

Healthcare industry BW

IHO: global consulting for the molecular diagnosis of leukaemia

IHO GmbH from Mannheim offers a professional solution for the international exchange of information and services concerning the molecular diagnosis of leukaemia. This drives forward the harmonisation of these methods and brings therapy monitoring to a new global level.



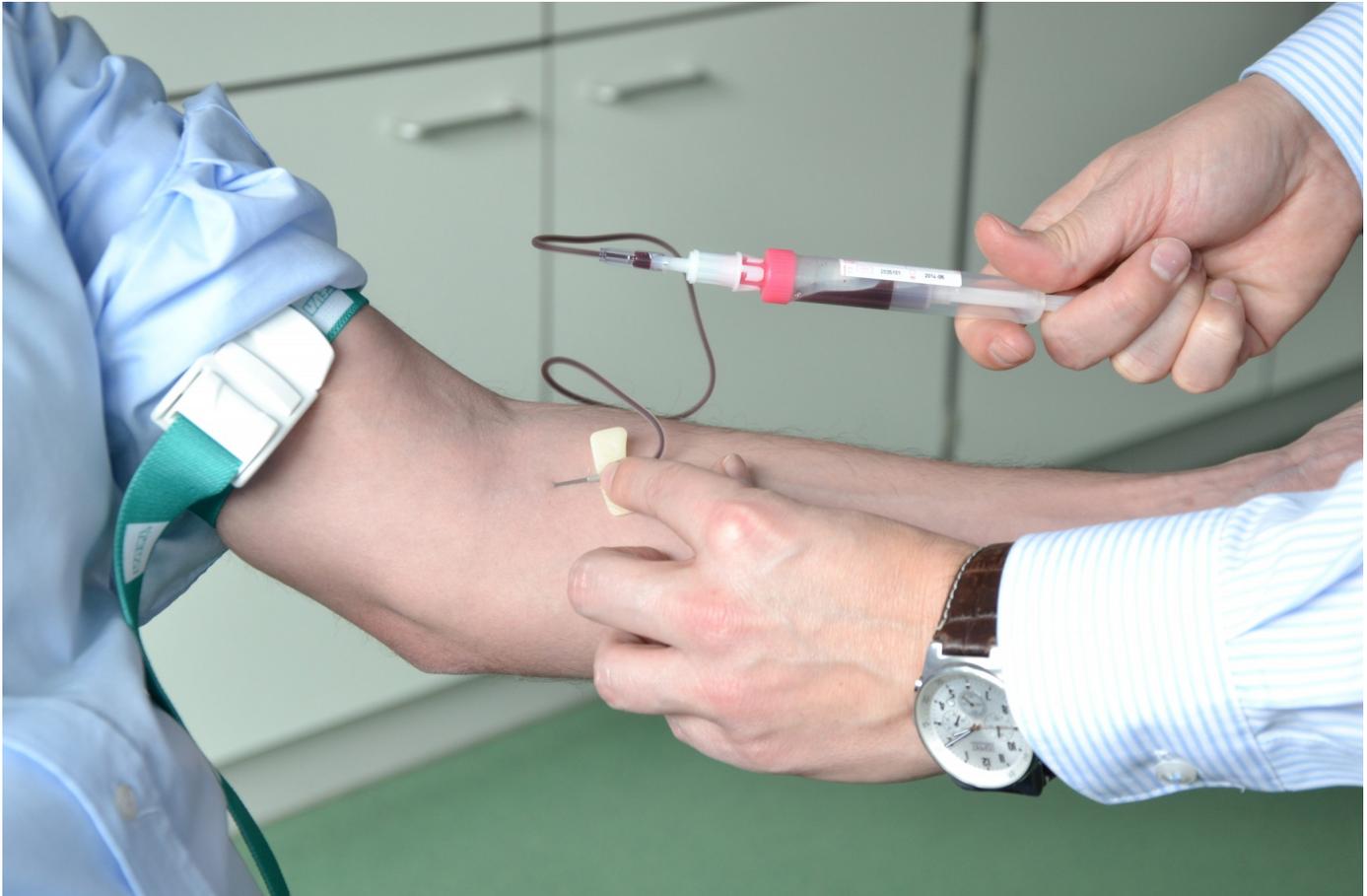
Prof. Dr. Martin Müller, an oncologist and haematologist from Mannheim, has been working for many years on the molecular diagnosis of CML (chronic myeloid leukaemia).
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Prof. Dr. Martin Müller worked at Mannheim University Hospital for 16 years, most recently as a senior physician, before going on to spin out IHO GmbH in 2014 in cooperation with biologist Dr. Christian Dietz and IT specialist Ralf Bieber. In addition to his medical work as an oncologist and haematologist, Müller has advanced molecular investigations in these areas and contributed to the laboratory in Mannheim becoming one of the leading centres on molecular diagnostics of leukaemic diseases in Europe. "For around ten years, the Institute for Hematology and Oncology, IHO, has been a reference laboratory for BCR-ABL diagnostics, especially in follow-up monitoring," says Müller. The quantitative measurement of BCR-ABL is applied to patients with chronic myeloid leukaemia, CLM for short, and detects a genetic modification that is characteristic of this cancer (see box).

