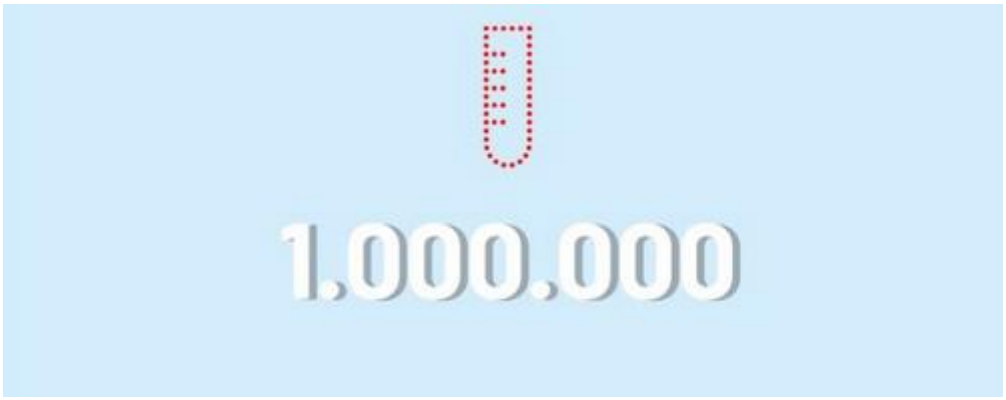
MLL News

October 12, 2022

1,000,000 Samples Since the MLL Was Founded

The MLL team has analyzed one million samples since our laboratory was established on August 1, 2005. Every day we do our best to continuously advance leukemia diagnostics and to enable every patient to receive the optimal therapy. Interdisciplinary teamwork and good communication with our submitters are essential for a reliable and rapid diagnosis. We want to thank you for the high level of trust placed in us and our diagnostics.



New: Quick Request Option for MLL Order Entry

For four years, we have been offering you, our submitters, digital order entry, the MLL order entry portal*. Query findings from anywhere and at any time, track the submitted sample live, place orders digitally, and much more: our order entry system is a modern alternative to paper-based requests.

Of course, we want to make our order entry as intuitive and user-friendly as possible for you. What can we do even better? What can be presented more clearly? We have discussed these and other questions with you and collected your feedback. Based on this, we have improved our order entry for you and once again made it more time-saving and intuitive. We are pleased to present all of the innovations to you in the following article.

Just a few clicks to the finished order

Brief information on diagnosis, material, disease status, and blood count – that's all we need from you here (see Fig. 1).

