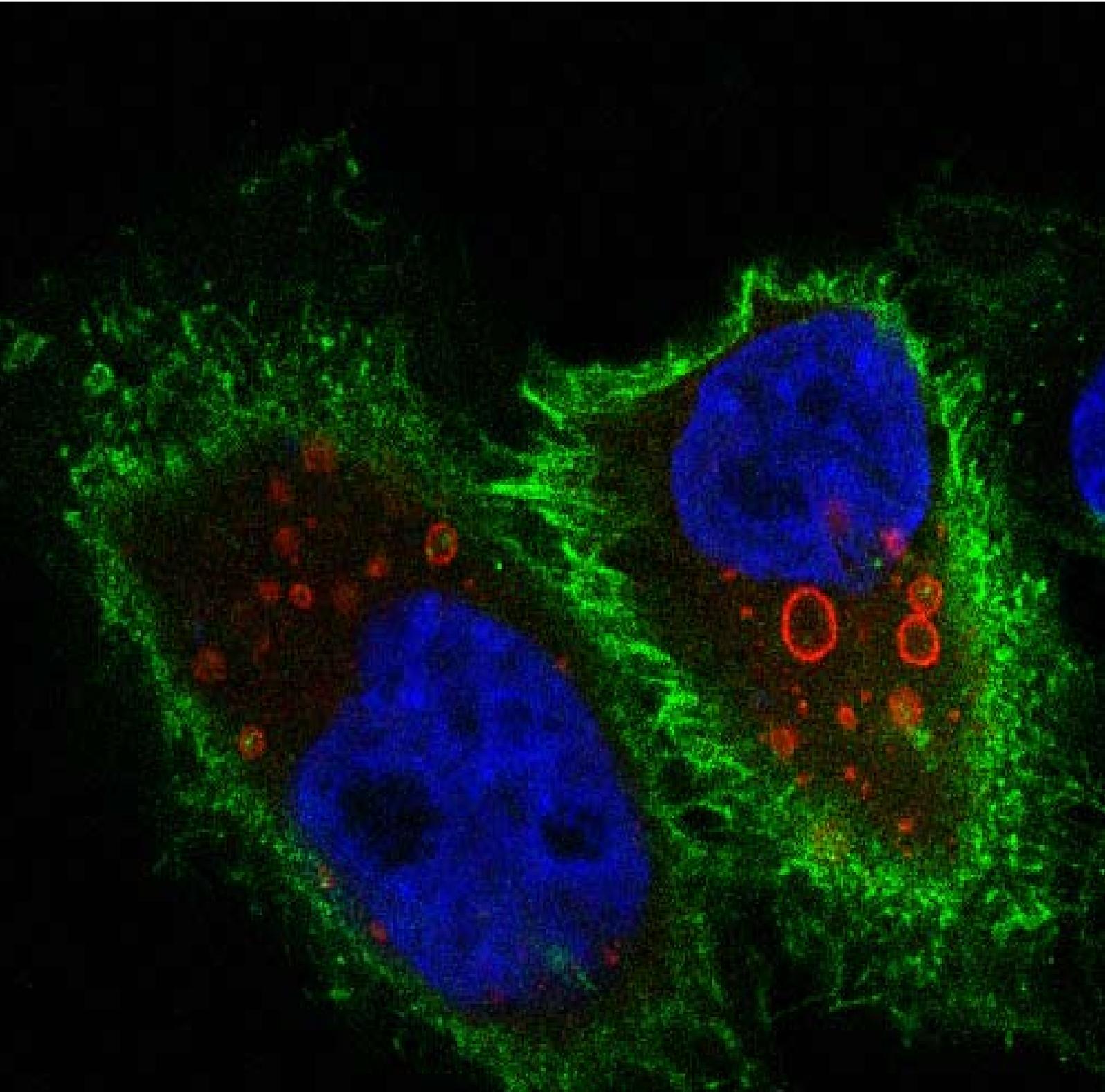


YOUR MONEY AT WORK

HOW THE SWISS PRIVATE BANKING COMMUNITY HELPS
SCIENTISTS TO FIND A CURE FOR CANCER



OUR STATED PRIORITY IS TO ADVANCE EFFORTS TO FIGHT CANCER WITH ALL AVAILABLE MEANS.

