MLL News

December 20, 2022

We want to say thank you: The MLL Annual Review for 2022

Even if the corona pandemic is no longer every day's top headline, the disease is still important in our practice, MLL MVZ, and in the MLL Munich Leukemia Laboratory. Naturally, this is especially true with regard to protecting the patients entrusted to us in our daily consultation hours, but it also applies to our employees. As in many practices and businesses, it is necessary to ensure that operations continue to function (seven days/week in the laboratory). Therefore, together with our staff, we are making every effort to improve our service again this year in the interests of the patients entrusted to us and those who send them to us as the number of requests increases.

That is why the year 2022 is of particular importance: The newly published guidelines for diagnostics, classification, prognosis assessment, and prognosis prediction change the laboratory workflow in many places – and sometimes the reporting times as well (turnaround time, TAT). The new classifications according to the WHO and ICC are of central importance, as is the newly published ELN on the diagnosis and therapy of AML and the IPSS-M for prognosis assessment in MDS, including molecular genetic markers. These publications and online versions (WHO) complement the ELN AML Guidelines for measurable residual disease (MRD) already published last year.

Not only do all these publications need to be taken into account, but they must also be harmonized. Only then are they implemented into the daily routine of our findings. As one example, we will be changing our findings to the new WHO 2022 terminology in January 2023.

This will make diagnostics more complicated – not only for every provider on the laboratory side but also for physicians and ultimately for our patients. A large amount of new therapeutic and prognostic information based on this will need to be considered. However, all of this factors into the progress of science and is now indispensable, especially in these times of precision medicine.

In addition to the introduction of new, specifically molecularly defined entities and prognosis scores, the hierarchy of the respective diagnosis also plays an important role in the diagnostic process: With the new classifications and guidelines, we are taking a big step toward genotype-based diagnostics while easing away from phenotype-based diagnostics (previously cytomorphology, histology, immunophenotyping, and immunohistology).

Today, chromosomal changes are joined by a variety of molecular genetic changes, such as fusion genes and variants/mutations. Gene expression patterns need to be considered as well. Without next-generation sequencing (NGS) – such as in the form of panel sequencing, in which many genes are examined in a patient-specific manner in a single approach – the mapping of these new guidelines in routine diagnostics would not even be possible.

From the above, it is easy to imagine just how complex the analysis and findings have now become. At the same time, the "user," namely our submitting physicians and our common patients, must not only understand the findings but also receive the best possible diagnosis and – especially – therapy.

That is why we are continuously working on simplifying the requests using request sheets, whether this is still done with paper, a PDF file, or even via our "Order Entry" digital requests platform. For example, the new quick request option in our Order Entry Portal has reduced the number of clicks required per request by 2/3, namely from 20 to 6.

From now on – also for everyone's convenience – we will be strictly following the new guidelines and allowing for a simple "request by guideline."

Furthermore, the diagnoses of CHIP and CCUS according to the WHO and CCUS according to the ICC have been included in the portfolio of diseases: as precursor diseases of MDS in the sense of a continuum. This must also be taken into account in the laboratory procedure and when reporting findings. In order to make the whole thing easier for later use, we have supplemented and expanded our "integrated report" and stored the new guidelines: This is currently being made available for the primary diagnoses of AML and MDS and – in the very foreseeable future – for multiple myeloma and CLL as well.

For difficult cases, we are enabling cutting-edge technologies like whole-genome sequencing and whole-transcriptome sequencing (WGS and WTS). The study which we started, "The Exciting Case" (ClinicalTrials.gov Identifier: NCT05046444), has already recruited more than 40 cases using WGS and WTS as parallel diagnostics in addition to today's optimal gold standard diagnostics. In one third of the cases, we were able to establish a definite diagnosis with the help of the new sequencing methods with otherwise unclear results from the gold standard diagnostics, thereby underlining their diagnostic significance.

