# MLL News

February 15, 2023

## New: The Hematology Genome Network Introduces Itself:

### Closer Networking Needed between Diagnosticians and Therapists

Together with the Comprehensive Cancer Center Klinikum Rechts der Isar TUM and the Comprehensive Cancer Center Mainfranken/Universitätsklinikum Würzburg, MLL has founded the Hematology Genome Network. The goal is to provide patients with access to new diagnostic approaches – including whole genome sequencing (WGS) – for complex clinical questions. WGS and other new technologies can then be performed during studies and projects, depending on the actual clinical question involved. In tumor boards, results are discussed together with clinical experts so that therapy options can be jointly evaluated. The implementation of the treatment recommendations and clinical outcomes are documented in a shared database. The plan is to use this data to redefine the value of state-of-the-art diagnostics in the new era of precision medicine.

### Starting with Two Pilot Projects

Two studies were launched on two topics that are currently relevant:

The purpose of the **"Exciting Case" study** is to clarify whether WGS can provide additional insights and optimize diagnosis, prognosis assessment, and perhaps therapy selection in patients for whom current standard diagnostics have left questions unanswered (further details and initial results).

The goal of the **"Mechanisms of Resistance in Multiple Myeloma to Targeted Therapies" study** is to investigate how many patients already have genetic alterations before or after targeted therapies that make resistances towards specific therapies likely (further details on this study).

### Anyone Can Become Active in the Hematology Genome Network

We would welcome your support for the Hematology Genome Network by contributing patients towards these two studies. Furthermore, you can also submit an application for membership before participating in the tumor boards or initiating studies and projects within the Hematology Genome Network yourself. The data will only be accessible to Network members for conducting further research.

### Making Goals a Reality

One mission of the Hematology Genome Network is to establish knowledge-generating patient care: Not only will data integrated from research projects and daily patient care to improve individual treatment, but – based on the experience and daily challenges of patient care – new research projects are also being developed whose results will in turn improve patient care. The Hematology Genome Network is therefore expected to help make personalized medicine a reality in hematology and to further improve patient care.

Author: Prof. Dr. med. Claudia Haferlach


## Hemoglobinopathies – Thalassemia and Abnormal Hemoglobins

**Background and Request for Testing**
Worldwide, approximately 5% of the population are carriers of hemoglobinopathies. Due to the ongoing migration situation, they are now playing an increasingly relevant role in hematology practice. Thalassemia has now become a frequent differential diagnosis in patients with a corresponding genetic background when it comes to clarifying the cause of microcytic hypochromic anemia. Together with abnormal hemoglobins, these are among the most common hereditary disorders. Over the past years, we have also regularly received requests for to carry out diagnostics in these areas.

In order to provide our colleagues with a central point of contact for this disease complex, which is growing increasingly relevant and frequent, we have expanded our range of tests at MLL to include complete diagnostics for the identification and characterization of hemoglobinopathies.

They can be requested using a special test order process. 1 x 3 ml EDTA blood (standard blood count tube), 1 x 7.5 ml EDTA blood, 1 x 7.5 ml of serum, and the patient's consent to allow the conducting of genetic analyses according to the Genetic Diagnostics Act are required.

**Typical indications for testing for hemoglobinopathy include the following:**

- Hypochromia and/or anemia after iron deficiency has been excluded
- Chronic hemolytic anemia
- Vascular occlusions of unknown origin
- Recurrent pain crises
- Unexplained severe infections
- Hydrops fetalis syndrome
- Positive family history

### Classification of hemoglobinopathies

Hemoglobinopathies include congenital quantitative (thalassemia) or qualitative (abnormal hemoglobins) disorders of the hemoglobin chain synthesis. The most common forms of thalassemia are α-thalassemia and β-thalassemia. The clinical spectrum ranges from blood count changes without clinical symptoms to transfusion dependency. Among the abnormal hemoglobins, HbS is of particular importance, as it is the basis for sickle cell disease. This is associated with chronic hemolytic anemia, recurrent vaso-occlusive pain crises, and resultant organ damage. Other regularly occurring hemoglobin structural variants are HbC, HbE, and HbD.

### Diagnostic Methods

If hemoglobinopathy is suspected, staged diagnosis consisting of blood count, iron status, hemoglobin differentiation using capillary electrophoresis, and other staged diagnostic methods, depending on the findings, are recommended:

- Hemoglobin differentiation: High-resolution capillary electrophoresis is used to separate and quantify the different hemoglobin fractions. This produces evidence of disorders in the β-globin gene complex or severe forms of α-thalassemia.
- Molecular genetics: Molecular genetic methods based on the findings are then employed to confirm the suspected diagnosis. Deletion-specific PCR is used to detect α-thalassemia, while abnormal hemoglobins or β-thalassemia are confirmed with next-generation sequencing (NGS). Rare forms like (γ)δβ-thalassemia are caused by large deletions. In these cases, multiplex ligation-dependent probe amplification (MLPA) is used.

