

## **Lymphoma Team**

### **Work program**

The advent of new immuno- and cell-therapies into the clinical practice of hematological neoplasms raised the need for a better understanding of tumor microenvironment (TME) in terms of cell composition and function. Deeper dissections of immune and stromal TME components in the context of peculiar malignancy subtypes might reveal new drug targets and optimize the personalization of current treatments. However, the study of TME remains challenging due to two main reasons: i) the phenotypic/functional heterogeneity of TME within and between patients, and ii) the difficulty of conciliating biological and clinical data in the context of controlled trials and real-world practice.

The research activity of the Laboratory of Diagnostic Hematology and Cell Therapy has long been devoted at applying the cutting-edge bioinformatic and mathematical approaches of TME dissection, exploiting public big data to generate and validate prognostic/predictive hypotheses in several hematological malignancies. Such approach is tightly interconnected with a retrospective/prospective activity of internal data recording (clinical and biological) of real-world cohorts as well as centralization of samples from prospective controlled multicentric clinical trials.

The research effort of the team has already provided large amounts of results in the field of the diffuse large B cell lymphoma and related subtypes, producing valuable prognostic gene panels (validated on NanoString technology), and allowing the conceptualization of new immunotherapy rationales for high-risk patients. Additional research lines are aimed at optimizing the diagnostics of rare lymphoma subtypes by transcriptomics as well as at producing new predictive tools for other hematological malignancies.

### **Team Composition**

#### Team Leader

Maria Carmela Vegliante, PhD –Hematology Unit IRCCS

#### Team members

Sabino Ciavarella  
Giacomo Loseto  
Carla Minoia  
Maria Stella De Candia  
Antonio Negri  
GianMaria Zaccaria  
Grazia Gargano  
Paolo Mondelli  
Anita Pappagallo  
Fabio Pavone  
Felice Clemente

### **Team Network**

- Department of Mathematics, University of Bari Aldo Moro, 70125 Bari, Italy
- FIL, Fondazione Italiana Linfomi
- Division of Diagnostic Haematopathology, European Institute of Oncology, IRCCS, Milan, Italy.
- August Pi i Sunyer Biomedical Research Institute (IDIBAPS) and Hospital Clinic, Barcelona Spain.

- Hematology Unit and Translational Research Laboratory, Azienda USL-IRCCS, Reggio Emilia, Italy.
- Tumor Immunology Unit, Department of Sciences for Health Promotion and Mother-Child Care "G. D'Alessandro", University of Palermo, Palermo, Italy

### **Key funding**

- Ricerca Corrente 2022-Ministry of Health
- Bando Roche per la ricerca indipendente 2020
- Fil Club -*FollEz study 2022*

### **Key publication**

- **NR1H3 (LXR $\alpha$ ) is associated with pro-inflammatory macrophages, predicts survival and suggests potential therapeutic rationales in diffuse large b-cell lymphoma.**  
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- **Prognostic value of lesion dissemination in doxorubicin, bleomycin, vinblastine, and dacarbazine-treated, interimPET-negative classical Hodgkin Lymphoma patients: A radio-genomic study.**  
Durmo R, Donati B, Rebaud L, Cottereau AS, Ruffini A, Nizzoli ME, Ciavarella S, Vegliante MC, Nioche C, Meignan M, Merli F, Versari A, Ciarrocchi A, Buvat I, Luminari S. *Hematol Oncol.* 2022 May 23.
- **Spatial transcriptome of a germinal center plasmablastic burst hints at MYD88/CD79B mutants-enriched diffuse large B-cell lymphomas.**  
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- **Electronic case report forms generation from pathology reports by ARGO, automatic record generator for onco-hematology.**  
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- **Predictive and Prognostic Molecular Factors in Diffuse Large B-Cell Lymphomas.**  
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- **A New Ensemble Method for Detecting Anomalies in Gene Expression Matrices.**  
Laura Selicato, Flavia Esposito, Grazia Gargano, Maria Carmela Vegliante, Giuseppina Opinto, Gian Maria Zaccaria, Sabino Ciavarella, Attilio Guarini, Nicoletta Del Buono. *Mathematics,* 2021-04 | Journal article.
- **18F-FDG PET/CT Cannot Substitute Endoscopy in the Staging of Gastrointestinal Involvement in Mantle Cell Lymphoma. A Retrospective Multi-Center Cohort Analysis.**  
Skrypets T, Ferrari C, Nassi L, Margiotta Casaluci G, Puccini B, Mannelli L, Filonenko K, Kryachok I, Clemente F, Vegliante MC, Daniele A, Sacchetti G, Guarini A, Minoia C. *J Pers Med.* 2021 Feb 13;11(2):123.
- **Primary, Bilateral and Diffuse Renal Non-Hodgkin's Lymphoma in a Young Woman Suffering from Turner Syndrome.** Rossini B, Skrypets T, Minoia C, Quinto AM, Zaccaria GM, Ferrari C, Maggioretti N, Mastorosa A, Gatti P, Casiello M, Ciavarella S, Guarini A. *J Pers Med.* 2021 Jul 7;11(7):644.
- **Hodgkin Lymphoma: A Special Microenvironment.**

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- **Intra-tumour heterogeneity of diffuse large B-cell lymphoma involves the induction of diversified stroma-tumour interfaces.**  
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- **A Spatially Resolved Dark- versus Light-Zone Microenvironment Signature Subdivides Germinal Center-Related Aggressive B Cell Lymphomas.**  
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- **The Tumor Microenvironment of DLBCL in the Computational Era.**  
Opinto G, Vegliante MC, Negri A, Skrypets T, Loseto G, Pileri SA, Guarini A, Ciavarella S. Front Oncol. 2020 Mar 31;10:351.
- **Diffuse large B-cell lymphoma: the stuff of cell-of-origin and microenvironment.**  
Pileri SA, Vegliante MC, Ciavarella S. Oncotarget. 2019 Jun 18;10(40):3991-3993.
- **Dissection of DLBCL microenvironment provides a gene expression-based predictor of survival applicable to formalin-fixed paraffin-embedded tissue.**  
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- **SOX11 promotes tumor angiogenesis through transcriptional regulation of PDGFA in mantle cell lymphoma.**  
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