For the past three years, we have been promoting projects where diagnostics are supported by artificial intelligence (AI). In cytogenetics, this has been part of routine practice for more than two years. In 2023, we will be able to introduce the AI algorithms into our routine diagnostics for the areas of molecular genetics, such as genome sequencing, and particularly for the daily routine of cytomorphological assessments for peripheral blood and bone marrow and for immunophenotyping. The results obtained in this way will be presented to the MLL colleagues who obtained the findings, checked, and included in the final findings.

In October 2022, the total number of submissions since MLL's inception surpassed the one million mark. What a special experience for us all!

At the same time, we are increasing our scientific output through our own publications and by participating in global research alliances. For example, this is true of the EU-funded HARMONY, GenoMed4All, and Intercept-MDS collaborations. Many collaborations involve leading research laboratories at universities worldwide. We consider it an important mission not only to make our data and our knowledge between cytomorphology and genome sequencing optimally and quickly available to each individual patient but also to offer them in cumulative publications to other researchers, scientifically interested parties, and clinically active colleagues.

More detailed lists of MLL's 2022 publications can be found on our website. Furthermore, we, Prof. Dr. med. Claudia Haferlach and Prof. Dr. med. Dr. phil. Torsten Haferlach, have also had the opportunity since this year to author the new WHO classification and contribute the cumulative knowledge of MLL there.

Once again, and for over 17 years now, we want to thank all of our employees for their excellent work this year. None of this would be possible without them!

We thank our submitters for their confidence in us and in our diagnostics. We owe a great debt of gratitude to all our partners who are working with us on the development of our laboratory workflows and on studies for introducing new drugs and, of course, to all the suppliers who keep us supplied, especially in times of supply bottlenecks.

More than ever, we are continuing to pursue our mutual goal of extending lives and increasing cure rates – thanks to the results of our diagnostics.

We wish you all a peaceful holiday season and especially positive and good developments for the coming year 2023.

Best regards,

Prof. Dr. med. Claudia Haferlach

Prof. Dr. med. Dr. phil. Torsten Haferlach

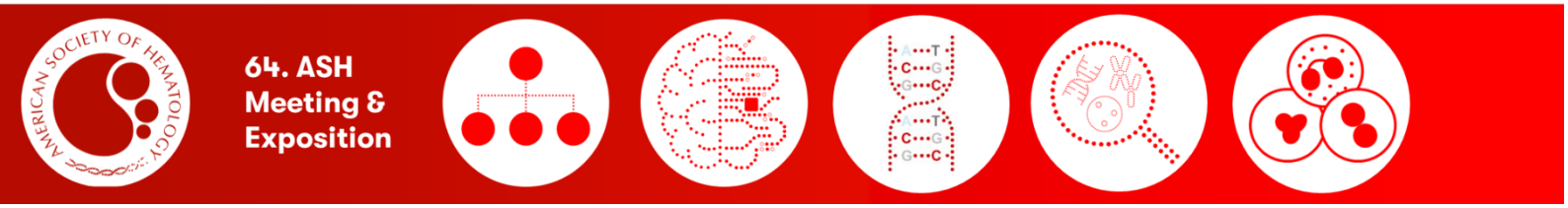
Prof. Dr. med. Wolfgang Kern

MLL at the 64th ASH Annual Meeting & Exposition – a Follow-Up Report

The 64th Annual Meeting & Exposition of the American Society of Hematology was held from December 10-13 in New Orleans this year.

MLL participated with 20 contributions, consisting of talks and poster presentations and covering the following topics:

- Classification (Haferlach C et al., Huber et al., Kern et al., Mueller M-L et al.)
- Artificial intelligence (Haferlach T et al., Nadarajah et al., Pohlkamp et al.)
- Genome and transcriptome sequencing (Blombery et al., Meggendorfer et al., Mueller H et al. (1), Truger et al.)
- Biological and clinical significance of certain genetic alterations (Meierhofer et al., Mueller H et al. (2), Stengel et al. (1), Stengel et al. (2), Stengel et al. (3), Summerer et al.)
- Pathogenesis, diagnosis, and prognosis of myelodysplastic neoplasms (MDS) (Baer et al. (1), Baer et al. (2), Weiss et al.)