... invests in cancer research worldwide

In the past ten years, we have supported numerous projects in Brazil, the UK, France, Italy, Norway, Sweden and Switzerland.

... generates over 2 million Swiss francs in research funding every year

Banks in Switzerland have introduced numerous clients to SWISS BRIDGE, each of which has donated substantial amounts to SWISS BRIDGE.

... annual SWISS BRIDGE AWARD for international researchers

The SWISS BRIDGE AWARD has become one of Europe's most important annual research awards. Only the best in class receive funding of up to 500,000 Swiss francs for their future projects.

... no expenses deducted from donations for research

Over the past ten years, the supporters and friends of the foundation have covered all the costs of public relations, fundraising and administration. This allows us to transfer 100% of donations designated for research to the respective research teams.

... world-class scientific standing

Both the Scientific Committee and the Patrons Committee include Nobel prize-winners and other world-renowned scientists.

... close co-operation with the UICC (a WHO institution)

To enable international investors and international researchers to rate the quality of SWISS BRIDGE, the organisation stipulates that recipients of SWISS BRIDGE funding outside Switzerland be a member of the Union Internationale Contre le Cancer in Geneva.

... "swissness" (trustworthy, modest and precise)

For ten years, SWISS BRIDGE has undertaken only modest PR activities, putting it on the shortlist of the most efficient and successful platforms raising funds for cancer research.

GREETINGS FROM OUR CHAIRMAN

From the Chairman of the Board

Having served for six years as Chairman of the Board of the SWISS BRIDGE Foundation, I come to realise how important the Swiss Private Banking Industry can be in our international, multi-disciplinary approach in cancer research. The generous support by numerous Swiss and foreign banks and their clients speak for their solidarity towards our continuous fight against cancer. Thanks to all persons and institutions who have given support and who will give further support to SWISS BRIDGE to intensify the fight against cancer.

From the Chairman of the Scientific Jury

Ten times has the SWISS BRIDGE AWARD been announced for a minimum of 500,000 Swiss francs contribution to Swiss and international cancer research teams. Many of the hundreds of innovative and cutting-edge cancer research projects submitted to SWISS BRIDGE have come across my desk, of which I would have preferred to approve many more than those which were selected for funding. Nevertheless, there is great optimism among the cancer research community, for which reason I commend the work of SWISS BRIDGE to you without reservation.

From the Co-founder and Member of the Board of Foundation

Thanks to the generous support of a broad group of friends and colleagues, Swiss Private Bankers, we have been able to collect important funds to fund outstanding cancer research projects across Europe. I am proud to be able to hand over the management of SWISS BRIDGE to my successor Heinz Waech, and to serve the institution, which I have built up and cared about in the past eleven years, as Member of the Board of Foundation. I appeal to you to join me in my goal to raise more money to support cancer research, to fulfil our vision to leave our descendants a precious legacy.



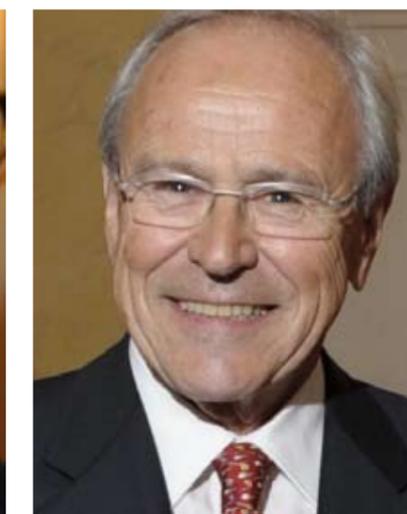
Giorgio Nosedà

Giorgio Nosedà
Chairman of the Board



Gordon McVie

Gordon McVie
Chairman of the Scientific Jury



Thomas Hoepli

Thomas Hoepli
Co-founder and
Member of the Board of Foundation

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ANNUAL SWISS BRIDGE AWARD

The SWISS BRIDGE AWARD – a success story

When I founded SWISS BRIDGE in 1997, it was my great concern that the funds I would generate for cancer research should only be invested in the most advanced research programme. What else could ensure this better than the announcement of the availability of funds to the research community. This procedure was quickly approved by the Board of the Foundation under the Chairmanship of Prof. Dr. Urs Metzger, and welcomed by the Scientific Board, headed then by Prof. Dr. Rolf Zinkernagel. Another important decision was to ask researchers to hand in a letter of intent with a very short description of their ideas. Out of these first submissions, 6–8 candidates were asked to present detailed projects.

