3.5.7 Research and Diagnosis of Inherited Metabolic Diseases

Publications:8 | Q1:5

COMPOSITION

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- **María Lourdes Ruiz Desviat.** Catedrática Bioquimica y Biología Molecular. Universidad Autónoma de Madrid. CBM "Severo Ochoa"
- **Pedro Ruiz Sala.** Investigadora Senior. 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 novel therapeutic strategies: RNA therapies, pharmacological chaperone, repurposing
- Development of animal and cellular models.
- 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

Doctoral theses

- **Vilas Lagoa A.** Desarrollo de modelos con fines diagnósticos y terapéuticos para la deficiencia de fosfomanomutasa 2.[dissertation]. Madrid: UAM: 2023(14/04/2023). Director: Pérez González MB. International Mention
- **Segovia Falquina C.** Generación de una plataforma de análisis funcional de variantes en PMM2 con fines diagnósticos y terapéuticos[dissertation]. Madrid: UAM: 2023(04/09/2023). Director: Pérez González MB, Gamez Abascal MA
- **Arribas Carreira L.** Implicaciones del metabolismo de la glicina en la salud y la enfermedad humana: Hiperglicinemia no Cetósica, una enfermedad con fenotipo clínico neurológico[dissertation]. Madrid: UAM: 2023(19/06/2023). Director: Rodríguez Pombo P PI19/01155

Final Degree Theses

- **González Garnacho I.** Estudio de la fisiopatología de la acidemia propiónica en modelos celulares neurales humanos derivados de iPSCs[dissertation]. Madrid: UAM: 2023(30/06/2023). Director: Richard Rodríguez EM
- **Alvera Alonso B.** Generación de modelos celulares y evaluación de terapia antisentido para defectos de splicing en enfermedades neurológicas[dissertation]. Madrid: UAM: 2023(30/06/2023). Director: Ruiz Desviat ML

