Cancer Predisposition and DNA Repair Syndromes

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DESCRIPTION

This research group works in the field of genetic diseases characterized by a high predisposition to cancer. Many of these syndromes are caused by mutations in DNA repair genes. These genes are important to avoid the accumulation of mutations and prevent cancer transformation. Research on these syndromes is crucial to unravel the mechanisms that protect us from cancer.

In the past few years, the team has identified and studied several genes involved in such syndromes and performed therapeutic research leading to two orphan drug designations by the European Medicines Agency.

Their researchers are also involved in several clinical trials on gene therapy and drug repurposing and investigate DNA repair genes involved in these syndromes as therapeutic targets against cancer in the general population.

There are an increasing number of novel therapeutic strategies based on the deep knowledge of the genetic causes of the disease. Therefore, a proper genetic diagnosis is important not only to provide adequate genetic counseling and clinical management to the patients and their families but also to provide personalized medicine based on genomic information.

MAIN LINES OF RESEARCH

- Genetics and molecular biology of cancer-prone genetic syndromes with a focus on familial breast cancer and Fanconi Anemia and related chromosome fragility syndromes such as ataxia telangiectasia.

- Development of new diagnostic and therapeutic tools in Fanconi anemia, including gene therapy, regenerative medicine, and drug repurposing.
- Mechanism of genomic instability and predisposition to cancer. Study of DNA repair mechanism and biological and clinical consequences of DNA repair failure.
- Fanconi/BRCA pathway in cancer. Implications of Fanconi genes in cancer and their use as therapeutic targets against cancer. Development of DNA repair inhibitors against cancer by synthetic lethality.
- Application of next-generation sequencing, genome medicine, and genome editing to better identify pathogenic mutations and perform functional studies of variants of known significance in rare diseases.

SCIENTIFIC CHALLENGES

- Optimization of our drug candidate to inhibit FA pathway in a valorization process under the financial help of a Proof of Concept Grant by the Spanish Ministry.
- Follow up of functional assay to classify variants of unknown significance in cancer predisposing genes.
- As we signed a collaboration agreement with US based Rocket Pharma Ltd for 10 years follow-up of FA patients undergoing gene therapy, we will continue to do so.
- Initiation of our AFAN clinical trial for the repurposing of afatinib to treat Fanconi anemia patients with advanced head-and-neck cancer.
- Performing a drug screening to find drugs reactivating the Fanconi pathway in cells expressing a FANCA mutant protein.
- Develop and apply advanced genomic medicine tools and pipelines for the detection of pathogenic mutations in genes involved in rare diseases.
- Validation of gene candidates identified and prioritized in a genome-wide CRISPR-Cas screen to identify synthetic lethal and viable interactions with the Fanconi/BRCA pathway.

ACTIVE GRANTS

- NIH Center Comprehensive Program for Natural History of Development of Squamous Cell Carcinoma in Fanconi AnemiaCo-PI: Neelam Giri, MD and Sharon A Savage, MD (National Institute of Health). Co-IP Spanish team: Jordi Surrallés. Fanconi Anemia Research Fund. 2022-2025. Total Funds Awarded (USD): $ 1,107,464. Surrallés team Budget: $ 80.000.
- Infraestructura de Medicina de Precisión asociada a la Ciencia y Tecnología (IMPaCT). Acción Estratégica en Salud 2017-2020, Programa de Medicina Genómica. Ref. IMP/00009. Proyecto coordinado por el Consorcio Centro de Investigación Biomédica en red M.P. CIBER. Duración 2021-2023. 7.249.990 €.
- The Fanconi anemia/BRCA pathway :Genomic medicine and advanced therapies. (FABRAT). Ref. PID2021-122411OB-I00. Proyectos de Generación de Conocimiento 2021. Modalidad: Investigación Orientada Tipo B. Ministerio de Ciencia e Innovación. (1set.2022-31set.2025). IP Jordi Surrallés. 417.000 €.
- Ayudas Programa Investigo 2022. Ref. 100048TG2. Agència de Gestió d'Ajuts Universitaris i de Recerca AGAUR. (2022-2024) IP Jordi Surrallés. 66.217,84 €.
- ACCI 29-Cellular models for high-content drug screening in Fanconi anemia therapeutics. Ref. ER22P7AC745. Acciones Cooperativas y Complementarias Intramurales Conv.2021 (ACCI). CIBERER. (01/10/2022-29/02/2024) IP Jordi Surrallés. 52.600 €.
- Federated network for functional genomics of undiagnosed and rare diseases-rarefunction. Acciones Cooperativas y Complementarias Intramurales 2021 (ACCI).Ref. ER22P4AC7322/2023 / CB06/07/0001. CIBERER. Coordinador Francisco Palau. PI grupo Jordi Surrallés/ Massimo Bogliolo). 73.500 €.
- Reposicionamiento de afatinib para HNSCC en pacientes con anemia de Fanconi. Ref. ICI22/00076. Proyectos de Investigación Clínica Independiente de la convocatoria 2022. Acción Estratégica en Salud. Instituto de Investigación Carlos III. (ene2023-dic2026) IP Jordi Surrallés. 396.101,20 €.
- Valorización y prueba de concepto de un inhibidor de la reparación del DNA por la via Fanconi/BRCA para el tratamiento del cáncer por letalidad