to draw from a well-funded bank account, which we did not have in the early days. Remembering the techniques, I used to apply in my former profession as an investment banker, I went out to bankers to inquire if they were willing to guarantee the payment of the prize monies, in case I was not able to find donations to pay for the planned award.



Isabel Mortara, Member of the Board of the Foundation SWISS BRIDGE, with Michel Meyrat, Chairman of the Board of the Stammach Foundation.

tutions were not called on the guarantee, they renewed their commitment for a second year. Thereafter we had accumulated sufficient funds to announce the award without extra support.

24 SWISS BRIDGE AWARD winners for 5 million Swiss francs

When at the beginning, we received some 15 to 20 submissions, the evaluation by the Scientific Jury was relatively easy to handle. When the award became better known in the research community, the flow of projects increased steadily until 2007, when we received over 150 letters of intent, of which 10 were selected for the final contest.

In the past nine years, 24 individual researchers from 12 leading cancer research institutions throughout Europe have received funding through the award. Three of them are portrayed in this magazine.

The tenth SWISS BRIDGE AWARD

After the announcement of the SWISS BRIDGE AWARD 2009 for a total amount of 500,000 Swiss Francs, the Jury will evaluate the projects submitted in the month of September. It has been announced, that approx. half of the award monies are earmarked for a Swiss and the other half for a foreign scientist. The prize-giving ceremony will be held on 20th October 2009 at the Tower Restaurant of the Zurich University. Applications to participate in this exquisite event can be made to info@swissbridge.ch.

Thomas Hoepli



From left: Prof. Arnold Koller, Dr. Giorgio Ghiringhelli, Prof. Giorgio Nosedà and Dr. Egon Zehnder at the SWISS BRIDGE AWARD 2008.

The first SWISS BRIDGE AWARD

There was however another problem: In order to announce reasonably important prize monies, you would have to be able

To my astonishment, six financial institutions agreed to participate in a syndicate to jointly guarantee more than half of the first SWISS BRIDGE AWARD funded with 500,000 Swiss francs. The confidence these institutions demonstrated motivated me to make even more efforts to find donors through my Swiss Private Banking contacts. Because the financial ins-

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A WOMEN'S GENETIC MAKE-UP IS IMPORTANT FOR RISK, TYPE, AND FATE OF BREAST CANCER

Professor Anne-Lise Børresen-Dale, SWISS BRIDGE AWARD 2004



In a project headed by Professor Anne-Lise Børresen-Dale, Department of Genetics, Institute for Cancer Research, Radiumhospitalet, Oslo University Hospital, she and her colleagues (see picture; Børresen-Dale [in the middle] with the two co-PIs V.N. Kristensen to the right and T. Sørli to the left) have demonstrated that breast cancers, at the molecular level, are many different diseases that behave differently and have various re-

sponse to the same therapy. With the project funded by SWISS BRIDGE during 2005–2007, they have been able to demonstrate that the patient's own genotype, the genetic make-up, influences both the risk to develop a certain subtype of breast cancer and how the tumour further develops. Advanced molecular analyses are expensive, but with the support from SWISS BRIDGE they were able to perform large-scale analyses at several molecular levels of tumours from hundreds of patients. The data derived from these analyses was then compared to the patient's own genotype, and the first markers that point to a higher risk of developing certain types of breast tumours were identified. These findings have paved the way for better understanding and estimation of breast cancer risk and development, and for more accurate diagnosis. This will hopefully lead to more personalised treatment by tailoring the therapy to subgroups that will improve drug response and patient prognosis.



