VIII POST SSIEM Freiburg Madrid 2022

Apreciados amigos

Es un placer para mí, una vez más, poder coordinar la **VIII reunión científica Post-SSIEM 2022**, que se celebrará en **MADRID** el próximo día **4 de Noviembre** y que nos ofrece la oportunidad de, como en años anteriores, poder resumir el congreso SSIEM que tuvo lugar en **Freiburg**, a todos aquellos profesionales interesados o que no pudieron asistir.

Los resúmenes que se os presentarán están divididos por los diversos errores congénitos del Metabolismo, dando a cada profesional una o varias vías metabólicas de las cuales considero que son expertos.

Cada uno de los ponentes va a exponer lo que ha considerado más novedoso y significativo de las diferentes charlas que tuvieron lugar durante el congreso, tanto Sesiones Plenarias, como Paralelas o Simposios.

Estoy segura de que también este año será todo un éxito y de gran interés y provecho para cada uno de nosotros.

Nos vemos en Madrid!!

Un saludo.

Dra. Mercedes Pineda

SOLO PARA PROFESIONALES DE LA SALUD

Organizado por: AECOM Asociación Española Para el Estudio de los Errores Congénitos del Metabolismo

Con la colaboración de: sanofi BIOMARIN Takeda ultragenyx pharmaceutical

SOLO PARA PROFESIONALES DE LA SALUD

VIII POST SSIEM Freiburg Madrid 2022

04 | NOVIEMBRE | 2022

HOTEL EUROBUILDING - MADRID - **Sala: ROMA 2**

Agenda

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Agenda 04 | NOV

09:30H. - 09:45 H. ▶ BIENVENIDA

Dr. Domingo González Lamuño | Presidente de la AECOM
Dra. Mercé Pineda | Coordinadora VII Post-ICIEM

09:45 - 10:00 H. SESIÓN I

Dra. María Bueno | Hospital Universitario Virgen del Rocío (Sevilla)

- **NUTRITION A DIETETIC GROUP MEETING**
  - / The gut microbiome in inherited metabolic disorders: the influence of the diet
  - / The changing face of PKU - the challenges of nutrition and dietetics in the era of new treatment approaches
  - / Overcoming nutritional problems in IEM post-transplant
  - / Efficacy and safety of empagliflozin in glycogen storage disease type Ib
  - / Pregnancies in phenylketonuria
  - / Pregnancies in other inborn errors of metabolism
- **SIMPOSIO RICORDATI: Optimization of long-term management of patients with organic acidaemia** (propionic and methylmalonic acidurias)
- **PLENARY SESSION 4: Reality meets Metabolism**
  - / Introduction into the session
  - / Sophie Hauenherm - Behind human understanding
  - / Measuring what matters to rare disease patients - patient-reported outcomes
  - / Academia-driven medicine development: towards new public- private partnerships
  - / Rare diseases: challenges and opportunities for social entrepreneurs

10:00 - 10:15 H. SESIÓN II

Dra. Montse Morales | Hospital 12 de Octubre (Madrid)

- **ADULT GROUP MEETING**
  - / Introduction and welcome
  - / Interference RNA treatment for acute porphyria
  - / Treatment of erythropoietic protoporphyria
  - / Liver complications in porphyrias
  - / Concluding remarks
  - / Epidemiological Trends and Outcomes of Children, Adolescents, and Adults Hospitalized with Inherited Metabolic Disorder: A Population Based Cohort Study
  - / Plasma globotriaosylsphingosine correlates strongly with disease severity in untreated Fabry disease patients: A tool to aid clinical decision making
  - / Effects of high versus low Phe intake on neurocognitive functioning and wellbeing in adults with PKU; The Phe eat or diet study
  - / Alpha-mannosidosis diagnosed in a 47-year-old male: the importance of re-visiting undiagnosed patients
- **ADULT GROUP MEETING**
- **SIMPOSIO SANOFI: Unmet Needs in Fabry disease: Where to go from here?**
- **PARALLEL SESSION 3A: Gene Therapy Clinical Trials**
  - / Sustained efficacy and safety at week 52 and up to three years in adults with glycogen storage disease type Ia (GSDIa): results from a phase 1/2 clinical trial of DTX401, an AAV8-mediated, liver-directed gene therapy
  - / Metabolic Abnormalities in Canavan Disease and Reduction in CNS N-acetyl-L-aspartate in Patients Receiving Systemic AAV9-mediated ASPA Gene Transfer
  - / RGX-111 gene therapy for the treatment of severe mucopolysaccharidosis type I (MPS I): Interim analysis of data from the first in human study
  - / AT845 gene replacement therapy for Late Onset Pompe disease: preliminary safety and efficacy data from FORTIS, a phase I/II open-label clinical study
  - / Safety and Efficacy of DTX301 in Adults with Late-Onset Ornithine Transcarbamylase (OTC) Deficiency: A Phase 1/2 Trial
  - / From Academic Clinical Development to an Approved Commercial Drug Administered in Multiple Highly Specialised Centres: arsa-cel, a Lentiviral Haematopoietic Stem-Cell Gene Therapy for Early-Onset Metachromatic Leukodystrophy (MLD)

