research group:

Calvitti, M., Antonelli, M., Moretti R., and R.C. Bautista, 2002. Oviposition response and development of the egg-pupal parasitoid *Fopius arisanus* on *Bactrocera oleae*, a tephritid fruit fly pest of olive in the Mediterranean basin. *Entomologia Experimentalis et Applicata*, 102(1): 65-73.

Moretti, R., and M. Calvitti, 2003. Mortality by parasitization in the association between the oo-pupal parasitoid *Fopius arisanus* and *Ceratitis capitata*. *BioControl*, 48(3): 275-291.

Bellini, R., M. Calvitti, A. Medici, M. Carrieri, G. Celli And S. Maini. 2007. Use of the Sterile Insect Technique against *Aedes albopictus* in Italy: First Results of a Pilot Trial, pp. 505-515. In Vreysen, M.J.B., A.S. Robinson, and J. Hendrichs (Eds.), *Area-Wide Control of Insect Pests: From Research to Field Implementation*. Springer, Dordrecht, The Netherlands.

Moretti, R. and Calvitti, M., 2008. Intrinsic competition between the parasitoids *Eretmocerus mundus* and *Encarsia formosa* in *Bemisia tabaci*. *Entomologia Experimentalis et Applicata*, 129: 44-53.

Calvitti, M., Moretti, R., Porretta D., Bellini R. and Urbanelli S., 2009. Wolbachia removal in the mosquito *Aedes albopictus*: effects on male fitness. *Medical and Veterinary Entomology*, 23: 132-140.

Calvitti, M., Moretti, R., Lampazzi E., Bellini R. and Dobson S. L., 2010. Characterization of a new *Aedes albopictus* (Diptera: Culicidae) - *Wolbachia pipientis* (Rickettsiales: Rickettsiaceae) symbiotic association generated by artificial transfer of the wPip strain from *Culex pipiens* (Diptera: Culicidae). *Medical Entomology*. 47(2):179-187.

Massimo Celino's Lab

ENEA (Italian Agency for New Technology, Energy and Sustainable Economic Development, <http://www.enea.it>) is a public institution operating in the fields of energy, environment and new technologies to support competitiveness and sustainable development. ENEA has 12 research sites, six of them integrated with computer centers. All ENEA main computational resources are integrated in the ENEA-GRID infrastructure which provides to ENEA researchers and their partners an easy access to the available multiplatform resources. The GRID infrastructure provides a full set of services for authentication, authorization, resource discovery and management. Many sectors of the computational science routinely perform high performance calculations in the ENEA GRID environment, with a particular attention to the CRESCO infrastructure (linux parallel computing platform with a total of about 2700 cores, www.cresco.enea.it). One of them is the computational Materials Science Laboratory (CMAST, Computational Materials Science and Technology, www.afs.enea.it/project/cmast) which gathers all the activities of ENEA and its partners in this field. CMAST provides a virtual environment where researchers, from both universities and industries, work together by sharing competences, software, specialized services and best practices. In the CMAST Laboratory classical and ab-initio molecular dynamics simulations are performed to study a wide range of materials and molecules with applications in energy and new-technology fields. Molecular systems from life-science and bio-inspired materials are also considered.

Training of the students will be performed in the CMAST laboratory by helping them in leading small scientific projects. Students will have the possibility to use the HPC infrastructure and the software

specialized in molecular modeling. Lessons and seminars on both high performance computing themes and on molecular modeling activities will be performed.

