Haematological Diagnosis

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DESCRIPTION

The general objective of our line is to introduce improvements in the diagnosis and monitoring of haematological neoplasms using immunophenotypic and molecular biology techniques.

For more than 20 years (first project 1994), we have received funding for our proposals from the ISCIII on the following topics:

1. Molecular mechanisms of leukemogenesis: Identification of the molecular mechanisms associated with chromosomal translocations, in which we ruled out the presence of point mutations of RAG1 and RAG2, (Leukemia 1995;9:229-30;Hum Mutat 1996;8:191-2; Leukemia 1996;10:1715-8;Leukemia 2002;16:1571);the implication of repetitive Alu sequences at the origin of some chromosomal translocations (IgH-ID4)(cloned for the first time in our laboratory)(Haematologica 2003; 88:994-1001) and the role of microsatellite instability inacute myeloid leukemias (limitations of BAT26, interference of LOH lesions and characteristics of some areas promoters of p53 response genes (Leuk Lymphoma 2008;49:1178-83;Leukemia 2004;18:1148-9;Ann Hematol 2005;84:368-75;Leuk Res 2008;32:186-8).
2. Importance of p53 lesions in hematological malignancies: B and T line acute lymphoblastic leukemias, chronic lymphoproliferative syndromes, acute myeloid leukemias with complex karyotype and 17p lesions, transformations of bcr-abl negative chronic myeloproliferative syndromes

(Genes Chrom Cancer 1995;14:106-11; Genes Chrom Cancer 1996;15:48-53, Leuk Lymphoma 1998;29:595-605;Haematologica 1999;84:757-8;Med Clin (Barc)2000;115:573-5;Haematologica 2002;87:908-17;Med Clin (Barc)2002;119:497-9).

3. Application of flow cytometry techniques in the haematology laboratory: population enumeration of lymphoid cells, identification of lymphoproliferative syndromes in peripheral blood, nodal expression, and marrow involvement. Description of the first broad distribution of CD123 in haematological malignancies, including first cases in hairy cell leukemia (Haematologica 2001;861261-9).
4. Study of acute leukemias with KMT2a lesions: description of the differential morphology compared to other cases with myelomonocytic differentiation, presence of p53 mutations, description of nodal forms of KMT2a neoplasms, identification of the characteristic phenotype (monocytic markers + immaturity), participation in international study in which the associated mutations were exhaustively described (Leukemia 1995;9:955-9;Leuk Res 1999;23:585-8;Haematologica 2001;86:218-9,Leukemia 2003;17:76-82;Cancer Genet Cytogenet 2003;142:8-12;Blood 2016:128:e1-9;Hematol Oncol 2017:35:778-88;Hemasphere 2019;3:e181).
5. Residual disease studies in acute leukemias with tandem approach (cytometry and biology molecular): application to LAL Ph+, AML with CBFb-MYH11 and RUNX1-RUNX1T1 rearrangements. Participation in the development of the standardised test for the quantification of WT1 and application to the monitoring of myeloid neoplasms using conventional chemotherapy, stem cell transplant, demethylating agents, and the development of a PCR-specific digitalis (Leukemia 2000;14:339-40;Haematologica 2003:88:637-45;Leuk Res 2005;29:1109-16;Leukemia2006;20:87-94;Leuk Res 2009;33:1643-9;J Clin Oncol 2009;27:5195-201;Leukemia 2013;27:2157-64;Biol Blood Marrow Transplant 2018;24:55-63;Eur J Haematol 2019;103:208-14;Ann Hematol 2020;99:765-72).
6. Application of genotypic techniques and new molecular platforms in haematological diagnosis focused on acute myeloid leukemias, multiple myeloma, lymphomas, and chronic lymphoproliferative syndromes (Haematologica 2002;87:828-35;

   Expert Rev Mol Diagn 2019;19:571-8;Blood 2013;121:1403-12;Blood 2013;121:4902-5;Leukemia2016;30:929-36; Cytometry B Clin Cytom 2018;94:121-8;Cytometry B Clin Cytom 2019;96:143-8)
7. Reference laboratory in the protocols of the CETLAM cooperative group: clinical and genotypic correlation work. Reference laboratory for the Novartis Ratify trial, which allowed the approval of midostaurin as first-line treatment in AML with FLT3 mutations. Work on allelic ratios: the importance of the load in the forecast. Design of protocols based on post-consolidation treatments according to molecular findings and MRD.

