

**Personal Information**

Name: **Laura Pacini**  
 Birthplace: Rome, Italy  
 Nationality: Italian  
 Work address: Saint Camillus International University of Health and Medical Sciences (UniCamillus), Via di Sant'Alessandro 8 , 00131 Rome  
 e-mail: laura.pacini@unicamillus.org

**Education**

**1987** Master's Degree *cum laude* in Biological Sciences, University of Rome "Tor Vergata"  
**1992** PhD in "Molecular and Cellular Biology", University of Rome "Tor Vergata"  
**1991-1993** Postgraduate Course in "Biotechnology Applications", University of Rome "Tor Vergata" (fellowship Montedison S.p.A)

**Research Fields**

**2011- to present** The study of cellular and molecular mechanisms underlying memory and cognitive processes based on activity-dependent synaptic plasticity. In particular, I focused on the molecular mechanisms that affect local protein synthesis and the formation of synapses. Dysregulation of these mechanisms leads to dysmorphogenesis of dendritic spines and a variety of neuropathological conditions including the most common form of inherited intellectual disability, Fragile X syndrome (FXS).

FXS is caused by the lack of expression of the FMR1 gene, which encodes the Fragile X Mental Retardation Protein (FMRP protein), and is involved in multiple aspects of neuronal mRNA metabolism such as transport, stability and local translation. My research activity is also aimed at understanding the contribution of the absence of FMRP to autism spectrum disorders (ASD) present in a high percentage of patients affected by FXS. The experimental models used include the murine model FMR1 KO and samples derived from blood / cells of patients with FXS.

In addition, some clinical studies have shown a reduced risk of cancer in individuals with FXS. Therefore, my research has expanded to include the role of FMRP in tumor progression. Recent work within the research group of Prof. Claudia Bagni has indeed documented that high levels of FMRP are correlated with indicators of aggressiveness and invasiveness of different types of cancer.

**1993-2009** Hepatitis C virus (HCV) molecular biology. Study of cellular systems for *in vitro* infection / replication of HCV.

**1987-1993:** Signal transduction and lipid intracellular messengers. Lipid metabolism in primary cultures of mouse keratinocytes and in human neuroblastoma cell lines. Mechanism of action of amphiphilic molecules on acetylcholinesterase activity.

**Research experience**

**2011- to present.** Staff Scientist, Laboratory of Molecular Neurobiology (Prof. Claudia Bagni), Department of Biomedicine and Prevention, Faculty of Medicine, University of Rome "Tor Vergata", Italy

**Collaboration Contracts:**

-Telethon GGP10150A: "*Mechanisms of reactivation of the FMR1 gene and analysis of pathways involved in the pathogenesis of fragile X syndrome: towards a drug-based therapy.*" (from 1/07/2012 to 30/06/2013)

-Associazione Italiana Sindrome X fragile: "*Role of the FMRP protein in gene regulation mediated by microRNAs in Fragile X Syndrome*" (from 1/11/ 2013 to 1/11/ 2014)

-Novartis Pharma: "Analysis of general protein synthesis in FXS patient fibroblasts"  
 (from 1/11/ 2014 to 30/04/ 2015)

**Research Contract** (Assegno di Ricerca) "Shaping and reshaping the synapses: from physiology to Intellectual Disability syndromes" (from 1/11/2015, renewed to 1/11/2018)

**1994-2009.** Senior Research Biologist in the Antivirals Department, Hepatitis C Virus project, Merck Research Laboratories/ IRBM, Pomezia, Rome.

Evaluation of HCV replication/infection systems based on cultured cell lines and primary human hepatocytes.

Development and automatization of biological assays required to support the development of preclinical candidates of HCV replicase and protease. Support to lead identification and lead optimization processes in collaboration with biotesting lab and chemistry department.

### **Fellowships and Trainings:**

**2014** 4th LIN Symposium “Synaptic function and synaptic pathology in disease” Tangermünde, Germany

**2013 – 2014** Visiting at VIB Center for the Biology of Disease, KU Leuven - Center for Human Genetics, Belgium.

**2013** Selected for the Neuroscience School of Advanced Studies “RNA and the Aetiology of Brain Disease” IBRO KEMALI College Cortona, Italy.

**1994** FASEB (Federation of American Societies of Experimental Biology) Conference on “Virus assembly”, Saxton River, Vermont USA.