Key publications from the project:

Kristensen, V. N., et al.: Genetic variation in putative regulatory loci controlling gene expression in breast cancer. PNAS, 103 (20): 7735–7740, 2006.

Naume, B, et al.: Presence of bone marrow micrometastasis is associated with different recurrence risk within molecular subtypes of breast cancer. Mol. Oncol. 1: 160–171, 2007.

Nordgard, S.H., et al.: Genes harbouring susceptibility SNPs are differentially expressed in the breast cancer subtypes. Breast Cancer Res. 9 (6): 113, 2007.

Dumeaux, V, et al.: Gene expression analyses in breast cancer epidemiology: the Norwegian women and cancer postgenome cohort study. Breast Cancer Res. 2008 Feb 13, 10 (1): R13.

Rønneberg, J.A, et al.: GSTP1 promoter haplotypes affect DNA methylation levels and promoter activity in breast carcinomas. Cancer Res. 68 (14): 5562–5571, 2008.

Nordgard, S.H., et al.: Genome wide analysis identifies 16q deletion associated with survival, molecular subtypes, mRNA expression, and germline haplotypes in breast cancer patients. Genes, Chromosomes and Cancer 47 (8): 680–696, 2008.

Kristensen, V.N., and Børresen-Dale, A.-L.: SNPs associated with molecular subtypes of breast cancer: On the usefulness of stratified Genome-wide Association Studies (GWAS) in the identification of novel susceptibility loci. Mol. Oncol. 2: 12–15, 2008

THE EPIGENOME OF THE VIRUSES ASSOCIATED WITH HUMAN CANCER

Dr. Manel Esteller, Director, Cancer Epigenetics and Biology Program (PEBC), SWISS BRIDGE AWARD 2006, Barcelona, mesteller@iconcologia.net

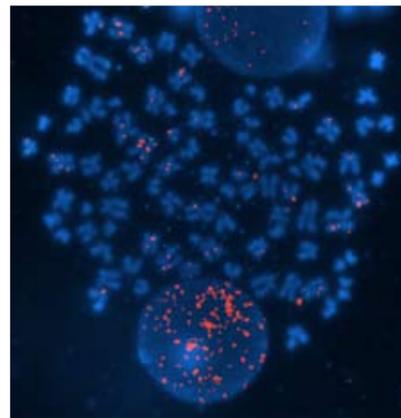
Epigenetics encompasses a large number of mechanisms, underlying embryonic development, differentiation, and cell identity including DNA methylation and histone modifications, and is increasingly recognised as being involved in human diseases such as cancer and imprinting disorders, among others. For the first time, it is possible to define whole epigenomes, which represent all epigenetic marks in a given cell type, thanks to the development of new powerful genomic technologies. In contrast to the human genome, human epigenomes vary between tissues, among individuals, and between healthy and disease states.



Under these circumstances, distinct epigenomes might explain why the same genetics can generate different features and diseases as occurs in monozygotic twins.

Determining the complete DNA methylome entails the description of all the methylated nucleotides in an organism. We decided to obtain the complete DNA methylomes of double-stranded DNA viruses associated with human cancer. The chosen option recalls the U.S. Department of Energy's establishment in

1994 of the Microbial Genome Program as a companion to its Human Genome Program. From the very start, the MGP achieved remarkable success, and microbial genomics has become one of the most exciting and high-profile fields in biology today. Thus, the complete description of the DNA methylomes of



model organisms, such as double-stranded DNA viruses, might have an enormous impact on the success of the human epigenome project.

Worldwide, it has been estimated that viral infections are etiologically linked to 15% of cancer cases, accounting for nearly 1.5 million new cases and 1,000,000 deaths annually. Three well-studied oncogenic viruses are the human papilloma virus (HPV), the hepatitis B virus (HBV) and the Epstein-Barr virus (EBV). All of these are double-stranded DNA viruses, that are not only involved in the development of infectious diseases (such as infectious mononucleosis and hepatitis), but also in the formation of cervical, liver and nasopharyngeal tumours and lymphomas, respectively. We have obtained the DNA methylomes of the HPV 16, HPV 18, HBV and analysed the dynamic changes in the viral DNA methylome and their functional relevance in the natural history of the disease.