Selected publications of the research group

- M.Celino, A.Montone, F.Cleri, A.Aurora, D.Mirabile Gattia, S.Giusepponi, M.Vittori Antisari, "Metallographic and numerical studies of the role of catalyst particles in MgH₂-Mg system", Def. and Diff. Forum, Vols 297-301 (2010) pp 263.
- M.Celino, F.Coppiari, A.Di Cicco, "Pressure effects on icosahedral short range order in undercooled copper", Solid State Science 12 (2010) 179-182.
- S.Giusepponi, M.Celino, F.Cleri, A.Montone, "Hydrogen storage in MgH₂ matrices:a study of Mg-MgH₂ interface using CPMD code on ENEA-GRID", Il Nuovo Cimento C 32 (2009) 139-142.
- G.Gianese, V.Rosato, F.Cleri, M.Celino, P.Morales, "Atomic-scale modelling of the interaction between short polypeptides and carbon surfaces", J. Phys. Chem. B 113 (2009) 12105-12112.
- B.Rakshit, S.Sanyal, [M.Celino](#), "First-Principles Lattice Dynamical Study of ScAs and ScSb at Zero and High Pressure", Solid State Communications 149 (2009) 1326-1329.
- [C.Massobrio](#), [M.Celino](#), [P.S.Salmon](#), [R.A.Martin](#), [M.Micoulaut](#), [A.Pasquarello](#), "Atomic structure of the two intermediate phase glasses SiSe₄ and GeSe₄", Phys. Rev. B 79, 174201 (2009).
- V.Artale, G.Bracco, G.Buffoni, M.Celino, P.D'Angelo, S.Migliori, A.Quintiliani, V.Rosato, G.Sannino, "Calcolo Numerico ad alte prestazioni", [Energia Ambiente e Innovazione, Bimestrale ENEA](#), Anno 54, luglio-agosto 2008.

Claudia Dalmastrì's Lab

Biodiversity of natural bacterial communities in soil: study of population structure at the molecular level and variation related to different environmental conditions and anthropogenic activity.

Opportunistic pathogens of the Burkholderia cepacia complex in natural habitat. Characterisation of environmental and clinical isolates to assess the presence of potential pathogenic strains in the environment: identification and typing by means of advanced tools.

Diversity of gut microbiota in insect: functional analysis to assess the role of microbiota in insects responsible of pathogenicity in plants

Selected publications of the research group

- Pirone L., Chiarini L., Dalmastrì C., Bevivino A., Tabacchioni S. (2005). Detection of cultured and uncultured Burkholderia cepacia complex bacteria naturally occurring in the maize rhizosphere. Env. Microbiol. 7(11):1734-1742.
- Chiarini L., Bevivino A., Dalmastrì C., Tabacchioni S., Visca P. (2006) Burkholderia cepacia complex species: health hazard and biotechnological potential. Trends Microbiol. 14(6):277-286.
- Dalmastrì C., A. Baldwin, S. Tabacchioni, A. Bevivino, E. Mahenthiralingam, L. Chiarini, C. Dowson. 2007. Investigating Burkholderia cepacia complex populations recovered from Italian maize rhizosphere by multilocus sequence typing. Env. Microbiol.9: 1632-1639.
- Baldwin A., Mahenthiralingam E., Drevinek P., Vandamme P., Govan J. R., Waine D. J., LiPuma J. J., Chiarini L., Dalmastrì C., Henry D. A., Speert D. P., Dowson C. G. (2007) Environmental Burkholderia cepacia complex isolates in human infections. Emerging Infectious Diseases 13:458-461.
- Tabacchioni S., Ferri L., Manno G., Mentasti M., Cocchi P., Campana S., Ravenni N., Taccetti G., Dalmastrì C., Chiarini L., Bevivino A., and Fani R. (2008) Use of the gyrB gene to discriminate among species of the Burkholderia cepacia complex. FEMS Microbiol Lett 281(2):175-182.
- Pirone L., Bragonzi A., Farcomeni A., Paroni M., Auriche C., Conese M., Chiarini L., Dalmastrì C., Bevivino A., and Ascenzioni F. (2008) Burkholderia cenocepacia strains isolated from cystic fibrosis patients are apparently more invasive and more virulent than rhizosphere strains. Environ Microbiol. 10:2773-2784.
- Cesarini S., Bevivino A., Tabacchioni S., Chiarini L., Dalmastrì C. (2010) RecA gene sequence and Multilocus Sequence Typing for species-level resolution of Burkholderia cepacia complex isolates. Letters in Applied Microbiology 49 (5): 580-588.
- Ferri L., Campana S., Tabacchioni S., Taccetti G., Cocchi P., Rivenni N., Dalmastrì C., Chiarini L., Bevivino A., Manno G., Mentasti M. and Fani R. (2010) Application of Multiplex Single Nucleotide Primer Extension (SNuPE) to the identification of bacteria: the Burkholderia cepacia complex case. J Microbiological Methods 80:251-256

Previous experience with Erasmus Students: Maite Sanpedro Pellicer, Valencia - Spain

Anna Giovanetti' s Lab

At the ENEA Casaccia research Center (<http://www.enea.it>) researches are carried on direct or non-targeted effects of ionizing radiation (bystander effect, genomic instability).

