3.5.8 Research and Diagnosis of Inherited Metabolic Diseases Group

Publications: 14
Q1: 5

COMPOSITION

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Fernando García Muñoz. Técnico de Laboratorio. CEDEM
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María Pilar Rodríguez Pombo. Profesora Titular. Universidad Autónoma de Madrid. CBM "Severo Ochoa"
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Pedro Ruiz Sala. Investigador Postdoctoral. CEDEM

STRATEGIC OBJECTIVE

- Development of multiomic approaches aimed at improving the diagnosis of hereditary metabolic diseases.
- Study of mitochondrial dysfunction and oxidative stress as a modifier of the clinical phenotype and as a potential therapeutic target in organic acidurias.
- Development of animal and cellular models.
- Development of novel therapeutic strategies: antisense therapy, pharmacological chaperone, repurposing.
- Pathophysiology studies targeted to identify new druggable targets.
- Registry of patients with hereditary metabolic diseases.

RESEARCH LINES

- Improved diagnosis of congenital defects of glycosylation and mitochondrial defects through the application of genomic techniques
- Identification of deep intronic mutations in metabolic disorders gene by transcriptional analysis. Functional validation in cellular splicing systems.
- Development of antisense therapy and pharmacological chaperones as therapeutic approaches
- Study of oxidative stress and evaluation of common signatures of neuropathogenicity and cardiotoxicity in congenital defects of glycosylation, organic acidemias and mitochondrial diseases.
- Evaluation of drugs aimed at the recovery of mitochondrial function and biogénesis.
- Search for biomarkers as predictors of severity and as systems for the evaluation of pharmacological therapies.
- Characterization of pathophysiology in a murine model of propionic acidemia.

- Identification of dysregulated miRNA in propionic acidemia and characterization of its association with pathology and its usefulness as biomarkers.
- Generation of iPS from patient-derived fibroblast with organic acidemia and congenital defects of glycosylation. Differentiation to hepatocytes, neural progenitors or cardiomyocytes.

RESEARCH ACTIVITY

Publications

- Alcaide P, Ferrer-López I, Gutiérrez L, Leal F, Martín-Hernández E, Quijada-Fraile P, Bellusci M, Morais A, Pedrón-Giner C, Rausell D, Correcher P, Unceta M, Stanescu S, Ugarte M, Ruiz-Sala P, Pérez B. Lymphocyte medium-chain acyl-coa dehydrogenase activity and its potential as a diagnostic confirmation tool in newborn screening cases. J Clin Med. 2022; 11(10): 2933. Article. IF: 3.9; Q2
- Briso-Montiano A, Vilas A, Richard E, Ruiz-Sala P, Morato E, Desviat LR, Ugarte M, Rodríguez-Pombo P, Pérez B. Hepatocyte-like cells differentiated from methylmalonic aciduria cblB type induced pluripotent stem cells: A platform for the evaluation of. BBA-Mol Basis Dis. 2022; 1868(9): 166433. Article. IF: 6.2; D1
- López-Márquez A, Martínez-Pizarro A, Pérez B, Richard E, Desviat LR. Modeling splicing variants amenable to antisense therapy by use of CRISPR-Cas9-based gene editing in HepG2 Cells. Methods Mol Biol. 2022; 2434: 167-84. Article. IF: 3.5; Q3
- Martínez-Pizarro A, Desviat LR. RNA solutions to treat inborn errors of metabolism. Mol Genet Metab. 2022; 136(4): 289-95. Review. IF: 3.8; Q2
- Martínez-Pizarro A, Leal F, Holm LL, Doktor TK, Petersen USS, Bueno M, Thony B, Pérez B, Andresen BS, Desviat LR. Antisense oligonucleotide rescue of deep-intronic variants activating pseudoexons in the 6-pyruvoyl-tetrahydropterin synthase gene. Nucleic Acid Ther. 2022; 32(5): 378-90. Article. IF: 4; Q2
- Martín-Rivada A, Conejero AC, Martín-Hernández E, López AM, Belanger-Quintana A, Villarroya EC, Quijada-Fraile P, Bellusci M, Calzada SC, Martínez AB, Stanescu S, Casanova MMP, Ruiz-Sala P, Ugarte M, González BP, Pedron-Giner C. Newborn screening for propionic, methylmalonic acidemia and vitamin B12 deficiency. Analysis of 588,793 newborns. J Pediatr Endocr Met. 2022; 35(10): 1223-31. Article. IF: 1.4; Q4
- Paredes-Fuentes AJ, Oliva C, Montero R, Alcaide P, Ruijter GJG, García-Villoria J, Ruiz-Sala P, Artuch R. Technical aspects of coenzyme Q(10) analysis: Validation of a new HPLC-ED method. Antioxidants. 2022; 11(3): 528. Article. IF: 7; D1
- Sánchez-Lijarcio O, Yubero D, Leal F, Couce ML, Gutiérrez-Solana LG, López-Laso E, García-Cazorla A, Pias-Peleteiro L, Brea BD, Ibáñez-Mico S, Mateo-Martínez G, Troncoso-Schifferli M, Witting-Enriquez S, Ugarte M, Artuch R, Pérez B. The clinical and biochemical hallmarks generally associated with GLUT1DS may be caused by defects in genes other than SLC2A1. Clin Genet. 2022; 102(1): 40-55. Article. IF: 3.5; Q2
- Segovia-Falquina C, Vilas A, Leal F, del Cano-Ochoa F, Kirk EP, Ugarte M, Ramón-Maiques S, Gámez A, Pérez B. A functional platform for the selection of pathogenic variants of PMM2 amenable to rescue via the use of pharmacological chaperones. Hum Mutat. 2022; 43(10): 1430-42. Article. IF: 3.9; Q2
- Soria LR, Makris G, D'Alessio AM, de Angelis A, Boffa I, Pravata VM, Rufenacht V, Attanasio S, Nusco E, Arena P, Ferenbach AT, Paris D, Cuomo P, Motta A, Nitzahn M, Lipshutz GS, Martínez-Pizarro A, Richard E, Desviat LR, Haberle J, van Aalten DMF, Brunetti-Pierri N. O-GlcNAcylation enhances CPS1 catalytic efficiency for ammonia and promotes ureagenesis. Nat Commun. 2022; 13(1): 5212. Article. IF: 16.6; D1
- Soriano-Sexto A, Gallego D, Leal F, Castejón-Fernández N, Navarrete R, Alcaide P, Couce ML, Martín-Hernández E, Quijada-Fraile P, Peña-Quintana L, Yahyaoui R, Correcher P, Ugarte M, Rodríguez-Pombo P, Pérez B. Identification of clinical variants beyond the exome in inborn errors of metabolism. Int J Mol Sci. 2022; 23(21): 12850. Article. IF: 5.6; Q1
- Stanescu S, Belanger-Quintana A, Fernández-Felix BM, Ruiz-Sala P, Alcaide P, Arrieta F, Martínez-Pardo M. Plasma CoQ10 status in patients with propionic acidaemia and possible benefit of treatment with ubiquinol. Antioxidants. 2022; 11(8): 1588. Article. IF: 7; D1
- Stanescu S, Belanger-Quintana A, Fernández-Felix BM, Ruiz-Sala P, del Valle M, García F, Arrieta F, Martínez-Pardo M. Interorgan amino acid interchange in propionic acidemia: the missing key to understanding its physiopathology. Amino Acids. 2022; 54(5): 777-86. Article. IF: 3.5; Q3
- Stanescu S, Bravo-Alonso I, Belanger-Quintana A, Pérez B, Medina-Díaz M, Ruiz-Sala P, Flores NP, Buenache R, Arrieta F, Rodríguez-Pombo P. Mitochondrial bioenergetic is impaired in Monocarboxylate transporter 1 deficiency: a new clinical case and review of the literature. Orphanet J Rare Dis. 2022; 17(1): 243. Review. IF: 3.7; Q2