One of the main findings of our study is the progressive increase in the DNA methylation content in these viruses from asymptomatic carriers, through benign lesions and premalignant disease, to full-blown human tumours. One particularly interesting possibility is that DNA methylation might be a device to camouflage the virus from our immune system. Most interestingly, the use of clinically approved DNA demethylating agents for the treatment of hematological malignancies, in addition to restore the expression of epigenetically silenced tumour suppressor genes of the host cell, might also reactivate the immune response, thereby enhancing its therapeutic benefits.

These issues go beyond basic research and might have a great impact in public health, since many millions of people in the world are carriers of these viruses. The potential clinical applications of these findings include the non-invasive detection of methylated viral genome in biological fluids, serum and blood. Above



all, the DNA methylomes obtained here, although owned by very small organisms, could be an excellent starting point for launching ultra-deep sequencing projects aimed at the complete description of the human DNA methylome, in a similar way to which microbial genomes stimulated the race to derive the human genome. Our viral DNA methylomes, in this regard, could be an excellent proof of principle for the successful completion of ongoing human epigenome projects.

GLIOMA CANCER STEM CELL SELF-RENEWAL

A. Ruiz i Altaba, University of Geneva Medical School, SWISS BRIDGE AWARD 2007



The SWISS BRIDGE AWARD has given us the freedom to pursue critical ideas and analyses on cancer stem cells. Specifically, it has allowed us to develop an in vivo competition assay to test for the behaviour of cancer stem cells in vivo. This is critical to understand how such cells, which are thought to be responsible for recurrence and metastases, act and therefore how one may go about to identify them and kill them in patients. Focusing mostly on glioblastoma multiforme, we have developed such "red/green assays" using cells purified from human patient samples.

These are transduced with lentivectors expressing green or red fluorescent proteins plus any gene or blocking construct we desire so as to manipulate specific activities in the recipient cells. Cells are then mixed with control untransduced

cells and injected orthotopically into the brains of immunocompromised mice, which allow the growth of the human cancerous cells. In vivo imaging allows us to follow the fate of cells and to quantify the introduced cell populations. These behave as if they were in the brain of the patient, grow, invade healthy regions and cause devastating disease.

Results so far indicate confirm the essential role of the HEDGEHOG-GLI1 pathway in the survival and maintenance of glioma cancer stem cells, supporting our previous findings (Clement et al., 2007), and setting the stage for novel discoveries. We are convinced that this exquisite assay and imaging will allow us to dissect the mechanisms of cancer stem cell self-renewal. Such results will surely provide new therapeutic avenues for so far incurable cancers.



FOUNDATION BIOBANK-SUISSE

The foundation biobank-suisse is a network of biobanks in Switzerland. It will allow getting a quick overview of the available biospecimens and data for research.

Biobanks became more and more important in recent years. New techniques allow analysing large quantities of samples and data in a short period of time. A single biobank is usually too small for such a task. The answer to this problem is networking between biobanks. A pattern of biobank networks is developing in many European countries and ultimately

linking of national or regional biobank networks at a European level will lead to the infrastructure so desperately needed.

The biggest issue we are facing is the different structures of the different biobanks. This is asking for an individual approach. The same applies for the different ethical, legal and social issues.

Informed consent is probably the most critical issue we already identified earlier. Therefore we together with the data protection managers of the canton Zurich and Basel City and the Swiss Academy of Medical Sciences initiated a task force which is proposing a draft for the text for the informed consent.

We also started to participate at different congresses with our own booth. The premier was the annual meeting of USGEB (Union of the Swiss Societies for Experimental Biology) (picture). It was a big success and the participating researchers appreciated the idea of the foundation biobank-suisse very much. This congress and others which will follow are important to meet with researchers and to better get to know their needs. We are grateful for the significant donations of SWISS BRIDGE for the foundation biobank-suisse.