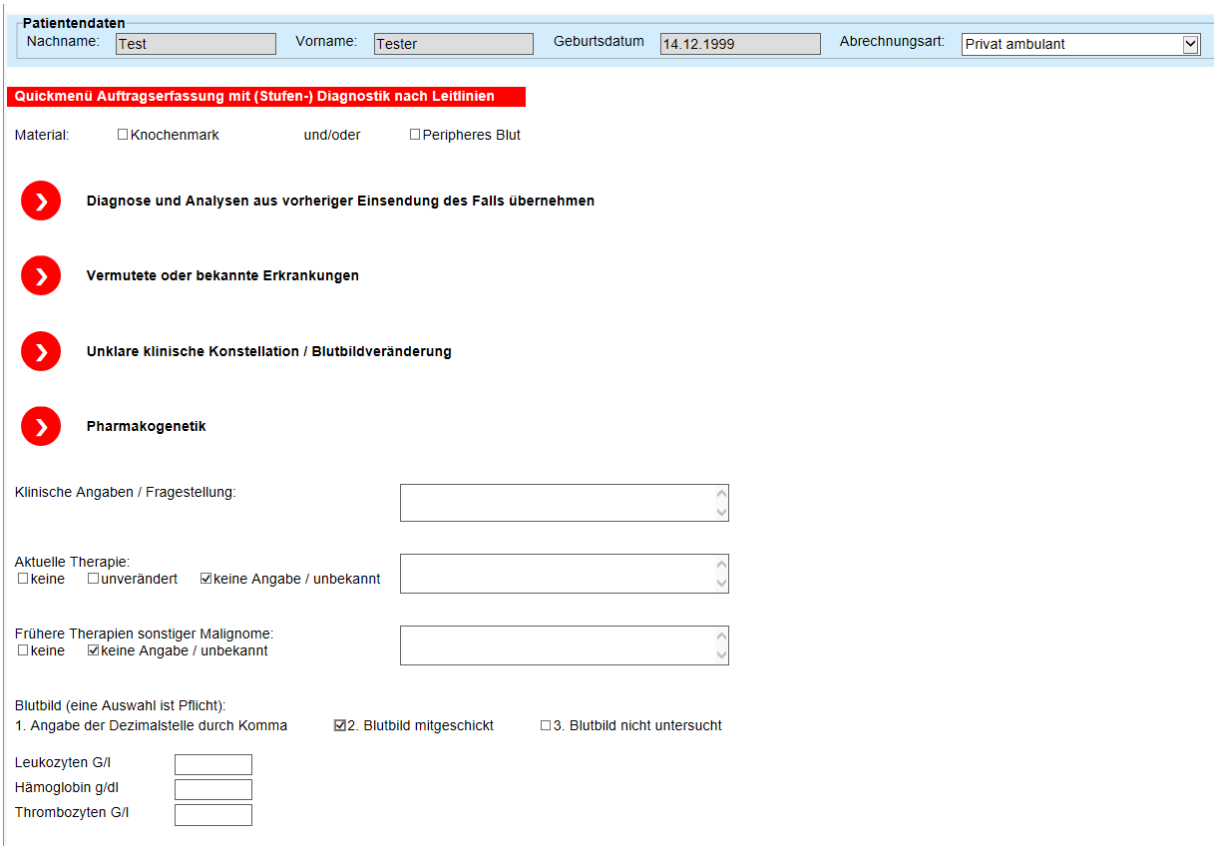


Fig. 1 Quick request order placement

All other information is filled in automatically, including in particular the selection of suitable diagnostic methods for the (suspected) diagnosis. In doing so, we are following the current guidelines and recommendations of the professional associations.

Before submitting the order, you have the option to do a final review. Individual adjustment of the order is of course still possible here (see Fig. 2).

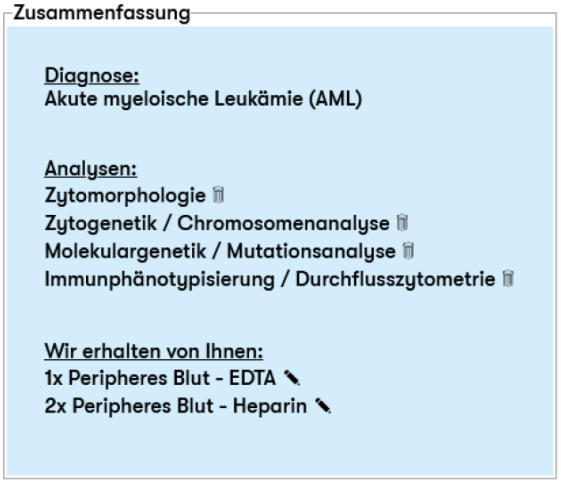


Fig. 2 Adjustment of analyses and material in the summary

If you want to add detailed information, e.g., the testing of individual genes, this can be done in the usual entry form in the separate menu for detailed requests.

If you do not have certain diagnostic methods performed by us, we can now save this information so that these analyses are no longer proposed by the algorithm. So please let us know by email or phone if this is the case for you.

Individual standard profiles

Another request that we have often heard from you in this context is saving individual profiles based on the (suspected) diagnosis. For the most common disease entities, you normally have to repeatedly submit identical requests for testing: For these cases, wouldn't it be more convenient to send the preferred request for these with a single click?

To comply with this request, we have created some profiles for the most common diagnoses. Except for the material, all of the information is already filled in, either according to your personal wishes or according to current guidelines and recommendations (see Fig. 3).