Research projects

Pérez González MB. Enfoque cross-ómico para el descubrimiento de la base genética de errores innatos del metabolismo y para una intervención terapéutica personalizada (PI19/01155). ISCIII. 2020-2022.

Managment centre: UAM

Pérez González MB. Estudio observacional: Estudio a-REVEAL. Chiese Therapeutics. 2021-2022.

Managment centre: UAM

Pérez González MB. Identificación y diagnóstico de la deficiencia AADC. PTC Therapeutics. 2021-2022.

Managment centre: UAM

Richard Rodríguez EM. Acidemia propiónica: impacto en el epigenoma y el proteoma en relación con el fenotipo cardiaco y neurológico. Fundacion Ramón Areces. 2021-2023.

Managment centre: Fundación Severo Ochoa

Richard Rodríguez EM. Acidemia propiónica: impacto en el epigenoma y el proteoma en relación con el fenotipo cardiaco y neurológico. Fundación Ramón Areces. 2021-2024.

Managment centre: UAM

Ruiz Desviat LM. Delivery of RNA therapy. European cooperation in Science and Technology (CA17103). EU Cost Action. 2018-2022.

Managment centre: UAM

Ruiz Desviat LM. Mecanismos responsables del fenotipo patológico en enfermedades neurometabólicas raras y aproximaciones terapéuticas personalizadas (PID2019-105344RB-I00). MCINN. 2020-2023.

Managment centre: UAM

Cibers and Retics

Pérez González MB. Centro de Investigación en Red de Enfermedades Raras. (CIBERER) (CB06/07/0004). ISCIII. (31/12/2024). UAM

Patents and trademarks

Pérez González B, Ruiz Desviat L, Jorge Finnigan A, Ugarte Pérez M, Martínez Ruiz A, Underhaug J, Barnejee R, inventors; UAM, Universidad de Bergen, Universidad de Michigan, assignees; Compounds useful for the treatment of methylmalonic aciduria. P201330171; 2013 February 11.

Pérez González B, Gámez Abascal A, Yuste Checa P, Arduim Brasil S, Ugarte Pérez M, Martínez Ruiz A, Underhaug J, inventors; UAM, Universidad de Bergen, assignees; Compounds for treating congenital disorders of glycosylation. EP16382373.5; 2016.