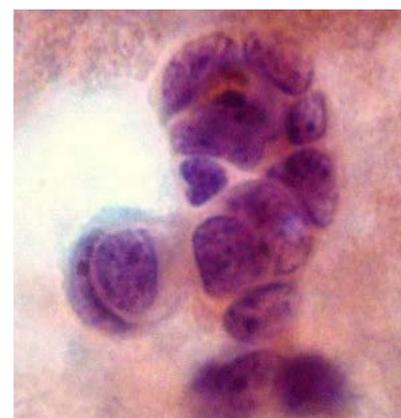


INSTITUTO NACIONAL DE CÂNCER (INCA) IN RIO DE JANEIRO (BRAZIL)

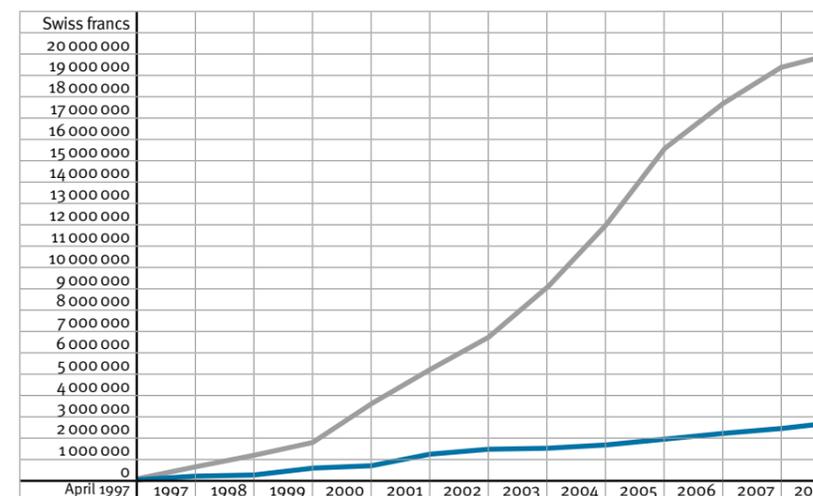
Over the past six years, SWISS BRIDGE has made substantial contributions to INCA to carry out the following projects:

- establishment of a national tumour and DNA bank in Brazil.
- gene expression profiling studies in Brazilian cancer patients.
- molecular heterogeneity of leukaemia and lymphomas.
- molecular markers and environmental interaction in the study of pathogenesis of childhood leukaemia in Brazil.

When the Chairman of our Scientific Committee visited the research team in Rio de Janeiro, he reported: "In summary, this group at INCA gets better and better, partly reflecting SWISS BRIDGE investment, and the reward in terms of scientific outcome is more than satisfactory."



COST/DONATION COMPARISON



■ Cumulated direct and indirect donations (including supporters and friends)

■ Cumulated costs of PR work and administration

Supporter and Friends of the Foundation

The costs for administration and public relation (including fundraising costs) have been born over the past 11 years by the Circle of Supporters and Friends of the Foundation.

This circle meets annually for the SWISS BRIDGE golf trophy, which in 2009 will take place in Lipperswil on 25th September. Interested golfers are invited to register under www.swissbridge.ch or at the address mentioned in page 4 herein.

Designated donations

Some of the donors, who have committed larger sums, have designated their contribution to specific institutions of their choice. With the approval of the Scientific Committee, projects in England, Italy, Brazil and Switzerland were supported.

Non-designated donations

Many donors entrust the decision for the use of funds to the Scientific Committee. By announcing the annual SWISS

BRIDGE AWARD on various electronic platforms, scientists all over Europe are invited to compete for a total of 500,000 Swiss francs prize monies annually (see page 5).

The Stammbach Chapter

For many years, the Stammbach Foundation in Basle has committed important funds to cancer research. Through the SWISS BRIDGE AWARD it has supported projects in Switzerland of highest quality without having to spend costs for a lengthy and expensive selection procedure.

Direct donations

Other foundations in Switzerland, like the above-mentioned Stammbach Foundation, have entrusted our Scientific Committee to select cancer research projects to spend their funds in accordance with the respective charter. This is a very effective way to contribute towards cancer research, profiting from a high-quality selection process at no costs. We would like to motivate other donors to make use of our outstanding scientific expertise.

Note of thanks

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