10:15 - 10:30 H. SESIÓN III

Dra. María Camprodón | Hospital Vall d'Hebrón (Barcelona)

- **SIMPOSIO AMICUS: The FACEs® of Fabry disease**
- **SIMPOSIO SPARK THERAPEUTICS: Immunogenicity and Investigational AAV Gene Therapy**
- **PARALLEL SESSION 3D: Disorders of Vitamins and cofactors**
  - / Oxidative stress and mitochondrial respiration impairment induced by sulfite in rat brain are prevented by the mitochondria-targeted antioxidant XJB-5-131
  - / Biochemical investigation of SAM mediated allosteric inhibition of MTHFR
  - / Influence of early identification and therapy on long-term outcomes in early-onset MTHFR deficiency
  - / Improved biochemical profile after hydroxocobalamin dose-escalation in cobalamin C defect
  - / Personalized modeling of altered metabolic states inborn errors of cobalamin metabolism
  - / Novel biochemical and clinical evidence reveals abnormal concentrations of acetylated amino acids in cerebrospinal fluid in acetyl-CoA transporter deficiency

10:30 - 10:45 H. SESIÓN IV

Dra. Raquel Yahyaoui | Hospital Materno Infantil de Málaga (Málaga)

- **ERNDIM Workshop**
  - / Chair's Update
  - / Common DPT sample
  - / Biomarkers for neurotransmitter diseases
  - / Biomarkers for mitochondrial diseases
  - / Open discussion: Future directions
- **PLENARY SESSION 2: Technology meets Metabolism**
  - / Introduction into session: Technology meets metabolism
  - / Single cell RNA sequencing: understanding liver cell differentiation and plasticity in health and disease
  - / Mechanistic modeling of human metabolism: monogenic and polygenic disorders
  - / Big data and artificial intelligence in medicine: the good, the bad and the ugly
- **PLENARY SESSION 3: Ethics meets Genetics**
  - / Introduction into session: Ethical questions with respect to the use of data, data management, genetic results, newborn screening
  - / Newborn screening by whole genome sequencing: opportunities and challenges
  - / Ethics of big data and whole genome screening: how to make chicken from chicken salad?
  - / A lifetime's knowledge at birth? What do we actually want to know?
  - / Plenary discussion
  - / Neurofilament light as a biomarker for involvement of the brain in classic infantile Pompe patients
  - / Bi-allelic variants in VPS16, encoding a subunit of HOPS/CORVET complexes, cause a mucopolysaccharidosis-like disease.
- **PARALLEL SESSION 2A: Mechanisms and Markers in Lysosomal Disorders**
  - / Lyso-Gb3 elicits a proteotoxic effect on a neuronal cell model
  - / Next-generation deep plasma proteomics reveals systemic and tissue-specific remodeling in Fabry Disease
  - / Quantitative nuclear magnetic resonance spectroscopy-based metabolomics of urine samples in metachromatic leukodystrophy: identifying indicators for neurodegeneration and disease progression
  - / LC-MSMS sulfatides measurement in dried blood spots for the diagnosis of metachromatic leukodystrophy
  - / Neurofilament light as a biomarker for involvement of the brain in classic infantile Pompe patients
  - / Bi-allelic variants in VPS16, encoding a subunit of HOPS/CORVET complexes, cause a mucopolysaccharidosis-like disease

10:45 - 11:00 H. SESIÓN VI

Dra. Angels García Cazorla | Hospital San Juan de Deu (Barcelona)