   We are currently dealing with the rapid molecular diagnosis of recently diagnosed AML (Helena Castellet, team member). We analyze mutations of NPM1, FLT3, CEBPA, IDH1, IDH2, KMT2a, and chromosomal translocations included in the AML-plex kit. We have incorporated the UBTF tandem analysis and metabolism studies in leukemia (published in 2025).

MAIN LINES OF RESEARCH

- Germ cells neoplasms. (Pratcorona Canela, Marta).
- Erythropathology. (González Álvarez, Nuria).
- Flow cytometry. (Leoz, Pilar).

SCIENTIFIC CHALLENGES

- Long-read sequencing and optical genome mapping applied to complex molecular abnormalities.

- Clonal evolution assessed by ddPCR and NGS.
- Metabolism parameters in the diagnosis and treatment of hematologic neoplasms.
- Structural studies to assess the pathogenic potential of mutants.
- Rare red cell disorders diagnosis.

ACTIVE & AWARDED GRANTS

- San José Alonso, Paula. Estados ferrodeficitaRíos enmascarados: valores de ferritina, hepcidina y receptor soluble de transferrina. FUND. JL CASTAÑO 2024. Fundación José Luis Castaño. Duration: 2024-2026. 12.000,00 €
- Sierra Gil, Jordi & Pratcorona Canela, Marta. Poblaciones subclonales de LMA y células madre leucémicas identificadas mediante secuenciación de ARN de una sola célula y citometría de flujo multiparamétrica: impacto en la respuesta al tratamiento. PI20/01621. Instituto de Salud Carlos III (ISCIII). Duration: 2021-2025. 304.920,00 €

DOCTORAL THESES DEFENDED

- Cisa Wieczorek, Sabina. Estudio metabólico de c-KIT en líneas celulares mieloides y LMA en casos con sobreexpresión de WT1. 03/12/2024. Universitat Autònoma de Barcelona. Supervisors: Nomdedeu Guinot, Josep Francesc; Blanco Vaca, Francisco. https://hdl.handle.net/10803/693201.