The main objectives are to:

- Characterize the radio-induced effects
- Analyse the role of signalling cytokines, oxidative stress and cellular membrane on the untargeted response
- Verify if antioxidant treatment is able to counteract radio-induced damage.
- Identify a set of biosensors for the early assessment of radiation exposure

Research includes studies at different levels of biological organization such in vitro, ex vivo, in vivo and human studies. The main parameters measured are: genetic damage (Comet assay, micronuclei, H2AX), apoptosis (DAPI, Annexin Cy3), ROS production (FACS and), cytotoxicity (MTT), signalling molecules and antioxidant enzymes (ELISA).

Selected publications of the research group

- Mancuso M Giovanetti A Brittebo E "Effects of dichlobenil on the ultrastructural morphology" *Toxicol Pathol* 25:186, 1997
- Giovanetti A Mancuso M Lombardi C Massa E "Analysis of lung damage induced by TCE inhalation in mice fed diets with low, normal and high copper content" *Toxicol Pathol* 26:628, 1998
- Bergstrom U, Giovanetti A, Piras E, Brittebo E "Methimazole-induced damage in the olfactory mucosa effects on ultrastructure and glutathione levels" *Toxicol Pathol* 31:19, 2003
- R Amendola, E Basso, P Pacifici, E Piras, A Giovanetti, G Romeo "Mouse RET, cAbl, and TP53 gene fragmentations detected in COMET-FISH assay act as in vivo bio-markers of radiation exposure" *Rad Res* 165,5:553-561, 2006
- C Limatola, V Massa, C Lauro, A Giovanetti, S Nuccitelli, A Spinedi. "Evidence for a role of glycosphingolipids in CXCR4-dependent cell migration". *FEBS Lett.* 581(14):2641-2646, 2007.
- Giovanetti, E. Basso, T. Deshpande "Persistence of Genetic Damage in Mice Exposed to low dose of X Rays" *Int J Rad Biol.* Volume 84 Issue 3, 227-235, 2008
- Giovanetti, S. Fesenko, M.L. Cozzella, L. D. Asencio, U. Sansone "Bioaccumulation and biological effects in the earthworm *Eisenia fetida* exposed to natural and depleted uranium", *J Environm Radioact*, 101, 6: 509-516, 2010

Silvia Tabacchioni's Lab

The microbiology ENEA's group has a long-standing expertise in (i) the use of microorganisms as plant growth promoters (biofertilizers) and biocontrol agents, (ii) microbial ecology, in particular in the field of culture-dependent and culture-independent analyses of natural microbial communities, and in (iii) bioconversion of biomasses, in particular in the field of fermentation processes using wastes as substrate (industrial and urban wastes) for the production of chemicals and biofuels.

Our expertise includes the phenotypic and genotypic characterization of different bacterial species as potential biofertilizers and biocontrol agents and their application in greenhouse and field experiments

Our expertise includes the development and application of PCR-based methods such as cloning, sequencing, Denaturing Gradient Gel Electrophoresis (DGGE), multilocus sequence typing (MLST) and culturing of bacteria from a variety of environmental samples (e.g. soil, rhizosphere, freshwater, lake sediment, and sewage sludge samples) as well as statistical analyses of molecular data.

Our expertise includes the set up of batch and fed-batch fermentation processes for the production of lactic acid from milk whey and whey permeate, and of hydrogen through dark fermentation of the organic fraction of solid urban wastes, as well as the development and application of analytical methods such as Gas Chromatography (GC) and High Performance Liquid Chromatography (HPLC).

