Juvenile myelomonocytic leukemia: International classification model allows for customized treatment

Scientists of the German Cancer Research Center (DKFZ), the National Center for Tumor Diseases (NCT) Heidelberg and the Medical Center University of Freiburg, together with international colleagues, have now defined a globally valid uniform methodology for the use of methylation status as a biomarker in juvenile myelomonocytic leukemia (JMML) based on a database of 255 patients. The classification method is designed to be used in everyday clinical practice. One of the aims of the researchers is to identify high-risk patients more quickly in order to give them access to innovative treatments in clinical studies.

Juvenile myelomonocytic leukemia (JMML) is a rare blood cancer of early childhood. Previous research activities have shown that JMML patients can be divided into three groups based on certain genetic markers, DNA methylation. Depending on the subgroup, statements can be made about the course of the disease. Scientists of the German Cancer Research Center (DKFZ), the National Center for Tumor Diseases (NCT) Heidelberg and the Medical Center University of Freiburg, together with international colleagues, have now defined a globally valid uniform methodology for the use of methylation status as a biomarker in JMML based on a database of 255 patients. The classification method is designed to be used in everyday clinical practice. One of the aims of the researchers is to identify high-risk patients more quickly in order to give them access to innovative treatments in clinical studies.

The National Center for Tumor Diseases (NCT) Heidelberg is a joint institution of the German Cancer Research Center (DKFZ), Heidelberg University Hospital (UKHD) and German Cancer Aid (DKH).

Joint press release from NCT Heidelberg and KiTZ.

Juvenile myelomonocytic leukemia (JMML) mainly affects children, usually before the end of the second year of life. So far, blood stem cell transplantation is the only form of treatment. If this therapy is not successful, the disease is often fatal.

Researchers have found out that the development of cancer is not only a purely genetic process. Markers on the genetic material can also promote the uncontrolled growth of cells. Scientists have therefore also examined the genetic material of JMML cells for the occurrence of certain chemical genetic markers, DNA methylation. These so-called epigenetic changes control the activity of individual genes. “Depending on how strongly the DNA is methylated, JMML patients can be divided into three groups: Patients in whom the genetic material of the tumor cells is strongly methylated usually show characteristics that are associated with an increased risk of relapse after stem cell transplantation. In another group of patients whose tumor genome is only weakly methylated, the disease usually progresses milder. A third group has a medium level of DNA methylation,” reports Daniel Lipka, head of the Section Translational Cancer Epigenomics in the Department of Translational Medical Oncology at DKFZ and the NCT Heidelberg. The analysis of DNA methylation status is therefore now also used as a biomarker to better assess the...
In the present study, international scientists and physicians have defined a standardized methodology for subgrouping JMML based on the DNA methylation pattern. For this purpose, the genetic analyses of 255 patients were evaluated and clinically and biologically characterized. "Our analysis was able to detect the methylation pattern as the only significant factor that can predict overall survival in this particular disease," reports Maximilian Schönung, first author of the publication and scientist in the Section Translational Cancer Epigenomics of the Department of Translational Medical Oncology at DKFZ and at the NCT Heidelberg. The researchers tested the method in an independent patient group and also investigated whether the analyses produce reliable results at different locations and with different technical conditions. The results of the group classification were in 98 percent agreement and thus proved the high reliability of the classification method. "Thanks to the international standard procedure, JMML patients can now be more reliably assigned to the three subgroups. In particular, high-risk patients for whom an allogeneic blood stem cell transplantation is not curative can now be identified more quickly," says Christian Flotho, scientist in the German Consortium for Translational Cancer Research (DKTK) at the University of Freiburg Medical Center. "For this challenging group of patients, we are working together with the European study group EWOG-MDS to develop clinical studies that will open up access to innovative treatment options," adds Lipka.

