Congrès du **Club Hématopoïèse et Oncogénèse**

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Au nom du bureau et du comité d'organisation du Congrès du Club Hématopoïèse et Oncogénèse (Docteur Françoise PORTEU, Docteur Cyril BROCCARDO, Docteur Philippe BRUNET DE LA GRANGE, Docteur Marie-Laure ARCANGELI, Docteur Adlen FOUDI, Docteur Dominique BLUTEAU, Docteur Paulo DE SEPULVEDA, Docteur Christel GUILLOUF, Docteur Nathalie MAZURE, Docteur Fabienne MEGGETTO).

The annual congress of the Club of Hematopoiesis and Oncogenesis (CHO) held from September 29th to October 2th, 2021 at the Centre Belambra de la Presqu'Ile de Giens, France. We welcomed a total of 125 people, still with some international participants despite uncertainties of travel and quarantine between foreign countries. The general feeling form the participants was that our congress was impatiently expected due to the cancellation of last year congress because of COVID restrictions.

The general topics of the congress are normal hematopoiesis, oncogenesis related to hematology, and also sessions dedicated to oncology non-related to hematology. The goal behind this diversity is the scientific cross-fertilization between those fields, as well as an expected porosity between normal and pathological mechanisms.

During the congress, we heard impressive talks on the latest published knowledge, as well as unpublished data. The use of many innovative approaches, including single-cell techniques, omics, 3D-cell and tissue imaging, numerous animal models, bioinformatics, modelization allow to push the limits of the unknown in our fields of Hematopoiesis and Oncogenesis. We have tried to present a wide range of topics : basic hematopoiesis and cancer, the role of metabolic pathways in hematopoiesis and malignancies, genetics, genome stability, etc.

Here are some highlights of our congress.

Ten national and international speakers were invited. It was Pr. Julien BERTRAND (Université de Genève, Suisse) that gave the opening lecture with his conference entitled “How to expand HSCs: a tale of zebrafish tails”. Beyond this pun, Pr. Bertrand exposed us the molecular and cellular mechanisms governing the expansion of hematopoietic stem cells (HSC), using zebrafish as a model of investigation. His research led him to dissect the non-cell-autonomous genetic pathways controlling HSC expansion, and to decipher the cooperation between the vascular niche and myeloid cells to protect, maintain and expand HSCs in the caudal hematopoietic tissue.
Pr. Sandrine SARRAZIN (Centre d’Immunologie de Marseille-Luminy, CIML, Marseille) brought us into this fascinating (artificial) frontier between hematology and immunity, and reconciled them (!). She and others showed that HSCs can directly sense both cytokines released during infection and inflammation, and pathogen associated molecular patterns. Her presentation on ‘Immunomodulation and immune memory in HSC: new functions for new therapeutic applications?’ led us to understand how HSC can directly ‘molecularly’ sense a gram-negative bacteria, and that HSC can present an immune memory. She concluded that HSC are not only at the top of hematopoietic development but also at the heart of the immune response.
Pr. Els VERHOEYEN (C3M, Nice; CIRI-EVIR, Lyon) introduced us into the world of immuno-metabolism thanks to her talk on ‘GAPDH over-expression in the T cell lineage leads to a rare T cell lymphoma through a NF-κB dependent mechanism’. Based on a transgenic mouse model overexpressing GAPDH exclusively in the T cell lineage, she was able to investigate the role of GAPDH in T cells and T cell malignancies. In particular, her mouse model recapitulated key molecular and pathological features of human angioimmunoblastic T cell lymphoma (AITL). She identified a non-canonical NF-κB pathway activated by GAPDH and demonstrated that a newly developed NF-κB inducing kinase inhibitor prolonged AITL-bearing mouse survival. Finally, Pr. Els VERHOEYEN presented very interesting non-viral

vector tools to modify genetically CD34+ HSC with a high efficacy. She welcomes collaborative works using these tools.