Selected publications of the research group

- 1) Chiarini L., Mara L., Tabacchioni S. (1992) Influence of growth supplements on lactic acid production in whey ultrafiltrate by *Lactobacillus helveticus*. *Appl Microbiol Biotechnol* 36: 461-464.
- 2) Di Cello F., Bevivino A., Chiarini L., Fani R., Paffetti D., Tabacchioni S., Dalmastrì C. (1997) Biodiversity of a *Burkholderia cepacia* population isolated from maize rhizosphere at different plant growth stages. *Appl Environ Microbiol* 63: 4485-4493.
- 3) Tabacchioni S., Chiarini L., Bevivino A., Cantale C., Dalmastrì C. (2000) Bias caused by using different isolation media for assessing the genetic diversity of a natural microbial population. *Microb Ecol* 40: 169-176.
- 4) Fiore A., Laevens S., Bevivino A., Dalmastrì C., Tabacchioni S., Vandamme P., Chiarini L. (2001) *Burkholderia cepacia* complex: distribution of genomovars among isolates from the maize rhizosphere in Italy. *Environ Microbiol* 3: 137-143.
- 5) Dalmastrì C., Fiore, A., Alisi, C., Bevivino, A., Tabacchioni, S., Giuliano, G., Sprocati, A.R., Segre, L., Mahenthalingam, E., Chiarini, L., and Vandamme, P. (2003) A rhizospheric *Burkholderia cepacia* complex population: genotypic and phenotypic diversity of *Burkholderia cenocepacia* and *Burkholderia ambifaria*. *FEMS Microbiol Ecol* 46: 179-187.
- 6) Pirone, L., Chiarini, L., Dalmastrì, C., Bevivino, A., Tabacchioni, S. Detection of cultured and uncultured *Burkholderia cepacia* complex bacteria naturally occurring in the maize rhizosphere. *Env Microbiol* 7:1734-1742.
- 7) Dalmastrì, C., Baldwin, A., Tabacchioni, S., Bevivino, A., Mahenthalingam, E., Chiarini, L., Dowson, C. (2007) Investigating *Burkholderia cepacia* complex populations recovered from Italian maize rhizosphere by multilocus sequence typing. *Environ Microbiol* 9:1632-1639.
- 8) Lal, S., Paganin, P., Chiarini, L., Bevivino, A., Dalmastrì, C., Tabacchioni, S. Eutrophic lake sediments host a community of H₂ producing strains of *Penibacillus polymyxa*. IX Convegno FISV, 26-29 settembre 2007 Riva del Garda, Italy.
- 9) Paganin, P., Chiarini, L., Bevivino, A., Dalmastrì, C., Izzo, G, Tabacchioni S. Archeal and bacterial community composition of plankton and sediment from Averno lake. X Convegno FISV, 24-27 settembre 2008 Riva del Garda, Italy.
- 10) Aldrovandi, A, Marsili E, Stante, L, Paganin, P, Tabacchioni, S, Giordano, A. (2009) Sustainable power production in a membrane-less and mediator-less synthetic wastewater microbial fuel cell. *Biores Technol* 100: 3252-3260).

ISTITUTO SUPERIORE DI SANITA', ROME (WWW.ISS.IT)

Gemma Calamandrei's Lab

Section of Neurotoxicology and Neuroendocrinology, Department of Cell Biology and Neuroscience, Istituto Superiore di Sanità (National Institute of Health), Rome, Italy

The research activity carried out in our laboratory is focused on animal models of neurodevelopmental disorders, and also involves the use of transgenic mouse strains to assess the role of defective genes and of their interaction with environmental risk factors. Experiments are mainly concerned with characterization of rodents' neurobehavioural phenotype with special emphasis on social and communicative behaviour (ultrasonic vocalizations) at different developmental stages. Experimental protocols also imply administration of drugs/neurotoxicants to pregnant females, with the aim of analysing both short and long-term effects of these exposure on offspring behaviour. Neurochemical and neurohormonal correlates of the behaviors in study are also studied in collaboration with other research groups working at the ISS. Statistical data analysis with complex designs are applied.

