MLL News

06/09/2020

Leukemia diagnostics during the pandemic

In the past few months, we have all been confronted with an entirely new situation. Our patients belong to the high-risk group by definition. Hospitals, outpatient clinics, and medical practices have had to be restructured and reorganize their priorities. Workflows had to be re-examined with regard to factual and time-related aspects with hygiene in mind. The goal has been to ensure continued care for patients, while at the same time protecting the employees trained for that very purpose.

For the MLL too, this has led to entirely new situations. Terms such as *social distancing*, *compulsory masks*, *home office* and *lockdown* were previously not on the list of challenges faced for providing our services.

We therefore thank all our colleagues and you, the senders, for the flexible and constructive cooperation over the past few months in the interest of our shared mission of providing the best care possible for our patients in this new situation.

Like many others, we too are modifying and reviewing our current workflows. Hence, we will be striving to achieve greater flexibility, particularly in our communication with you, the senders, and collaboration partners in the interest of our shared patients and duties. This applies above all for the continued expansion of our digital platforms, which supplement and are increasingly replacing the usual communication media such as phone, fax, and e-mail. We are working intensively on further increasing the user-friendliness and simplifying the local installation of our **Order Entry Portal**, which allows for the digital "order entry" and tracking of the samples. Already highly popular is the **Online Findings Portal** we provide for accessing your patients' findings in digital form around the clock ("MLL Befundportal," all findings retroactively up till September 2017). The initial responses from more than a hundred users have been highly positive.

You will find more information on these portals and login/registration requests at www.mll.com/orderentry and www.mll.com/befundportal. We look forward to contacting you in the future to inform you in more detail about these highly effective new options for even more flexible and effective communication.

For all of you, and in particular our patients, we hope that the situation continues to stabilize in this "new normal." Moreover, we look forward to continued

collaboration. Please do not hesitate to let us know of your suggestions for improving our offerings – as soon as an idea occurs to you!

Sincerely yours,

C. Haferlach, T. Haferlach, W. Kern

Identifying resistance mutations in targeted therapies

Over the past few years, the use of targeted therapies has proven effective for various forms of hematological neoplasia, and increasingly become routine. The rational molecular design of such active substances allows for the targeted blocking of intracellular signal chains in malignant cells, resulting e.g. in cell cycle arrest or ideally apoptosis.

Unfortunately, resistance occurs even against such tailored therapies. It has increasingly become possible to explain their molecular mechanisms. For one, under therapy are a growing number of new mutations in various target genes of targeted drugs or in the genes of associated molecular pathways which could lead to a loss of effectiveness.

The targeted analysis of such resistance mutations can, particularly in the event of the absence of a response or a decreasing response, be proof of potential drug resistance and provide a rationale for the modification of the therapy. Naturally, patient compliance should be ensured before this is done.

Accordingly, MLL strives to offer the analysis of such resistance mutations in the target genes of various active substances according to the state of the art, and recently expanded its portfolio to this effect.

Currently, the following analyses are being offered in this context:

- *IDH2* mutations for Enasidenib resistance in AML
- *BCR-ABL1* mutations for resistance to common tyrosine kinase inhibitors or against the new allosteric Abl inhibitor Asciminib in CML and ALL
- *BCL2* mutations for Venetoclax resistance (e.g. in CLL, mantle cell lymphoma and follicular lymphoma)
- *BTK* mutations and *PLCG-2* mutations for Ibrutinib resistance in CLL

On our order form (current version at **www.mll.com**), these analyses can be found under the sections for the respective disease. The same applies for our digital order entry system. Please feel free to contact us for any suggestions or questions regarding this.

