3.5.8 Dyslipidemias of Genetic Origin and Metabolic Diseases

Publications: 5 | **Q1:** 4

COMPOSITION

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STRATEGIC OBJETIVES

- Improve early diagnosis of genetic dyslipidemias, especially Familial Hypercholesterolemia (FH), through the use of advanced genomic technologies such as next-generation sequencing (NGS).
- Optimize the identification of affected family members through cascade genetic screening programs, promoting a cost-effective strategy for cardiovascular prevention.
- Develop and apply in vitro functional studies to characterize genetic variants in genes involved in FH (LDLR, APOB, PCSK9), enhancing their clinical classification and understanding their biological impact.
- Promote personalized medicine in patients with genetic dyslipidemias by integrating genetic and functional data to predict treatment response and guide individualized therapeutic decisions.
- Explore new genetic and epigenetic mechanisms involved in non-monogenic or unexplained dyslipidemias, expanding the understanding of the molecular basis of lipid metabolism.
- Promote training, scientific dissemination, and multidisciplinary collaboration, both nationally and internationally, in the field of hereditary cardiovascular diseases.

RESEARCH LINES

1. Molecular Diagnosis of Genetic Dyslipidemias
- Implementation and optimization of NGS sequencing protocols for the study of FH and other genetic dyslipidemias.
- Family screening strategies in different healthcare settings.

2. Functional Studies of Genetic Variants
- Validation of cell-based assays to determine the pathogenicity of variants in LDLR, APOB, and PCSK9.
- Genotype-phenotype correlation based on the variant and its functional impact.

3. Discovery of New Genetic and Epigenetic Causes
- Identification of new candidate genes through genomic studies in patients without known pathogenic variants.
- Investigation of the role of microRNAs in the regulation of LDLR, PCSK9, and other genes involved in lipid metabolism.
- Study of potential epigenetic mechanisms underlying complex forms of dyslipidemia.
- Definition and implementation of a workflow for systematic analysis of variants in the LDLR 3'UTR region in patients with suspected Familial Hypercholesterolemia.

4. Personalized Medicine and Treatment Response
- Evaluation of the influence of variant type on the response to lipid-lowering therapies.
- Pharmacogenetic analysis and study of molecular predictors of therapeutic response or resistance.

5. Rare and Underdiagnosed Dyslipidemias
- Genetic and clinical characterization of rare dyslipidemias (e.g., familial chylomicronemia, dysbetalipoproteinemia).
- Development of diagnostic algorithms integrating genomics, biochemistry, and clinical phenotype.

6. Metabolic Myopathy
- Identification of the genetic-molecular cause in patients with suspected metabolic etiology myopathy.

RESEARCH ACTIVITY

Publications

- **Escudero-Ferruz P, Ontiveros N, Cano-Estrada C, Sutcliffe DJ, Jinnah HA, Torres RJ, López JM.** A new physiological medium uncovers biochemical and cellular alterations in Lesch-Nyhan disease fibroblasts. Mol Med. 2024; 30(1): 3. Article. IF: 6.4; Q1
- **Major TJ, Takei R, Matsuo H, Leask MP, Sumpter NA, Topless RK, Shirai Y, Wang W, Cadzow MJ, Phipps-Green AJ, Li ZQ, Ji AC, Merriman ME, Morice E, Kelley EE, Wei WH, McCormick SPA, Bixley MJ, Reynolds RJ, Saag KG, Fadason T, Golovina E, O'Sullivan JM, Stamp LK, Dalbeth N, Abhishek A, Doherty M, Roddy E, Jacobsson LTH, Kapetanovic MC, Melander O, Andrés M, Pérez-Ruiz F, Torres RJ, Radstake T, Jansen TL, Janssen M, Joosten LAB, Liu RQ, Gaal OI, Crisan TO, Rednic S, Kurreeman F, Huizinga TWJ, Toes R, Lioté F, Richette P, Bardin T, Ea HK, Pascart T, McCarthy GM, Helbert L, Stiburková B, Tausche AK, Uhlig T, Vitart V, Boutin TS, Hayward C, Riches PL, Ralston SH, Campbell A, MacDonald TM, Nakayama A, Takada T, Nakatochi M, Shimizu S, Kawamura Y, Toyoda Y, Nakaoka H, Yamamoto K, Matsuo K, Shinomiya N, Ichida K, Lee C, Bradbury LA, Brown MA, Robinson PC, Buchanan RRC, Hill CL, Lester S, Smith MD, Rischmueller M, Choi HK, Stahl EA, Miner JN, Solomon DH, Cui J, Giacomini KM, Brackman DJ, Jorgenson EM, Liu HB, Susztak K, Shringarpure S, So A, Okada Y, Li CG, Shi YY, Merriman TR.** A genome-wide association analysis reveals new pathogenic pathways in gout. Nat Genet. 2024; 56(11): 2392-406. Article. IF: 29; D1
- **Otero JS, Rodríguez-Jiménez C, Prieto JM, Rodríguez-Antolín C, Álvarez AC, Blanco FA, Rodríguez-Nóvoa S.** Functional Analysis of 3′UTR Variants at the LDLR and PCSK9 Genes in Patients with Familial Hypercholesterolemia. Hum Mutat. 2024; 2024: 9964734. Article. IF: 3.7; Q2
- **Prior-de Castro C, Gallego MAM, Gómez-González C, Martín RD, Rodríguez-Antolín C, Rodríguez-Jiménez C, Mate AD, de Lucas EZ, Maiz MRD, Gómez CD, Batres SA, Sánchez MCP, Torres RJ.** Molecular diagnosis of cystic fibrosis by RNA obtained from nasal epithelial cells. J Cyst Fibros. 2024; 23(4): 788-95. Article. IF: 6.0; Q1
- **Villafuerte B, Carrasco-López C, Herranz A, Garzón L, Simón R, Natera-de-Benito D, Alikhani P, Tenorio J, Garcia-Santiago F, Solis M, del-Pozo A, Lapunzina P, Ortigoza-Escobar JD, Santisteban P, Moreno JC.** A Novel Missense Variant in the NKX2-1 Homeodomain Prevents Transcriptional Rescue by TAZ. Thyroid. 2024; 34(7): 942-8. Article. IF: 6.7; Q1

Research projects

- **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.** Plataforma: dislipemias de origen genético y enfermedades metabólicas. Varios Financiadores. 2021-Ongoing. 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
- **Torres Jiménez R.** Alteracion del desarrollo neuronal en la enfermedad de Lesch Nyhan: papel de ZMP, hipoxantina y estres energetico. Fundació Marató TV3. 2021-Ongoing. Managment centre: FIBHULP
- **Torres Jiménez R.** Alteraciones del desarrollo neuronal en células pluripotentes humana HPRT deficientes (PID2020-113124RB-C22). MICIIN. 2021-2025. 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.