Selected publications of the research group

- The female urine sniffing test: a novel approach for assessing reward-seeking behavior in rodents. Malkesman O, Scattoni ML, Paredes D, Tragon T, Pearson B, Shaltiel G, Chen G, Crawley JN, Manji HK. *Biol Psychiatry*. 2010;67(9):864-71.
- Early behavioural markers of disease in P301S tau transgenic mice. Scattoni ML, Gasparini L, Alleva E, Goedert M, Calamandrei G, Spillantini MG. *Behav Brain Res*. 2010;208(1):250-7.
- Gestational exposure to the organophosphate chlorpyrifos alters social-emotional behaviour and impairs responsiveness to the serotonin transporter inhibitor fluvoxamine in mice. Venerosi A, Ricceri L, Rungi A, Sanghez V, Calamandrei G. *Psychopharmacology (Berl)*. 2010;208(1):99-107.
- Unusual repertoire of vocalizations in the BTBR T+tf/J mouse model of autism. Scattoni ML, Gandhi SU, Ricceri L, Crawley JN. *PLoS One*. 2008;3(8):e3067.
- Prenatal chlorpyrifos exposure alters motor behavior and ultrasonic vocalization in CD-1 mouse pups. Venerosi A, Ricceri L, Scattoni ML, Calamandrei G. *Environ Health*. 2009;8:12.
- Long-term effects on hypothalamic neuropeptides after developmental exposure to chlorpyrifos in mice. Tait S, Ricceri L, Venerosi A, Maranghi F, Mantovani A, Calamandrei G. *Environ Health Perspect*. 2009;117(1):112-6.

Giovanni Laviola's Lab

The major interest of the lab is "behavioural neuroscience", specifically development and validation of animal models of neuro-psychiatric diseases. The lab is particularly interested in the modulation of animal behavior by means of pharmacological and non-pharmacological tools (socio-environmental factors, hormones and drugs). The research training will consist in active involvement in experiments with animal model of diseases aimed to look at alterations of motivational and socio-emotional parameters. The experience will include behavioural testing using mice and rats, including drug-induced conditioned place preference; drug self-administration; tests of anxiety and depression; tests for social affiliation / aggressivity; tests to model "decision making", a process involving the inhibition of sub-cortical drives and a pre-fronto-cortical elaboration. A particular interest is devoted to the infant and adolescent phase in laboratory rodents, a window of vulnerability for the onset of behavioural disorders.

Thanks to a precious collaboration with another group at the same Institute, training can now exploit the possibility to measure metabolic parameters in brain areas of rodents, by means of the technique of in vivo magnetic resonance spectroscopy (MRS). In particular, experiments will deal with the challenging attempt to link altered behaviour with functional activation in forebrain brain areas, suggestive of localized changes in brain energy metabolism.

Selected publications of the research group

Adriani W, Laviola G (2002) Spontaneous Novelty Seeking and Amphetamine-induced Conditioning and Sensitization in Adult Mice. Evidence of Dissociation as a Function of Age at Weaning. *Neuropsychopharmacology* 27: 225-236.

Adriani W, Macri S, Pacifici R, Laviola G (2002) Peculiar Vulnerability to Nicotine Oral Self-administration in Mice during Early Adolescence. *Neuropsychopharmacology* 27: 212-224

Adriani W, Della Seta D, Dessi-Fulgheri F, Farabollini F, Laviola G (2003) Altered profiles of spontaneous novelty seeking, impulsive behaviour, and response to d-amphetamine in rats perinatally exposed to bisphenol-A. *Environmental Health Perspectives* 111: 395-401

Adriani W, Laviola G (2003) Elevated levels of impulsivity and reduced place conditioning with d-amphetamine: Two behavioral features of adolescence in mice. *Behavioral Neuroscience* 117: 695-703

Adriani W, Caprioli A, Granstrem O, Carli M, Laviola G (2003) The spontaneously-hypertensive-rat as an animal model of ADHD: Evidence for impulsive and non-impulsive subpopulations. *Neurosci Biobehav Rev* 27: 639-651

Adriani W, Granstrem O, Macri S, Izykenova G, Dambinova S, Laviola G (2004) Behavioral and neurochemical vulnerability during adolescence in mice: Studies with spontaneous consumption or imposed administration of nicotine. *Neuropsychopharmacology* 29: 869-878