- **PARALLEL SESION 1B: Organic Acidurias**
  - / Altered glutamine anaplerosis in MMUT deficiency.
  - / A network medicine approach identifies key TCA cycle enzymes as potential therapeutic targets in organic acidemias
  - / Cognitive functions are not necessarily spared in early diagnosed individuals with glutaric aciduria type 1 - a national prospective study over 20 years
  - / Newborn screening and disease variants predict neurological outcome in isovaleric aciduria
- **SIMPOSIO PTC BIO: Transformative science in action: Gene therapy for AADC deficiency**
- **PARALLEL SESSION 3C: Mitochondrial Disorders**
  - / Discovery and replication of novel biomarkers for mitochondrial diseases in a cohort of 2,000 individuals
  - / Unlocking the mitochondrial genome for gene therapy and modelling disease
  - / Reversal of m.3243A>G related defects to advance drug screening "hits" towards clinical trials
  - / Inborn disorders of the malate aspartate shuttle lead to disturbed NAD+/NADH redox balance, glycolysis and defective serine biosynthesis
  - / Ryanodine receptor type 3 variants cause acute episodes of rhabdomyolysis related to abnormal calcium homeostasis and impaired autophagy
  - / 3-methylglutaconic aciduria type II: The molecular mechanism responsible for the mitochondrial dysfunction
- **PARALLEL SESSION 4A: GENE AND INNOVATIVE THERAPIES**
  - / Eladocagene Exuparvovec Gene Therapy Improves Motor Development in Patients With Aromatic L-Amino Acid Decarboxylase Deficiency
  - / Intracerebral gene therapy in 2 patients with aromatic-L acid decarboxylase (AADC) deficiency
  - / Hematopoietic Stem & Progenitor Cell Gene Therapy for Hurler Syndrome: interim clinical results and extensive metabolic correction
  - / Novel Gene Supplementation, Genome Editing and Cellular Therapeutic Approaches to Treat Glutaric Aciduria Type I
  - / Sustained efficacy of neonatal AAV gene therapy for maple syrup urine disease in mice
  - / Pegzilarginase efficacy in Arginase 1 Deficiency: results of the PEACE pivotal phase 3 trial

11:00 - 11:15 H. SESIÓN V

Dra. Mireia del Toro | Hospital Vall d'Hebron (Barcelona)

- **SIMPOSIO CHIESI: What matters most? Improving care in Lysosomal Storage Disorders (LSDs)**
- **PARALLEL SESSION 4C: Neurometabolic disorders**
  - / Identifying the mechanism by which creatine represses expression of AGAT
  - / ASS1 deficiency is associated with impaired neuronal differentiation in zebrafish larvae
  - / Identification of Cln5 as S-depalmitoylase highlights the significance of reversible protein palmitoylation in childhood dementia and Alzheimer's disease
  - / Cerebrospinal fluid amino acids glycine, serine, and threonine in nonketotic hyperglycinemia
  - / COX11 defects are a novel cause of an infantile-onset mitochondrial encephalopathy.
  - / The time has come for newborn screening for pyridoxine-dependent epilepsy
- **PARALLEL SESSION 1D: Novel Disease Insights**
  - / ARSK deficiency- a novel subtype of mucopolysaccharidosis
  - / Glutaminase deficiency impairs neuronal function and can be partially rescued with glutamate supplementation.
  - / A case of 3-MCC leading to the discovery of a novel neurodevelopmental syndrome caused by bi-allelic loss-of-function variants in RABGAP1
  - / Bi-allelic variants in NAE1 cause intellectual disability, ischiopubic hypoplasia, stress-mediated lymphopenia and neurodegeneration.
  - / Infantile Superoxide Dismutase 1 Deficiency Syndrome (ISODDES) is an infantile- onset motor neuron disease with impaired glutathione metabolism
  - / A previously undescribed combination of juvenile ALS with crystalline retinopathy caused by a de novo mutation in SPTLC2 causing a shift in substrate specificity of Serine Palmitoyl Transferase towards longer chain acyl-CoA's

P A U S A C ☕ F É

12:00 - 12:15 H. SESIÓN V

Dra. Amaya Belanger | Hospital Ramón y Cajal (Madrid)