**1993 -1994** Fellowship at Istituto di Ricerche Biologia Molecolare IRBM P. Angeletti, Pomezia (Rome)

**1992** FEBS (Federation of European Biochemical Societies) ‘short-term Fellowship’ at Department of Biochemistry and Cell Biology, Faculty of Veterinary Medicine, Institute of Biomembranes, Utrecht The Netherlands (Prof. Van Golde).

**1989** NATO Advanced Course "Dynamics and Biogenesis of membranes", Cargese (Corse).

### **Recent Meetings attended**

**2014** - LIN Symposium “Synaptic Function and Synaptic Pathology in Disease” Tangermunde, Germany.

**2016** - 3<sup>rd</sup> DNF Symposium, UNIL Lausanne, Switzerland.

**2016** - International Child Neurology Association. “Is Autism a treatable disorder?” Rome, Italy.

**2016** - NCCR Synapsy “The Neurobiology of Mental Health”. Geneva, Switzerland.

- **Reviewer** for *Neuroscience*

- **Revision** for *EDISES Edition “WOLFE–ELEMENTI DI BIOLOGIA”* (chapters 1, 2, 3)

### **Academic Appointments:**

**2019:** Researcher (Lecturer) in Applied Biology - Saint Camillus International University of Health and Medical Sciences (UniCamillus), Rome

**2011-2018 :** Adjunct Professor of Biology (SSD BIO13), Faculty of Medicine, University of Rome “Tor Vergata”

Laurea magistrale a ciclo unico in Medicina e Chirurgia: Biologia e Genetica (9CFU)

Lauree Triennali:            Tecniche Audioprotesiche (2CFU)  
    Tecniche delle Prevenzione nell’ambiente e nei luoghi di lavoro (2 CFU)  
    Tecniche di Laboratorio Biomedico (2CFU)  
    Tecniche di Radiologia medica per immagini e radioterapia (1CFU)  
    Tecniche Ortopediche (1CFU)

Direct supervision of the following student theses:

Undergraduate Theses: Silvia Rea, Giorgia Pedini, Eleonora Rosina, Giovanna Menduti, Franceschina Sasso