Laviola G, Adriani W, Rea M, Aloe L, Alleva E (2004) Social withdrawal, neophobia, and stereotyped behavior in developing rats exposed to neonatal asphyxia. *Psychopharmacology* 175: 196-205

Adriani W, Rea M, Baviera M, Invernizzi W, Carli M, Ghirardi O, Caprioli A, Laviola G (2004) Acetyl-L-carnitine reduces impulsive behaviour in adolescent rats. *Psychopharmacology* 176: 296-304

Adriani W, Giannakopoulou D, Bokulic Z, Jernej B, Alleva E, Laviola G (2006) Response to novelty, social and self-control behaviors, in rats exposed to neonatal anoxia: Modulatory effects of an enriched environment. *Psychopharmacology* 184: 155-65.

Adriani W, Leo D, Greco D, Rea M, Di Porzio U, Laviola G, Perrone-Capano C (2006) Methylphenidate administration to adolescent rats determines plastic changes on reward-related behavior and striatal gene expression. *Neuropsychopharmacology* 31: 1946-1956

Adriani W, Deroche-Gamonet V, Le Moal M, Laviola G, Piazza PV (2006) Pre-exposure during or following adolescence differently affects nicotine rewarding properties in adult rats. *Psychopharmacology* 184: 382-390

Laviola G, Adriani W, Gaudino C, Marino R, Keller F (2006) Paradoxical effects of prenatal acetylcholin-esterase blockade on neuro-behavioral development and on drug-induced stereotypies in reeler mutant mice. *Psychopharmacology* 187: 331-344.

Adriani W, Canese R, Podo F, Laviola G (2007) 1H MRS-detectable metabolic brain changes and reduced impulsive behavior in adult rats exposed to methylphenidate during adolescence. *Neurotoxicology and Teratology* 29: 116-25

Previous experiences with Erasmus students:

Isabelle Olivier (AMIENS): isa-ka@hotmail.fr

Fernando Santos (PORTO) fjoaogsantos@gmail.com

Susanne Koot (UTRECHT) susanne.koot@chello.nl

Blandine Duvillard (LYON): Bd007@bouygtel.fr

Ana Nichole Chaves (MONTE CAPARICA): nickass12@hotmail.com

Adrien Borsik (PARIS-DESCARTES): adrienborsik@gmail.it

Francesca Maranghi's Lab

Food and Veterinary Toxicology Unit

Research activity on risk assessment of chemicals in the food chain acting on endocrine homeostasis (Endocrine Disrupters – EDs) for susceptible/vulnerable phases of development (childhood). Elaboration of *in vivo* experimental models to identify and characterize long-term effects following exposure to chemicals with neuro-endocrine, reproductive and immune activity. Targeted *in vivo* toxicological studies (juvenile toxicity/reproductive-developmental toxicity). Histopathological analysis, evaluation and characterization of biomarkers of effect, toxicogenomics and phenotypic anchoring in sex steroids-targeted tissues. Evaluation of the potential association between ED exposure and increased risk of childhood diseases by development of bio-monitoring programs linking together environment, food and life style, using and characterizing biomarkers of exposure and their correlation with health status.

