

ABSTRACT BOOK

UPDATES ON GENETICS AND EPIGENETICS OF HEMATOLOGICAL MALIGNANCIES: FROM KNOWLEDGE TO APPLICATIONS

20-22 November, 2024

Josep Carreras Leukaemia Research Institute (IJC)

Badalona, Barcelona



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DE CIENCIA, INNOVACIÓN
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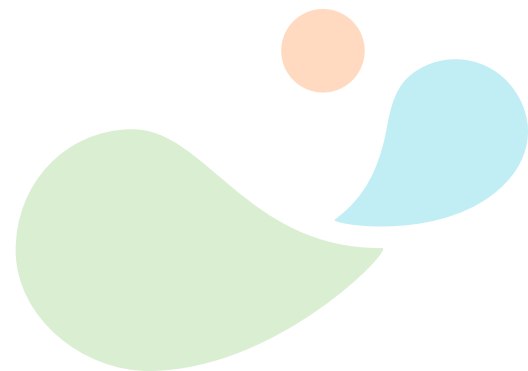
04/2024 - 03/2030



Josep Carreras
LEUKAEMIA
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WELCOME

We are pleased to welcome you to the Symposium “**Updates on Genetics and Epigenetics of Haematological Malignancies: From Knowledge to Applications**”. Organized by Josep Carreras Leukaemia Research Institute, the meeting will be held at the headquarters of the Josep Carreras Leukaemia Research Institute, Badalona, Barcelona, from **20th-22nd November 2024**.

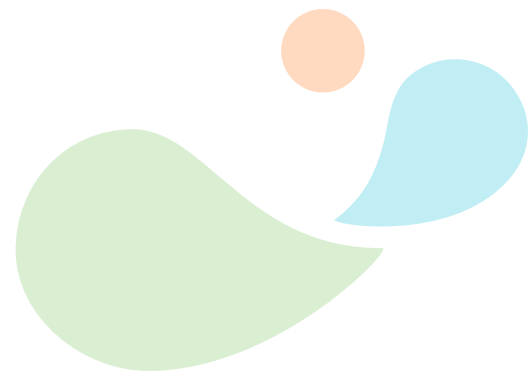
During the symposium, world-class experts will share their views and thoughts on their journey against cancer from multiple points of view: cell biology, immunology, genetics, epigenetics and computational biology, among others. Together, we will gather an interdisciplinary representation of the finest researchers, from the basic and clinical sciences, to present their latest publications and discuss with their peers openly.

The latest technologies like single cell analysis, next generation sequencing and genome editing will be also key players of the event, with experts on the field commenting on the endless possibilities they open for research and diagnosis.

We hope that the conference will meet all expectations and that fruitful discussions and new collaborations will be established as a result.

Warm regards,

Laura Belver, Anna Bigas, Marcus Buschbeck and Manel Esteller.



PROGRAMME

UPDATES ON GENETICS AND EPIGENETICS OF HEMATOLOGICAL MALIGNANCIES: FROM KNOWLEDGE TO APPLICATIONS

Wednesday, 20 November

- 13:30 – 14:30 Registration
- 14:30 – 14:40 Welcome - Manel Esteller
Josep Carreras Leukaemia Research Institute (IJC), CIBERONC
- 14:40 – 15:25 Opening Lecture, introduced by Manel Esteller
Ross Levine
Memorial Sloan Kettering Institute, New York, USA
"Deciphering and Targeting Clonal Evolution to AML"
- 15:30 – 16:30 **Session 1 - Stem Cells and Premalignancy**
Session Chair: [Gregoire Stik](#)
Senior lectures (20+10)
Michael Milsom
German Cancer Research Center (DKFZ), Heidelberg, Germany
"Pre-malignant programming of hematopoietic stem cells during aging and inflammation"

Florian H. Heidel
Hannover Medical School (MHH), Germany
"Epigenetic regulators as targets and effectors of cell signaling"
- 16:30 – 16:45 Selected Short talk (10+2)
Michael Scherer
German Cancer Research Center (DKFZ), Heidelberg, Germany
"Unraveling clonal identity and cell state in hematopoiesis from single-cell DNA methylation data"
- 16:45 – 17:10 Group Photo and Coffee break
- 17:15 – 17:30 Selected Short talk (10+2)
Cristina Lopez-Rodriguez
Department of Medicine and Life Sciences, Universitat Pompeu Fabra, Barcelona, Spain
"Fine-tuning of hematopoiesis under inflammatory stress"
- 17:30 – 18:00 Senior lecture (20+10)
Vincenzo Calvanese
Josep Carreras Leukaemia Research Institute (IJC), Catalonia, Spain
"Chromatin and transcriptional modulation in human blood stem cell self-renewal"
- 18:00 – 19:30 IJC Poster session "get to know us", Cocktail and Networking
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PROGRAMME