Ph.D. Thesis : Franceschina Sasso, Laura D’Andrea

Current PhD students: Giorgia Pedini, Eleonora Rosina, Giulia Cencelli

## Publications

- Alfedi, G., Luffarelli, R., Condò, I., Pedini, G., Mannucci, L., Massaro, D.S., Benini, M., Toschi, N., Alaimo, G., Panarello, L., **Pacini, L.**, Fortuni, S., Serio, D., Malisan, F., Testi, R., Rufini, A. **Drug repositioning screening identifies etravirine as a potential therapeutic for friedreich's ataxia (2019)**. Accepted in the journal of *Movement Disorders*.
- Rosina E., Battan B., Siracusano M., Di Criscio L., Hollis F., **Pacini L.**, Curatolo P. and Bagni C. **Disruption of mTOR and MAPK pathways correlates with severity in idiopathic autism (2019)**. accepted in the journal of *Translational Psychiatry*.
- Jacquemont S<sup>#</sup>, **Pacini L<sup>#</sup>**, Cencelli G<sup>§</sup>, Jønych AE<sup>§</sup>, Rozenberg I, He Y, D'Andrea L, Pedini G, Eldeeb M, Willemsen R, Gasparini F, Tassone F, Hagerman R, Bagni C\* and Gomez-Mancilla B\* (2018) **Protein synthesis levels are increased in a subset of individuals with Fragile X syndrome**. *Hum Mol Genet* 27 (2): 2039-2051. <sup>#</sup>Both authors contributed equally to this manuscript.
- Zalfa F, Panasiti V, Carotti S, Zingariello M, Perrone G, Sancillo L, **Pacini L**, Luciani F, Roberti V, D'Amico S, Coppola R, Abate SO, Rana RA, De Luca A, Fiers M, Melocchi V, Bianchi F, Farace MG, Achsel T, Marine JC, Morini S, Bagni C (2017). **The fragile X mental retardation protein regulates tumor invasiveness-related pathways in melanoma cells**. *Cell Death Dis.* 8(11), e3169.
- Filippini A, Bonini D, Lacoux C, **Pacini L**, Zingariello M, Sancillo L, Bosisio D, Salvi V, Mingardi J, La Via L, Zalfa F, Bagni C, Barbon A (2017). **Absence of the Fragile X Mental Retardation Protein results in defects of RNA editing of neuronal mRNAs in mouse**. *RNA Biol* 14(11):1580-1591.
- Yrigollen CM, **Pacini L**, Nobile V, Lozano R, Hagerman R, Bagni C and Tassone F (2016). **Clinical and Molecular Assessment in a Female with Fragile X Syndrome and Tuberous Sclerosis**. *J Genet Disor Genet Rep.* 5:3.
- Pasciuto E, Ahmed T , Wahle T, Gardoni F, D'Andrea L , **Pacini L**, Jacquemont S, Tassone F, Balschun D, Dotti CG, Vegh Z, D'Hooge R, Müller UC, Di Luca M, De Strooper B and Bagni C (2015). **Dysregulated ADAM10-mediated processing of APP during a critical time- window leads to synaptic deficits in fragile X syndrome**. *Neuron* 87(2):382-98.
- Pasciuto E, Borrie SC, Kanellopoulos AK, Santos AR, Cappuyns E, D'Andrea L, **Pacini L** and Bagni C (2015). **Autism Spectrum Disorders: translating human deficits into mouse behavior**. *Neurobiology of Learning and Memory* 124:71-87. *Featured on the cover*.
- Janusz A, Milek J, Perycz M, **Pacini L**, Bagni C, Kaczmarek L, Dziembowska M (2013). **The Fragile X mental retardation protein regulates matrix metalloproteinase 9 mRNA at synapses**. *J Neurosci.* 33(46):18234-41.
- Pacini B, Avolio S, Ercolani C, Koch U, Migliaccio G, Narjes F, **Pacini L**, Tomei L, Harper S (2009). **2-(3-thienyl)-5,6-dihydroxypyrimidine-4-carboxylic acids as inhibitors of HCV NS5B RdRp**. *Bioorganic and Medicinal Chemistry Letters*.19 (21):6245-9.
- Pacini L**, Graziani R, Bartholomew L, De Francesco R, Paonessa G (2009). **Naturally occurring hepatitis C virus subgenomic deletion mutants replicate efficiently in huh-7 cells and are trans-packaged in vitro to generate infectious defective particles**. *J Virol.* 83(18):9079-93.
- Pacini L**, Bartholomew L, Vitelli A, Migliaccio G (2004). **Reporter substrates for assessing the activity of the hepatitis C virus NS3-4A serine protease in living cells**. *Anal Biochem.* 331(1):46-59.
- Tomei L, Altamura S, Bartholomew L, Biroccio A, Ceccacci A, **Pacini L**, Narjes F, Gennari N, Bisbocci M, Incitti I, Orsatti L, Harper S, Stansfield I, Rowley M, De Francesco R, Migliaccio G (2003). **Mechanism of action and antiviral activity of benzimidazole-based allosteric inhibitors of the hepatitis C virus RNA-dependent RNA polymerase**. *J Virol.* 77(24):13225-31.
- Trozzi C, Bartholomew L, Ceccacci A, Biasiol G, **Pacini L**, Altamura S, Narjes F, Muraglia E, Paonessa G, Koch U, De Francesco R, Steinkuhler C, Migliaccio G (2003). **In vitro selection and characterization of hepatitis C virus serine protease variants resistant to an active-site peptide inhibitor**. *J Virol.* 77(6):3669-79.
- Pacini L**, Vitelli A, Filocamo G, Bartholomew L, Brunetti M, Tramontano A, Steinkühler C, Migliaccio G (2000). **In vivo selection of protease cleavage sites by using chimeric sindbis virus libraries**. *J Virol.* 74 (22):10563-70.
- Filocamo G, **Pacini L**, Nardi C, Bartholomew L, Scaturro M, Delmastro P, Tramontano A, De Francesco R, Migliaccio G. (1999). **Selection of functional variants of the NS3-NS4A protease of hepatitis C virus by using chimeric sindbis viruses**. *J Virol.* 73 (1):561-75.
- Pieroni L, Santolini E, Fipaldini C, **Pacini L**, Migliaccio G, La Monica N (1997). **In vitro study of the NS2-3 protease of hepatitis c virus**. *J Virol.* 71(9):6373-80.
- Pacini L**, Limatola C, De Laurenzi V, Ricci I, Spinedi A (1997). **Arachidonic acid modulates [14C]stearic acid incorporation into phosphatidylinositol, in human neuroblastoma cells**. *J*

