V POST SSIEM Atenas MADRID 2018

Apreciados amigos

Es un placer para mí, una vez más, poder coordinar la **V reunión científica Post-SSIEM 2018**, que se celebrará en Madrid el próximo día 26 de Octubre y que nos ofrece la oportunidad de, como en años anteriores, poder resumir el congreso SSIEM que tuvo lugar en Atenas, 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,

M. Pineda

Dra. Mercedes Pineda Marfa (Col. 6125)
Neuropediatra del Hospital Sant Joan de Déu de Barcelona

EU/MPRL/0105/Sept2018

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AVALADO POR:
AECOM · SEMI · Grupo de Enfermedades Minoritarias · Sociedad Española de Errores Innatos del Metabolismo

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V POST SSIEM Atenas MADRID 2018

26/10/18

Lugar_ COAM Colegio Oficial de Arquitectos de Madrid
Hortaleza, 63 | 28004 Madrid "Salón de Actos de Planta Jardín"

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AGENDA 26/10/18

9:00 RECOGIDA DE DOCUMENTACIÓN

9:30 **PRESENTACIÓN**
Dr. David Gil ▶ Presidente AECOM
Dra. Mercé Pineda ▶ Coordinadora Post-SSIEM

9:40 **SESIÓN I** ▶ **Dr. C. Colón** ▶ Hospital Clinico Universitario de Santiago de Compostela

ERNDIM Meeting
ERNDIM Workshop
- Chair's update.
- Common DPT sample.
- Laboratory diagnostic aspects of the new defects in purine and pyrimidine metabolism.
- Clinical aspects of the new defects in purine and pyrimidine metabolism.

Educational Session: Diagnostic Challenges in the "OMICS" Era
Plenary Session 4: Next-Generation Diagnostic
- C13 Dynamic Studies in Fibroblasts.
- Transcriptomics in Rare Disease Diagnostic.
- Discovering New Pathways and Diseases. The Role of Metabolism.

Simposio Alnylam: RNA Unterference: Harnessing Technology with the Potencial to Advance the Management of Rare Diseases
- Overview of RNAi therapeutics.
- Clinical Presentation of AHP – A Case based approach.
- Clinical Presentation of Primary Hyperoxaluria – A Case based approach.

09:55 **SESIÓN II** ▶ **Dra. M. del Toro** ▶ Hospital Vall d'Hebron (Barcelona)

Plenary Session 1: Biochemical Defects as Developmental Disorders
- Biochemical Defects Leading to Abnormal CNS Development.
- Bone Development and Remodeling in Metaolic Disorders.
- Lessons from Pluripotent Stem Cell Models.

Plenary Session 2: Inborn Error of Metabolism and the Immune System
- Glycosylation and Human Immune System Function.
- The Immune System in Inborn Errors of Metabolism.
- Inborn Errors of Metabolism and Cancer: The Case of Gaucher Disease.

Parallel Session 1B: New Treatments
- Safety and efficacy of KH176 in adult patients with mitochondrial disease due to the m.3243A>G mutation (KHENERGY).
- Fragment-based drug discovery for inborn errors of metabolism: Primary hyperoxaluria I as exemplar target.
- Organoids to evaluate novel treatment strategies for intrahepatic cholestatic disease.
- An observational study of patients with cerebral adrenoleukodystrophy (CALD) treated with allogeneic hematopoietic stem cell transplant.
- Lenti-D hematopoetic stem cell gene therapy for cerebral adrenoleukodystrophy: safety and efficacy outcomes from an ongoing Ph 2/3 trial.
- Long-term safety and efficacy of combined therapy of high-dose ambroxol and imiglucerase in neuronopathic Gaucher disease.

Simposio BioMarin: Reshaping the Odyssey of MPS IVA and VI
- Facilitating the journey of MPS IVA with early diagnosis and treatment.
- MPS IVA – My personal Odyssey.
- How long-term treatment reshapes the Odyssey of MPS VI.

