3.5.8 Dyslipidemias of Genetic Origin and Metabolic Diseases Group

Publications:3 | **Q1:**3

COMPOSITION

Sonia María Rodríguez Novoa.
Facultativo Especialista de Área. Responsable del Laboratorio de Genética de Enfermedades Metabólicas. Hospital Universitario La Paz

- **Ana Carazo Álvarez.** Técnico de Laboratorio. Hospital Universitario La Paz
- **Amanda Herranz Cecilia.** Facultativo Especialista de Área en Bioquímica Clínica. Hospital Universitario La Paz
- **Irene Hidalgo Mayoral.** Facultativo Especialista de Área en Genetica. FIBHULP
- **Álvaro del Monte Vergara.** Investigador Predoctoral. Hospital Universitario La Paz
- **Carmen Rodríguez Jiménez.** Facultativo Especialista de Área en Bioquímica Clínica. Hospital Universitario La Paz
- **Elena Sevilla Alonso.** Investigadora Predoctoral. Hospital Universitario La Paz
- **Javier Sanguino Otero.** Investigador Posdoctoral. Hospital Universitario La Paz
- **Rosa Torres Jiménez.** Investigadora Senior (Contrato Miguel Servet - I2) Jefe de Laboratorio. FIBHULP

STRATEGIC OBJECTIVE

- Our research is especially focused on the molecular diagnosis of dyslipidemias of genetic origin. Among dyslipidemias, Familial Hypercholesterolemia (FH) stands out for its impact on health. FH is an important risk factor in the development of early cardiovascular disease. Patients with pathogenic variants in the main genes involved in FH (LDLR, APOB, PCSK9, and LDLRAP1) are at high risk of premature coronary disease. The autosomal dominat hipercolesterolemia is caused by pathogenic variants at LDLR, APOB or PCSK9 genes. Patients with FH have a 50% of having a child with the condition. In this context, early detection of genetic alterations in patient´s relatives is essential in order to stablish an early treatment. Genetic studies of the family have proven to be cost-effective. The massively parallel sequencing technology (NGS) provide an useful tool to carry out this type of studies. However, it is important not only the detection of new variants but the characterization of them to determine their impact or pathogenicity. For this purpose, our research group has developed and validated functional in vitro studies for the characterization of genetic variants in the main genes associated with FH.
- An important percentage of patients with hypercholesterolemia do not present pathogenic variants in the most frequent genes. Our group has a line of research focused on the search for new candidate genes and epigenetic causes related with altered lipid metabolism. We have developed in vitro studies to determine the impact of microRNAs on the expression of LDLR and PCSK9.
- In addition to FH, we also study other genetic dyslipidemias such as familial hypertriglyceridemia and other "rare" dyslipidemias that are often not diagnosed with the usual diagnostic tools.

RESEARCH LINES

- Molecular diagnosis of familial hypercholesterolemia by massive sequencing of a panel of genes. Study of the exome to detect new candidate genes.
- Functional studies of genetic variants in LDLR, PCSK9 and APOB in cellular model.
- Study of microRNAs as modulators of cholesterol regulation and their impact on familial hypercholesterolemia.
- Molecular diagnosis of hypertriglyceridemia and other "rare" dyslipidemia.
- Genetic diagnosis of metabolic diseases.

SCIENTIFIC REPORT 2023

RESEARCH ACTIVITY

Final Degree Theses

- **García Mesa J.** Estudio del carácter oligogénico de la hipercolesterolemia mediante secuenciación masiva de panel customizado y exoma completo[dissertation]. *Madrid: Universidad Francisco de Vitoria: 2023(30/06/2023). Director: Rodríguez Jiménez C, Rodríguez Novoa S.*

Publications

- **Guijarro-Eguinoa J, Arjona-Hernández S, Stewart S, Pernía O, Arias P, Losantos-García I, Rubio T, Burdiel M, Rodríguez-Antolín C, Cruz-Castellanos P, Higuera O, Borobia AM, Rodríguez-Novoa S, de Castro-Carpeño J, de Cáceres II, Rosas-Alonso R.** Prognostic impact of dihydropyrimidine dehydrogenase germline variants in unresectable non-small cell lung cancer patients treated with platin-based chemotherapy. Int J Mol Sci. 2023; 24(12): 9843. Article. IF: 4.9; Q1
- **Rodríguez-Jiménez C, de la Peña G, Sanguino J, Poyatos-Peláez S, Carazo A, Martínez-Hernández PL, Arrieta F, Mostaza JM, Gómez-Coronado D, Rodríguez-Nóvoa S.** Identification and functional analysis of apob variants in a cohort of hypercholesterolemic patients. Int J Mol Sci. 2023; 24(8): 7635. Article. IF: 4.9; Q1
- **Stewart S, Dodero-Anillo JM, Guijarro-Eguinoa J, Arias P, De las Huertas AGL, Seco-Meseguer E, García-García I, García ER, Rodríguez-Antolín C, Carcas AJ, Rodríguez-Novoa S, Rosas-Alonso R, Borobia AM.** Advancing pharmacogenetic testing in a tertiary hospital: a retrospective analysis after 10 years of activity. Front Pharmacol. 2023; 14: 1292416. Article. IF: 4.4; Q1

Research projects

- **Rodríguez Novoa SM.** Diagnóstico genético de la hipercolesterolemia familiar mediante secuenciación masiva. Estudio funcional de nuevas variantes y detección de mosaicismo. Estudio de miRNAs (PI18/00917). ISCIII. 2019-2023. Managment centre: FIBHULP
- **Rodríguez Novoa SM.** Impacto de las variantes genéticas en región 3´UTR de los genes causantes de la Hipercolesterolemia Familiar: regulación del metabolismo de lípidos mediante miRNAs. (PI21/01239). ISCIII. 2022-2024. Managment centre: FIBHULP
- **Rodríguez Novoa SM.** Renal tubular and markers of bone turnover in hbv monoinfected patients during long term tretament with entecavir or tenofovir (P11/30). Bristol-Myers Squibb International Corporation. 2011-Ongoing. Management centre: FIBHULP
- **Rodríguez Novoa SM.** Plataforma: dislipemias de origen genético y enfermedades metabólicas. Varios Financiadores. 2021-Ongoing. Managment centre: FIBHULP

Patents and trademarks

- **Rodríguez Novoa SM, del Monte Vergara A, Rosas Alonso R, Queiruga Parada J, Yuste González F, authors; FIBHULP, assignee.** Trademark name: Pharma Genfinder; CM18332183; 2020 November 05.

PHARMA GENFINDER

- **Ibáñez de Cáceres I, de Castro Carpeño J, Jiménez Hernández J, Rodríguez Antolín C, Rodríguez Jiménez C, Rosas Alonso R, Cruz Castellanos P, Burdiel Herencia M, Pernía Arias O, Diestro Tejada MD, Esteban Rodríguez MI, inventors; FIBHULP, assignee.** miR-151A-3p as an universal endogenous control for exosome cargo normalization. EP19382252.5 (EP3719144), PCT/EP2020/059774 PCT Direct, EP20719957.1 (EP3947733), US17/601,657; 2019 April 05.