MLL News

October 15, 2021

A Difficult Case: What the Diagnostics of Tomorrow Will Look Like

We have all learned: “Common things are common, except when the diagnosis is rare.” So far so good. Thanks to the large number of cases with increasingly networked data and by taking the current WHO classification as a basis, it is possible for even rare diagnoses to be assigned with greater precision today. This becomes more difficult, however, if the individual findings of the diagnostics chain and the blood values do not fit together in a conclusive way – or if any uncertainty simply remains even though the patient is definitely clinically ill. So what is the next step?

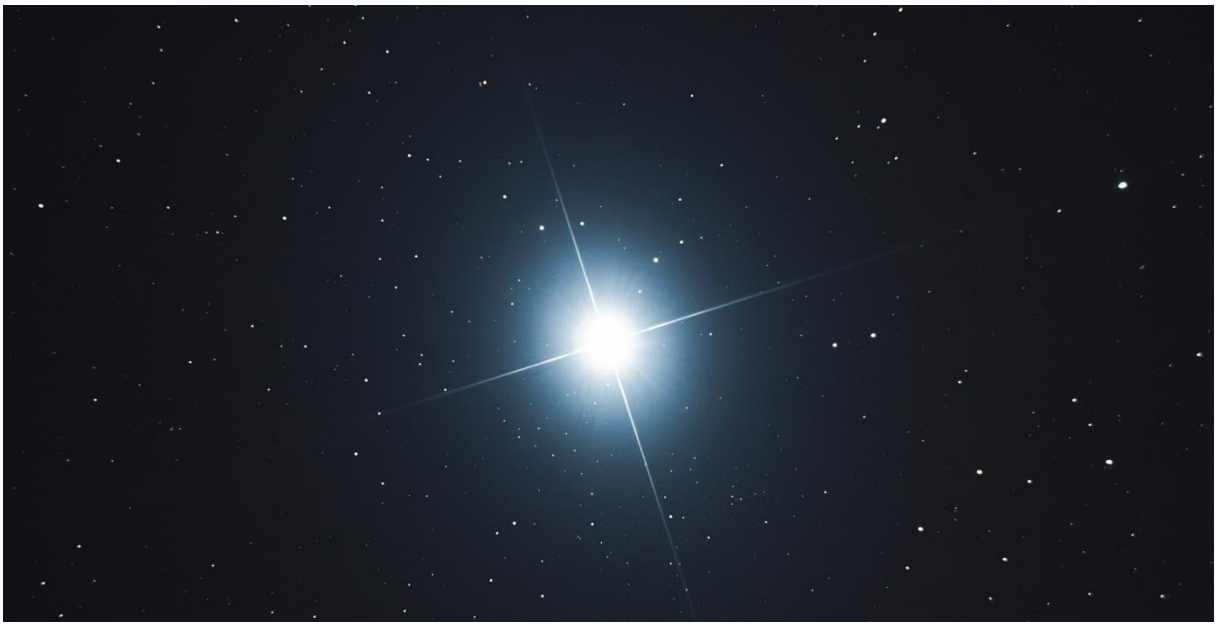
It is precisely here where MLL’s collaboration with Illumina® starts: with our new research project SIRIUS (Solving Riddles Through Sequencing). In this prospective study, which was recently accepted in American study register NCT (NCT05046444), we want to investigate the extent to which a precise genomic and transcriptomic profile (whole genome and whole transcriptome sequencing, WGS, WTS) helps to provide the most likely diagnosis in a complicated case.

As a run-up to this, not only have thousands of hematological diseases been diagnosed according to the latest scientific findings and the data saved at MLL over the last 16 years, but 5,500 genomes and transcriptomes of 30 different diagnoses have been sequenced in the last four years as well. All of this data is now available as a basis for the SIRIUS study.

The study protocol specifies that “difficult cases” be studied in parallel with today’s WHO/Onkopedia gold standard and simultaneously with WGS and WTS. The genomic profile is then compared with all 5,500 profiles of our collection in order to identify the “closest neighbor.” We also expect that good clinical annotation will provide us with valuable information. The ultimate goal is not only to arrive at the best possible diagnosis but possibly the indication of a specific therapy as well. As always, we will determine the precise costs for rendering these services in addition to the time needed to obtain the findings in each instance. In close consultation with the clinical colleagues who have sent us the material, we will then attempt to identify the findings and make patient-related decisions.

So where does the study name SIRIUS come from, you ask? Like the ancient mariners who sailed all over the world using only a sextant and the stars, we now want to use SIRIUS (the brightest star in the night sky) for orientation concerning what diagnostics will look like in the near future.

Author: Prof. Dr. med. Dr. phil. Torsten Haferlach



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 senders 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 10 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, 2021.

Start survey

Thank you very much for taking part. We look forward to your feedback!