10:10 **SESIÓN III** ▶ **Dra. M. O'Callaghan** ▶ Hospital Sant Joan de Deu (Barcelona)

Simposio BioMarin: Genetics: Your Role in Completing the Diagnostic Puzzle in CLN2 Disease
- The picture on the puzzle: Natural history of CLN2.
- Solving the mystery puzzle earlier with genetic testing.
- Connecting the dots for early diagnosis and benefits of early intervention.

Parallel Session 3A: Mitochondrial Disorders
- Update Lecture: What is New in Mitochondrial Disorders.
- Elucidating the complexity of mitochondrial membrane lipids in Barth Syndrome.
- Mutations in QRSL1, GATB, and GATC encoding glutamyl-tRNAGln amidotransferase subunits cause a lethal mitochondrial cardiomyopathy.
- Genetic defects causing complex movement disorders and basal ganglia degeneration in childhood.
- A novel complex neurological phenotype due to homozygous mutation in FDX2.

Simposio Actelion: 10 years of progress and innovation in Niemann-Pick disease Type C: from new insights in pathophysiology to effective therapy
- Current and evolving hypotheses of the pathogenesis and underlying mechanisms of NP-C.
- Diagnostic workup for NP-C in 2018: how do recent advances impact your clinical practice?.
- Spotlight on miglustat: findings from the first 10 years of effective treatment for NP-C.

10:25 **SESIÓN IV** ▶ **Dra. M. Morales** ▶ Hospital 12 de Ocubre (Madrid)

Adult Group Session: Expanded newborn screening (eNBS), waht does it mean for adult metabolic medicine?
- The moving targets of expanded newborn screening for inborn errors of metabolism.
- Expanded NBS for X-ALD and implications for adult AMN Patients.
- Ethical considerations regarding presymptomatic testing in adults from expanded in neonates.

Adult Group Session: Oral Presentations
Parallel Session 4C: Metabolic Disorders in Adults
- Changes in cornstarch dosing in adults with glycogen storage disease type Ia.
- Retrospective observational study on 53 adult patients with suspected metabolic myopathy.
- Does a period of restricted phenylalanine intake influence the decision to be on PKU diet? An audit on maternal phenylketonuria experience.
- Adult patients with hereditary fructose intolerance are characterized by an increased intrahepatic triglyceride content.
- Late-onset diagnosis of urea cycle disorders: results from an adult French cohort of 49 patients.
- Treatment with chenodeoxycholic acid in cerebrotendinous xanthomatosis: clinical, neurophysiological and brain structural outcomes.

10:40 **SESIÓN V** ▶ **Dr. M. Bueno** ▶ Hospital Virgen del Rocio (Sevilla)

Dietician group / Nutrition & Dietetic Session
- Chalenges of protein requirements - Differences between general and guideline IMD.
- Acute nutritional ketosis and exercise in GSD IIIa.
- Recent advances in the nutritional management of infant onset LAL-D.

Dietician group / Nutrition & Dietetic Session
- The use of Modified Mediteranean Diet in the therapeutic approach of Aminoacidopathies and Glut I deficiency.
- GMP - The unfolding story in children with PKU.
- GA1 mangement after 6 years of age.

Simposio BioMarin: PKU: Inside the Trojan Horse
- PKU, The Trojan Horse, discovering the surprises within.
- Unwanted guests in adul PKU: Comorbidities.
- Mild hyperphenylalaninemia: Surprisisng effects.
- Screening for BH4 response: A good start is half the battle.