- **SIMPOSIO BIOMARIN: Creating waves with PALYNZIQ® (pegvaliase): Three years of experience in Europe**
- **PARALLAEL SESSION 2B: New Perspectives in Phenylketouria**
  - / Characterization of a humanized PKU mouse carrying the frequent splicing variant c.1066-11G>A
  - / Cognitive deficits emerge in early-treated adult PAH-deficient mice following discontinuation of pegvaliase therapy.
  - / Investigation of the phenylalanine hydroxylase proteostasis network reveals potential therapeutic targets for phenylketonuria
  - / Searching for new potential biomarkers in adults with Phenylketonuria
  - / A long non-coding RNA (lncRNA) transcript HULC regulates phenylalanine hydroxylase activity and could act as a new therapeutical agent in phenylketonuria.
  - / A CRISPR/Cas9 genome-edited PAH-deficient cell line for studying PKU
- **PARALLEL SESSION 3B: Aminio Acid**
  - / Efficacy and pharmacokinetics of betaine in CBS and cblC deficiency: a cross over randomized controlled trial
  - / Branched Chain Ketoacid Dehydrogenase Kinase (BCKDK) deficiency: A treatable neurodevelopmental disease amenable to newborn screening
  - / The impact of liver transplantation on health-related quality of life in intoxication-type inborn errors of metabolism
  - / Nutrigenomics on the fly: a systematic animal model approach to finding dietary treatments for inherited metabolic diseases
  - / Isoleucine to valine substitutions by IARS1 help maintain cellular function during nutritional stress
  - / Genetic correction of ornithine delta-aminotransferase mutation and metabolomic analyses of iPSC lines derived from gyrate atrophy patients

12:15 - 12:30 H. SESIÓN VIII

Dra. Mar O´Callahan | Hospital San Juan de Deu (Barcelona)

- **PARALLEL SESSION 1A: New Therapies in Lysosomal Disorders**
  - / Retargeting phenylbutyrate, ursodeoxycholic acid, pyrimethamine and betaine for beta-glucocerebrosidase recovery in gaucher disease fibroblasts resulting from homozygous p.L483P mutation
  - / Four-year real-world effectiveness of eliglustat in treatment-naïve and switch patients enrolled in the International Collaborative Gaucher Group (ICGG) Gaucher Registry
  - / AZ-3102, a novel brain-penetrant small molecule, significantly improves survival in Sandhoff disease mice
  - / The first successful in utero enzyme replacement therapy treatment of a child with CRIM negative infantile-onset Pompe disease
  - / Interim 73-week cohorts A, B, and C results of a Ph1/2 study of intravenous DNL310 (brain-penetrant enzyme replacement therapy) in MPS II
  - / RGX-121 gene therapy for the treatment of severe mucopolysaccharidosis type II (MPS II): Interim analysis of data from a Phase 1/2 study
- **SIMPOSIO ORCHARD THERAPEUTICS: Reaching new hights in ex vivo gene therapy - therapeutic advances for early onset MLD patients**
- **SIMPOSIO BIOMARIN: Improving the diagnostic pathway in MPS and treating Morquio A in the real world: best practice and findings from MARS**

12:30 - 12:45 H. SESIÓN IX

Dr. Isidro Vitoria | Hospital La Fe (Valencia)

- **EHOD MEETING**
- **PARALLELL SESSION 1C: Glycosylation and Carbohydrate Disorders**
  - / Sodium D, L-3-hydroxybutyrate in the treatment of GLUT1 deficiency syndrome
  - / Anaplerotic therapy using Triheptanoin for patients with glycogen storage disease type I (GSD I): clinical trial results
  - / Investigating metabolic adaptations in PMM2-CDG
  - / Functional platforms for the characterization of PMM2-CDG clinical variants
  - / Oral sialic-acid supplementation in NANS-CDG: Results of a single center, open label, observational pilot study
  - / Cellular fluxomics to study sugar metabolism in Galactosemia and Congenital Disorders of Glycosylation
- **PARALLEL SESSION 4B: Urea cycle disorders**
  - / Neurometabolic impact of liver transplantation in six patients with argininosuccinate lyase deficiency (ASLD)
  - / In vivo lentiviral gene therapy for argininosuccinic aciduria
  - / Proof of concept of in vivo mRNA therapy in a mouse model of argininosuccinic aciduria
  - / O-GlcNAcylation enhances CPS1 catalytic efficiency for ammonia and promotes ureagenesis.
  - / In vivo assessment of ureagenesis using stable isotope tracing to monitor disease and treatment efficacy
  - / Severity-adjusted evaluation of newborn screening on the metabolic disease course in cytosolic Urea Cycle Disorders