From Genome to Exome to RNA Sequencing – an Interview Regarding Our New MLLSEQ Sequencing Service

MLLSEQ is the name of the sequencing service and the affiliate company of MLL Münchner Leukämielabor that was relaunched around five months ago. With the slogan, "We are the next generation – Sequencing Service," MLLSEQ is offering its extensive next generation sequencing (NGS) knowledge – from library preparation to sequencing only – along with detailed bioinformatic processing and visualization of the data generated. Along with the strategic reorientation on 6/1/2021 there have been a lot of changes: Ever since, MLLSEQ – formerly MLL Dx – has sported a new name and outfit, with the color *deep purple* dominating its new brand identity, the corporate design, and above all its new logo. The website https://mllseq.com/has been completely overhauled as well.

So why the change from MLL Dx to MLLSEQ? What has changed since the reorientation of the label? And how exactly are the sequencing processes at MLLSEQ run? So, it's high time

for a talk with Dr. rer. nat. Manja Meggendorfer, head of the areas of “Molecular Genetics” and “Research and Development” at MLL.

Sarah Kurz (S): Manja, together with BLACKSPACE design studio, you have created the new brand and corporate identity plus a new website in an exciting process. What led you to do this?

Manja Meggendorfer (M): *There is truly a demand for high-throughput sequencing services. We offer the sequencing capacity and corresponding know-how, coupled with the rapid processing times that we know and practice based on our everyday work with acute diseases. However, since these same qualifications are used in various fields besides leukemia diagnostics, it became clear to us that we had to make a fresh start with our sequencing service itself and become more independent. With the new label, logo, and associated website, we want to call attention to our sequencing service – even outside of routine leukemia diagnostics.*

S: And how have things been for you since the strategic reorientation? What has changed since then?

M: *With MLLSEQ, we are able to introduce ourselves and present what we offer in a whole new way that would not have been possible for us as a clinical diagnostics laboratory. Our new website and presence in social media alone has reaped a lot of positive feedback on our new label and its reception; its reach is very different, as we are able to support international scientists from a vast range of fields.*

S: From genome to exome to RNA sequencing – the new MLLSEQ website provides detailed information on your sequencing offer and the different services. Can anyone interested in a specific sequencing service get in touch with you?

M: *Yes, that’s right. We see ourselves as a partner in science, and we are glad to provide support right from the project planning phase by bringing our experience to bear with regard to what is possible from a sequencing perspective, where boldness or caution is advised, and which controls for clean bioinformatic processing are necessary. Naturally, there are plenty of scientists who have an extremely high level of expertise in the field themselves. For them, we are also happy to offer our sequencing-only service, where we sequence even completely prepared libraries precisely according to the desired requirements.*

S: For example, let’s say that an international client wants to commission MLLSEQ to perform genome sequencing. What do the next steps look like? It would be great if you could give us a glimpse of what goes on at MLLSEQ on a normal day.

M: *Our new website lists various ways of contacting us: either via a contact form or “Request a quote” along with specific information on the sequencing project. We put together a suitable offer based on that. And then the sample can be sent to us. After arriving at the laboratory, each sample is given a barcode for tracking and is entered into the database*

used to define the analysis being conducted. A single genome analysis takes ten days on average. Along with a list of the quality controls performed, our client receives either a data table or the links for downloading the fastq files. This depends entirely on the request.

S: Can you say which projects MLLSEQ will be working on in the future and how the service and brand will be developing further in the upcoming months and years?

M: *Whole exome sequencing (WES) and RNA sequencing are increasingly in demand. More and more, we are receiving single-cell RNA sequencing as a finished library for sequencing. Liquid biopsy is yet another promising area that is gaining in importance in solid oncology. We have learned that having important industrial partners at our side is extremely helpful. For example, we are working closely together with Illumina and are Propel-certified, which makes us stand out as a sequencing service provider. Likewise, we are striving with IDT – Integrated DNA Technologies, where we procure our panel samples – to develop quick service for custom panels. And I can think of other technology providers off the top of my head as well with whom we could work together on projects and further development.*

S: Thank you very much for your time and the exciting interview.

Dr. rer. nat. Manja Meggendorfer is a graduate biologist and head of the areas of Molecular Genetics and Research and Development at MLL Münchner Leukämielabor. After her studies in Tübingen and Munich, she completed her doctorate in the field of cell nuclear architecture at LMU Munich (human genetics) in close collaboration with the Institute of Virology at the Munich Helmholtz Center. During her postdoc time, she focused on the research of HIV in neuronal stem cells before switching to MLL 10 years ago to work as a scientist in leukemia diagnostics. Through her postgraduate studies resulting in an MBA in Health Care Management, she is qualified not only for scientific publications, the molecular genetic findings of our leukemia samples, but also for the transfer of new technologies into routine molecular genetic diagnostics. She owes her considerable expertise in the field of next generation sequencing not least to her leadership in the 5000 genome project within MLL.