10:55 **SESIÓN VI** ▶ **Dr. L. Aldámiz** ▶ Hospital de Cruces (Bilbao)

Parallel Session 2C: Novel Diagnostic Approches
- Contribution of functional studies to validate disease-causing variants identified by NGS in patients with inborn errors of metabolism.
- Large-scale, untargeted metabolomic profiling identifies novel biomarkers and clarifies DNA variants of uncertain significance.
- Signature oligosaccharides change the way we diagnose and monitor the mucopolysaccharidoses.
- Cross-omics: merging whole exome sequencing with untargeted metabolomics.
- Integrated UPLC-HR-MS and NMR detection of inborn errors of metabolism in urine.
- A technological upgrade for newborn mass urine screening in the Province of Quebec: from TLC to MS/MS.

Simposio Shire: Lysosomal storage disorders: from genes to biomarkers and clinical outcomes
- Gaucher disease, Fabry disease and mucopolysaccharidosis type II (MPS II): from genotype to phenotype.
- Biomarkers as predictors of clinical outcome in Gaucher disease, Fabry disease and MPS II.
- Impact of long-term enzyme replacement therapy (ERT): Gaucher-related bone disease.
- Impact of long-term ERT: outcomes in Fabry disease and MPS II.

Simposio Sanofi Genzyme: Substrate Reduction Therapy in Gaucher disease: from clinical development to real-world experience and treatment monitoring
- Gaucher disease treatment options and SRT development.
- Real-world experience and long-term eliglustat outcomes.
- Old and new biomarkers in Gaucher disease; Lyso-GL-1 in the clinic.

COFFEE BREAK

11:45 **SESIÓN VII** ▶ **Dra. A. Belanger** ▶ Hospital Ramón y Cajal (Madrid)

Simposio Nutricia: Nutrition in PKU
- Effects of inadequate amino acid mixture intake on nutrient supply of adult patients with PKU.
- Role of personalised nutritional mangemente in PKU patients - BH4 users.
- Role of personalised nutritional management in PKU patients - off diet adult PKU patients.

Parallel Session 1C: Phenylketonuria and Neurotransmitter Disorders
- Clinical characterization of tremor in patients with Phenylketonuria.
- Does early treatment of PKU patients with sapropterin dihydrochloride affect brain development?.
- Cerebral creatine deficiency and lower weight gain in a new KI rat model of creatine transporter deficiency.
- AGIL-AADC gene therapy in children with AADC deficiency increases dopamine production and sustains motor milestones.
- Neurotransmitter trafficking defect in a patient with the clathrin (CLTC) alteration presenting with hyperphenylalaninemia and Parkinsonism.
- Proteomic study on neurotransmitter defects find several biomarkers pointing towards neurodevelopment dysregulation.

Simposio APR: Physiological absorption of amino acids: rationale and expected benefits
- The physiological utilization of amino acids in PKU.
- The Physiomimic technology and impact on prolonged release and taste masking of amino acids.
- Absorption kinetics of amino acids in humans: the basis for a new option for PKU management.
- Panel discussion: expectations for PKU patients.

Parallel Session 3B: Disorders of Fatty Acid and Ketone Metabolism
- Update Lecture: Inborn Errors of Metabolism and Autophagy.
- MiRNA analysis provides new insights into propionic acidemia related cardiomyopathy.
- Propionate anions produce acute and sustained remodelling of calcium transients in rat ventricular myocytes.
- α-galactosidase A activity modulates DNA methylation of androgen receptor promoter in Fabry disease vascular endothelial cells.
- The satellite cell paradox in Pompe disease: breaking the barriers for regeneration.

12:00 **SESIÓN VIII** ▶ **Dr. D. Gonzalez-Lamuño** ▶ Hospital Marqués de Valdecilla (Santander)

Simposio Amicus: A Closer Look at the Therapeutic Goals in the Management of Fabry Disease
- Decoding Fabry Disease: A systemic and Multi-organ Disease.
- Defining Treatment Success in the Management of Fabry Disease.
- Migalastat in the Real World - Experience from a Fabry Center of Excellence.

Plenary Session 3: Old Players in New Roles
- Cholesterol: More than Meets the Eye.
- Mitochondria and Neurodegeneration.
- Inborn Errors of Metabolism as Risk Factors of Parkinson Disease.

