SEMINAR CYCLE

of the PhD in Neuroscience of Turin

1st Appointment

Dr. Laura Baroncelli

Senior Researcher at Neuroscience Institute of CNR
and IRCCS Fondazione Stella Maris, Pisa

"Creatine Transporter Deficiency: the long journey to successful therapy"

24th January, 2024 h 14:00 PM

The lecture will last 1 hour and it will be followed by discussion

Host: Prof. E. Boda & Prof. M. Giustetto

Great Hall A – Anatomy Institute
C.so Massimo d'Azeglio 52
Link: https://bit.ly/3NCbFUe

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DR. LAURA BARONCELLI

Dr. Baroncelli graduated in Biology at the University of Pisa in 2005 and trained in the PhD program in Neurobiology at the Scuola Normale Superiore from 2006 to 2009. Following a fellowship at Scuola Normale Superiore, she was awarded in 2010 a two-year post-doctoral fellowship at the Accademia Nazionale dei Lincei, in Italy. Since 2011, she is Tenured Researcher at the Neuroscience Institute (IN) of CNR in Pisa. In 2017, she was awarded a six- month travel grant within the program "Post-Doctoral Fellowship- 2017" of Fondazione Umberto Veronesi for a training period with two-photon microscopy at the University Medical Center of Göttingen. Moreover, she is responsible of the group for the research in rare neurodevelopmental disorders and co-responsible of the fNIRS lab at the Stella Maris Institute.

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DR. LAURA BARONCELLI

Her scientific production was highly fruitful leading to the publication of 58 original research papers in international peer-reviewed journals. She was awarded personal fundings by Fondazione Roma, LUMOS Pharma, Italian Ministry of Health, Lejeune Foundation, Telethon Foundation, European Joint Programme for Rare Diseases and Fondazione San Paolo for the study of creatine-related and other neurodevelopmental disorders. She is also Academic Editor of Neural Plasticity and Scientific Report, and reviewer for various international journals and national agencies.

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ABSTRACT

Creatine Transporter (CrT) Deficiency (CTD) is an X-linked neurodevelopmental disorder, early presenting with cerebral creatine (Cr) depletion, intellectual disability, behavioural problems, autistic-like features and epilepsy. Although rare, CTD is a life-long illness with a major impact on patients and care givers. There is no cure for this devastating disorder, and the pathogenic mechanisms of the disease remain still elusive, hampering the identification of suitable therapeutic targets. Thus, achieving a better understanding of the neurobiological bases of CTD and searching for therapies are challenges that need to be addressed in parallel by the scientific community. Using a knockout murine model recapitulating the key features of the human disorder, we studied how Cr depletion affects the development and function of different cell population in the brain. We found that parvalbumin (PV) inhibitory interneurons are particularly vulnerable to the metabolic disruption induced by Cr deficit, leading to structural and functional alterations in these cells.

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Also, the selective loss-of-function of CrT in PV neurons is sufficient to cause cognitive impairment and increased susceptibility to epilepsy, demonstrating the fundamental role of these cells in the pathogenesis of CTD. On the therapeutic side, we are investigating gene therapy as a possible disease-modifying treatment. Using AAV-mediated delivery, we found that the administration of a functional copy of the CrT gene to newborn KO mice results in the expression of transgenic CrT in the brain, increasing Cr levels, brain connectivity and improving the behavioral performance of mice. However, CrT overexpression also brings toxic effects, indicating that the therapeutic window for CTD is narrower than expected.

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