As with all cancers, CML can be treated more effectively the sooner the disease is diagnosed. "Due to effective treatment options, very few CML patients die from the disease nowadays. This makes diagnostic follow-up monitoring even more important than before," says Müller. The molecular

analysis of genetic modifications does not require any clever wizardry. The PCR devices needed for the amplification and hence easier detection of the gene region of interest are standard equipment in all modern laboratories. "PCR can be performed by anybody really, at least as long as only yes/no statements are required. However, findings can be misinterpreted and lead to an incorrect evaluation of disease progression," says Müller.

Correct quantification increases treatment quality



Blood samples from the patient are used for molecular leukaemia diagnostics. In the case of CML, quantitative PCR is used to determine the ratio between cells with or without BCR-ABL mutation.

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IHO GmbH is specifically focused on correct BCR-ABL quantification. Quantitative real-time PCR is rather complex in methodological terms and can lead to erroneous results as well as results that differ from laboratory to laboratory. The values of the PCR runs are only comparable when aligned to the International Scale (IS) and compared with suitable reference material. IHO GmbH provides the reference material required. The material is processed in such a way that it can also be sent to remote regions of the world. "We work with freeze-dried cells, i.e. with a mixture that contains a specific ratio of abnormal and healthy cells. The material is stored at room temperature and can be shipped without cooling or dry ice," says Müller. Prior to measurement, the cells are dissolved in buffer solutions and processed. The laboratories are then able to compare the absolute values from the PCR runs involving patient material with the reference material values.

"No other company offers the kind of reference material we do," says Müller highlighting the company's unique selling point. Although commercial measuring systems with calibrators are available, these calibrators have to be used for each individual measurement. "This is often not practical for cost reasons, especially in poorer countries," says Müller. He also points out that ring

tests from reference laboratories show that the same system can lead to completely different results. "This is less down to the kits and protocols used, but mainly due to the fact that the extracted RNA is transcribed in DNA, which in turn affects the conversion factor. Moreover, RNA extraction is not always as good as one would like."

This is IHO GmbH's strong point because "our service covers the entire process. We use four different calibrators and the material has been extensively validated. In addition, we can check whether the extracted RNA is good enough," says Müller. The IHO team evaluate the PCR runs themselves, so that customers can be sure of the quality and can identify and eliminate faults, for example in the pipetting scheme used. In some regions, the technical equipment is also not suitable for carrying out BCR-ABL quantification with the required sensitivity. Therefore, one of IHO GmbH's services is complete sample analysis - including reference checking, help with interpreting the results and troubleshooting.

GISMO to drive forward molecular cancer diagnostics on the global level



IHO GmbH's information system, GISMO, is aimed at facilitating the global exchange of information between laboratories and contributing to the harmonisation of molecular diagnostics.

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IHO GmbH's services are embedded in an information system called GISMO (global in-depth supervised monitoring system for laboratory diagnostics). It forms the core of the start-up company and manages the medical molecular diagnostics of CML with the help of computers. GISMO functions globally and with an easy-to-use tool, thanks to the programming skills of IHO co-founder Ralf Bieber. "The system is not yet fully online. We still have to check back with our customers, small companies in India or China that are carrying out BCR-ABL analyses for the first time particularly need our support, also in terms of communication," says Müller.

It is from such customer contact that the team learns where the system is particularly difficult to implement, which then enables GISMO to be further optimised. There will be greater exchange of information and the system will be increasingly automated. Müller and his co-founders are already thinking ahead. In the long term, they want to use their expertise to integrate diagnostics in other leukaemias and even solid tumours. The overall objective is to generate internationally comparable results and to harmonise diagnostics globally. This will ultimately benefit all patients. At the moment, the company's management team is carrying out intensive talks with interested parties in China, India and South America, i. e. countries where many regions lack state-of-the-art laboratory equipment, and which can particularly benefit from IHO's services. "In principle, we believe there is huge clinical need and a large market, both in European countries like Romania, as well as in Asia," says Müller.

About CML

A gene translocation is the cause of chronic myeloid leukaemia (CML). In this case, chromosomes 22 and 9 exchange part of their genetic material, which results in the BCR (from

chromosome 22) and ABL (from chromosome 9) genes being arranged side by side. This leads to the production of a fusion protein BCR-ABL in the cell. The attached ABL protein portion prevents the BCR protein from exerting its normal inhibitory function in cell division. This leads to uncontrolled cell growth and leukaemia develops. Since genetic modification affects only somatic cells and not germ line cells, the disease is not passed on to progeny.

Article

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Further information

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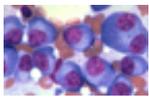
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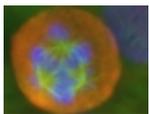
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