In this article, we will be presenting the research projects that we had the pleasure of presenting at the ASH conference. The MLL presentations covered a wide range of hematology topics – from classification and genetics to prognostics and artificial intelligence. In addition, we were also there with many poster presentations. If you would like to read in more in-depth about them – and about our talks – you will find more information about all of this year's contributions at the end of this article.

Genetics as the Mainstay of New Classifications

The year 2022 has brought major changes to hemato-oncology – first and foremost, the new classification of the World Health Organization (WHO). Moreover, the "international consensus classification" appeared as well, which raised the question: Does the parallel use of two classifications make diagnosis more difficult for physicians and patients? This question is addressed by Huber et al. using the examples of AML and MDS who also elaborated differences and similarities between the WHO and ICC classifications. What both have in common is that genetics plays a solid supporting role and genetics-based definitions are gaining in importance. However, the fact that the search for the best possible classification is never over is illustrated by the project of Haferlach et al. For example, according to the WHO and ICC, while cytomorphology is essential for diagnosing MDS, this method – unlike genetics – naturally involves a certain amount of subjectivity. As shown by the results of Haferlach et al., however, a purely genetic classification of MDS would be readily feasible and also of clinical relevance.

Genetics Improves Prognosis

This year's publication of the "Molecular International Prognostic Scoring System" (IPSS-M) represents an important innovation in assessing the prognosis for MDS (Bernard et al. NEJM 2022). By taking molecular genetic information into account, the IPSS-M improves on the IPSS-R prognostic score established for MDS. The predictive superiority of the IPSS-M over the IPSS-R is validated by Baer et al. in an independent cohort. Both the IPSS-M and the personalized prognostic models of Nazha et al. and Bersanelli et al. (both JCO 2021) take molecular genetic factors into account. As Baer et al. show, however, the three molecular models differ in the parameters they select. Age in particular is an important factor here. This varies the prognostic power of each model depending on whether overall survival or leukemia-free survival / leukemic transformation is in focus.

Both the WHO 2022 classification of MDS and the molecular prognostic scores for MDS take *TP53* alterations into account, that may be a consequence of deletion, mutation, or copy-neutral loss of heterozygosity. A distinction needs to be made between single-hits (one of the changes mentioned) and double-hits (≥2 changes). In a cohort of 1,520 patients with MDS and AML, Stengel et al. identify *TP53* double-hit as the most important prognostic factor. The incidence of *TP53* double-hit seems to depend on the proportion of blasts. While single-hit still predominates in cases with *TP53* alteration(s) in MDS with <5% blasts, double-hit prevails in MDS with ≥5% blasts as well as in AML.

Artificial Intelligence (AI) on Its Way into Routine Diagnostics

Even though the contributions have very different strongpoints, the development from phenotype to genotype emerges as a common theme. The increasing importance of (molecular) genetics is also generating more and more highly complex data. The ability to evaluate and make the best possible use of this data in the future will depend on the need for artificial intelligence increasing at the same time, including in our laboratory. In this context, Nadarajah et al. are now validating a previously presented classifier in a prospective cohort. Here, the AI succeeds in assigning samples to 33 entities with great accuracy and at high

speed. Besides genetics, artificial intelligence is also finding its way into all other diagnostic areas of hematology. For cytomorphology, Haferlach et al. show with the prospective BELUGA study that an AI-driven and cloud-based platform for providing differential blood images improves reproducibility and reduces processing times.

