

## **Titles and Research experiences**

**1989:** First degree in Biological Science (Laurea in Biologia) University of Milan. Graduated with maximum score of 110 cum laude. Focused her studies on the heterochromatic DNA structure.

**1993:** PhD in Cellular and Molecular Biology. Research activity from 1989 to 1992 working on the identification and characterization of proteins involved in the formation of constitutive heterochromatin.

**1993–1997:** NIH, Bethesda, USA. PostDoc fellow in Dr. Alan P. Wolffe's laboratory at the National Institute of Child Health and Human Development, NIH, Bethesda, USA. She concentrated her activity on the role of chromatin and transcription factors in the regulation of transcription. Furthermore she studied the molecular mechanisms of gene silencing mediated by DNA methylation.

**1998–2004:** University of Insubria, Varese. University Researcher in Molecular Biology at the Department of Structural and Functional Biology. Focusing her attention on the molecular mechanisms responsible for gene silencing driven by DNA methylation and the mechanisms involved in acute promyelocytic leukemia onset.

**2005–march 2014:** University of Insubria, Varese. Associate professor in Molecular Biology at the University of Insubria. Principal investigator of the Laboratory of Genetic and Epigenetic Control of Gene Expression (University of Insubria, Busto Arsizio, Varese) and of the San Raffaele Rett Research Center (Division of Neuroscience, DIBIT, San Raffaele, Milan). Mainly focusing on Rett syndrome and *MECP2* and *CDKL5*-associated disorders.

**April 2015-today:** University of Milan, Associate professor in Molecular Biology.

**2013:** qualified full professor in Molecular Biology and in Applied biology.

## **Current research activity**

Even though her previous research domain was in chromatin structure and gene transcription, since the last five years, the research activity supervised by N.L. is exclusively dedicated to *MECP2* and *CDKL5* related disorders. In particular, in the past she has contributed to demonstrate that the repressive role of DNA methylation occurs through the formation of a repressive chromatin structure and has participated to the demonstration that MeCP2 interacts with the Sin3A/HDAC complex. More recently, her laboratory has significantly contributed to the knowledge of CDKL5, an X-linked kinase capable to interact with MeCP2 and responsible of several forms of mental retardation associated to infantile spasms. Furthermore, her group has identified the first kinase (HIPK2) capable of specifically phosphorylating MeCP2, both *in vitro* and *in vivo*.

Currently, the laboratory is mainly interested in characterizing the role of MeCP2 in cortical development and its regulation by phosphorylation. To this purpose a novel knock-in mouse simulating a pathogenic mutation of MeCP2 leading to incorrect phosphorylation and Rett syndrome has just been generated and its severe symptoms are under investigation. Furthermore, the group has recently identified a novel association of MeCP2 with the centrosome and we are further detailing these studies addressing their involvement on neuronal maturation and functioning. We are also deeply investigating a novel event of phosphorylation of MeCP2 and its possible implication in Rett syndrome. Concerning CDKL5,

the group is mainly involved in characterizing the neuronal stimuli involved in its regulation and the consequences of its deficiency with a particular interest on the synaptic domain. During this period N.L. has established several national and international contacts with experts in the field.

Since 2005 N.L. is actively collaborating with the Italian Association of parents, proRETT research who is also substantially supporting her research activities. Together with proRETT she has organized the first (2007) and second (2009) editions of the European Working Group of Rett Syndrome a scientific meeting that has been attended by most of the researchers involved in the field. She has also contributed to the organization of the 6 World Rett Syndrome Congress that was held in Paris in 2008 and is organizing the one that will be held in Edinburg in October 2010.

### **Main teaching activity**

- Molecular Biology II (2000-2010, University of Insubria)
- Approaches of Molecular Biology (2002-2012, University of Insubria)
- Epigenetic Mechanisms regulating gene expression (2005-2015, University of Insubria)
- Molecular Biology I (2002-2015, Univeristy of Insubria)
- Epigenetics (2004-2015, University of Vita e Salute)
- She has made several lectures in national and iinternational PhD courses.
- NL has cured several three years, specialistic and PhD thesis.

### **Awards**

Along the years she obtained several personal grants such as AIRC (6 times), Telethon (3 times), Prin, FIRB, IRSA, Fondazione Cariplo (2 times), Foundation Jerome Le Jeune and has participated to projects supported by ERANET and Ministero della Salute (2 times).

**1997:** 1997 NIH Fellows Award for Research Excellence.

**2004-today:** member of the Italian association of molecular biology SIBBM.

**2007-2012** secretary of Società Italiana di Biofisica e Biologia Molecolare., directed by Dott. Valerio Orlando. Member of the scientific and organization board of Federazione Italiana Scienza della Vita.