Publications

- **Álvarez M, Ruiz-Sala P, Pérez B, Desviat LR, Richard E.** Dysregulated cell homeostasis and mirnas in human ipsc-derived cardiomyocytes from a propionic acidemia patient with cardiomyopathy. Int J Mol Sci. 2023; 24(3): 2182. Article. IF: 4.9; Q1
- **Arribas-Carreira, L; Dallabona, C; Swanson, MA; Farris, J; Ostergaard, E; Tsiakas, K; Hempel, M; Aquaviva-Bourdain, C; Koutsoukos, S; Stence, NV; Magistrati, M; Spector, EB; Kronquist, K; Christensen, M; Karstensen, HG; Feichtinger, RG; Achleitner, MT; Merritt, JL; Pérez, B; Ugarte, M; Grünewald, S; Riela, AR; Julve, N; Arnoux, JB; Haldar, K; Donnini, C; Santer, R; Lund, AM; Mayr, JA; Rodríguez-Pombo, P; Van Hove, JLK.** Pathogenic variants in GCSH encoding the moonlighting H-protein cause combined nonketotic hyperglycinemia and lipoate deficiency. Hum Mol Genet. 2023; 32(6): 917-33. Article. IF: 3.1; Q3
- **Bravo-Alonso I, Morin M, Arribas-Carreira L, Álvarez M, Pedrón-Giner C, Soletto L, Santolaria C, Ramón-Maiques S, Ugarte M, Rodríguez-Pombo P, Ariño J, Moreno-Pelayo MA, Pérez B.** Pathogenic variants of the coenzyme A biosynthesis-associated enzyme phosphopantothenoylcysteine decarboxylase cause autosomal-recessive dilated cardiomyopathy. J Inherit Metab Dis. 2023; 46(2): 261-72. Article. IF: 4.2; Q1
- **Himmelreich N, Bertoldi M, Alfadhel M, Alghamdi MA, Anikster Y, Bao XH, Bashiri FA, Ben Zeev B, Bisello G, Ceylan AC, Chien YH, Choy YS, Elsea SH, Flint L, García-Cazorla A, Gijavanekar C, Guemues EY, Hamad MH, Hismi B, Honzik T, Huebschmann OK, Hwu WL, Ibanez-Mico S, Jeltsch K, Julia-Palacios N, Kasapkara ÇS, Kurian MA, Kusmierska K, Liu N, Ngu LH, Odom JD, Ong WP, Opladen T, Oppeboen M, Pearl PL, Pérez B, Pons R, Rygiel AM, Shien TE, Spaull R, Sykut-Cegielska J, Tabarki B, Tangeraas T, Thoeny B, Wassenberg T, Wen YX, Yakob Y, Yin JGC, Zeman J, Blau N.** Prevalence of DDC genotypes in patients with aromatic L-amino acid decarboxylase (AADC) deficiency and in silico prediction of structural protein changes. Mol Genet Metab. 2023; 139(3): 107624. Article. IF: 3.7; Q2
- **Marín-Quílez A, Di Buduo CA, Díaz-Ajenjo L, Abbonante V, Vuelta E, Soprano PM, Miguel-García C, Santos-Mínguez S, Serramito-Gómez I, Ruiz-Sala P, Peñnarrubia MJ, Pardal E, Hernández-Rivas JM, González-Porras JR, García-Tuñón I, Benito R, Rivera J, Balduini A, Bastida JM.** Novel variants in GALE cause syndromic macrothrombocytopenia by disrupting glycosylation and thrombopoiesis. Blood. 2023; 141(4): 406-21. Article. IF: 21.0; D1
- **Musokhranova U, Grau C, Vergara C, Rodríguez-Pascau L, Xiol C, Castells AA, Alcantara S, Rodríguez-Pombo P, Pizcueta P, Martínell M, García-Cazorla A, Oyarzábal A.** Mitochondrial modulation with leriglitazone as a potential treatment for Rett syndrome. J Transl Med. 2023; 21(1): 756. Article. IF: 6.1; Q1
- **Peña-Burgos EM, Regojo RM, de Pipaón MS, Santos-Simarro F, Ruiz-Sala P, Pérez B, Esteban-Rodríguez MI.** Neuropathological findings in short-chain enoyl-coa hydratase 1 deficiency (echs1d): case report and differential diagnosis. Pediatr Devel Pathol. 2023; 26(2): 138-43. Article. IF: 1.3; Q3
- **Tangeraas T, Constante JR, Backe PH, Oyarzábal A, Neugebauer J, Weinhold N, Boemer F, Debray FG, Ozturk-Hism B, Evren G, Tuba EF, Ummuhan O, Footitt E, Davison J, Martínez C, Bueno C, Machado I, Rodríguez-Pombo P, Al-Sannaa N, de los Santos M, López JM, Ozturkmen-Akay H, Karaca M, Tekin M, Pajares S, Ormazabal A, Stoway SD, Artuch R, Dixon M, Morkrid L, García-Cazorla A.** BCKDK deficiency: a treatable neurodevelopmental disease amenable to newborn screening. Brain. 2023; 146(7): 3003-13. Article. IF: 10.6; D1

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. 2020-2023. *Managment centre: UAM*
- **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.** Mecanismos responsables del fenotipo patológico en enfermedades neurometabólicas raras y aproximaciones terapéuticas personalizadas (PID2019-105344RB-I00). MCINN. 2020-2023. *Managment centre: UAM*
- **Pérez González MB.** Mejora del diagnóstico y desarrollo de terapias para errores congénitos del metabolismo a través del análisis genómico, transcriptómico, epigenómico y funcional de pacientes y modelos (PI22/00699). ISCIII. 2023-2025. *Managment centre: FIBHULP*
- **Ruiz Desviat LM.** Rare neurometabolic diseases: from research in novel disease models to targeted therapies- (PID2022-137238OB-I00 MCINN). MCINN. 2023-2026. *Managment centre: UAM*

Cibers and Retics

- **Pérez González MB.** Centro de Investigación en Red de Enfermedades Raras (CIBERER). 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.
- **Ruiz-Desviat L, Martínez-Pizarro A, Picó S, Lucas JJ, Andrésen BS, inventors; UAM, CSIC,University of Southern Denmark, assignes; Splice shifting oligonucleotides for use in the treatment of diseases characterized by altered inclusion of microexons.** PCT/EP2022/077882, EP4163373A1 2023 April 12