If you would like a deeper insight into our various research projects, you can find overviews of these on our website. Links to the individual presentations and posters at this year's ASH conference can also be found below:

Talks

- Baer et al. (1) Risk Prediction in MDS: A Validation of the IPSS-M and Comparison to IPSS-R and to Two Other Personalized Prediction Tools. *Blood* 2022; 140 (Supplement 1): 1128–1129. doi: https://doi.org/10.1182/blood-2022-159939

- Haferlach C et al. MDS Classification - Do We Still Have to Count Blasts?. *Blood* 2022; 140 (Supplement 1): 1130–1131. doi: https://doi.org/10.1182/blood-2022-162147

- Haferlach T et al. Machine Learning Algorithm Correctly Identifies 95% of Cells in Differential Count of Blood Smears: A Prospective Study on >29,000 Cases and >17 Million Single Cells. *Blood* 2022; 140 (Supplement 1): 1909–1910. doi: https://doi.org/10.1182/blood-2022-165863

- Huber et al. AML and MDS Classification According to Who 2022 and International Consensus Classification: Do We Invent a Babylonian Confusion of Languages?. *Blood* 2022; 140 (Supplement 1): 555–556. doi: https://doi.org/10.1182/blood-2022-162326

- Nadarajah et al. Evaluation of a Transparent Artificial Intelligence (AI) Disease Classification System with Whole Genome Sequencing (WGS) and Whole Transcriptome Sequencing (WTS) Data in a Prospective Study with 325 Cases. *Blood* 2022; 140 (Supplement 1): 1915–1916. doi: https://doi.org/10.1182/blood-2022-169093

- Stengel et al. (3) Interplay of *TP53* Allelic State, Blast Count and Karyotype on Survival of Patients with AML and MDS. *Blood* 2022; 140 (Supplement 1): 2073–2074. doi: https://doi.org/10.1182/blood-2022-159388

Poster

- Baer et al. (2) Molecular Evolution of Ccus Already Follows the Same Rules As MDS Progression. *Blood* 2022; 140 (Supplement 1): 8598–8599. doi: https://doi.org/10.1182/blood-2022-162168

- Blombery et al. Novel Non-Coding, Coding and Structural Variants in Hairy Cell Leukemia from Whole Genome Transcriptome Sequencing. *Blood* 2022; 140 (Supplement 1): 3546–3547. doi: https://doi.org/10.1182/blood-2022-163300

- Kern et al. Identification of Phenotypic Subgroups of Acute Myeloid Leukemia, Defined By Differentiation According to Who 2022 Classification. *Blood* 2022; 140 (Supplement 1): 8908–8909. doi: https://doi.org/10.1182/blood-2022-165918

- Meggendorfer et al. Detecting the Unusual without Compromising Diagnostic Accuracy - a Prospective WGS/Wts Pilot Study in Acute Leukemias Provided Additional Information for Diagnosis, Prognosis and Treatment. *Blood* 2022; 140 (Supplement 1): 4959–4960. doi: https://doi.org/10.1182/blood-2022-159428

- Maierhofer et al. Detection of Novel Occult Germline Multi-Exon Deletions in Patients with *DDX41* Familial Predisposition to Myeloid Malignancy. *Blood* 2022; 140 (Supplement 1): 8676–8677. doi: https://doi.org/10.1182/blood-2022-163064

- Mueller H et al. (1) Benchmarking of Whole Genome Sequencing (WGS) and Whole Transcriptome Sequencing (WTS) As Diagnostic Tools for Determining the Mutation Status of IGHV Genes in CLL. *Blood* 2022; 140 (Supplement 1): 7826–7827. doi: https://doi.org/10.1182/blood-2022-162209

- Mueller H et al. (2) Proximally Biased V(D)J Recombination and Evolution of Non-Productive Clones in B-Cell Precursor Acute Lymphocytic Leukemia with *KMT2A*::*AFF1* Fusion Genes. *Blood* 2022; 140 (Supplement 1): 6348–6349. doi: https://doi.org/10.1182/blood-2022-162382

- Mueller M-L et al. Evaluation of Analysis Strategy for Cytoplasmic Lineage-Associated Markers in Mixed-Phenotype Acute Leukemia (MPAL) As Devised By Who Classification 2022. *Blood* 2022; 140 (Supplement 1): 3172–3173. doi: https://doi.org/10.1182/blood-2022-168548

- Pohlkamp et al. A Fully Automated Digital Workflow for Assessment of Bone Marrow Cytomorphology Based on Single Cell Detection and Classification with AI. *Blood* 2022; 140 (Supplement 1): 10725–10726. doi: https://doi.org/10.1182/blood-2022-168780

- Stengel et al. (1) *RUNX1* Mutated AML and MDS: Similarities, Differences and Molecular Factors Leading to Disease Progression. *Blood* 2022; 140 (Supplement 1): 2990–2991. doi: https://doi.org/10.1182/blood-2022-159379
- Stengel et al. (2) *IDH2* mutations in Hematological Malignancies: Distribution, Hot Spots, Clonal Development and Identification of a Novel (cyto-)Genetically Defined Subgroup. *Blood* 2022; 140 (Supplement 1): 3405–3406. doi: https://doi.org/10.1182/blood-2022-158979

- Summerer et al. Myeloid Neoplasms with *MYC*-Positive Double Minutes, a Specific Subgroup? *Blood* 2022; 140 (Supplement 1): 9142–9143. doi: https://doi.org/10.1182/blood-2022-166102

- Truger et al. How Whole Genome and Transcriptome Sequencing (WGTS) Can Contribute to Unsolved Cases in Hematology That Have Undergone Extensive Standard Diagnostic Workup: A Prospective Head-to-Head Study. *Blood* 2022; 140 (Supplement 1): 7824–7825. doi: https://doi.org/10.1182/blood-2022-166129

- Weiß et al. Application of a Flow Cytometric Core Marker Set in the Diagnostic Workup of Patients with Suspected Myelodysplastic Syndromes. *Blood* 2022; 140 (Supplement 1): 4067–4068. doi: https://doi.org/10.1182/blood-2022-165987

Authors: Dr. rer. nat. Ines Schmidts, Dr. rer. nat. Constanze Kühn

Transcriptome Analysis with B-ALL and MLN-TK

Whole transcriptome sequencing (WTS) is becoming increasingly important in the routine diagnostics of leukemia. In addition to the holistic detection of fusion transcripts, transcriptome analysis also makes it possible to determine subtype-specific expression profiles for more accurate stratification of patients. Thus, according to the new WHO classification (5th edition), some subtypes can only be determined by analyzing gene expression profiles. Therefore, for both B-ALL and MLN-TK, we have included transcriptome analysis in our routine workflows and offer it accordingly.

Transcriptome Analysis with B-ALL

B-ALL is primarily classified into its subtypes genetically by determining copy number alterations of individual chromosomes or whole chromosome sets and by detecting translocations and corresponding fusion transcripts. In addition, we also know of groups where no known fusions are detectable in the patients, yet their expression profile is hardly distinguishable from that of patients with defined translocations – these include *BCR::ABL1*-like or *ETV6::RUNX1*-like B-ALL. The ability to detect fusion transcripts and create expression profiles is a strength of transcriptome analysis, which is why we have started using it to determine B-ALL subtypes. After whole transcriptome sequencing, we use an algorithm trained via machine learning that can distinguish and classify 18 different B-ALL subtypes based on their expression profiles (ALLSorts, Schmidt B *et al.*, Blood Adv. 2022 Jul 26;6(14):4093-4097). Only the subgroups with deviating numbers of chromosomes (hyper/hypodiploid) are not reliably detected by this method. In contrast, however, other groups, such as *BCR::ABL1*-like, *ETV6::RUNX1*-like, and *DUX4* rearrangements, can only be detected using such a method.

Transcriptome Analysis with MLN-TK

The newly named entity myeloid/lymphoid neoplasia with eosinophilia and tyrosine kinase gene fusion bears in its very name the diagnostic criterion of detection of a tyrosine kinase gene fusion. While the most commonly detected fusions are *FIP1L1::PDGFRA*, *ETV6::PDGFRB*, *ZNF198::FGFR1*, and also *PCM1::JAK2*, other tyrosine kinase gene fusions can also occur in rare cases. Due to its therapeutic relevance, when MLN-TK is suspected, an extended and broad-based screening – after ruling out known fusions – is recommended as part of a stepwise diagnostic process. The advantage of transcriptome analysis is being able to simultaneously determine aberrant tyrosine kinase expressions as well as rare tyrosine kinase gene fusions along with known ones. The sequence of a detected fusion can also be used to identify whether it occurred within the reading frame and whether it leads to a functional tyrosine kinase, which then serves as a potential target for corresponding inhibitors.

Transcriptome analysis is on our request form as a diagnostic method for both B-ALL and MLN-TK.

Author: Dr. rer. nat. Manja Meggendorfer

WHO, ELN and IPSS-M: Adjusting Our Diagnostic Service

The year 2022 yielded important advances for the diagnostic and prognostic classifications of hematologic neoplasms. On the one hand, there are the preliminary publications on the new WHO classification and the new ICC (International Consensus Classification). On the other, new ELN guidelines for AML with modifications of the previous risk categories and the IPSS-M score for MDS have been published. The latter, as the successor to the IPSS-R, incorporates molecular genetic alteration into the risk stratification for the first time.

Increasing Complexity Enables More Differentiated Decision-Making Processes

The new WHO classification further advances the paradigm shift "from phenotype to genotype." The final diagnosis is increasingly based on objectifiable genetic characteristics and less and less for example on the morphological phenotype, which is often only reproducible to a limited extent. An increasing incorporation of molecular genetic features is also occurring in the prognostic characterization of myeloid neoplasms. While the new ELN score allows the risk classification to still be done "by hand" on the basis of a summary table, the IPSS-M factors in the mutation status of 31 genes, including the *TP53* allele status, among others. Calculating the IPSS-M score is only possible using an online calculator tool..

Naturally, this places increased demands on you and on us in our everyday diagnostic work, but it also enables more individualized prognoses and therapy planning. We are eagerly awaiting the results of prospective therapy studies based on the new prognostic scores.

Adjustment of the Diagnostic Offerings at MLL

We are of course adapting our diagnostic services to the above-mentioned innovations. We are planning to use the new WHO diagnoses in our findings across the board by early 2023 (after publication of the final WHO version in book form).

The prognostic scores for AML (according to ELN) and MDS (IPSS-M) published in 2022 have already been incorporated in our examination order (https://www.mll.com/en/request-form/mll_request_form.pdf) in the form of specific molecular genetic panels.

Integration of the New Classifications and Scores in Our "Integrated Findings"

Many of you are familiar with MLL's "Integrated Report" (IR), which provides another interpretation of the examination findings prepared at MLL for MDS and AML cases. It contains the diagnosis according to the WHO, conventional prognostic classifications, and recommendations for any MRD markers or targeted therapies. The Integrated Report is generated by an algorithm and validated by a physician if the required diagnostic methods have been performed in advance at MLL and additional required blood count (MDS) details have been transmitted to us.

Both the modified ELN score for AML as well as the IPSS-M have already been implemented in our Integrated Report to help you manage the increasing flow of diagnostic data. Furthermore, users of our digital order entry system have the option of submitting any missing blood count data via the subsequent request tool included in the system, after which they will receive an IR for MDS cases.

Similar to our standard methods (see above), the diagnoses in the IR will also be adjusted according to the new WHO classification at the beginning of 2023.

Author: Dr. med. Christian Pohlkamp

Events

MLL Academy 2023

The next MLL Academy will be held from April 24th until April 28th, 2023. During the five-day workshop on the subject of "state of the art diagnostics in hematological malignancies", participants can expect a mix of theoretical and practical content as well as joint discussions, all concerning the diagnosis of leukemias and lymphomas. Please register until 15th of February 2023.

Click here to register and go to the program

Most Recent Publications with MLL Involvement

- Chitadze G et al. Somatic TP53 mutations are pre-leukemic events in acute lymphoblastic leukemia. Blood. 2022. **View publication**

- Cuppen E et al. Implementation of Whole-Genome and Transcriptome Sequencing Into Clinical Cancer Care. JCO Precis Oncol. 2022. **View publication**

- Haertle L et al. Single Nucleotide Variants and Epimutations Induce Proteasome Inhibitor Resistance in Multiple Myeloma. Clin Cancer Res. 2022. **View publication**

- Huber S et al. SF3B1 mutated MDS: Blast count, genetic co-abnormalities and their impact on classification and prognosis. Leukemia. 2022. **View publication**

- Huber S et al. SF3B1 mutations in AML are strongly associated with MECOM rearrangements and may be indicative of an MDS pre-phase. Leukemia. 2022. **View publication**

- Huber S et al. Mutations in spliceosome genes in myelodysplastic neoplasms and their association to ring sideroblasts. Leukemia. 2022. **View publication**

- Kern W, van de Loosdrecht A. Flow cytometry in the diagnosis of myelodysplastic syndromes. Cytometry B Clin Cytom. 2022. **View publication**

- Kern W et al. Multicenter prospective evaluation of diagnostic potential of flow cytometric aberrancies in myelodysplastic syndromes by the ELN iMDS flow working group. Cytometry B Clin Cytom. 2022. **View publication**

- Kubota Y et al. Significance of hereditary gene alterations for the pathogenesis of adult bone marrow failure versus myeloid neoplasia. Leukemia. 2022. **View publication**

- Le Pannérer MM et al. Different Gene Sets Are Associated With Azacitidine Response In Vitro Versus in Myelodysplastic Syndrome Patients. Hemasphere. 2022. **View publication**

- Maggioni G et al. A sex-informed approach to improve the personalised decision making process in myelodysplastic syndromes: a multicentre, observational cohort study. Lancet Haematol. 2022. **View publication**

- Makishima H et al. Germline DDX41 mutations define a unique subtype of myeloid neoplasms. Blood. 2022. **View publication**

- Müller J et al. How T-lymphoblastic leukemia can be classified based on genetics using standard diagnostic techniques enhanced by whole genome sequencing. Leukemia. 2022. **View publication**

- Othman J et al. Overlapping features of therapy-related and de novo NPM1-mutated AML. Blood. 2022. **View publication**

- Pagliuca S et al. Molecular landscape of immune pressure and escape in aplastic anemia. Leukemia. 2022. **View publication**

- Schenz J et al. Increased prevalence of clonal hematopoiesis of indeterminate potential in hospitalized patients with COVID-19. Frontiers in Immunology. 2022. **View publication**

- Stölzel F et al. Biallelic TET2 mutation sensitizes to 5'-azacitidine in acute myeloid leukemia. JCI Insight. 2022. **View publication**

- Thrun MC et al. A Bioinformatics View on Acute Myeloid Leukemia Surface Molecules by Combined Bayesian and ABC Analysis. Bioengineering (Basel). 2022. **View publication**

- Walter W et al. Artificial intelligence in hematological diagnostics: Game changer or gadget? Blood Rev. 2022. **View publication**

- Zeidan AM et al. Prognostic implications of mono-hit and multi-hit TP53 alterations in patients with acute myeloid leukemia and higher risk myelodysplastic syndromes treated with azacitidine-based therapy. Leukemia. 2022. **View publication**

➢ Click here to go to all publications

MLL Münchner Leukämielabor GmbH
Max-Lebsche-Platz 31
81377 Munich, Germany

Phone: +49 89 990 17 0
Fax: +49 89 990 17 111
Email: info@mll.com
Website: www.mll.com