sintética (Fanconinib). Ref. PDC2022-1333233-100. Ministerio de Ciencia e Innovación. Proyectos I+D+i Pruebas de Concepto 2022. (2023-2024). IP Jordi Surrallés. 150.000 €.

- Precision Medicine in FA: drug screening to identify a mutation specific drug. (Fanconi-cure). Convocatoria "Proyectos Colaborativos" en Cataluña (IBEC.Institute for Bioengineering of Catalonia). Plan Complementario de Biotecnología aplicada a la Salud del programa NextGeneration Europe. 2022. IP Jordi Surrallés. 178.650 €.
- Catalan Interhospital web of genetic variants to improve genetic diagnosis in rare diseases. Agència finançadora: Fundació La Marató de TV3. Financiació (en milers d'euros): 399.932,70 euros. Duració: 2021-2023. Codi Expedient: FLMTv3 202040. IP Benjamín Rodríguez.

GRANTS AWARDED

- AFAN trial. Phase Ib/II study to investigate the safety and efficacy of Afatinib when administered as therapy in Fanconi anemia patients with unresectable and / or metastatic locoregionally advanced squamous cell carcinoma of the oral cavity, oropharynx or hypopharynx or larynx. (FARF) Fanconi Anemia Research Fund. Conv. FARF Research Grant Award (RGA) Program. (30/04/2023-29/042027). PI Jordi Surrallés. 296.303 €.
- Development and implementation of a functional genomics platform for undiagnosed hereditary cancer. (IMPaCT_VUSCan). Convocatoria proyectos de investigación de medicina personalizada (2022). Subdirección General de Evaluación y Fomento de la Investigación. Ministerio de Ciencia e Innovación. Ref. PMP22/00064. Multicéntrico. IP Coordinadora Concepción Lázaro García (IDIBELL).01/01/2023-31/12/2025. Presupuesto global 3.182.544 €. Presupuesto grupo Surrallés 144.320 €.
- SGR-Cat 2021 (AGAUR). Genomic medicine and rare diseases group. Ref. 2021-SGR-00835. (2023-2025) IP Jordi Surrallés. 40.000 €.
- Inestabilidad Genómica. Proyecto colaborativo. Ref. RED2022-134164-T. REDES DE INVESTIGACIÓN. Plan Estatal de Investigación Científica, Técnica y de Innovación. Ministerio de Ciencia e Innovación (2023-2024). IP Coordinador Andrés Aguilera (CABIMER) / Jordi Surrallés. 20.000 €.
- Grupo de Bioinformática: Actualización en el análisis de datos de NGS para el diagnóstico. Convocatoria Grupos de Trabajo (GdT) 2023. CIBERER.

DOCTORAL THESES DEFENDED

- Moreno Niño, Olga Maria. Caracterización genética de la anemia de fanconi en población colombiana, relación con el fenotipo clínico y citogenético. Universitat Autònoma de Barcelona. 09/09/2023. Supervisors: Benítez, Javier; Surrallés, Jordi.
- Pérsico, Ilaria. Dealing with the main challenges of fanconi anemia molecular diagnosis and therapy. 24/03/2023. Universitat Autònoma de Barcelona. Supervisors: Surrallés Calonge, Jordi; Bogliolo, Massimo; D'Adamo, Adamo Pio. http://hdl.handle.net/10803/689721

SCIENTIFIC PRODUCTION

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