Thursday, 21 November

- 09:00 – 11:00 **Session 2 - Premalignancy, Immune Niches and Disorders**
Session Chair: Marcus Buschbeck
Senior lectures (20+10)
George Vassiliou
Wellcome-MRC Cambridge Stem Cell Institute, Cambridge, UK
"Clonal haematopoiesis and leukaemia prevention"
- Bruno Paiva**
Clinica Universidad de Navarra, Centro de Investigación Médica Aplicada (CIMA), Spain
"Immunogenomic research in monoclonal gammopathies"
- Alberto Orfao**
University of Salamanca, CIBERONC, Spain
"Oncogenetic pathways and immune response in systemic mastocytosis: from bone marrow mastocytosis to advanced disease subtypes"
- Brigitte Schlegelberger**
Hannover Medical School (MHH), Germany
"How to deal with genetic predisposition to hematologic malignancies"
- 11:00 – 11:20 Coffee break
- 11:30 – 13:00 **Session 3 - Biology and Treatment of Myeloid Neoplasms**
Session Chair: Manel Esteller
Senior lectures (20+10)
Iannis Aifantis
New York University (NYU), New York, USA
"Mapping of tumor-immune system interactions in myeloid neoplasms"
- Matteo Della Porta**
Humanitas Cancer Center, Milan, Italy
"A single cell multi-omics approach to understand the mechanisms of leukemic evolution in patients with myelodysplastic syndromes"
- Courtney DiNardo**
MD Anderson, Houston, USA
"Individualizing AML Therapy: Best Practices and Novel Therapeutics in 2024"
- 13:00 – 13:15 Selected Short talk (10+2)
Alessandra Ferrelli
The Francis Crick Institute, London, UK
"Developing a humanised in vivo model to study myeloproliferative neoplasms"
- 13:15 – 14:00 Lunch and Poster Session



PROGRAMME

Thursday, 21 November

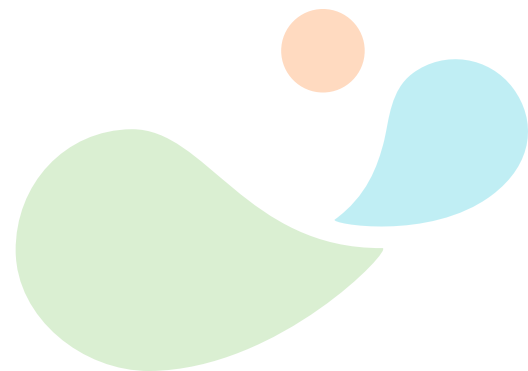
- 14:00 – 15:00 **Session 4 - Epigenetics and Chromatin Dynamics in Hematological Malignancies**
Session Chair: Biola M. Javierre
Senior lectures (20+10)
Manel Esteller
Josep Carreras Leukaemia Research Institute (IJC), CIBERONC, Catalonia, Spain
"Epigenetics and Epitranscriptomics in Hematological Malignancies"
- Christoph Plass**
German Cancer Research Center (DKFZ), Heidelberg, Germany
"Enhancer hijacking in acute myeloid leukemia"
- 15:10 – 15:55 Selected Short talk (10+2)
Andreas Lennartsson
Karolinska Institutet, Solna, Sweden
"Targeting Polycomb in the treatment of KMT2A-rearranged acute myeloid leukemia"
- Alba Maiques-Diaz**
Clínic Foundation for Biomedical Research - August Pi i Sunyer Biomedical Research Institute (IDIBAPS), Barcelona, Spain
"Chronic lymphocytic leukemia hijacks germinal center B cell transcriptional and epigenetic mechanisms to proliferate"
- Ruslan Sadreyev**
Massachusetts General Hospital, Boston, USA
"AML aggressiveness is driven by chromatin remodeling and expression changes of core regulators"
- 16:00 – 16:15 Coffee break
- 16:20 – 17:20 **Session 5 - Biology and Treatment of Acute Leukemias**
Session Chair: Laura Belver
Senior lectures (20+10)
Jan Cools
KU Leuven, Center for Human Genetics, Belgium
"Transcriptional deregulation in T-cell acute lymphoblastic leukemia"
- Maria L. Toribio**
Centro de Biología Molecular "Severo Ochoa", Madrid, Spain
"Pre-TCR targeting as a Selective Immunotherapy for T-cell Acute Lymphoblastic Leukemia"
- 17:30 – 17:45 Selected Short talk (10+2)
Alexander Waclawiczek
German Cancer Research Center (DKFZ), Heidelberg, Germany
"Four Leukemic Stem Cell Types mediate Resistance and Response in Acute Myeloid Leukemia"
- 17:45 – 18:45 Poster session, Cocktail and Networking