12:45 - 13:00 H. SESIÓN X

Dr. Antonio González Meneses | Hospital Virgen del Rocío (Sevilla)

- **SIMPOSIO SANOFI: Olipudase alfa: a new treatment for patients with ASMD**
- **PARALLEL SESSION 2D: Novel Diagnostic Technologies**
  - / Analysis of urinary oligosaccharide excretion patterns by UHPLC/HRAM-MS for rapid detection of oligosaccharidoses
  - / Discovery of new plasma biomarkers for Sjögren Larsson syndrome by untargeted lipidomics
  - / Unmasking the functional impact of variants of uncertain significance using knock-in cell lines generated by CRISPR/Cas9
  - / Liver-on-a-tube: Hollow fiber membrane technology to study liver metabolism and disease
  - / Multiplexing complexome profiling to foster routine protein complex profiling in medical research
  - / Expanded phenotyping by microscopic imaging
- **SIMPOSIO ASTELLAS: Pompe Disease: A Metabolic Disease Impacting Muscle and Potential Muscle-directed Gene Therapeutic Approaches**
- **PLENARY SESSION 5: Metabolism meets Genetics**
  - / Introduction into the session
  - / How genetics changed the face of mitochondrial disease
  - / Understanding variant pathogenicity using multi-omic pipelines
  - / The epigenetic clock and metabolism
- **SIMPOSIO SANOFI: Pompe disease, a new era: the latest avalglucosidase alfa clinical data and early real-world experiences**

13:00 - 13:15 H. SESIÓN XI

Domingo González Lamuño | Hospital de Valdecilla (Santander)

- **PLENARY SESSION 1: Environment meets Metabolism**
  - / Introduction into the session
  - / Genetics and the microbiome
  - / Exercise testing and prescription in metabolic diseases
- **SIMPOSIO TAKEDA: Optimizing early diagnosis in lysosomal storage diseases and innovation for the future**
- **PLENARY SESSION 6: Epigenetics meets Genetics**
  - / Introduction into the session
  - / Clinical epigenomics meets metabolic diseases and environment
  - / Developmental plasticity: the 3rd dimension of phenotypic variation and disease risk
  - / Beck-Fahrner syndrome: Delineation of a human Mendelian disorder of the DNA demethylation machinery

13:00 - 13:15 H. SESIÓN XII

Dra. Mª José de Castro | Hospital Médico Universitario de Santiago de Compostela

- **SIMPOSIO MEDSCAPE/ULTRAGENIX: Clinician and Patient Perspectives in the Management of Long-Chain Fatty Acid Oxidation Disorders**
- **GARROD AWARD LECTURE**
- **SIMPOSIO TRAVERE: Classical Homocystinuria and Development of a New Enzyme Replacement Therapy**
- **PARALLEL SESSIOIN 2C: Disorders of Fat Metabolism**
  - / Biochemical studies in fibroblasts to interpret variants of unknown significance in the ABCD1 gene
  - / Upregulation of glycogen cycling with a triheptanoin diet replenishes glycogen stores in very long chain acyl-CoA dehydrogenase deficient mice (VLCAD-/-)
  - / Thermo-sensitive mitochondrial trifunctional protein deficiency presenting with episodic myopathy
  - / Restoring succinyllysine antigenic signal and improving O2 consumption of CPT II deficient cells treated with anaplerotic compounds
  - / Plasma metabolomics during anabolic conditions among subjects with a fatty acid oxidation disorder compared to normal controls
  - / Systemic corticosteroids for the treatment of acute episodes of rhabdomyolysis in lipin-1-deficient patients
- **KOMROWER LECTURE**
  - / On pathways and blind alleys
- **PLENARY SESSION 7: Special awards Session**
  - / Characterization of the 1,5-anhydroglucitol transporter SGLT5 that was found to be mutated in a G6PC3-deficient child with a mild form of neutropenia
  - / Tailored amino acid treatment for mitochondrial ARS and QARS1 deficiencies
  - / O-GlcNAcylation enhances CPS1 catalytic efficiency for ammonia and promotes ureagenesis
  - / Deficient protein glycosylation and compromised functional integrity of PMM2 deficient neurons and brain organoids

13:30H. CIERRE VIII POST-SSIEM 2022 Y COCKTAIL