Parallel Session 3D: Inborn Errors of Metabolism as Autophagy Disorders
- Structural insights into drug therapy of mitochondrial fatty acid oxidation disorders.
- Impact of UX007 and dietary management on major clinical events in a 78- week single-arm openlabel phase 2 LC-FAOD study.
- Metabolomics profiling in dried blood spots differentiates clinical phenotypes in VLCADD.
- 3-hydroxybutyrate (3-HB) treatment in MADD: a systematic literature review and international retrospective cohort study.
- Restoration of VLCAD in null mice and mutant human fibroblasts using novel mRNA technology: Model to treat fatty acid β-oxidation disorders.
- Targeting cardiolipin: a new therapeutic approach to treat LCHAD and mitochondrial TFP deficiencies.

12:15 **SESIÓN IX** ▶ **Dra. M.L. Couce** ▶ Hospital Clínico Universitario de Santiago de Compostela

Garrod Lecture: Triheptanoin versus triactanoin for long-chain fatty acid oxidation disorders
Simposio Orphan Europe: Optimising long-term outcomes of patients with Propionic and Methylmalonic Acidaemias
- Challenges with protein restriction & malnutrition in the long-term management of PA & MMA patients.
- Overcoming these long-term management challenges: From an in-country experience to a Europe-wide investigator trial (LOTUS).
- Optimising long-term outcomes with Carbaglu: current and future data. A 4-year follow-up case study & outlines of the PROTECT and CAMP studies.

Simposio Sobi: Rethinking potential in management of Urea Cycle Disorders
- Current Treatment Strategies in Urea Cycle Disorders.
- Revision of Guidelines for Management of Urea Cycle Disorders.
- Nutritional Management of UCDs – Opportunities for Optimal Treatment Outcomes.

Plenary Session 6: Treating Inborn Errors of Metabolism
- Treating Lysosomal Storage Diseases: What have we Learnt?.
- Lessons from Brain Energy Metabolism: Therapy and Outcome Measures in Clinical Trials.
- Beyond Gene Therapy.

12:30 **SESIÓN X** ▶ **Dr. I. Vitoria** ▶ Hospital La Fe (Valencia)

Simposio Sanofi Genzyme: The Sands of Time in Fabry Disease
- Classic versus Late Onset phenotypes versus Polymorphisms and the importance of Lyso GL-3.
- Tissue and Podocyte GL-3 clearance.
- Adult Treatment Guidelines and the importance of DOSE.

Parallel Session 2B: Lysosomal Storage Disorders
- Update Lecture: Neuronal Ceorid Lipofuscinoses.
- Efficient and effective newborn screening for lysosomal disorders.
- Novel treatment of MPS II (Hunter Syndrome) with SB-913 ZFN-mediated in vivo human genome editing: Update from a Phase 1/2 clinical trial.
- Antisense oligonucleotides promote exon inclusion in iPSC-derived skeletal muscle cells from Pompe patients.
- Benefit of MGTA-456 cord blood expansion in enhancing donor derived microglial engraftment as treatment for inherited metabolic disorders.

Parallel Session 4A: Amino Acid Disorders and Organic Acidurias
- Update Lecture: Branched Chain Amino Acid Metabolism: From Rare to More Common Disorders.
- Interplay of enzyme replacement therapy, diet and betaine in murine cystathionine beta-synthase-deficient homocystinuria.
- Surrogate biomarkers for clinical trial design in methylmalonic acidemia (MMA): A bench to bedside approach.
- Identification of a multi-protein complex for mitochondrial cobalamin and methylmalonyl-CoA processing.
- Newborn screening, a disease-modifying intervention for glutaric aciduria type 1.