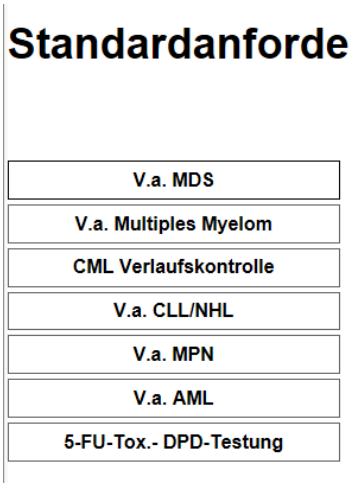


Fig. 3 Our standard requests

We would be happy to expand or modify these profiles according to your individual requirements. Send us your preferences for each of the diagnoses by email or phone, and we will save them for you as specific standard profiles in your personalized order entry module.

Conclusion

The workflows and processes in each of your practices and clinics, and thus also the procedure for order entry, are very heterogeneous:

Some of you prefer to prepare requests for testing in detail yourself, while others want to place it as quickly and easily as possible given the high time pressure.

It is therefore important to us to respond to your individual needs and to provide an efficient and customized method of order entry.

If you would also like to benefit from the advantages of flexible digital order entry or have any questions about the new quick request, please contact us over the phone at +49 (0)89 99017-551 or via email at orderentry@mll.com.

*Please note, that the MLL Order Entry Portal is only available in German language at this time.

Author: Julia Hennig

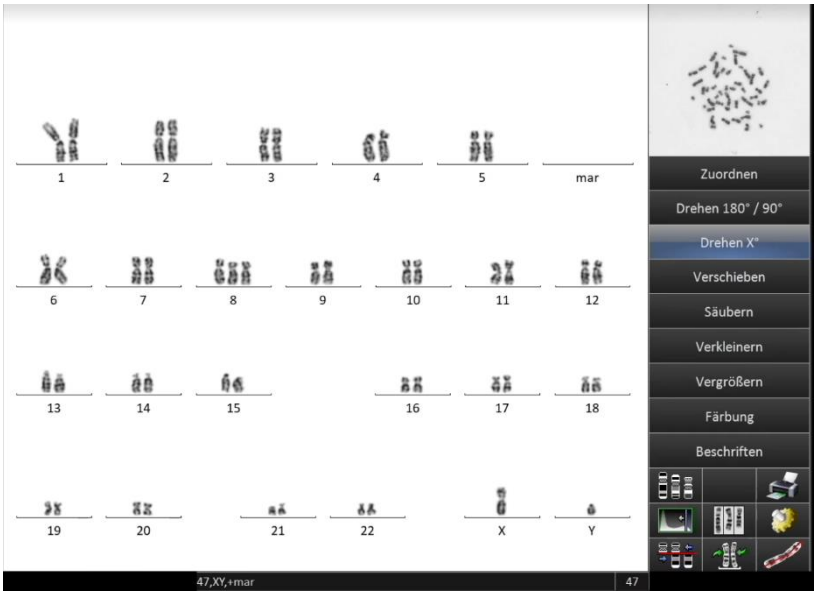
We Value Your Opinion

Our goal is to offer top-notch leukemia diagnostic services to patients and strive for continuous improvement. We therefore want to find out how satisfied and happy the submitters of samples are with our services. We take your feedback very seriously and use it as a tool for self-improvement.

We would appreciate if you could spare ten minutes of your time to complete our anonymous survey. Please use the opportunity to evaluate the cooperation with us and give us specific feedback. The following link will take you to the survey. The survey will be conducted until October 31, 2022.

Click here to partake in the survey.

Chromosome Analysis 5.0 – Automation, Digitization, and Artificial Intelligence



The method

Chromosome analysis is considered a labor-intensive and demanding method, the implementation and interpretation of results of which places high demands on the skills of personnel.

