Nephrology

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DESCRIPTION

The Kidney Diseases Research Group is dedicated to advancing understanding and improving outcomes across a broad spectrum of kidney disorders, with a strong focus on inherited kidney diseases. Key projects explore autosomal dominant polycystic kidney disease from a gender and reproductive perspective, improve genetic diagnostics using advanced genomic tools, and develop predictive models for Autosomal Dominant Alport Syndrome. Innovative approaches, including artificial intelligence and natural language processing, aim to revolutionise diagnostic precision and patient identification through deep phenotyping and electronic health record analysis.

Beyond inherited conditions, the group investigates glomerulopathies, such as IgA nephropathy and thrombotic microangiopathy, as well as the renal implications of inflammatory bowel disease. In chronic kidney disease (CKD), research encompasses bone health, dialysis-related genetic damage, and the role of the gut microbiota. The group also delves into the mechanisms of inflammation-induced fibrosis and transplant-related complications, including graft inflammation, fibrosis pathways, and EPLETS in kidney transplantation.

Uniting clinical, molecular, and computational approaches, this multidisciplinary team is at the forefront of kidney research, aiming to enhance diagnosis, treatment, and long-term management for diverse patient populations.

MAIN LINES OF RESEARCH

- Inherited Kidney Diseases:
  - The FEMALE PKD project focuses on a comprehensive approach to autosomal dominant polycystic kidney disease from a gender perspective, with a primary emphasis on reproductive and hormonal aspects, assessing the impact on hepatic and renal factors in women. (Furlano, Monica Maria).
  - To improve the genetic diagnostic yield of patients with suspected monogenic nephropathy, with previous negative genetic tests (gene panel/exome/MUC1), incorporating new genomic techniques that can contribute to identifying the etiological diagnosis of their kidney disease. (Ars Criach, Elisabet).
  - A cohort of individuals with Autosomal Dominant Alport Syndrome (ADAS) is being studied to identify genetic and epigenetic determinants of phenotypic variability, as well as transcriptomic profiling for characterisation of associated molecular signatures. Clinical data are being integrated to develop a predictive tool for assessing the risk of progression to advanced chronic kidney disease in ADAS patients. (Pilco Teran, Melissa Lorena; Torra Balcells, Roser; Furlano, Monica Maria; Ars Criach, Elisabet).
  - Inherited kidney diseases remain underdiagnosed, despite being the most common cause of early-onset chronic kidney disease (CKD), partly due to the challenges posed by clinical diagnosis given their heterogeneity. The use of artificial intelligence to develop clinical diagnostic tools represents a paradigm shift. Currently, clinical diagnostic tools for rare diseases (none of which are specifically designed for inherited kidney diseases) are based on ontologies. Still they have not been widely implemented due to their limited precision in describing these particular conditions. Within the framework of this project, an extensive curation of terms using HPO (Human Phenotype Ontology) annotations has been conducted, resulting in a precise description of these diseases in the context of deep phenotyping. The quality of this data will enable the development of clinical diagnostic tools, enriched not only with this curated information but also with real patient data using machine learning techniques. (Torra Balcells, Roser).
  - Identification of undiagnosed patients with inherited kidney disease by using natural language processing to extract data from electronic health records. (Torra Balcells, Roser).
- Glomerulopathies:
  - Study of the role of crescents in IgA nephropathy. Characteristics, prognosis, and treatment optimisation. (Marco Rusiñol, Helena)
  - Study of kidney diseases in patients with inflammatory bowel disease. Investigating possible association and prognosis. (Marco Rusiñol, Helena).
  - Clinical and histological patterns of renal thrombotic microangiopathy (TMA). TMA is a renal histological lesion caused by endothelial injury, usually associated with microangiopathic haemolysis; however, in some cases it may be limited to the kidney, requiring renal biopsy (RB) for diagnosis. Current knowledge of its histopathology is insufficient to understand its etiopathogenesis and thus to guide its treatment. We aim to describe the clinical and histological presentation of renal TMA in order to observe whether there are differences between patients with and without peripheral haemolysis, as well as between the different etiologies or triggers of TMA. This information would improve the diagnostic and etiological approach to renal TMA and guide its management.
- Chronic Kidney disease: Patients with chronic kidney disease (CKD) have a higher risk of fractures compared to the general population. Bone strength is determined not only by quantity (measured by DXA) but also by bone quality. Impact microindentation (IMI) is a technique that globally measures bone strength. This project investigates the behaviour of bone strength, as measured by

