SWISS BRIDGE

INVEST IN CANCER RESEARCH WORLDWIDE

YOUR MONEY AT WORK

Bulletin September 2014

A review of projects initiated and supported over the past years

A PRECIOUS LEGACY

After 17 years of successful operations, our mission remains to collect donations from Swiss and international clients of banks and foundations in Switzerland to support cancer research worldwide.

I have decided to continue campaigning to raise more funds to fulfil our vision to «leave our descendants a precious legacy». *Thomas Hoepli*

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Various Research Projects and Partner Organisations supported

Over the past 17 years, SWISS BRIDGE has invested designated and non-designated donations of approx. CHF 27 Million in cancer research projects (including the SWISS BRIDGE AWARD).

biobank-suisse SWISS BRIDGE is a founding member of this Swiss foundation

biobank-suisse has been established in 2005 by Oncosuisse, a partner organisation of the Swiss Cancer League, Berne, and coordinates activities and operates a data-base, which allows accredited researchers a quick search for human bio-specimens (tissue and liquids) and related data, donated by patients for biomedical research. This year, the activities of biobank-suisse are integrated in a new biobank platform, as proposed by the Swiss National Fund (SNF). We see this development with pride as confirmation of a policy to pursue the establishment of a network of biobanks in Switzerland.

ecancer.org SWISS BRIDGE is a founding member of this online publishing company

In the past seven years ecancer.org has supported cancer communication and education across the globe. The website includes free news, videos, education and a peer review journal as well as a Spanish and Portuguese language equivalent for Latin America. Since launch ecancer.org has been visited by 2 million people from 193 countries. Over 10 million oncology education videos have been watched and 10,000 ecancer members have signed up.
Thousands of articles have been submitted and peer reviewed with over 350 published in the open access cancer journal, enabling all doctors, scientists, researchers and patients to access important research data. 87% of doctors who watched an ecancer video said that the information would definitely improve their clinical practice or research. Patients are directly benefiting from the education of doctors as they receive better treatment and best practice care whilst undergoing their difficult cancer journey.
ecancer is able to offer all these resources at no cost to the user due to charitable support and grants.

AGORA SWISS CANCER CENTRE LAUSANNE

SWISS BRIDGE supports two projects at the Ecole Polytéchnique Fédérale de Lausanne (EPFL) under the leadership of Prof. Douglas Hanahan, Director of the Institut Suisse de Recherche sur le Cancer (ISREC) with CHF 200’000, starting from early this year.

Overcoming resistance to targeted therapy for colon cancer
Cancers are being increasingly treated with drugs that specifically kill cancer cells while sparing normal organs. These “targeted drugs” are very selective and initially effective. Unfortunately, cancers often find ways to escape from being killed by such treatments. For example, certain forms of colon cancer can be beneficially treated with drugs that precisely target the EGFR, a molecule that promotes tumor growth. Eventually, however, treated tumors often become resistant to the drug after initially responding, resulting in relapse to disease progression.

With the support of Swiss Bridge Foundation, the De Palma and Petrova groups joined forces to develop new mouse models of colon cancer that develop resistance to anti-EGFR drugs. The new cancer models, by mimicking the clinical failures observed in cancer patients with this targeted drug, will enable testing of innovative combination therapies designed to circumvent the occurrence of drug resistance that limits clinical benefit.

SWISS BRIDGE AWARD

Over the past 14 years, CHF 7'350'000.00 was awarded to 36 research teams in nine countries. This is what beneficiaries of more recent awardees tell us:

2009 – Prof Dr Matthias Egger of the Social and Preventive Medicine at the University of Berne received CHF 200'000 for the project **«AIDS-defining cancers in Southern Africa in the Era of ART»**

Sub-Saharan Africa is the region most affected by the HIV/AIDS epidemic: 21 million adults and 2,3 million children in the region are HIV-positive. Kaposi Sarcoma develops in patients with immunodeficiency and is the most frequent cancer in HIV-positive children and adults in Southern Africa. With the support of the Swiss Bridge 2009 Award we analysed data from a large collaboration of HIV cohort studies, the International epidemiological Databases to Evaluate AIDS. We showed that about 80 % of these cancers can be prevented if patients receive antiretroviral therapy to control their underlying HIV-infection. Despite this success the remaining risk of Kaposi Sarcoma is higher that the risk for any other cancer in HIV-negative persons. More efforts are needed to identify and treat HIV-infected children and adults early on and to ensure that all patients in need of antiretroviral therapy receive it.