Vital cells capable of division are required, which are cultured for one to three days with subsequent preparation of the metaphases and staining of the chromosomes using a specific banding technique. What is known as Giemsa banding gives each chromosome a specific band pattern, which enables the chromosomes to be clearly identified and chromosomal changes to be detected. The metaphases are captured using a computer-based imaging system on the microscope and then digitally processed to create the karyograms. Based on the analysis of at least 20 karyograms, a karyotype formula is derived and a cytogenetic report is generated.

Reduction of the turnaround time by AI

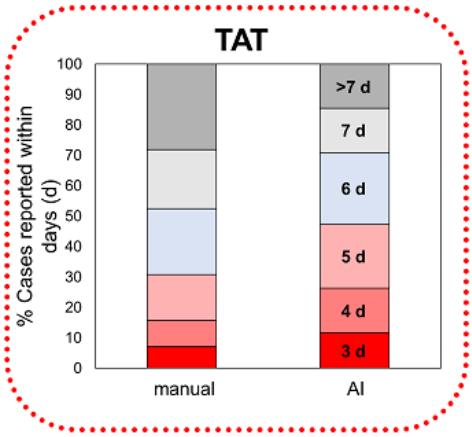
At MLL, automated processes – from fully automated cell processing to metaphase preparation as well as staining, medium, and spotting robots – have been used in the chromosome analysis laboratory for many years and are constantly being further developed. In collaboration with MetaSystems, MLL has also trained DNNs (deep neural networks) for object recognition, quality assessment, and classification of human

chromosomes. Since the end of 2019, such AI-based algorithms have been routinely used in chromosome analysis and are under continuous development. A karyogram can now be created fully automatically and manual image processing steps are no longer necessary.

We have summarized what this looks like in practice for you in a video. Click here to watch the video.

- Time required to create a karyogram manually: approx. two to three minutes
- Time required to generate a karyogram using AI (including subsequent checking by a cytogeneticist): approx. 25 seconds

The use of AI has significantly reduced the turnaround time (TAT) in chromosome analysis. Results can now be reported within ≤5 days for almost 50% of cases compared to approximately 30% of cases before the use of AI. Similarly, the proportion of cases with a turnaround time longer than seven days has been reduced from 28% to 15%.



AI-based quality assessment of metaphases also enables broad analysis across different quality levels, ensuring objective assessment of the entire case. In addition, the use of AI facilitates the targeted search for metaphases with aberrant karyotype, which in particular allows for better detection of small aberrant clones.

Relevance for leukemia diagnostics

Even considering the rapid progress in the field of whole genome sequencing, chromosome analysis remains an essential part of the diagnosis of hematologic neoplasias. The relevance of chromosome analysis is demonstrated by the following aspects, among others:

- Cost-effectiveness
- In some cases, the only possibility to detect small clones due to proliferation advantage during cultivation
- Single-cell analysis:
  - Distinguish between independent clones, e.g., between clones of a myeloid and concurrent lymphoid disease
  - Distinguish between clonal evolution (further development of a clone) and potential secondary hematological disease in an independent clone
- Karyotype as an independent prognostic factor in many hematologic neoplasias (e.g., IPSS-R in MDS or complex karyotype in CLL)
- Karyotype in some cases decisive for therapy (e.g., in AML with myelodysplasia-related changes)

Automation and the use of AI have transformed chromosome analysis, which was considered to be a laborious process, into a faster and more sensitive method that remains highly relevant in many hematologic neoplasias. For guidance in which cases a chromosome analysis is indicated, you will find recommendations on our website regarding the range of methodologies for the respective question or suspected diagnosis.

Authors: Christina Glashoff, Dr. rer. nat. Dr. Isolde Summerer

MLL Introduces Itself: Our Quality Management

Since being founded, MLL has been synonymous with quality and reliability. In order to provide patients with the best leukemia diagnostics, the MLL team has established a quality management (QM) system that is practiced by all employees and coordinated by the QM team. The QM team is responsible for the laboratory-wide implementation of existing quality requirements and ensures the continuous improvement of existing processes.