Original publication

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Further information to leukemia illnesses in the child age, their research and a patient service for second opinions finds it on the web page of the Hopp child tumor center Heidelberg (KITZ): www.kitz-heidelberg.de

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National Center for Tumor Diseases Heidelberg (NCT) The National Center for Tumor Diseases (NCT) Heidelberg is a joint institution of the German Cancer Research Center, Heidelberg University Hospital (UKHD) and German Cancer Aid. The NCT’s goal is to link promising approaches from cancer research with patient care from diagnosis to treatment, aftercare and prevention. This is true for diagnosis and treatment, follow-up care or prevention. The interdisciplinary tumor outpatient clinic is the central element of the NCT. Here, the patients benefit from an individual treatment plan prepared in interdisciplinary expert rounds, so-called tumor boards. Participation in clinical studies provides access to innovative therapies. The NCT thereby acts as a pioneering platform that translates novel research results from the laboratory into clinical practice. The NCT cooperates with self-help groups and supports them in their work. Since 2015, the NCT Heidelberg has maintained a partner site in Dresden. The Hopp Children’s Cancer Center (KiTZ) was established in Heidelberg in 2017. The pediatric oncologists at KiTZ work together in parallel structures with the NCT Heidelberg.

German Cancer Research Center (DKFZ)
The German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) with its more than 3,000 employees is the largest biomedical research institution in Germany. More than 1,300 scientists at the DKFZ investigate how cancer develops, identify cancer risk factors and search for new strategies to prevent people from developing cancer. They are developing new methods to diagnose tumors more precisely and treat cancer patients more successfully. The DKFZ’s Cancer Information Service (KID) provides patients, interested citizens and experts with individual answers to all questions on cancer.

Jointly with partners from the university hospitals, the DKFZ operates the National Center for Tumor Diseases (NCT) in Heidelberg and Dresden, and the Hopp Children’s Tumour Center KiTZ in Heidelberg. In the German Consortia for Translational Cancer Research (DKTK), one of the six German Centers for Health Research, the DKFZ maintains translational centers at seven university partner locations. NCT and DKTK sites combine excellent university medicine with the high-profile research of the DKFZ. They contribute to the endeavor of transferring promising approaches from cancer research to the clinic and thus improving the chances of cancer patients.

The DKFZ is 90 percent financed by the Federal Ministry of Education and Research and 10 percent by the state of Baden-Württemberg. The DKFZ is a member of the Helmholtz Association of German Research Centers.

Heidelberg University Hospital (UKHD) Heidelberg University Hospital (UKHD) is one of the most important medical centers in Germany; Heidelberg University’s Medical Faculty is one of Europe's most prestigious biomedical research facilities. Their shared objective is the development of innovative diagnostics and treatments and their prompt implementation for the benefit of the patient. The hospital and faculty employ approximately 13,000 individuals and are involved in training and qualification. Every year approximately 65,000 patients are treated as inpatients and 56,000 as day patients in more than 50 specialized clinical departments with around 2,000 beds, with more than 1 million patients being treated as outpatients. Together with the German Cancer Research Center and German Cancer Aid, the Heidelberg University Hospital established The National Center for Tumor Diseases (NCT) Heidelberg as the leading oncology center of excellence in Germany. The Heidelberg Curriculum Medicinale (HeiCuMed) is at the forefront of medical training in Germany. At present 3,700 aspiring physicians and doctors are studying in Heidelberg.
The Hopp Children’s Cancer Center Heidelberg (KiTZ) The “Hopp Children’s Tumor Center Heidelberg” (KiTZ) is the pediatric oncological institution of the German Cancer Research Center, the University Hospital Heidelberg and the University of Heidelberg. Like the National Center for Tumor Diseases (NCT) Heidelberg, which focuses on adult oncology, the KiTZ is based on the US-American model of the so-called “Comprehensive Cancer Centers” (CCC) in terms of type and structure. The KiTZ is also a therapy and research center for oncological and hematological diseases in children and adolescents. Its goal is to scientifically investigate the biology of childhood cancer and severe blood diseases and to closely link promising research approaches to patient care - from diagnosis to treatment and aftercare. Children suffering from cancer, especially those for whom no established treatment options are available, are given an individual therapy plan at the KiTZ, established in tumor conferences by experts from various disciplines. Many young patients can participate in clinical studies and thus gain access to new treatment options. Thus, the KiTZ is a pioneering institution for transferring research knowledge from the laboratory to the clinic.

Original publication: