Título del Proyecto	**CHAnging Rare disorders of LysInE metabolism (CHARLIE)**
Nº de expediente asignado	AC20/00088
Abstract	Rare inborn errors of lysine metabolism such as pyridoxine-dependent epilepsy (PDE) and glutaric aciduria type 1 (GA1) cause debilitating, often progressive neurologic symptoms. Although early detection via better diagnostics and newborn screening enables initiation of a medical diet, this therapy is often not effective resulting varying outcomes and considerable disease burden. Our international CHARLIE project synergizes the expertise of GA1 and PDE patient representatives, basic and clinical scientists, to collaboratively identify biomarkers, new disease mechanism, and importantly develop and test new therapies. One strategy inhibits the upstream enzyme, with the potential to reduce build-up of damaging metabolites thereby preventing brain damage. We will first apply this genetic therapy in PDE and GA1 model systems, such as neuronal stem cells and mouse models. Furthermore, we will investigate gene therapy to rescue the deficient GA1 enzyme and reduction of highly reactive toxic molecules in PDE. To evaluate and compare the efficacy of these different treatment approaches, we will perform behavioural, biochemical, morphological, enzymatic, untargeted metabolomics analyses. With our patient advocacy organizations, we will prioritize the most promising treatment strategy/-ies as well as enhance trial readiness. To inform the families, professionals, and stakeholders, we will organize regular meetings. Together we will pursue knowledge translation from bench to bedside, e.g. clinical trials and drug access, towards improved outcomes for PDE and GA1 patients and families.
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Enlaces:	https://www.ciberisciii.es/areas-tematicas/grupo-de-investigacion?id=17098