The QM team

The quality management team consists of three employees, who devote themselves to all matters relating to QM with a high level of professional and social competence. All three employees have been working for the company for several years and act as an important interface between the laboratory areas and management. Close cooperation with all departments plays an extremely important role in our company. The QM team is headed by Dr. Christine Käppel.

Although we do not have direct contact with our patients and referring physicians, we are nevertheless convinced that our work makes an important contribution to the diagnosis, therapy, and well-being of patients. This fills us with pride and motivates us to give our best every day.

A normal day in quality management

The tasks in quality management are demanding and varied, so that no two days are ever alike. As part of the overall implementation of the quality requirements applicable in the laboratory and the improvement of the existing processes, the QM team takes care of, among other things,

- independent planning, execution, and follow-up of internal audits
- cooperation with authorities, accreditation bodies, and cooperation partners in the performance of external audits
- optimization and expansion of digital processes in QM
- supervision of the company's risk management and error management
- conducting employee training as part of QM
- review and implementation of new regulatory requirements for the laboratory
- determination of quality indicators as part of the annual management review

It is precisely this variety and versatility that makes these activities so much fun and exciting for us. Together with our colleagues from the entire laboratory, we thus represent an important cornerstone that contributes to the high quality standards of our analyses.

What's next?

As in the other areas of the laboratory, the digitization and automation of processes will become increasingly important in QM. The QM team actively develops digital QM solutions

in order to set new standards and to be best prepared for the future. In addition, our area of responsibility will expand significantly as a result of additional partners in the context of clinical studies as well as new legal and normative requirements. Whatever tasks we face in the future, we are eagerly awaiting them and look forward to continuing to make our contribution to the best possible leukemia diagnostics.

Would you also like to influence where the lab's journey is headed? If so, you are cordially invited to participate in our annual user satisfaction survey (participation possible until October 31, 2022). We take your resulting suggestions, criticism, and wishes very seriously and will do our best to take them into account in the future. We would like to thank you in advance for taking part in our survey!

Author: Dr. rer. nat. Christine Käppel

Events

Oncology Symposium 2022

For the fourth time now, the Trillium Academy cordially invites you to the oncological symposium with the motto "From biomarkers to therapy." The event will take place on Friday, October 21, 2022 – live on site at MLL or virtually via live stream. The symposium series offers an insight into modern oncological precision medicine, which combines innovative diagnostic methods and therapeutic strategies to form a greater whole. Our newsletter subscribers benefit from a discount code on the basic ticket price.

Click here to register and enter your discount code

MLL advanced training event on November 16, 2022 – WHO, ICC, ELN/AML, and IPSS-M: The importance of genetics for myeloid entities ranging from CCUS to AML

Our advanced training event in hybrid format is entering its second round: Due to the large number of innovations in the diagnostic guidelines, we want to invite you to the event "WHO, ICC, ELN/AML, and IPSS-M: The role of genetics for myeloid entities ranging from CCUS to AML" being held on November 16, 2022, from 4 p.m. to 6 p.m. The event will take place live on site at the MLL, with virtual participation also being made possible.

Detailed information about the program and registration

Most Recent Publications with MLL Involvement

- Open publication
- Duncavage EJ et al. Genomic Profiling for Clinical Decision Making in Myeloid Neoplasms and Acute Leukemia. Blood. 2022. Open publication
- Haferlach C, Heuser M. Diagnostik bei unklaren Zytopenien - wie und wann suchen wir nach klonaler Haematopoese? Die Innere Medizin. 2022. Open publication
- Hehlmann R et al. Impact of emerging ACA on survival in chronic myeloid leukemia (CML). Leukemia. 2022. Open publication

- Ryland G et al. Description of a novel subtype of acute myeloid leukemia defined by recurrent CBFB insertions. Blood. 2022. Open publication
- Schmidts I et al. Precision Medicine in Therapy of Non-solid Cancer. Handb Exp Pharmacol. 2022. Open publication
- Valent P et al. Proposed Refined Diagnostic Criteria and Classification of Eosinophil Disorders and Related Syndromes. Allergy. 2022. Open publication

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