SCIENTIFIC PRODUCTION

- Abril AG, Alejandre J, Mariscal A, Alserawan L, Rabella N, Roman E, López J, Navarro F, Serrano E, Nomdedeu JM, Vidal S. Titers of IgG and IgA against SARS-CoV-2 proteins and their association with symptoms in mild COVID-19 infection. Scientific Reports. 2024; 14(1):12725. DOI:10.1038/s41598-024-59634-y. PMID:38830902. IF:3,800 (Q1/2D). Document type: Article.
- Andrés JV, Nomdedéu J, Aguado HJ, González D, Minguell J, Joshi N, Teixidor J, Tomàs J, Selga J, García Y, Noriega DC, Mateos E, Pereda A, Cervera MC, Balvis P, García A, Rodríguez M, Castro M, Moreta J, Olías B, Amaya P, Boluda J, Bárcena L, Blas JA, Freile P, Castillón P, Lanuza L, Cabria J, Valle J, García J, Bonome C, Cano MD, Benjumea A, Chico M, Fernández A, Saura E, Sánchez P, Ricón FJ, García EM, Medrano I, Cuadrado F, Pérez MI, García S, Del Pozo P, García FM, García E, Guijarro A, Navas I, Videla M, Muñoz JM, Querolt J, de Santamaría GTL, Serra T, Carrasco MC, Pena S, Otero V, Fernández F, Martínez A, Galián E, Hernández JM, Renau M, Campuzano B, Carreras A, Vives M, Camacho P, Jornet M, Muñoz A, Gámez C, Plaza N, Benito J, Cuenca A, Alonso L, Mingo J, Briso R, Barbería A, Chouza L, Ojeda C, Ajuria E, Díaz R, Gasset A, Domínguez A, Gosálbez J, Pérez I, Riera L, Roche A, Macho M, Criado G, Cabello HG, Cunchillos J, Saló JC, Espona J, Salamanca C, García P, Blasco J, Sevilla P, Cano JR, Martínez S, Carabelli GS, Slullitel P, Astore I, Hernández C, Marín J, Córdova JC, Sánchez N, García G, Rodríguez A, Pérez JM, Piñeiro A, Mandía A, De Caso J, Benito M, Murillo AD, De La Herrán G, Nunes N, Pérez NE, De Sande M, García XD, de Cortázar UG, Sánchez DE, PIPPAS GRP. Predictors of outcomes after internal fixation of periprosthetic femoral hip fractures Subgroup analysis of the peri-implant and peri-prosthetic fractures Spanish registry (PIPPAS). INJURY-INTERNATIONAL JOURNAL OF THE CARE OF THE INJURED. 2024; 55(10):111715. DOI:10.1016/j.injury.2024.111715. PMID:39032221. IF:2,200 (Q2/3D). Document type: Article.
- Arguello M, Mozas P, Albiol N, López M, Sierra J, Nomdedéu J, Martínez C, Moga E, Piñeyroa JA, Delgado J, Osorio S, Moreno C. Risk scores predicting disease progression in early-stage CLL: Comparative analysis and usefulness of IGHV subset #2 to improve their accuracy. CANCER. 2024; 131(1). DOI:10.1002/cncr.35552. PMID:39264834. IF:6,100 (Q1/2D). Document type: Article.
- Halik A, Tilgner M, Silva P, Estrada N, Altwasser R, Jahn E, Heuser M, Hou HA, Pratcorona M, Hills RK, Metzeler KH, Fenwarth L, Dolnik A, Terre C, Kopp K, Blau O, Szyska M, Christen F, Krönke J, Vasseur L, Löwenberg B, Esteve J, Valk PJM, Duchmann M, Chou WC, Linch

DC, Döhner H, Gale RE, Döhner K, Bullinger L, Yoshida K, Damm F. Genomic characterization of AML with aberrations of chromosome 7: a multinational cohort of 519 patients. Journal of Hematology & Oncology. 2024; 17(1):70. DOI:10.1186/s13045-024-01590-1. PMID:39160538. IF:29,500 (Q1/1D). Document type: Article.

- Hernández A, González T, Sobas M, Sträng E, Castellani G, Abáigar M, Valk PJM, Ramiro AV, Benner A, Metzeler KH, Azibeiro R, Tettero JM, Martínez J, Pratcorona M, Elicegui JM, Mills KI, Thiede C, Sanz G, Döhner K, Heuser M, Haferlach T, Turki AT, Reinhardt D, Schulze R, Barbus M, Hernández JM, Huntly B, Ossenkoppele G, Döhner H, Bullinger L. Rearrangements involving 11q23.3/KMT2A in adult AML: mutational landscape and prognostic implications - a HARMONY study. LEUKEMIA. 2024; 38(9). DOI:10.1038/s41375-024-02333-4. PMID:38965370. IF:12,800 (Q1/1D). Document type: Article.
- Orgueira AM, Encinas MMP, Varela ND, Wang YH, Mora E, Díaz M, Montoro MJ, Marín HP, Ortega FR, Tormo M, Jerez A, Nomdedeu J, Sánchez CD, Arenillas L, Cárcel P, Romero MTC, Cirici BX, Arango ER, Barreto R, Benlloch L, Lin CC, Tien HF, Míguez CP, Crucitti D, Campelo MD, Valcárcel D. Validation of the Artificial Intelligence Prognostic Scoring System for Myelodysplastic Syndromes in chronic myelomonocytic leukaemia: A novel approach for improved risk stratification. BRITISH JOURNAL OF HAEMATOLOGY. 2024; 204(4). DOI:10.1111/bjh.19341. PMID:38411250. IF:5,100 (Q1/2D). Document type: Article.