3.5.9 Dyslipidemias of Genetic Origin and Metabolic Diseases Group

Publications: 2
Q1: 0

COMPOSITION

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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.
- Study of microRNAs as modulators of cholesterol regulation and their impact on familial hypercholesterolemia.
- Functional studies of genetic variants in LDLR, PCSK9 and APOB in cellular model.
- Molecular diagnosis of hypertriglyceridemia and other "rare" dyslipidemia.
- Genetic diagnosis of metabolic diseases.

RESEARCH ACTIVITY

Doctoral theses

Rodríguez Jiménez C. Implementación de la validación funcional de las variantes en LDLR, APOB, PCSK9 y LDLRAP1 para confirmar el diagnóstico genético de la Hipercolesterolemia Familiar en la práctica asistencial. [dissertation]. Madrid: UAM: 2022 (13/12/2022).

Director: Rodríguez Novoa S.

Final Degree Theses

Asensio Rodríguez M. Caracterización de nuevos biomarcadores de riesgo cardiovascular en pacientes con sospecha de Hipercolesterolemia Familiar (FH). [dissertation]. Madrid: Universidad Francisco de Vitoria: 2022(14/07/2022).

Director: Rodríguez Novoa S.

Publications

- Gómez-González C, Pizarro-Sánchez C, Rodríguez-Antolín C, Pascual-Pascual I, García-Romero M, Rodríguez-Jiménez C, de Sancho-Martin R, del Pozo-Mate A, Solis-López M, Castro CPD, Torres RJ. Hereditary spastic paraplegia associated with a novel homozygous intronic noncanonical splice site variant in the AP4B1 gene. Ann Hum Genet. 2022; 86(3): 109-18. Article. IF: 1.9; Q4
- Pacio-Míguez M, Parrón-Pajares M, Gordon CT, Santos-Simarro F, Jiménez CR, Mena R, Arenas IR, Montano VEF, Fernández M, Solis M, del Pozo A, Amiel J, García-Miñaur S, Palomares-Bralo M. Broadening the phenotypic spectrum of EVEN-PLUS syndrome through identification of HSPA9 pathogenic variants in the original EVE dysplasia family and two sibs with milder facial phenotype. Am J Med Genet A. 2022; 188(9): 2819-24. Article. IF: 2; Q3

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. 2019-2022.

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.

Managment 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.

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.