

**Barbara Stöckl:**

*Prof. Gadner, you are the medical director of St. Anna Children's Hospital, the director of the St. Anna Cancer Research Institute, a paediatrician, as well as the coordinator of the EU- Project "Forschen heilt Krebs" ("Overcoming Cancer With Research").*

*The children's cancer research at St. Anna will be celebrating its 20<sup>th</sup> anniversary this year. Your research institute has developed into a positive establishment. How did this success story begin?*



**Prof. Gadner:** When I took over as medical director of St. Anna Children's Hospital in 1980, research was no real issue yet. We were more concerned with discovering ways and means to reduce the death rates of two thirds of cancer-stricken children. Owing to modern methods of treatment, we were effectively able to achieve a recovery rate of 70 percent throughout Austria within a few short years. However, further progress appeared hopeless and we did not know how to continue. The logical consequence was to initiate research, whereby the foundations for developing the research institute were created owing to a compassionate public relations campaign by the "Initiative betroffener Eltern" ("Initiative of Concerned Parents"). By means of research, we were hoping to develop better insight into the biology of cancer cells, and subsequently, to discover new and adapted treatment methods.

*How successful is the cancer treatment for children in comparison to the treatment for adults today?*

**Prof. Gadner:** As a matter of fact, it has been possible to boost the survival rate of cancer-stricken children up to 75 percent in the past 20 years. In comparison, the treatment results of adults were – at around 50 percent – a lot worse. This can be chiefly attributed to the fact

that the spectrum of cancer illnesses found in adults – with 80 percent being carcinomas – are principally different than those found in children. Children are usually affected by leukaemia, lymphomas, as well as the so-called embryonic tumours, which are also known as sarcomas. Carcinomas in children only make up approximately one percent and are, thus, rare.

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*Barbara Stöckl:*

*Doz. Kovar, you are a molecular biologist and academic director at the St. Anna Children's Cancer Research Institute.*

*What are the differences between children's cancer research and adult cancer research?*



**Doz. Kovar:** Cancer is the result of an accumulation of genetic alterations, which increase with age as well as with exposure to environmental impacts. These external factors do not play such a large role among children because they are still young. This is the reason why the tumour range among children and youths are substantially different from those found in adult patients. As a result, we can assume that a significantly smaller number of alterations are present in the genes, which play a key role in the regulation of cells.

*What are chief responsibilities of the St. Anna Children's Cancer Research Institute?*

**Doz. Kovar:** Statistically seen, the current treatment methods of cancer in children and youths are already very successful. However, there are large inter-individual differences which affect the recovery rate, as well as the side effects and late effects. This is the reason why, in addition to basic research, we perceive secondary research for the individualisation of therapy (adaptation to the expected course of disease) as our most important task. In addition, we support clinical research and recognize the importance of communicating and educating the general public, especially to young people, on sciences. All these areas are examined in four sequential events at the Academy of Sciences this week (November 18<sup>th</sup> – 22<sup>nd</sup>).

*Barbara Stöckl:*

*Prof. Ladisch, you are director of the Center for Cancer and Transplantation Biology at the Children's National Medical Center in Washington, and are Vice Chairman of the University Department of Paediatrics, where you successfully built a paediatric research institute, leading the research unit as scientific director from 1998 on for seven years. As an expert in paediatric research, you have been a long-term scientific advisor to the St. Anna Children's Cancer Research Institute*

*Which developments have been observed in children's cancer research over the last few decades?*



**Prof. Ladisch:** It is very important to understand childhood cancer and its treatment. Generally, cancer in children has been a disease with a poor outcome, if left untreated. In the 1950s, researchers succeeded in developing strategies to fight against leukemia. Childhood leukemia was the first example of a form of cancer (adult or paediatric) against which research developed a really successful treatment, based on the principle of new combination treatments. This big success spurred optimism for more research.

Because of this justified enthusiasm, in the last decades research in childhood cancer has been taken to new levels, and the CCRI is particularly geared to these new scientific directions. I would give two examples: (1) *Unravelling the molecular biology of cancer cells.* has now allowed paediatric oncologists to distinguish between tumours that need more treatment and those requiring less therapy, resulting in a better outcome for those more severely affected and less therapy (and therefore less dangerous side effects) for those at lower risk. (2) *Study of the circuitry of the cancer cell.* The study of the cancer cell itself has uncovered the pathways by which the abnormal cells mentioned by Dr. Kovar are able to assure their own survival, and the result has been the development of specific inhibitors of these signals. These signalling inhibitors have already shown success in improving the treatment of some forms of cancer and offer further promise for the future. So, these two

examples show that significant advances in childhood cancer research can be successfully applied and lead to better treatments for our young patients.