IMI, in different CKD scenaRíos: in prevalent hemodialysis patients, peritoneal dialysis patients, and newly transplanted patients. We study the relationship between IMI and other aspects of the bone phenotype (biomarkers, DXA, TBS, 3D-DXA), as well as its evolution over time. (Lloret Cora, Maria Jesús).

- Cardiovascular risk: This line investigates how positional (e.g., standing vs. lying down) and temporal (day-night) variability in blood pressure affects target organ damage in elderly patients with hypertension. The study aims to identify patterns of blood pressure fluctuation that may contribute to cardiovascular, renal, or cerebrovascular complications. Preliminary results suggest that greater variability in blood pressure—especially exaggerated nocturnal dips or postural changes—is significantly associated with increased markers of organ damage, including left ventricular hypertrophy, microalbuminuria, and white matter lesions on brain imaging. These findings underscore the importance of monitoring blood pressure dynamics beyond static measurements and support personalized approaches in managing hypertension in older adults. (Fernández De La Llama, Patricia).
- Dialysis: Evaluation of genetic damage in CKD and hemodialysis patients, and search for solutions (supplementation with antioxidants, switch to another hemodialysis technique, elimination of bisphenol A) and starting a new line about Genetic damage and gut microbiota in hemodialysis patients. (Coll Piera, Elisabet).
- Inflammation and fibrosis: The primary objective of this topic is to study inflammation-induced fibrosis. The focus is on the infiltration of M2 macrophages in renal tissue and their relationship with fibrosis and progression to chronic kidney disease. This study has produced several articles on cadaveric versus living donor transplantation and, more recently, the role of macrophages in the difference in prognosis between ANCAS MPO vs. PR3 vasculitis (in preparation). (Díaz Encarnacion, Maria Montserrat; Bardaji De Quixano, Beatriz).
- Transplantation: Advances in molecular HLA typing have made it possible to quantify mismatches at the epitope level, revealing that eplet incompatibility, particularly at HLA-DR/DQ loci, may play a critical role in graft outcomes and the development of donor-specific antibodies in kidney transplant recipients. Our research focuses on the impact of HLA class II eplet mismatches (HLA-DR/DQ) on kidney transplant outcomes, particularly their association with tacrolimus levels, graft survival, and acute rejection. (Guirado Perich, Lluís).

SCIENTIFIC CHALLENGES

- General: Navigating ethical approvals and compliance with research regulations (IRB), too much paperwork, lack of help, lack of blueprints. Lack of good and available statistical support.
- Dialysis:
  - Evaluation of mortality in patients with malnutrition in Hemodialysis.
  - Evaluation of low acute phase angle as a marker of increased mortality in hemodialysis patients
- Genetic kidney diseases:
  - Setting up a targeted RNA sequencing approach using a comprehensive renal gene panel to enrich RNA obtained from blood samples with transcripts involved in kidney diseases.
  - Procurement of a muticentric cohort of pregnant women woth ADPKD
  - Validation of the curation of HPO terms for inherited kidney diseases by European expert centres. Seek funding for developing an ML tool.