### Tests Offered at MLL

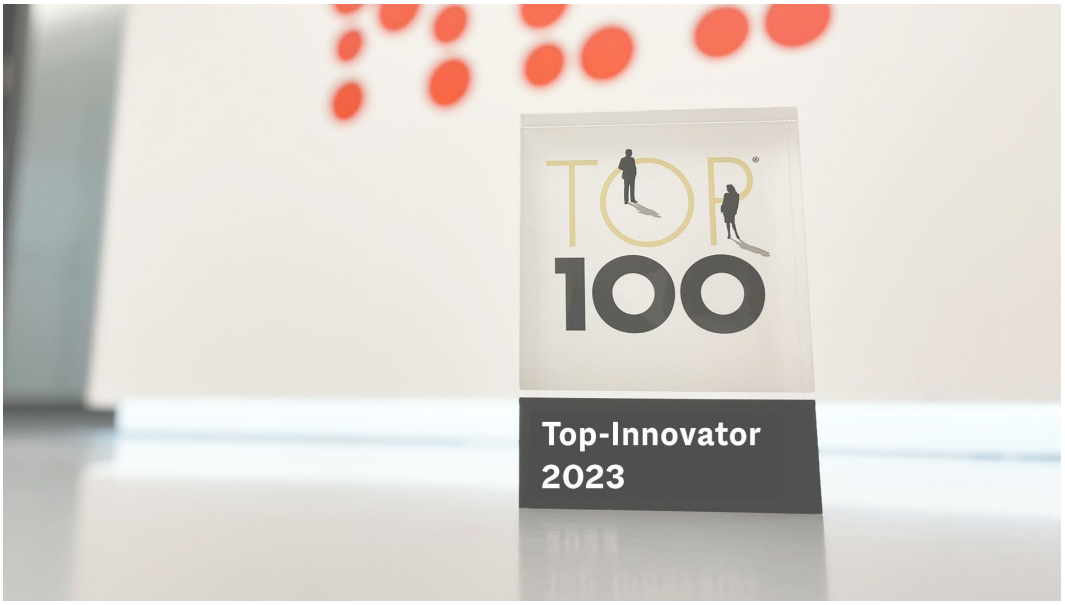
All of the above methods are now routinely offered at MLL. We hope that this will satisfy the wishes of colleagues who make requests from us. If you have any questions on this topic or the diagnostic procedure, please contact Dr. Dr. med. Armin Piehler.

Author: Dr. Dr. med. Armin Piehler

## MLL Munich Leukemia Laboratory Receives the TOP 100 Seal Again

MLL Munich Leukemia Laboratory was once again able to score points with its innovative spirit to receive the TOP 100 seal for the fifth time in a row. This award, which is presented as part of the TOP 100 Innovation Competition, is only given to especially innovative medium-sized companies. On June 23, 2023, Ranga Yogeshwar, science journalist and mentor of the competition, will personally congratulate MLL on its success at the German SME Summit in Augsburg.

Information on the Award




## MLL Introduces Itself: Our Knowledge Management

Every day, the MLL team works together to provide patients worldwide with the best possible therapy through rapid and targeted leukemia diagnostics. But what exactly does the day-to-day work of the more than 250 employees look like? What departments and areas are there? Our magazine series, "MLL Introduces Itself," provides you with an insight into our laboratory. This section also introduces you to our Knowledge Management Department.

As the name suggests, knowledge management is all about knowledge – knowledge that has been generated daily since MLL's inception to advance leukemia diagnostics and therapy for the benefit of patients.

### Knowledge Management Team

The Knowledge Management Department is one of the newest departments at MLL. The team is staffed by three scientists: Dr. rer. nat. Sabine Riedel leads the team and is supported by two experienced medical writers. In order to learn first-hand about MLL's needs and goals and to support all specialist departments in their day-to-day work, Knowledge Management communicates very regularly with all diagnostic areas and with the Research & Development and Corporate Communications departments.

### Storing and Bundling of Knowledge and Making it Accessible

Large amounts of data of different kinds are generated at MLL each day: both data from routine laboratory operations as well as data yielded by scientific projects. There is a coordinated routine for storing this data. But what happens with the rest, such as the lectures or information prepared about the various leukemic diseases, MLL internal workflows, and much more? Currently, Knowledge Management is implementing suitable software with which each employee will be able to quickly and reliably search for and find information and data. Such a digital system will ensure that the latest information will always be available and accessible to the entire MLL team. This tool will also serve to support the professional development of MLL employees, which is a top priority.

