

## **A second chance for children with cancer**

**Today most cases of childhood cancer can be cured. However, in about 20 percent of cases children suffer a recurrence of the cancer following therapy and they ultimately succumb to the disease. With a new project called INFORM\*, scientists from the German Cancer Research Center (DKFZ) and the German Consortium for Translational Cancer Research (DKTK) aim to provide these children with a second avenue toward cures. The work is based on an analysis of the tumor's complete genetic information at the time of relapse. The data allows researchers to discover factors that promote tumor growth and investigate whether novel, targeted drugs can help cure the individual child's disease. The goal is to identify genomic alterations in all cases of recurrent cancer in children across Germany and search for drugs that precisely target the tumor of each affected child. German Cancer Aid (Deutsche Krebshilfe) and the German Childhood Cancer Foundation (Deutsche Kinderkrebsstiftung) will now provide about €1.1 million to fund a two-year feasibility study.**

The most urgent problem in pediatric oncology today is the recurrence of cancer in the wake of intensive radiotherapy and chemotherapy. "In Germany, about 500 children are affected by a recurrence of cancer each year," says Prof. Otmar Wiestler, Chairman of the Management Board and Scientific Director of the DKFZ. "When cancer recurs, usually all effective treatment options have already been exhausted, and the drugs that were initially effective often fail. Therefore we are urgently searching for new treatment options for these children."

An analysis of a tumor's complete genetic information at the time of relapse allows today's scientists to identify factors that promote tumor growth in each individual case. Often it is possible to identify a matching drug that specifically inhibits these growth-promoting factors.

"About one quarter of children with cancer suffer from a relapse after treatment, and in most of these cases there is no more hope for a permanent cure," says DKFZ's Prof. Stefan Pfister, chief coordinator of the INFORM research network. "Judging from our experience so far, analyses of the tumor genomes might offer a second chance of survival for about half of these children. Our goal is for all cases of recurrent childhood cancer across Germany to search for a drug that precisely matches the tumor of each affected child."

Chemotherapy and radiotherapy damage all kinds of rapidly dividing cells, including those of tumors and healthy tissue. Novel, "intelligent" drugs, on the other hand, target specific cellular alterations that typically occur in cancer. A match can only be found for a particular tumor by analyzing its complete genome and detecting which of the many possible cancer-related alterations have occurred.

The central issue for INFORM is now to conduct a feasibility study based on comprehensive genome analyses at the DKFZ, aiming to determine what information about a tumor's genome will most likely lead to more effective treatments for affected children. The scientists will concentrate on 12 types of cancer with the highest recurrence rates in children. First it will be necessary to document the exact type and number of mutations found in individual cancer types that can be targeted by "intelligent" drugs. If agents are already available to address the mutations detected in an individual patient's tumor cells, a physician can use this to decide, with the individual patient, whether a specific drug can be used. If there is not yet a drug to

target a specific cancer-promoting alteration in cells, the information will be useful in developing new agents.

After the completion of the feasibility study, the pediatric oncologists plan a clinical trial based on German Drug Laws (Arzneimittelgesetz) to investigate whether individualized therapies based on genomic information offer better outcomes than conventional treatments following a relapse.

Unfortunately, patient health insurance plans do not currently cover the costs to analyse children's tumor genomes nor provide the expensive targeted drugs needed for treatment. Part of the costs for genome and data analyses and documentation will be covered by funding from the DKFZ and the German Consortium for Translational Cancer Research (DKTK) (€2.5 million), German Cancer Aid (Deutsche Krebshilfe), and the German Childhood Cancer Foundation (Deutsche Kinderkrebsstiftung).

"Innovative cancer research is a major concern of the Deutsche Krebshilfe," says Gerd Nettekoven, Managing Director of German Cancer Aid. "Only advances in research will enable us to improve the treatment and care of people suffering from cancer. This is the motivation for the Deutsche Krebshilfe's support of the highly-innovative INFORM project."

Ulrich Ropertz, Chairman of the German Childhood Cancer Foundation, says: "We want all children with cancer to have a chance of survival – through targeted therapies, with as few side effects as possible. This is why the promotion of research is so important. With joint funding by DKTZ and DKFZ, the German Cancer Aid and the German Childhood Cancer Foundation aim to forge new paths in pediatric oncology through the INFORM network project."

Another supporter of INFORM is the charity "BILD hilft e.V – Ein Herz für Kinder" ("A Heart for Children"). Donations to this charity help finance the other big cost element – that of the new drugs, which in most cases are not covered by health insurance companies because of a lack of data from clinical trials. A major fundraising gala on German TV under the title "Ein Herz für Kinder" (Saturday, December 6, 2014 on ZDF) has helped raise public awareness of and support for the initiative by presenting a young girl whose tumor genome analysis represents a second chance for a cure.

*\*INFORM stands for Individualized Therapy for Recurrent Malignant Tumors in Children. Scientific project coordinators are:*

- Prof. Stefan Pfister (chief coordinator, DKFZ),
- Prof. Angelika Eggert (chair of the Society of Pediatric Oncology and Hematology GPOH, Charité Berlin)
- Prof. Peter Lichter (coordinator of Molecular Diagnostics in INFORM, DKFZ)
- Prof. Olaf Witt (coordinator of the INFORM Registry study, DKFZ and Heidelberg University Hospital)

***The Society for Pediatric Oncology and Hematology (GPOH) draws together eleven study groups and over 50 participating recruitment centers across Germany in the INFORM project.***

The German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) with its more than 3,000 employees is the largest biomedical research institute in Germany. At DKFZ, more than 1,000 scientists investigate how cancer develops, identify cancer risk factors and endeavor to find new strategies to prevent people from getting cancer. They develop novel approaches to make tumor diagnosis more precise and treatment of cancer patients more successful. The staff of the Cancer Information Service (KID) offers information about the widespread disease of cancer for patients, their families, and the general public. Jointly with Heidelberg University Hospital, DKFZ has established the National Center for Tumor Diseases (NCT) Heidelberg, where promising approaches from cancer research are translated into the clinic. In the German Consortium for Translational Cancer Research (DKTK), one of six German Centers for Health Research, DKFZ maintains translational centers at seven university partnering sites.

Combining excellent university hospitals with high-profile research at a Helmholtz Center is an important contribution to improving the chances of cancer patients. DKFZ is a member of the Helmholtz Association of National Research Centers, with ninety percent of its funding coming from the German Federal Ministry of Education and Research and the remaining ten percent from the State of Baden-Württemberg.

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