12:45 **SESIÓN XI** ▶ **Dr. A. Gonzalez Meneses** ▶ Hospital Virgen del Rocio (Sevilla)

Simposio Sobi: Hereditary tyrosinemia type 1: Identification
- Inclusion of HT-1 in German newborn screening panel - Learnings and implementation.
- Implications of early or later detection in clinical practice - Updated recommendations for optimal management of HT-1 patients detected through newborn screening.
- Nutritional management of HT-1 - Achieving a successful diet therapy.
- Current analytical performance of succinylacetone and nitisinone determination in dried blood spot samples – Important aspects in clinical practice.

Parallel Session 1A: Glycosylation and Carbohydrate Disorders
- Fertility in classical galactosaemia, N-glycan, hormonal and inflammatory gene expression interactions.
- Link between glycemia and hyperlipidemia in Glycogen Storage Disease type IA.
- Tracing the fate of galactose in PGM1-CDG.
- Defining a new immune deficiency syndrome; MAN2B2-CDG.
- Ngly1 pathogenic variant causing deglycosylation defect, masquerading as mitochondrial hepatocerebral cytopathy.
- Longitudinal follow-up of 75 PMM2-CDG patients.

Simposio Chiesi: Discover alpha-mannosidosis: from disease to management
- Alpha-mannosidosis: an overview.
- Digging into alpha-mannosidosis complexity: Real life experience.
- Velmanase alfa clinical development: key results and learnings.
- Managing alpha-mannosidosis.
- Discover alpha-mannosidosis from disease to management: conclusion.

Parallel Session 3C: Peroxisomal Disorders
- GOT2 deficiency: a novel disorder of the malate aspartate shuttle resulting in serine deficiency.
- Pharmacologic inhibition of hepatic O-GlcNAcase enhances ureagenesis and ammonia detoxification.
- Identification of energy balance dysregulation in a mouse model of muttype methylmalonic aciduria.
- Biallelic SLC13A3 mutations cause reversible leukoencephalopathy with increased urine excretion of alphaketoglutarate.
- Dichotomous effect of mutations causing X-linked sideroblasmic anaemia and protoporphyria explained by the first human ALAS2 structure.
- Expanding the neurological spectrum of seipin deficiency (BSCL2), a complex lipid defect.

13:00 **SESIÓN XII** ▶ **Dra. A. Garcia Cazorla** ▶ Hospital Sant Joan de Deu (Barcelona)

Parallel Session 2A: Nutrition and Dietetics
- Update Lecture: Long Term Neurological Effects of Special Diets.
- Prospective study: Glycomacropeptide and conventional amino acid protein substitutes in children effect on blood phenylalanine and growth.
- Effect of phytosterols on serum lipids of children with hypercholesterolemia.
- Quality of dietary carbohydrates affects gut microbial community of phenylketonuric subjects.
- Body composition in hepatic glycogen storage disease: relationship with uncooked cornstarch.

Plenary Session 5: Metabolic Pathways and Subcellular Organelles: New Connections
- One Gene, One Enzyme,.. Several Reactions! How do we deal with Enzyme Promiscuity?.
- Bridging the Gap: Linking Cellular Metabolism and Protein Glycosylation in the Golgi.
- Organelle Interplay - Peroxisome Interactions in Health and Disease.

Simposio Centogene: Multi-omics approach in diagnosis of rare diseases
- Metabolic diseases in the view of a neurologist – clinical and diagnostic observations.
- Proteomics and metabolomics supporting clinical diagnosis in rare diseases.

Late Breaking News
- Squalene synthase deficiency; clinical, biochemical and molecular characterization of a novel defect in cholesterol biosynthesis.
- Failure to eliminate a phosphorylated glucose-analog leads to neutropenia in patients with G6PT and G6PC3 deficiency.
- Sialic acid catabolism by N-acetylneuraminate pyruvate lyase is essential for muscle function
- Solving the unknown in Mendelian Metabolic diseases: Glutaminase deficiency, a Novel Repeat Expansion Disorder identified through Deep Phenomics and Genomics.

CIERRE REUNIÓN