PROGRAMME

Friday, 22 November

- 09:00 – 10:30 **Session 6 - Biology and Treatment of Lymphomas and Myelomas**
Session Chair: Tomàs Navarro
Senior lectures (20+10)
Anna Bigas
Josep Carreras Leukaemia Research Institute (IJC), Hospital del Mar Research Institute, CIBERONC, Catalonia, Spain
"From Stem Cell Biology to Cancer Therapeutics"
- Teresa Palomero**
Columbia University, New York, USA
"Navigating the Molecular Landscape of Peripheral T-Cell Lymphomas: from Somatic Mutations to Mouse Models and Beyond"
- Francesco Bertoni**
Institute of Oncology Research, Bellinzona, Switzerland
"Mechanisms of resistance to BCR signaling inhibitors in B-cell lymphomas"
- 10:30 – 11:00 Selected Short talk (10+2)
Nuno R. dos Santos
i3S - Institute for Research and Innovation in Health - University of Porto, Porto Portugal
"Antibody blockade of the PSGL-1 immune checkpoint enhances T-cell responses to B-cell lymphoma"
- Wim Vanden Berghe**
University of Antwerp, Antwerp, Belgium
"Resolving epigenetic sensitization mechanisms of ferroptosis signaling to overcome therapy resistance in multiple myeloma"
- 11:00 – 11:20 Coffee break
- 11:30 – 11.40 Molecular Oncology Poster Presentation Awards
- 11:40 – 12.10 Closing Lecture, introduced by Manel Esteller
Ari Melnick
Weill Cornell Medicine, New York, USA
"Epigenetic mechanisms and targeted therapies for B cell lymphoma"
- 12:10 – 12:15 Final remarks and Farewell



Embryonic hematopoietic stem and progenitor cells show differential susceptibility to leukemic transformation upon acquisition of JMML-associated KrasG12D mutation

Giulia Quattrini¹, Cristiana Barone¹, Alessandro Muratore¹, Filipa Timóteo-Ferreira¹, Gloria Zambelli¹, Tiphanie Durfort¹, Roberto Orsenigo², Cristina D'Orlando¹, Raffaella Meneveri¹, Barbara Vergani¹, Sofia De Marco¹, Cristina Bianchi¹, Silvia Brunelli¹, Emanuele Azzoni¹

¹St. Anna Children's Cancer Research Institute (CCRI) Vienna, Austria

²School of Medicine and Surgery, University of Milano-Bicocca, Monza, Italy

³Biomedical Research in Melanoma-Animal Models and Cancer Laboratory, Vall d'Hebron Research Institute (VHIR), Vall d'Hebron Hospital Barcelona-UAB, Barcelona, Spain

Juvenile myelomonocytic leukemia (JMML) is a rare pediatric myeloproliferative neoplasm caused by a mutation in the RAS pathway. JMML is clinically heterogeneous and often originates prenatally, but the precise identity of disease propagating cells is still unclear. To investigate the cellular origin of JMML, we generated a preclinical model (Cdh5-CreERT2::KrasLSL-G12D::R26tdTomato transgenic mice) in which we can selectively target the KrasG12D to distinct subset of hematopoietic progenitors emerging from Cdh5+ hemogenic endothelium during embryonic development. Here, we demonstrate that embryonic hematopoietic progenitors show differential susceptibility to JMML-associated mutations. Targeting KrasG12D to erythromyeloid progenitors (EMPs) at E7.5, results in a low-penetrance myeloproliferative disorder with late onset (Fig2A), suggesting that EMPs are not the main cells of origin of JMML. Unexpectedly, targeting KrasG12D to fetal-restricted hematopoietic stem and progenitor cells (HSPCs) at E8.5 or HSCs at E10.5, caused lethal fetal liver (FL) anemia, due to defective erythroid differentiation (Fig1B), more severe if targeted to fetal HSPCs. To circumvent embryonic lethality, we induced KrasG12D in a mosaic-like fashion in HSPCs at E8.5 or HSCs at E10.5, which caused a fully penetrant leukemic phenotype in adult mice with a strong increase in the myelomonocytic lineage (Fig2B), more aggressive and transplantable (Fig2E,F) when induced the latter. These data suggest that both fetal-restricted HSPCs and HSCs could be involved in the pathogenesis of JMML, and that disease heterogeneity could be partially explained by variability in the cell of origin. We are currently analyzing the molecular and epigenetic changes KrasG12D-linked. Since our preliminary data suggest that patients-derived JMML HSPCs exhibit features of enhanced inflammation, we are investigating its role in disease onset and/or progression using our murine model and humanized mice model (PDX) of JMML.