Other exciting knowledge management tasks include the following:

- Writing scientific texts for internal and external uses
- Research for publications
- Assistance with the preparation of presentations
- Updating of scientific content on our website
- Identification of scientific projects, topics, and trends for internal and external communication
- And much more...

**The Knowledge of Tomorrow**

Knowledge about the prevention, diagnosis, and therapy of leukemia is constantly expanding, with more and more new findings and data being generated. As a result, our knowledge management activities at MLL are always exciting and diverse. In the Knowledge Management Department, we are looking forward to supporting scientists even more in the evaluation and publication of scientific projects in the future. We also intend to develop and structure the training of new employees by expanding our knowledge management tool.

Author: Dr. rer. nat. Sabine Riedel

## Research Report 2022

As in every year, we didn't just stand still over the last year but instead did all we possibly could every day to advance the best possible leukemia diagnostics for our patients. We have summarized all the highlights and milestones from our research for you in our Research Report 2022. To make reading easier and to communicate our data more clearly, we have included various graphs and summaries. We hope you enjoy reading it!

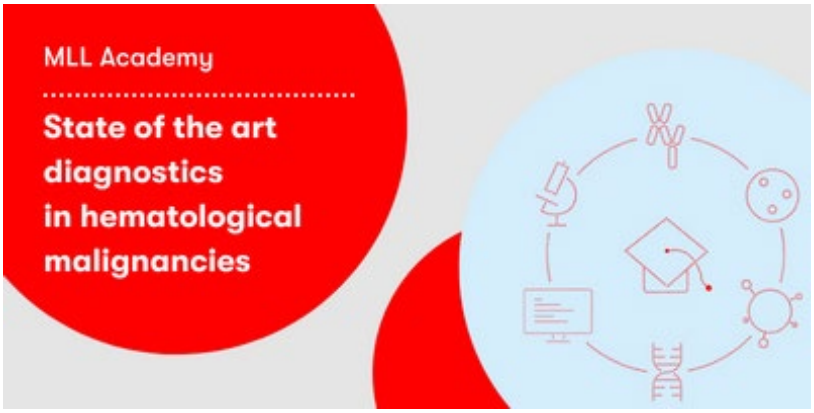
### About the Research Report 2022


## Events

## MLL Academy 2023

The next MLL Academy will be held on April 24-28, 2023. At the five-day workshop on the topic "State-of-the-art diagnostics in hematological malignancies", the twelve participants can expect a mixture of theoretical and practical content, along with joint discussions on leukemia and lymphoma diagnostics. Registration is still possible up until March 31, 2023.

Click here to register and go to the program




## MADE 2023 Microscopy Courses

For the first time together, Würmtal Laboratory and MLL Munich Leukemia Laboratory are organizing the microscopy course series MADE (*Mikroskopieren* (microscopy), *Analysieren* (analysis), *Diskutieren* (discussion), *Einpacken* (Packing)). Altogether, we are offering three courses (MADE by Yourself, MADE for the Future, MADE @ home) at different times.

Click here to register and go to the program

## Most Recent Publications with MLL Involvement

- Baer C et al. Risk prediction in MDS: independent validation of the IPSS-M - ready for routine?. Leukemia. 2023. View publication
- Brandstoetter T et al. SBNO2 is a critical mediator of STAT3-driven hematological malignancies. Blood. 2023. View publication
- Graf I et al. N-terminal pro-brain natriuretic peptide is a prognostic marker for response to intensive chemotherapy, early death, and overall survival in acute myeloid leukemia. Am J Hematol. 2023. View publication
- Haferlach T, Walter W. Challenging gold standard hematology diagnostics through the introduction of whole genome sequencing and artificial intelligence. Int J Lab Hematol. 2023. View publication
- Mansouri L et al. Different prognostic impact of recurrent gene mutations in chronic lymphocytic leukemia depending on IGHV gene somatic hypermutation status: a study by ERIC in HARMONY. Leukemia. 2022. View publication
- Mas-Peiro S, Pergola G, Berkowitsch A, Meggendorfer M, Rieger MA, Vasa-Nicotera M, Dimmeler S, Zeiher AM. Long-term risk associated with clonal hematopoiesis in

patients with severe aortic valve stenosis undergoing TAVR. Clin Res Cardiol. 2023. View publication

- Porwit A et al. Multiparameter flow cytometry in the evaluation of myelodysplasia: Analytical issues: Recommendations from the European LeukemiaNet/International Myelodysplastic Syndrome Flow Cytometry Working Group. Cytometry B Clin Cytom. 2022. View publication
- Stengel A et al. Specific subtype distribution with impact on prognosis of TP53 single hit and double hit events in AML and MDS. Blood Adv. 2023. View publication

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