**How is the St. Anna Children's Cancer Research Institute assessed in the field of international biomedical research from abroad?**

**Prof. Ladisch:** Because paediatric cancers are rare, it is particularly important to be able to systematically examine research results and their implications for diagnosis and treatment. The most effective way to do this in a rare disease is to intimately link the research to the clinical care of patients with these diseases, ideally through integration and physical proximity of the research institute and the hospital caring for the patients. This was the concept underlying the development of and is the concept underlying the current expansion of the CCRI.

St. Anna Children's Cancer Research Institute is a perfect example of undertaking targeted research, application and diagnosis in the same institution. Consequently the CCRI is highly respected internationally. In other words, the St. Anna Kinderkrebsforschung is among the leading institutions in this field worldwide. This is evidenced by the frequent invitation of St Anna investigators to discuss their work at international meetings, as well as by the publication of their exciting new findings in highly regarded international journals.

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**Barbara Stöckl:**

*Doz. Ladenstein, you are a doctor at St. Anna Children's Hospital and manage the department of Studies and Statistics at the St. Anna Children's Cancer Research Institute.*

*The St. Anna Children's Cancer Research Institute is located in close proximity to St. Anna Children's Hospital. What advantages does this provide to cancer-stricken children?*



**Doz. Ladenstein:** Children and youths with cancer require the best type of therapy possible. This can only be ensured within the framework of high quality trial platforms. These [platforms] guarantee optimal standard therapies and monitor innovative therapy concepts, optimised concomitant therapies, systematic monitoring, as well as therapy concepts due to insufficient responses. The integration of research questions into the diagnosis as well as into further therapy processes leads to risk-adapted treatment strategies, and thus, to maximum individual benefit for the child concerned. A network of clinical treatment and

support, as well as concomitant research, ensures that special attention is paid to the milestones achieved during the course of therapy. Thus, positive new progress is recognized in time. Research shows that children in clinical trials demonstrate better clinical progress and have higher survival rates than children outside of these trials.

*From a clinical standpoint, what problems are the most urgent, and must be solved with the support of the Children's Cancer Research Institute?*

**Doz. Ladenstein:** Cancer illnesses in children require highly complex treatment concepts and innovation, in order to improve the chances of recovery. The implementation of therapy optimisation and high quality treatment, integrated with research aspects, is clinical research. This is why the department for Studies and Statistics is a part of the St. Anna Children's Cancer Research Institute. The survival rate of cancer-stricken children has increased from under 20 percent to 80 percent in the past 30 years through therapy optimised studies (TOS). In line with the EU Clinical Trials Directive (2001/20/EC) and its implementation into the Austrian AMG in 2004, the necessary requirements in trials for children have increased – even in standard therapies. Now, public utility institutions must meet similar requirements to those found in the pharmaceutical industry. Special infrastructure and organisational structures are now required, in order to continue to provide child-friendly, legal, methodically valid and efficient trials for children. Without TOS, a 30 percent decrease in the survival rate of cancer-stricken children in Austria can be expected. Thus, the appropriate financial resources are needed for these patients, in order to run clinical trial centres as well as national and international research networks. This is the only way to further increase the survival rates of children and youths together. We hope to achieve a political regulation regarding the issue of resources. Relevant requests, in the form of detailed projects, have been submitted to the Ministry of Finance as well as to the Ministry of Health several times already.

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**Barbara Stöckl:**

*Doz. Kovar, you have been the director at St. Anna's Children's Cancer Research Institute for seven years now. During your career as a researcher, what have been the most promising developments, which have significantly influenced cancer therapy options for children and youths?*

**Doz. Kovar:**

At this point, I have to mention the adaptation of therapy intensity in children with leukaemia. The existence of defined and detectable molecular quantities is adapted to circulating tumour cells at specific times during the course of the illness. Likewise, the molecular-genetic analysis and description of the neuro-blastoma has resulted in the fact that certain patients were able to completely forgo chemotherapy. Regarding new treatment options, research has led to a better understanding of cellular signal paths (so-called receptor tyrosine kinase), which are now successfully employed in therapy.

*What significance does science communication hold for your institute?*

**Doz. Kovar:** Science communication is very important to us because we are aware of our responsibility to give something back to our many sponsors, who make our research possible. We also want to demonstrate what their commitment has contributed to. The St. Anna's Children's Cancer Research Institute is chiefly financed through donations – for 20 years now! We also feel a special responsibility for our youths – on the one hand, to educate them on these issues, and on the other hand, to spur their interest for science. Our public forum on November 20 at the Academy of Sciences, which is supported by the EU and organised by a science-communication project “Overcoming Cancer With Research” by our institute, is also intended for this purpose.