- Neurooncol.* 31(1-2):141-6.
19. Limatola C, **Pacini L**, Candi E, Spinedi A (1997). **On the role of agonist-evoked Ca<sup>2+</sup> mobilization in sustaining the ongoing phosphoinositide hydrolysis. A study on intact SK-N-BE(2) neuroblastoma cells subjected to muscarinic stimulation.** *J Neurooncol.* 31(1-2):129-32.
  20. Filocamo G, **Pacini L**, Migliaccio G (1997). **Chimeric sindbis viruses dependent on the NS3 protease of hepatitis C virus.** *J Virol.* 71(2):1417-27.
  21. Limatola C, **Pacini L**, Ricci I, Spinedi A (1996). **Phosphoinositide-derived diacylglycerol conversion to phosphatidic acid is a receptor-dependent and compartmentalized phenomenon in human neuroblastoma.** *Neurosci Lett.* 219(2):127-30.
  22. Santolini E, **Pacini L**, Fipaldini C, Migliaccio G, La Monica N (1995). **The NS2 protein of hepatitis C virus is a transmembrane polypeptide.** *J Virol.* 69(12):7461-71
  23. **Pacini L**, Limatola C, Palma E, Spinedi A (1994). **Effects of perphenazine on the metabolism of inositol phospholipids in SK-N-BE(2) human neuroblastoma cells.** *Biochem Pharmacol.* 48(8):1655-7.
  24. Limatola C, **Pacini L**, Spinedi A (1993). **Pertussis toxin effect on carbachol-elicited stimulation of phosphoinositide hydrolysis in human neuroblastoma SK-N-BE(2).** *Clin Chem Enzymol Commun.* 6(1-2):49-54.
  25. **Pacini L**, Limatola C, Frati L, Luly P, Spinedi A (1993). **Muscarinic stimulation of SK-N-BE(2) human neuroblastoma cells elicits phosphoinositide and phosphatidylcholine hydrolysis: Relationship to diacylglycerol and phosphatidic acid accumulation.** *Biochem J.* 289(1):269-75.
  26. Spinedi A, **Pacini L**, Limatola C, Luly P, Farias RN (1992). **Phenothiazines inhibit acetylcholinesterase by concentration-dependent-type kinetics. A study with trifluoperazine and perphenazine.** *Biochem Pharmacol.* 44(8):1511-4.
  27. Spinedi A, **Pacini L**, Luly P, Lombardi U, Nistico G (1992). **Rubidium shows effects different from lithium on phosphatidylinositol metabolism in a cell line of human neuroblastoma.** *Funct Neurol.* 7(4):305-8.
  28. Spinedi A, **Pacini L**, Limatola C, Luly P, Farias RN (1991). **A study of human erythrocyte acetylcholinesterase inhibition by chlorpromazine.** *Biochem J.* 278(2):461-3.
  29. Spinedi A, **Pacini L**, Limatola C, Luly P (1991). **Phosphoinositide turnover in human neuroblastoma cells (SK-N-BE).** *Biochem Soc Trans.* 19(2).
  30. **Pacini L**, Spinedi A, Piacentini M, Limatola C, Farrace MG, Autuori F, Luly, P (1990). **Ca<sup>2+</sup>-dependence of arachidonic acid redistribution among phospholipids of cultured mouse keratinocytes.** *Biochimica et Biophysica Acta - Lipids and Lipid Metabolism.* 1045(3):213-8.
  31. Spinedi A, Limatola C, **Pacini L**, Piacentini M, Luly P (1990). **Effects of  $\alpha$ -difluoromethylornithine treatment on arachidonic acid incorporation into SK-N-BE human neuroblastoma cell lipids.** *Clin Chem Enzymol Commun.* 2(4-6):363-9
  32. Spinedi A, **Pacini L**, Piacentini M, Melino G, Luly P (1990). **Arachidonic acid incorporation and redistribution in human neuroblastoma (SK-N-BE) cell phospholipids.** *J Neurochem.* 54(3):778-82.
  33. Spinedi A, **Pacini L**, Luly P (1989). **A study of the mechanism by which some amphiphilic drugs affect human erythrocyte acetylcholinesterase activity.** *Biochem J.* 261(2):569-73.

I authorize the use of my data according to the legislative decree 196/2003