2009 – Prof Dr Steven C. West of the London Research Institute, Cancer Research UK, South Mimms UK received CHF 150'000 for the project **«Interplay between the cancer predisposition disorders Fanconi Anemia, Bloom's Syndrome and BRCA2 breast cancer».**

Dr West's team at the London Research Institute was awarded the prize to study how our genetic material (DNA) is protected from chemical damage, radiation, and from everyday agents in the environment. His work has defined a variety of 'DNA repair processes' that specifically recognise lesions in DNA and repair them back to normal. Importantly, his work with three cancer predisposition disorders – Fanconi anemia, Bloom's Syndrome, and breast cancers caused by mutations in the BRCA2 gene – revealed defects in these basic DNA repair processes, and he has defined the mechanisms by which cells with defective repair processes can become tumourigenic. It is expected that future efforts will lead to the development of novel therapies and/or drugs that will utilise this knowledge to kill the cancer-causing cells.

2010 – Andrea Alimonti M.D. of the Oncology Institute of Southern Switzerland, Bellinzona, received CHF 250'000 for the project **«Manipulation of senescence pathways for cancer therapy: from experimental models to clinic».**

Tumor-infiltrating myeloid cells areshown to produce interleukin-1 receptor antagonist (IL1RA), which suppresses senescence in tumour cells by interfering with the production of secreted senescence-promoting factors and impedes pro-senescence therapies in a mouse model, suggesting that interleukin-1 receptor antagonist secretion might be involved in therapeutic resistance. This is the first study to describe that senescence in cancer can be antagonize by a subset of tumor infiltrating immune cells acting in a cell non-autonomous manner. This discovery also open at the possibility that immune cells secreting IL1RA may prevent aging and that treatments that enhance IL1RA may be used for life elongation in humans, which will be the future objective of our research together with cancer. In the second paper (Cell reports) we have demonstrated that treatments that reprogram the senescence secretome in tumors can be used to enhance the efficacy of chemotherapy by activating a strong tumor immune response.

2010 – Anna Sablina Ph.D. at the University of Leuven, Belgium received CHF125'000 for the project **«the Role of the RalA signalling pathway in human cancer».**

The RAS oncogenes are mutated in about 30% of all human cancers. Mutational activation of RAS proteins results in aggressive cancers with poor prognosis and poor response to existing therapies. Currently, there is a pressing clinical need for therapies specifically for patients with RAS mutated tumors.
Here we found that the RAS proteins are reversibly modified by the attachment of a small protein called ubiquitin as well as identified enzymes controlled this modification. Notably, ubiquitination of the RAS family members dramatically affects their functioning and tumorigenic properties. The results of our studies not only advance our understanding of the RAS signaling in cancer development and progression, but also could lead to novel therapeutic strategies for RAS-mutated tumors.

2011 – Prof Shail Izraeli, MD of the Sheba Medical Center at Ramat Gan, Israel, received CHF 150'000 for the project **«from inflammation and allergy to high risk childhood leukemia – the TSLP-JAK-STAT leukemogenic pathway».**

The two major challenges in treating children with blood cancer (leukemia) are overcoming high risk leukemia and lowering short and long-term toxicity of current chemotherapy. Both of these goals can be achieved through discovery of the abnormal genes and proteins that «drive» leukemia and designing specific therapies that target these abnormalities. The research sponsored by the Swiss Bridge Foundation was based on our earlier discovery of an unusual mechanism driving childhood leukemia. We discovered that in a subtype of very high risk childhood leukemia there is a genomic mutation that leads to the expression of a cell surface molecule (called «CRLF2») that otherwise is activated in allergic reactions. This cell surface protein transmits growth and proliferation signals into the cell activating proteins called JAK and STAT. We also found mutations that turn JAK into a particularly active transmitter of this growth signal. In our research we aim at understanding how these aberrations cause leukemia. We express the mutated genes and proteins in normal human white blood cells and examine their gradual development into leukemia. This research has a potentially strong translational impact as drugs that inhibit the JAK pathway, that were originally developed for allergic and arthritic disorders, may prove to be very useful in this type of leukemias. Indeed clinical trials with these drugs are on their way.

2011 – Prof Monika Hegi PhD of the University Hospital Lausanne received CHF 175'000 for the project **«Epigenetic aberrations in low grade glioma, identification of novel therapeutic targets and biomarkers for response to treatment».**

Low grade gliomas are a difficult to treat brain tumor that affect young patients. We have obtained tumor tissues of patients treated in a randomized clinical trial, either with radiotherapy or an alkylating agent. First results have revealed that the time of progression free survival was not different between the two treatment options. Hence it is of utmost importance to determine whether patients whose tumors belong to different molecular subclasses according to our analysis differ in their sensitivity to either of the treatments.
However, there are at least 3 molecular subclasses We are currently evaluating. We have molecularly sub-classified were able to perform genome-wide DNA methylation profiling of 150 tumors form patients At present we are investigating if the molecular subtypes of low grade glioma that we have established.