MLL News

08/19/2020

15 Years of MLL Munich Leukemia Laboratory: an anniversary without celebrations

We opened the MLL on August 1, 2005. Back then we had 29 employees; now we have over 200, 180 of whom are active.

The number of samples at the MLL and the possibilities for diagnostic methods have developed in parallel with hematology in the last 15 years. Diagnostics with all its possibilities and needs is becoming more and more exciting for us. It is growing in importance for patients and attending physicians. This is true regarding the description of the disease and its risk profile during diagnosis, as well as to the analyses of the course of the disease, whose numbers have increased sharply, which contribute to therapy management. The total number of samples sent to the MLL in the last 15 years is now over 750,000.

We would have liked to celebrate this milestone with our donors and employees as befits such an occasion. However, due to the current situation, all plans have been put on hold with our site also on lock down.

Our primary goal is still to provide all patients with the most current comprehensive diagnostics and in the shortest time possible. We also see it as our duty to document increasingly complex findings in as comprehensible a manner as possible. We are always grateful for any feedback and advice on how to improve our service!

With so much important data, we continue to believe our second important duty is to evaluate this data scientifically and to make the resulting knowledge available through lectures and publications. For us, the need also instinctively arises to not remain still and regard the present as given.

Thus, a special thanks goes to our donors: We need progression parameters, including for patient therapy, at many sites, to turn the data into lectures and publications. Many of you support us intensely, always taking into account the necessary data protection. We thank you most sincerely for this support, which will benefit future research approaches, guidelines and individual patient care through publications.

We are taking care of automation and digitization to improve our workflow not only due to the increasing number of cases but also to avoid errors. Since 2009, the entire system has been implemented in an accredited environment (ISO 15189) currently with over 600 SOPs.

Especially in the present time, bioinformatics, its knowledge and contributions also play a very important role at the MLL; they are essential to our services and further development of the laboratory. In view of this, we have also established the implementation of artificial intelligence for research projects at many sites, gradually introducing it into the routine and accrediting it. We have noticed an additional gain

regarding the validity of the findings and have achieved, at the same time, a reduction in turn-around times. All these algorithms also help us to minimize errors. Before using the findings from these algorithms, including AI, the result is checked and finally validated in every case by our hematologists, scientists and responsible MTAs.

We enjoy the common spirit of our laboratory as hematologists and molecular biologists who lead a large team of extremely committed employees from a variety of professions, arriving at findings cooperatively. In this way, we can always set a goal for new things and ultimately re-experience and enliven the passage of the first year every time.

As managing directors, we are also proud that, for the second time in a row, we have been voted Germany's TOP 100 more innovative and medium-sized companies and that we were able to put ourselves in the competition in this aspect as well.

We would like to continue committing ourselves to advancing leukemia diagnostics of mostly phenotype-based to more genotype-based approaches, and in accordance with the WHO classification and its further development. Another primary goal is to further digitize and automate the processes taking place and to make them even faster and safer especially via algorithms, including artificial intelligence. To have the knowledge in the field of hematology present in each individual case and make it available in the interest of individual patients. We believe that this can only be meaningfully illustrated in the future by means of such automation and the use of algorithms.

We look forward to continuing cooperation with you as our donors and employees as we fulfill our common duty here everyday in expert fashion. See behind – go beyond!

Best regards,

C. Haferlach, T. Haferlach, W. Kern

MLL Dx – the new website is live

The MLL Munich Leukemia Laboratory has been providing comprehensive diagnostics for leukemia and lymphoma patients in our health system for 15 years. Molecular

genetics has been an increasingly important component. The demand for comprehensive diagnostics, including from neighboring countries, is rising. Why not also offer this service outside the German health system? The three managing directors asked this question before the idea of establishing MLL Dx – MLL diagnostics – took shape. MLL Dx was founded as an affiliate of MLL in 2018 and has been visible through its own web site since July 2020.

MLL Dx benefits from the extensive experience from the routine diagnostics performed at the MLL. The services and knowledge of the MLL and MLL Dx are thus directly intertwined and are a potent offer for requesting physicians, researchers and the pharmaceutical industry.

Sequencing options have developed rapidly in recent years; thus, the sequencing of entire genomes and exomes have become a reality. In this area, the MLL has learned a lot from its 5,000 genome project. MLL Dx now provides this knowledge, our laboratory experience and bioinformatics to scientists and physicians nationally and internationally. In the field of next-generation sequencing, our offers range from the preparation of samples for the sequencing (library prep) of individual genes, gene panels, as well as exomes, genomes and transcriptomes to sequencing only where we can efficiently incorporate samples that have already been prepared and are thus ready for sequencing into our sequencing planning. There are also different levels of bioinformatic analysis that our clients can access. Thus, our client decides to what extent we perform the data analysis through our in-house pipelines or if he would like to perform them himself.

In addition to the sequencing service, leukemia diagnostics and clinical studies have expanded MLL Dx's portfolio. MLL Dx stands on the following three pillars to respond flexibly to requests for leukemia diagnostics outside the German health system and to perform even better than before as a partner and reference laboratory in international clinical studies. The diagnostics offered cover all areas of cytomorphology, cytogenetics, immunophenotyping and molecular genetics. Thus, MLL Dx also covers comprehensive leukemia and lymphoma diagnostics as the MLL has done for 15 years. In addition, MLL Dx was successfully accredited in accordance with ISO 15189 and ISO 17025 last year, including new methods such as genome and transcriptome sequencing.

In addition to MLLi, MLL Dx complements the MLL family with diagnostics outside the German health system, as well as a sequencing service, which is also intended to meet the scientific need.