Selected publications of the research group

- Maranghi F**, Tassinari R, Moracci G, Macri C, Mantovani A. Effects of a low oral dose of diethylstilbestrol (DES) on reproductive tract development in F1 female CD-1 mice. *Reprod Toxicol*. 2008 Oct;26(2):146-50.
- Maranghi F**, Tassinari R, Lagatta V, Moracci G, Macri C, Eusepi A, Di Virgilio A, Scattoni ML, Calamandrei G. Effects of the food contaminant semicarbazide following oral administration in juvenile Sprague-Dawley rats.. *Food Chem Toxicol*. 2008 Dec 10.
- Maranghi F**, Rescia M, Macri C, Di Consiglio E, De Angelis G, Testai E, Farini D, De Felici M, Lorenzetti S, Mantovani A. Lindane may modulate the female reproductive development through the interaction with ER-beta: an *in vivo-in vitro* approach. *Chem Biol Interact*. 2007 Aug 15;169(1):1-14. Epub 2007 Apr 22.
- S. Tait, L. Ricceri, A. Venerosi, **F. Maranghi**, A. Mantovani and G. Calamandrei (2009). Long-Term Effects on Hypothalamic Neuropeptides after Developmental Exposure to Chlorpyrifos in Mice. *Environmental Health Perspectives* volume 117(1) January 2009
- Mantovani A, La Rocca C, **Maranghi F**. Endocrine disrupters: from research to risk assessment. *Epidemiol Prev*. 2009 Jan-Apr;33(1-2):5-7. Italian. No abstract available.
- De Angelis S, Tassinari R, **Maranghi F**, Eusepi A, Di Virgilio A, Chiarotti F, Ricceri L, Venerosi Pesciolini A, Gilardi E, Moracci G, Calamandrei G, Olivieri A, Mantovani A. Developmental exposure to chlorpyrifos induces alterations in thyroid and thyroid hormone levels without other toxicity signs in CD-1 mice. *Toxicol Sci*. 2009 Apr;108(2):311-9.
- A. Magrelli, G. Azzalin, M. Salvatore, M. Viganotti, F. Tosto, T. Colombo, R. Devito, A. Di Masi, A. Antoccia, S. Lorenzetti, **F. Maranghi**, A. Mantovani, C. Tanzarella, G. Macino, D. Taruscio. Altered microRNA expression patterns in Hepatoblastoma patients. *Translational Oncology* 2009 (in press).
- Caserta D, Maranghi L, Mantovani A, Marci R, **Maranghi F**, Moscarini M. Impact of endocrine disruptor chemicals in gynaecology. *Hum Reprod Update*. 2008 Jan-Feb;14(1):59-72.
- M. Clementi, G. Tiboni, R. Causin, C. La Rocca, **F. Maranghi**, F. Raffagnato, R. Tenconi. 2008. Pesticides and fertility: An epidemiological study in Northeast Italy and review of the literature. *Reproductive Toxicology* 2008, 26:1, 13-18.
- A. Mantovani, **F. Maranghi**, C. La Rocca, G. Tiboni, M. Clementi. The role of toxicology to characterize biomarkers for agrochemicals with potential endocrine activities. *Reproductive Toxicology* 2008, 26:1, 1-7.

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([HTTP://WWW.MARIONEGRI.IT/MN/EN/INDEX.HTML?L=EN](http://www.marionegri.it/mn/en/index.html?L=EN))

Tiziana Borsello's Lab

The lab of Tiziana Borsello Neuronal death and Neuroprotection is in the the Department of Neuroscience at the Mario Negri Institute of Milano. See the personal web site <http://www.neuronlab.org/index.oho> as well as the Institute web site <http://www.marionegri.it/mn/it/index.html>

The training is designed to appeal to students from varied backgrounds. The lab is working in the Neuroscience field with an emphasis on studying neuronal death, key modulators enzyme in neurodegenerative mechanisms and neuroprotection, especially neurodegenerative diseases This Is a practical training in the skills necessary for a career In a research environment (see the techniques) but have also a challenge of extending students theoretical knowledge. Therefore, the main aim is to equip undergraduates student from these different backgrounds for the next stage of their career to develop their master thesis . Learning Objectives. Students will learn the protocols and techniques needed to study neuronal death, activation of different signalling pathways, protein interaction and will see the application of this form in cell free,

Techniques: The Cargo Strategy As A Key Tool In Neuroprotection in vivo-AD and PD mice models. Primary neuronal culture; organ typical culture of hippocampus and cerebellum. Ceil line cultures. Routine histological techniques Basic biochemistry-techniques Molecular Biology techniques: DNA purification, manipulation of plasmids, sub cloning, constructions of targeting vector, mutagenesis, southern-blot, immunoprecipitation of proteins, western-blot, cells transfection. Imagine techniques: NeuroLucida and Neuroexplorer morphometric-analysls; Time-Lapse microscopy on living neurons for study synaptic morphology. Confocal, EM two-photon microscopies

Selected publications of the research group

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