Leukaemia Team

Work program

Acute myeloid leukaemia (AML) is a hierarchically organized myeloproliferative disorder that is caused by step- wise acquisition of different mutations that prime malignant transformation and affect normal maturation of myeloid precursor cells. Despite concerted efforts in the development of new treatments, many patients are refractory to current therapeutic approaches or have a high relapse rate, with the overall long-term survival of patients being below 40% and more than 60% of the patients over 65 years of age succumbing to the disease within one year of diagnosis. In current medical practice, the diagnosis, prognosis, and therapeutic choices are dictated by detection of genetic mutations and the measurement of specific biomarkers that are used to classify patients into risk categories. However, due to the heterogeneous nature of the disease, prognosis within these categories is highly variable.

The concept of disease stratification promises to provide great improvements in the diagnosis, prognosis, and treatment of cancer, but requires robust and readily measurable biomarkers in order to be feasible. In line with this, part of the research activity of the Laboratory of Hematology and Cell Therapy is devoted to the identification of novel molecular biomarkers through the establishment of bioinformatic pipelines and genetic and pharmacological manipulation approaches. In parallel, large efforts are made also to overcome the major limitations of the lack of clinically relevant experimental systems to study the molecular basis of how specific mutations drive leukaemogenesis. To circumvent this limitation, we are applying somatic cell reprogramming in combination with CRISPR/Cas9 genome editing to generate unique cellular platforms to study how the sequential acquisition of specific mutations rewire the epigenome to instruct myeloid transformation and drive clonal disease establishment. Finally, we apply single cell sequencing technologies (scRNA-seq and scATAC-seq) with the aim to precisely delineate the clonal substructure of leukaemia, including the evolutionary history of its development and the co-occurrence of its mutations, this being paramount to understand and overcome treatment resistance. Those technologies allow to study differences in cell composition, state and function in complex tissues and to obtain key insights into how different mutation reshape the epigenetic landscape to escape the immune therapy and reveal important information in what transcriptional circuitries mediate the process of disease relapse.

Team Composition

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- Hematology Unit and Translational Research Laboratory, Istituto Romagnolo per lo Studio dei Tumori "Dino Amadori, Meldola, Italy.
- Department of Biomedical Sciences, Institute of Medical Biochemistry, University of Veterinary Medicine, Vienna, Austria.

Key Funding

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Key Publications

- **Cell transcriptomic atlas of the non-human primate Macaca.**
  Fascicularis Han L*, Wei X*, Liu C*, Volpe G*, Zhuang Z*, Zou X*, Wang Z, Pan T, Yuan Y, Zhang X, Fan P, Guo P, Liu X, Wu L, Shi Q, Yu H, Huang Y, Lu H, Wang B, Cheng M, Xu J, Liu Y, Wang M, Wang C, Zhang Ym, Yu Y, Wong C, Lai G, Xu S, An Ward C, Isern J, Feng L, Liu Y, Guo X, Maxwell P, Barker N, Munoz-Canoves P, Gu J, Mulder J, Uhlen M, Liu S, Yang H, Wang J, Hou Y, Xu X , Esteban MA, Liu L. 2022, Nature.
  *Co-first author.
- **NR1H3 (LXRa) is associated with pro-inflammatory macrophages, predicts survival and suggests potential therapeutic rationales in diffuse large b-cell lymphoma.**
  Vegliante MC, Mazzara S, Zaccaria GM, De Summa S, Esposito F, Melle F, Motta G, Sapienza MR, Opinto G, Volpe G, Bucci A, Gargano G, Enjuanes A, Tabanelli V, Fiori S, Minoia C, Clemente F, Negri A, Gulino A, Morello G, Scattone A, Zito AF, Tommasi S, Agostinelli C, Vitolo U, Chiappella A, Barbui AM, Derenzini E, Zinzani PL, Casadei B, Rivas-Delgado A, López-Guillermo A, Campo E, Moschetta A, Guarini A, Pileri SA, Ciavarella S.. 2022, Hematological Oncology.
- **Single-cell landscape of the ecosystem in early-relapse hepatocellular carcinoma.**
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  *Corresponding author.
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  *Corresponding author.
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- **MYBL2 supports DNA double strand break repair in haematopoietic stem cells, a process which is defective in low MYBL2 expressing myelodysplastic syndrome patients**.
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- **Prognostic significance of high GFI1 expression in AML of normal karyotype and its association with a FLT3-ITD signature with normal karyotype acute myeloid leukaemia**.
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