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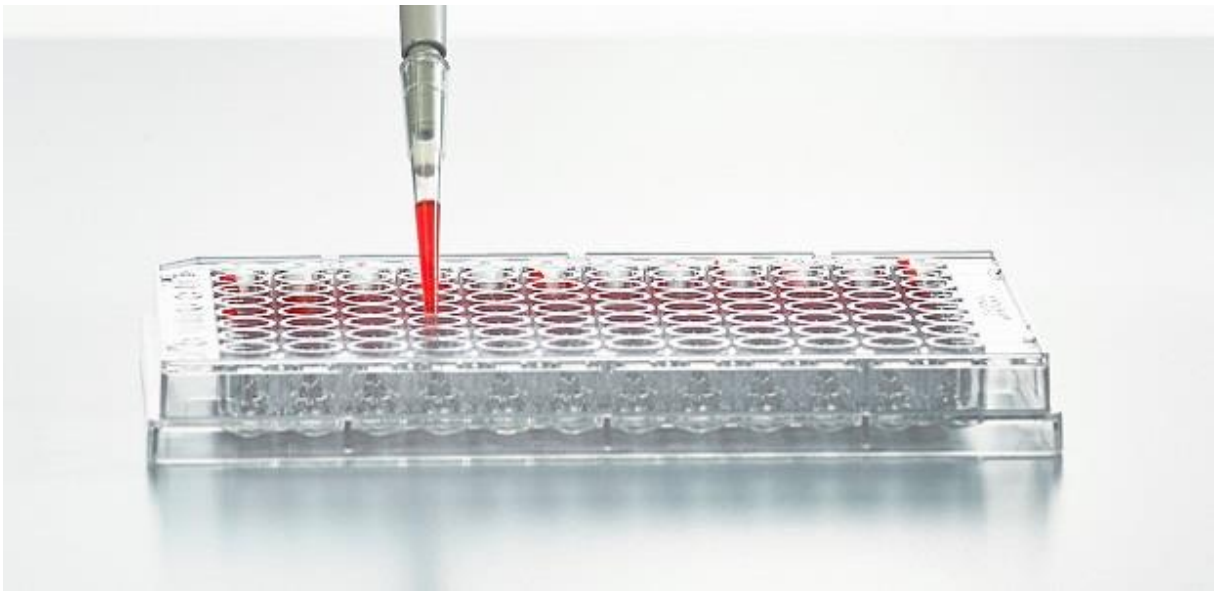

MLL uses AWS Cloud Computing infrastructure for NGS data

Thanks to the rapid advancement of sequencing technology, it has become easier to read an increasingly large amount of DNA. Gene panels are already standard in leukemia diagnostics, and a switch to exome sequencing is expected in the medium term. However, the ability to interpret this data has not grown by the same amount. For this purpose, high-performance computer clusters are necessary in order to analyze the large quantities of data for a standard next-generation sequencing (NGS) run.

With lower sequencing costs and the introduction of devices with significantly higher capacity, the sequencing throughput has increased. This means that the bottleneck has shifted away from sequencing and towards data processing and interpretation. The increasing availability of computer resources as a result of to cloud computing therefore competes with a large initial investment in local computer infrastructure.

Hence, MLL performed an initial evaluation of cloud computing for NGS in the context of the 5,000 genome project. It quickly became clear that this project would produce petabytes of data that would need to be processed and stored securely over the long term in a computer environment secured according to ISO 27001 and which complies with the GDPR. Building such infrastructure would have equated to a huge initial workload and costs for MLL. The maintenance costs would also be immense. With the decision to utilize cloud computing and the associated pay-per-use approach, that was no longer an issue, and we were able to focus completely on the goal of the project: better molecular leukemia diagnostics.

After the initial positive experiences with cloud computing as part of this research project, we decided to switch to cloud computing for the evaluation of the NGS routine diagnostics data as well, after we had to search for costly local solutions in the

previous years in order to ensure the same turnround time despite continuously increasing volumes of data.

Accreditation of the newly set-up NGS panel diagnostics in acc. w/ DIN EN ISO 15189 and DIN EN ISO/IEC 17025 with a pipeline developed specifically for this purpose utilizing Illuminas BaseSpace and AWS Cloud Computing was performed in early 2019. With this pipeline, the amount of daily patient data no longer has an influence on the processing duration, as the data of each patient can be processed in parallel and simultaneously in the cloud.

With the ability of cloud computing to scale almost infinitely, both with regard to processing as well as the storage of data, we consider ourselves to be well-equipped for the future development of NGS – whether it is via the expansion of the panels, whole exome, or whole genome sequencing. Furthermore, we are striving to shift additional workflows to MLL's dedicated partition on the AWS Cloud. As part of collaborative projects with AWS and its Envision engineering team, we are currently working, e.g. on scalable approaches, in order to perform cell differentiation in cytomorphology via artificial intelligence and automatically analyzing flow cytometry data in immune phenotyping without manual gating.

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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, obligation-free.

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