



ASSOCIAZIONE ITALIANA ACADEMIA METILMALONICA CON OMOCISTINURIA

CBLC - APS

Viale Tito Labieno, 36 - 00174 Roma – CF: 97926850583

Dear SSIEM,

We convey our sincere thanks for your support in financing our first patient-expert meeting, held in Florence on 20 and 21 October 2023. It represented a unique opportunity put together most of CBLC APS associated families alongside with outstanding experts in metabolic diseases which are carrying out studies on cblC disease with different approaches, and primary-standing institutions, allowing us to enhance knowledge of cblC and the further strengthen the network among the several stakeholders.

The meeting was highly appreciated by all the attendees for having combined a focus on patients and relevant families' day-by-day needs, fears and queries with a very high level of scientific content. It also paved the way for further potential future co-operation projects among the scientists attended because the outcome of the researches presented has stimulated new ideas and potential JV research paths.





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Please find below a summary of the topics discussed during the meeting.

20th October

- The Chairwoman of CBLC APS (R. Brindisi) opened the meeting with an overview of the association from its set up until nowadays, pointing out the impressive growth in terms of members (we represent by far the largest families' association in Europe focused on cblc, with c. 90 families), reference metabolic centres involved, research projects financed and national and international networks created.
- The vice Chairman (A. Costetti) continued the overview deep diving on the projects we have supported and on the actions taken to solve the emergency derived from the permanent withdrawal from the Italian market of the sole suitable drug authorized in Italy (OHB12, the most important drug in the context of cblc therapeutic treatment) occurred in 2022, highlighting the crucial importance of the synergies created between CBLC APS, AIFA and Stabilimento Chimico Farmaceutico Militare in order to handle timely and effectively such unexpected shortage.
- Such topic has been further discussed in the speeches held by such two important institutions (AIFA and Stabilimento Chimico Farmaceutico Militare) which described their relevant missions and scope of work and pointed out the importance of creating a virtuous network between the associations of patients (which represents the first line of defense, in particular in case of rare diseases, immediately raising potential or actual issues) and the institutions, which reacted promptly in analyzing the problem in its complexity and find out the best way to handle it (in this specific case authorizing and setting up a centralized import of a foreign drug to guarantee continuity of care).
- Dr. C. Dionisi Vici (Bambino Gesù Hospital) and subsequently Stefania Collet and Laura Gentile (OMAR), focused the attention, inter alia, on the rare siblings, i.e. brother and sisters of patients affected by a rare disease; such figure has been the subject of some studies/experiences (e.g. Nave Italia, Gruppi Esperienziali) aimed at better understanding their point of view and the impact on their own life, attitude and psychology deriving from having a brother/sister with a rare disease, thus trying to help them in finding a way to tackle their difficulties.
- Dr. B. Greco of Bambino Gesù hospital shared the outcome of a study on psychiatric and neurological status of adolescent cblc patients.
- S. Di Munno, member of the BoD of the CBLC APS, held a speech on the different fund raising activities of the association and the results reached so far, followed by the experience of the association "La Vita è un Dono" which has been supporting Bambino Gesù hospital for several years with donations overall amounting to more than €800K and co-financed with us a research project on cblc disease.

- We had the video testimony of D. Cassioli, a paralympic athlete (28 world titles, 27 European titles and 45 Italian titles) blind since his birth, considered the greatest paralympic water skier ever. He spoke about his story, how he managed to overcome the difficulties linked to his status and pointed out the importance of the sport also for children with handicaps.
- In this context, subsequently there was the witness of two members of Cblc aps who spoke about the experience of their relatives (brother and son, respectively) with sport (swimming and basketball) and music, and how such activities helped the patients in materially improving various aspects such as concentration and coordination skills, self-esteem and ability to relate to other people, proving that often these guys are able to overcoming limits which from outside seemed insurmountable.





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21st October

Such session was mostly dedicated to the outcome of the more recent studies on cblc disease from different standpoints, including scientific evidences of the currently available therapy and new frontiers that are being explored (also thanks to the projects financed by CBLC APS) to better understand the mechanism of the pathology at hand and new potential more effective therapies. The last part was focused on national and international networks. Please find below the main topics covered:

- Jean Louis Gueant (Professor of Biochemistry-Molecular Biology at Université de Lorraine, Head of Department): i) atophysiology, metabolic pathways, ii) the Epimutation
- Carlo Dionisi-Vici (Head of Metabolic Diseases Unit at Bambino Gesù hospital): from clinical diagnosis to neonatal screening
- Giacomo Bacci (Director at the Pediatric Ophthalmology Unit of Meyer hospital): Maculopathy in CblC: etiopathological hypotheses and possible treatments
- Amelia Morrone (Head of Diagnostic Laboratory of Nervous System and Metabolic Diseases, Molecular and Cellular Biology at Meyer hospital): The genetics of CblC
- Chiara Parati (Hospital Pharmacist at Niguarda hospital): Hydroxocobalamin and Betaine: how and why they work
- Francesca Menni (Representative for metabolic diseases at the High Intensity Care Pediatrics of the Milan Policlinic): Homocysteine and Methionine: interpretation and metabolic balance
- Marco Spada (Director of Metabolic Diseases Unit at Regina Margherita hospital): The use of the I-Port, prenatal treatment, home monitoring with Guthrie
- Sabrina Signorini /Antonella Luparia (Center for Developmental Neurophthalmology at IRCCS Fondazione Istituto Neurologico Nazionale C. Mondino): Early neuropsychomotor rehabilitation and transferability to home
- Daniela Ricci (Child Neuropsychiatrist of the National Low Vision and Rehabilitation Centre at Gemelli hospital): Early neurodevelopmental characterization in children with cobalamin C defect
- Giancarlo Parenti (Professor of Pediatric and Head of Pediatric Metabolic Diseases Unit at Federico II university hospital)/ Ivan Conte (Responsible of Medaka Core Facility at Telethon Institute of Genetics and Medicine and Assistant Professor of Molecular Biology at Federico II University): Study on the Medaka fish
- Silvia Vilasi (Researcher of Biophysics Institute at National Research Council): A biophysical approach for studying pathological mutants of MMACHC involved in CblC disease
- Anna Sidorina (Chemical Analyst at Bambino Gesù hospital): first outcome of the metabolomics study through a state-of-the-art mass spectrometer



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- Laura Tinti (Representative of Proteomic Services at Fondazione Toscana Life Sciences):
Therapeutic perspectives: enzymatic therapy
- Alessio Cantore (Group Leader at San Raffaele Telethon Institute for Gene Therapy and Researcher of histology at Vita-Salute San Raffaele University): Therapeutic perspectives: gene therapy.
- Round table Networks and Institutions:
 - The MetabErn network in Europe (C. Bellettato)
 - MetabErn Italia (C. Dionisi-Vici)
 - SIMMESN (A. Pession)
 - E-HOD (M. Huemer) video contribution
 - SIFO (C. Parati)
 - AIFA (D. Di Giorgio – O. Cruciani)
 - SCFM (G. Picchioni / L. Margheriti)

Your sincerely,
On behalf of **CBLC APS**