Author: Sarah Kurz

Good Findings Start with Preanalytics – Our Sample Receipt Area Introduces Itself

Every day, the MLL team focuses its combined efforts on making it possible for patients around the world to receive the best therapy thanks to quick and targeted leukemia diagnostics. But how does a normal workday look for the 200 or so employees? What are the different departments and areas? Our new magazine series "Introducing MLL" will be offering you a glimpse into our laboratory. In the first part, we want to present our Sample Receipt area.

The Sample Receipt area is where all patient samples first arrive at MLL and is therefore the first place where the sample material undergoes a quality inspection. The Sample Receipt employees receive the samples, and they record and check the patient master data, the sender data, and the quantity and type of sample material. It is at this time that all sample containers are labeled with a unique barcode, which allows the samples to be unambiguously identified at all times and is used to steer them in the laboratory information system as they pass through MLL.

Sample Receipt Team and Order Control

Eight Sample Receipt employees under the technical leadership of Mr. Florian Wimmer are responsible for this initial step. Most of the team members are medical specialists, periodically assisted by working students over the past few months.

In order to guarantee the senders of samples the highest possible quality, every work step at MLL is subject to strict guidelines and requirements. This process starts as soon as a sample is received at our laboratory: Together with medical laboratory assistants from the various analytical areas, the Sample Receipt employees check whether the sample material is suitable for the analyses requested. In addition, each submitted sample is examined by the scientists and physicians at MLL in view of the clinical question involved. This stringent order control process guarantees that all submitted samples are checked individually to ensure the very highest level of quality in the subsequent analysis. We contact the physician who sent in the sample whenever anything is unclear or there are questions, such as if the type of sample material is unsuitable for the analyses.

A Typical Workday

A typical workday in the MLL Sample Receipt area starts with recording the samples we receive in the mail and from courier services. Since many samples are received at the same time and need to be distributed quickly to the analytics areas, these peak times demand particularly careful and efficient work from our employees. After this phase, the employees in the Sample Receipt area manage any necessary follow-up tasks that arise from the initial results of the cytomorphology or immunophenotyping or are initiated by the senders themselves. In addition, phone calls are answered, missing billing information is filled in, and shipping materials are sent to the senders. The Sample Receipt area is therefore a central hub between the individual MLL analysis areas on the one hand and the senders on the other.

Outlook

In the future, the consistent promotion of automation and digitalization in the sample receipt process will be critical. Sample transport systems can assist the employees in distributing the samples. By expanding the electronic order entry system, we want to increase direct communication between the physician information system and the laboratory information system – not only to minimize the chance of confusion and thereby achieve even greater patient safety but also to optimize the transmission of findings and follow-up management for the senders.

Author: Assoc. Prof. Gregor Hörmann, MD, PhD

Important dates

Oncological Symposium 2021

Oncological Symposium 2021 will take place on November 5, 2021. The successful symposium series "From Biomarkers to Therapy" will be entering its third round. The event offers insights into modern oncological precision medicine, which combines innovative diagnostic methods and therapeutic strategies into a greater whole. The symposium will take place virtually and also as a face-to-face event at MLL Münchner Leukämielabor. As a new subscriber to the MLL Newsletter, you will receive a discount for the basic ticket (€49.00 instead of €79.00) **by entering the code OS21MLL**.

More information and a link for registration can be found here.

Shaping the Medicine of Tomorrow Together

In order to expand our dedicated team, we are looking for medical specialists (m/f/d) with a focus on hematology/oncology, laboratory medicine, or pathology for the area of cytomorphology or for the area of immunophenotyping and for biologists (m/f/d) with a focus on cytomorphology – to start immediately or at any time.

You can find all information about the job posting, the application, and other job offers here.

Most Recent Publications with MLL Involvement

- Chen YT et al. *Prognostic gene expression analysis in a retrospective, multinational cohort of 155 multiple myeloma patients treated outside clinical trials*. Int J Lab Hematol. 2021. Open publication
- Ottema S et al. *The leukemic oncogene EVI1 hijacks a MYC super-enhancer by CTCF-facilitated loops*. Nat Commun. 2021. Open publication
- Radakovich N et al. *A Geno-Clinical Decision Model for the Diagnosis of Myelodysplastic Syndromes*. Blood Adv. 2021. Open publication
- Stengel A et al. *Mutational patterns and their correlation to CHIP-related mutations and age in hematological malignancies*. Blood Adv. 2021. Open publication
- van der Werf I et al. *Splicing factor gene mutations in acute myeloid leukemia offer additive value if incorporated in current risk classification*. Blood Adv. 2021;5(17):3254-3265. Open publication
- Wojtuszkiewicz A et al. *Maturation State-Specific Alternative Splicing in FLT3-ITD and NPM1 Mutated AML*. Cancers (Basel). 2021;13(16):3929. Open 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
E-mail: info@mll.com
Website: www.mll.com