**2010-today:** Academic Editor for PlosONE

**2011:** Commendatore della Repubblica Italiana

**2012-today:** member of the Italian association of Neuroscience SINS.

**2013-today:** Academic Editor for Peer J.

She has been referee for several journals and request of proposals including PRIN 2007, Futuro in Ricerca 2010, the International Rett Syndrome Foundation, USA, Fondazione Pierfranco e Luisa Mariani and the French National Research Agency

## 2010-2015 Publications

1. Conti V, Gandaglia A, Galli F, Tirone M, Bellini E, Campana L, Kilstrup-Nielsen C, Rovere-Querini P, Brunelli S, Landsberger N. (2015) MeCP2 affects skeletal muscle growth and morphology through non cell-autonomous mechanisms. *Plos one* 10(6): e0130183.
2. Bedogni F, Cobolli Gigli C, Pozzi D, Rossi RL, Scaramuzza L, Rossetti G, Pagani M, Kilstrup-Nielsen C, Matteoli M, Landsberger N. (2015) Defects During Mecp2 Null Embryonic Cortex Development Precede the Onset of Overt Neurological Symptoms. *Cereb Cortex*. 2015 May 15. pii: bhv078. [Epub ahead of print]
3. La Montanara P, Rusconi L, Locarno A, Forti L, Barbiero I, Tramarin M, Chandola C, Kilstrup-Nielsen C, Landsberger N. (2015) Synaptic synthesis, dephosphorylation, and degradation: a novel paradigm for an activity-dependent neuronal control of CDKL5. *290(7):4512-27*.
4. Bergo A, Strollo M, Gai M, Barbiero I, Stefanelli G, Sertic S, Cobolli Gigli C, Di Cunto F, Kilstrup-Nielsen C, Landsberger N. (2015) Methyl-CpG binding protein 2 (MeCP2) localizes at the centrosome and is required for proper mitotic spindle organization. *J Biol Chem*. 290(6):3223-37.
5. Kilstrup-Nielsen C, Landsberger N. (2015) Rett Syndrome: From the Involved Genes to Treatment Chapter of the book *Neurobiology of Brain Disorders*, Edited by Elsevier.
6. Bellini E, Pavesi G, Barbiero I, Bergo A, Chandola C, Nawaz MS, Rusconi L, Stefanelli G, Strollo M, Valente MM, Kilstrup-Nielsen C, Landsberger N. (2014). MeCP2 post-translational modifications: a mechanism to control its involvement in synaptic plasticity and homeostasis? *FRONT CELL NEUROSCI* doi: 10.3389/fncel.
7. Rusconi F, Paganini L, Braida D, Ponzoni L, Toffolo E, Maroli A, Landsberger N, Bedogni F, Turco E, Pattini L, Altruda F, De Biasi S, Sala M, Battaglioli E. (2014). LSD1 Neurospecific Alternative Splicing Controls Neuronal Excitability in Mouse Models of Epilepsy. *CEREB CORTEX*. Apr 15. [Epub ahead of print]
8. Bedogni F., Rossi R.L., Galli F., Cobolli Gigli C., Gandaglia A., Kilstrup-Nielsen C., Landsberger N. (2014). Rett syndrome and the urge of novel approaches to study MeCP2 functions and mechanisms of action. *NEUROSCI BIOBEHAV REV*. 46 Pt 2:187-201.
9. Colombo E., Bedogni F., Lorenzetti I., Landsberger N., Previtali S.C., Farina C. (2013). Autocrine and immune cell-derived BDNF in human skeletal muscle: implications for myogenesis and tissue regeneration. *J PATHOL*. Vol. 231(2), p. 190-8.
10. Williamson SL, Giudici L, Kilstrup-Nielsen C, Gold W, Pelka GJ, Tam PP, Grimm A, Prodi D, Landsberger N, Christodoulou J. (2012). A novel transcript of cyclindependent kinase-like 5 (CDKL5) has an alternative C-terminus and is the predominant transcript in brain. *HUMAN GENETICS*, 131(2), 187-200,
11. C. Kilstrup-Nielsen, L. Rusconi, P.L. Montanara, D. Ciceri, A. Bergo, F. Bedogni, N. Landsberger (2012). What We Know and Would Like to Know about CDKL5 and Its Involvement in Epileptic Encephalopathy. *NEURAL PLASTICITY*, 2012:728267.
12. Ricciardi S, Boggio EM, Grosso S, Lonetti G, Forlani G, Stefanelli G, Calcagno E, Morello N, Landsberger N, Biffo S, Pizzorusso T, Giustetto M, Broccoli V. (2011). Reduced AKT/mTOR signaling and protein synthesis dysregulation in a Rett syndrome animal model. *HUMAN MOLECULAR GENETICS*, vol. 20(6), p. 1182-1196.

13. Rusconi L, Kilstrup-Nielsen C, Landsberger N. (2011). Extrasynaptic N-methyl-D aspartate (NMDA) receptor stimulation induces cytoplasmic translocation of the CDKL5 kinase and its proteasomal degradation. *THE JOURNAL OF BIOLOGICAL CHEMISTRY*, vol. 286, p. 36550-36558.
14. Forlani G, Giarda E, Ala U, Di Cunto F, Salani M, Tupler R, Kilstrup-Nielsen C, Landsberger N. (2010). The MeCP2/YY1 interaction regulates ANT1 expression at 4q35: novel hints for Rett syndrome pathogenesis. *HUMAN MOLECULAR GENETICS*, vol. 19(16), p. 3114-3123.