Dr. Vera PANCALDI (CRCT, Toulouse) delivered a presentation on 'Data integration and single cell approaches to characterise the tumour microenvironment'. Her field game is solid cancers as well as hematological malignancies. She manipulates immunofluorescence multiplex imaging and multi-omics data to define cell identity and phenotype in a spatial context.

Dr. Claire FRANCASTEL (Université Paris-Diderot, Paris) recalled us that the vast majority of mammalian genomes does not code for proteins, and focused on the role of those non-coding genomic regions. She explored the functional links between transcription of DNA repeats, DNA methylation (responsible for silencing repetitive elements and for maintaining genome stability), and molecular and cellular programs. She worked on a rare human genetic disease with chromosomal instability, the Immunodeficiency, Centromeric instability, Facial anomalies syndrome, where compromised centromere integrity is directly linked to constitutive alterations of DNA methylation of centromeric DNA repeats.

With Dr. Eirini TROMPOUKI (Max Planck Institute of Immunobiology and Epigenetics, Freiburg, Germany), we continued into the field of repetitive elements, but this time from the perspective of developmental and regenerative hematopoiesis. She explained us how repetitive elements are transcribed during hematopoietic stem cell development and chemotherapy-induced regeneration, how repetitive element RNAs act as signals for innate immune receptors of the RIG-I-like receptor family, and how RNA sensing of repetitive elements actively shapes cellular transitions.

Pr. Michaela FONTENAY (Université de Paris, Institut Cochin, Paris) talked about the 'Splicing factor SF3B1 and DNA replication in erythropoiesis' based on her research on myelodysplastic syndromes (MDS). She explored the molecular causes of DNA damage and subsequent DNA repair, and their differences between high-risk and low-risk MDS.

Pr. Raphael ITZYKSON (Institut de recherche Saint-Louis, Paris) explained us his work on the 'Clonal Architecture in acute myeloid Leukemias'. He developed the concept of richness and evenness, two distinct dimensions of clonal diversity, that can be explored by genetic annotations of acute myeloid leukemias samples. Emerging single-cell technologies can be instrumental to decipher clonal architecture.

Dr. Maria Carolina FLORIAN (Bellvitge Biomedical Research Institute, Barcelona, Spain) is interested in the 'Aging of the hematopoietic stem cell niche'. Changes in the HSC niche are responsible of specific alterations of HSC behavior. She demonstrated that aged labelling retaining HSCs (the most quiescent HSC subpopulation with the highest regenerative capacity and cellular and epigenetic polarity) reside predominantly in perisinusoidal niches. Moreover, she demonstrated that sinusoidal niches are uniquely preserved in shape, morphology and number upon ageing. Altogether, she identified that perisinusoidal niches are uniquely preserved and protect HSCs from ageing.

Dr. Elodie SEGURA (Institut Curie, Paris) presented her work on the 'mechanisms of monocyte differentiation in steady-state and inflammation'. Circulating monocytes can differentiate into monocyte-derived macrophages (mo-mac) or dendritic cells (mo-DC). In this lecture, she questioned the mechanism of balance of mo-DC versus mo-Mac fate commitment, and identified transcription factors that repress mo-Mac differentiation and enable monocyte to commit to the mo-DC pathway. She proposed potential therapeutic targets to re-direct monocyte differentiation in inflammatory disorders.

Four "young" researchers recently recruited by research institutions such as INSERM and CNRS were also invited to present their previous work and new teams and projects. In our eyes, this "young researchers" session is important to get to know their background and their project. It also helps to introduce our CHO community and to enlarge the CHO network.

The organizing committee also selected additional 16 communications from the submitted abstracts for oral presentations. Among these 16 presentations, three by students or post-doctoral fellows were rewarded for their work, their great precision, clarity and synthesis: Céline Phillipe (BARTS cancer institute, London) on 'Vitamin B5 and Succinyl-CoA improve ineffective erythropoiesis in SF3B1 mutated myelodysplasia', Donia Hidaoui (INSERM U1287, Institut Gustave Roussy, Villejuif, Université Paris-Saclay) on 'Eradication of hematopoietic stem cells from patients with chronic myelomonocytic leukemia by combining DNA demethylating agents and histones methyltransferase inhibitors', and Veronica Alonso-Perez (CEA iRCM, Fontenay-aux-Roses)on 'Modelling pediatric ETO2-GLIS2-driven AMKL in human $CD34^{+}$ cells indicates that fetal liver and bone marrow cells are the most sensitive to transformation'.