More information about MLL Dx's services, methods and offers is available at www.mlldx.com.

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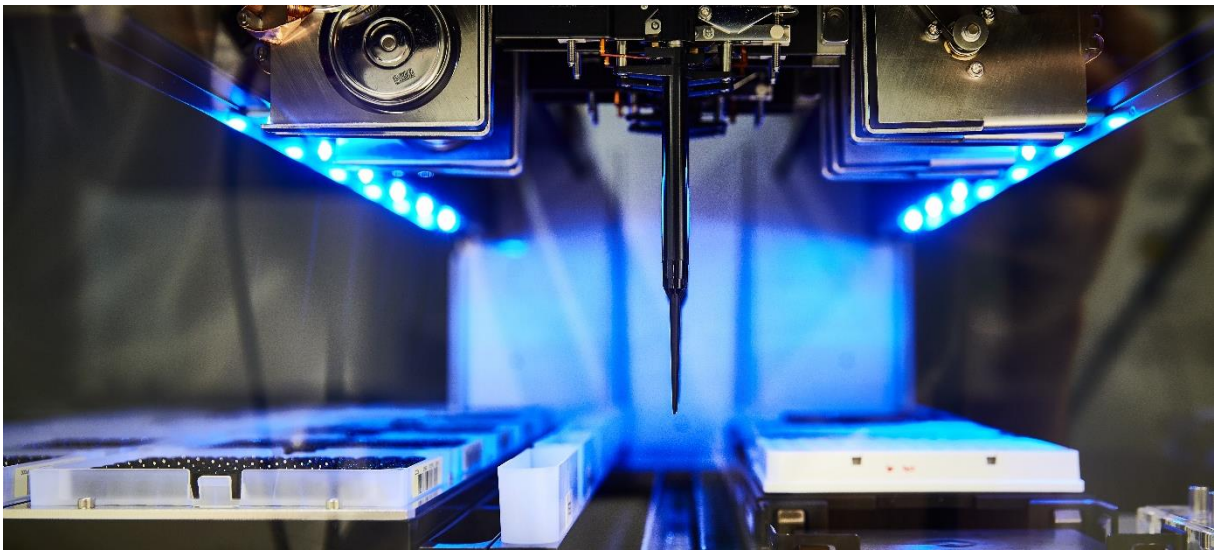

Diagnostic perspectives – WGS and WTS

The diagnosis and classification of hematological neoplasia is a complex process. Various diagnostic technologies (cytomorphology, histology, cytogenetics, immunophenotyping and molecular genetics) are needed to meet the clinical challenges for a rapid, accurate and therapeutically relevant diagnosis for each patient. Genetic testing in particular has changed considerably in recent years, making it a quick and comprehensive option for a variety of issues.

Conventional molecular tests have so far been mainly based on the study of genes or gene regions known to be associated with hematological neoplasia. However, for many patients, these tests do not yet provide a conclusive, molecularly justifiable diagnosis. However, recent improvements in sequencing technology and bioinformatics have made time and cost-effective sequencing of the individual genome (WGS) and transcriptome (WTS) a reality. This allows for an equally wide range of molecular information to be collected with a single approach and without prior knowledge and any previously necessary limitation to known genetic aberrations. This can, for example, improve the determination of clonal markers, which can be helpful in the diagnosis of cytopenia of unclear origin.

The WGS opens up the possibility of creating a complete and personalized molecular profile for each patient by simultaneously analyzing somatic changes such as individual nucleotide variants (SNV), small insertions and deletions (indels), structural variants (SV) and variations in the number of copies (CNV). In particular, this advantage can be seen in cases with limited material, such as with multiple myeloma, where the isolation of a sufficient number of plasma cells is often difficult, limiting the number of possible tests. However, assessing the clinical relevance of SNVs and indels is also a major challenge for which there is neither a gold standard nor a standardized pipeline.

The WTS has been established in diagnostics for about 20 years, mostly in the form of microarray experiments, and is used to determine gene expression and detect fusion transcripts. With the introduction of RNA-Seq, the analysis is performed

without prior knowledge for known biomarkers or fusions. RNA-Seq can be used by determining specific expression profiles for the classification of hematological neoplasia, as well as for prognosis assessment. Gene expression is used in acute lymphocytic leukemia (ALL), for example, to identify cases that are similar to BCR-ABL1-positive ALL despite the lack of t(9;22) in its expression pattern and potentially benefit from treatment with kinase inhibitors. In addition, SNVs, indels and CNVs can be determined to a limited extent; however, accuracy is not (yet) comparable to DNA-based analyses.

As part of the 5,000 genome project, more than 4,500 genomes and their transcriptomes have already been sequenced and analyzed at the MLL to gain better research insight into the molecular genetic profile of the various subgroups of hematological neoplasia. The data generated in this way already contributes to the understanding and knowledge of the accuracy of WGS and WTS data. One goal is also to test a practical and efficient use of WGS and WTS for routine diagnostics.

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Digital order entry platform enables online order submission

In an era where administrative processes are increasingly being digitized, you can avail yourself of our web-based portal for digital order submission. Apart from the reliable transmission of all the necessary data, it also offers, for example, the ability to post-edit orders (even after material submission) and to view findings online.

Click here to submit a registration request.

Important dates

Oncology Symposium 2020

In the wake of the resounding success of the 2019 Oncology Symposium “From Biomarker to Therapy Recommendation”, the event will be taking place again in 2020, and also be offered in digital format. Experts from the field of diagnostics met in 2019 to report on the important role of biomarkers as a guide for personalized medical approaches and to give insights into their experience in oncological diagnostics.
The next iteration of this successful event will take place on 11/13/2020. Register now, at no obligation.

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