ACTIVE & AWARDED GRANTS

- Ars Criach, Elisabet. Heterogeneidad clínica, genética y alélica de las enfermedades renales hereditarias de debut temprano: nuevas causas moleculares de anomalías congénitas del riñón y el tracto urinario. PI19/01633. Instituto de Salud Carlos III (ISCIII). Duration: 2020-2024. 93.170,00 €

- Ars Criach, Elisabet. Estudio genómico y transcriptómico de pacientes con nefropatía no filiada con sospecha de causa monogénica. PI23/00426. Instituto de Salud Carlos III (ISCIII). Duration: 2024-2026. 102.500,00 €
- Díaz Encarnacion, Maria Montserrat. Papel de la vía del succinato en la inflamación de los riñones procedentes de donantes cadáver. FMM 2019. Fundación Mutua Madrileña. Duration: 2019-2024. 99.997,00 €
- Fernández De La Llama, Patricia. Primary care interventions to prevent maternal and child chronic diseases of perinatal and developmental origin. RD21/0012/0019. Instituto de Salud Carlos III (ISCIII). Duration: 2022-2024. 124.080,00 €
- Furlano, Monica Maria. FEMALE PKD: abordando la poliquistosis renal autosómica dominante desde una perspectiva de género. PI24/00823. Instituto de Salud Carlos III (ISCIII). Duration: 2025-2027. 138.750,00 €
- Lloret Cora, Maria Jesús. Estudio del comportamiento de biomarcadores de recambio óseo durante el primer año post-trasplante renal. BECA FEIOMM 2022 INVESTIGACIÓN CLÍNICA. Sociedad Española de Investigación Ósea y Metabolismo Mineral. Duration: 2022-2022. 7.000,00 € (F. Puigvert)
- Torra Balcells, Roser. Utilisation of artificial intelligence and systems biology for diagnosis and personalised risk assessment of inherited kidney diseases, with a focus on Alport syndrome. MARATO 202036-30. Fundació La Marató de TV3. Duration: 2021-2024. 112.500,00 €
- Torra Balcells, Roser. Búsqueda de enfermedades renales hereditarias no sospechadas: una aguja en un pajar. PI22/00361. Instituto de Salud Carlos III (ISCIII). Duration: 2023-2025. 123.420,00 €
- Torra Balcells, Roser. Inflamación e inmunopatología de órganos y sistemas. RD21/0005/0006-1. Instituto de Salud Carlos III (ISCIII). Duration: 2022-2024. 105.765,00 €
- Torra Balcells, Roser. RICORS2040-Renal. RD24/0004/0002. Instituto de Salud Carlos III (ISCIII). Duration: 2025-2027. 171.699,00 €
- Torra Balcells, Roser. Contratos para la intensificación de la actividad investigadora en el Sistema Nacional de Salud 2024. INT24/00049. Instituto de Salud Carlos III (ISCIII). Duration: 2025-2026. 60.000,00 €

DOCTORAL THESES DEFENDED

- Ruiz García, César Emilio. Efecto de los bisfenoles sobre el daño genómico en pacientes con Enfermedad Renal Crónica en Hemodiálisis. 20/09/2024. Universitat Autònoma de Barcelona. Supervisors: Coll Piera, Elisabet; Pastor Benito, Susana; Torra Balcells, Roser. https://hdl.handle.net/10803/693008
- Salas Gama, Karla. Toma de decisiones compartida y proceso de selección de la modalidad de diálisis en pacientes con enfermedad renal crónica avanzada. 19/09/2024. Universitat Autònoma de Barcelona. Supervisors: Bolibar Ribas, Ignasi; Díaz Gómez, Joan Manel. https://hdl.handle.net/10803/692760.

SCIENTIFIC PRODUCTION

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- Blasco M, Quiroga B, García JM, Torra R, Ortiz A, de Sequera P. Estudio genético en pacientes jóvenes con enfermedad renal crónica avanzada de etiología no filiada. Diseño del estudio GENSEN. NEFROLOGIA. 2024; 44(4). DOI:10.1016/j.nefro.2023.09.002. PMID:39054238. IF:2,000 (Q2/5D). Document type: Article.
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