The 35 papers selected for poster presentations were also presented by their author as a one-minute/slide "quick-fire" oral presentation to the full audience and an explanation to a poster presentation. Three students were awarded for the quality and originality of their quick-fire presentation, which often did not lack humor: Mathieu Desaunay (CRCM, CNRS, INSERM U1068, Institut Paoli-Calmettes, UMR7258, FNCLCC, Aix Marseille Université : UM105) on the 'Interaction between Fes kinase and the Vault particle plays a primordial role in protecting cells from transformation', Laura Jamrog (Laboratory of Hematopoietic Stem Cells and Leukemia (LSHL) INSERM U1274, UMR-E008 IRCM, IBFJ – CEA, Université de Paris-Université Paris-Saclay, Fontenay-aux-Roses, France) on the 'Role of a fusion between the RANBP2/NUP358 nucleoporin and ABL1 tyrosine kinase in the relapse of a pediatric T-ALL: from targeted therapy of a single case to generalization to more pediatric ALL', and Giulia Scorrano (CRCM, Inserm U1068, Institut Paoli-Calmettes, Université Aix-Marseille UM105, CNRS UMR7258, Marseille) for 'KIT promotes kynurenine uptake and metabolism by the kynurenine pathway in myeloid leukemia'.

This year again, the poster session was very much appreciated for the interactions that took place and the attendance that it had. It is a real place for scientific exchanges between teams, researchers, seniors and juniors. Four committees were formed to discuss the posters' works. The four committees each selected their best presentation/explanation, resulting in four student/postdocs being awarded: Gurvan Hermange (Centralesupelec, Université Paris-Saclay, Lab MICS ; INSERM, UMR 1287, Gustave Roussy, Villejuif, France INSERM) on 'Inferring the dynamics of mutated hematopoietic stem and progenitor cells induced by IFNα in myeloproliferative neoplasms', Charly Le Maout (CEA DRF/ JACOB/ IRCM/ UMRE008-U1274 Fontenay-aux-Roses) on 'Inflammatory microenvironment impacts T-cell acute lymphoblastic leukemia progression, Charly Courdy (CRCT, Inserm U1037) on 'Autophagy, a new potential therapeutic target in JAK2V617F Myeloproliferative Neoplasms' and Jean-Edouard Martin (Inserm UMR1287, Gustave Roussy, Villejuif) on the 'Role of TP53 alterations in leukemic transformation of JAK2 V617F mutated myeloproliferative neoplasms'.

Altogether, during the conferences, the poster session but also the social events, we observed an intense participation to the discussion, and great emulation between participants. They easily exchange ideas and suggestions, they share views and thoughts.

Finally, three new initiatives are to be noted for this 2021 edition of the CHO annual conference. Two initiatives focused on strengthening the involvement and responsibility of young participants. On the one hand, they were offered to participate -on a voluntary basis- to chair the sessions, and on the other hand, four young people were integrated in the poster juries. These two initiatives were very well received. Then, at the level of communication, we were able to benefit from the talents of a communication officer made available to us by the CRCT of Toulouse. On this occasion, the CHO created a Twitter account CHO_HEMATO to report the highlights of the congress.

Importantly, the CHO board members and myself would like to thank the French Cancer Society for its important moral and financial support.

The next meeting of Club of Hematopoiesis and Oncogenesis (CHO) will be held on October 12th-15th 2022 at the Centre Belambra de la Presqu'Ile de Giens, France. We invite you to visit regularly our website for update : https://www.cho-hemato.fr/ .

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