## **Projects**

The projects supported financially by the foundation, in full or in co-funding, are outlined below. Please note that these outlines are in plain, non-specialist language. More detailed information and references to publications are available on request.

Last update: January 2023

## A) Cancer research and clinical studies on cancer

## Clinical study on ovarian cancer (ETH Zürich, University Zürich (UZH), University Hospital Basel (USB))

Tumor Profiler Center: Klinische Studie zu Eierstockkrebs (2022 - ongoing)

The Tumor Profiler Center collaboration seeks to obtain a more comprehensive analysis of a tumor by complementing the usual data (morphology and genetics) with data on biochemistry, molecular characterization of tumor cells, response to therapies, and evaluating this information with computer modeling in order to determine optimised therapies. The aim is to identify biomarkers which are relevant for the choice of the most effective therapy in the individual cases. The results must be verified in clinical studies.

This clinical study is focused on a cohort of ovarian cancer patients. Ovarian cancer is relatively infrequent but highly lethal. In Switzerland every year about 700 women develop this form of cancer. It does not generate specific early symptoms and in most cases it is detected when it already is at an advanced stage. The standard first line platin-based therapy is frequently followed by relapse and resistance to the drug. The currently available treatments are frequently ineffective.

The aim of the clinical study is to verify how the recommended individualised therapies, as determined by the profiler method, improve the outcome of the treatment.

The budget of the clinical study is large and a very substantial contribution is requested to private institutions. The foundation provides financial support at the level of 4% of the budget over four years.

# Project on treatment of acute lymphoblastic leukemia (ALL) (Children's Research Center - Kinderspital Zürich)

Determinants of necroptosis - an alternative cell death pathway to eliminate resistant leukemia (B. Bornhauser)
(2022 - ongoing)

There has been remarkable progress in the treatment of acute lymphoblastic leukemia (ALL), but in a considerable number of cases relapse occurs and drug resistance develops, with adverse outcome. Drug resistance is mainly due to failure of leukemia cells to activate apoptosis (programmed cell death mechanism). The research team has found that an alternative mechanism (necroptosis) can be triggered in specific ALL drug resistant cases. The aim of this project is to identify the biological, molecular and genetic factors that drive the necroptotic mechanism, and therapeutic agents that may enhance the response, for implementation in clinical treatment.

The foundation provides financial support at the level of approximately 30% of the overall project budget over three years.

#### TAXIS international phase-III trial (Basel University Hospital)

Tailored axillary surgery with or without axillary lymph node dissection followed by radiotherapy in patients with clinically node-positive breast cancer (TAXIS). A multicenter randomized phase III trial (Walter P. Weber).

(2021 - ongoing)

Complete lymph node removal through conventional axillary dissection has been the standard treatment for breast cancer patients for a long time. This radical intervention can induce long-lasting heavy side-effects such as pains and limitations in movements. The aim of the TAXIS trial, an international collaboration led by Prof. Weber at the Basel University Hospital, is to evaluate the treatment based on tailored axillary surgery in conjunction with radiotherapy, which could assure an optimal effectiveness without the side effects of the conventional treatment. The foundation provides financial support over three years for an amount that that covers the cost of treatment of the patients recruited in Switzerland.

# Project on radiation therapy quality improvement program (RTQA) (University Hospital Zurich)

Clinical Trials associated Radiation Therapy Quality Improvement Program for a prospective randomized trial on high-precision radiosurgery for brain metastases conducted by the Comprehensive Cancer Center Zurich (N. Andratschke)

(2021 - ongoing)

Brain metastases that appear in conjunction with various types of cancer are generally treated with stereotactic radiosurgery, the timing of which is controversial. The Comprehensive Cancer Center Zurich (CCCZ) is initiating a randomized phase III clinical trial to address this issue. Currently however there are no agreed radiotherapy quality assurance (RTQA) standards for high-precision brain radiosurgery within clinical trials. This project aims at implementing an RTQA strategy within the CCCZ trial and eventually to transfer modern quality standards into clinical routine practice. The foundation provides financial support at the level of 22% of the overall project budget over two years.

### **Project on circulating tumor cells (Basel University and University Hospital)**

Three-dimensional culture of circulating tumor cells on a microchip technology to enable real-time personalized drug screening (F. Schwab) (2019 - 2020)

The study is conducted by Dr Fabienne Schwab, Basel Unispital (USB) in the frame of a translational research project led by Prof. N. Aceto at the Basel University. The aim of the study is to single out and analyse the tumor cells circulating in the blood (CTC) in order to investigate the biology and formation of metastases.

The CTCs are detected and isolated using microfluidic technologies. The sequencing of the genome allows to gain insight in the metastasis formation process. The effects of different medicaments can then be investigated on ex vivo cultures of CTCs with the aim of developing effective personalized therapies.

In this study, a microchip of novel conception is developed so as to integrate the culture of CTCs and the study of medicaments in vitro.

The most recent published article can be found at the link:

https://www.nature.com/articles/s41378-022-00467-y

#### Project on photodynamic therapy for cancer (EPFL - Lausanne)

Combined use of exogenous agents and photobiomodulation to improve cancer photodynamic therapy with protoporphyrin IX (G. Wagnières) (2019 - 2020)

Photodynamic therapy (PDT) is a technique to detect and treat tumor lesions with the help of photosensitizers (PS). The PS are chemical substances that concentrate in tumoral tissues and become toxic when exposed to light, thereby killing the tumoral cells. PDT is unfortunately not always effective because the photosensitizer is often produced in insufficient quantity and is not homogeneous.

The aim of this project, led by Dr. G. Wagnières in the functional and metabolic imaging laboratory at the EPFL, is to develop a novel method to increase the quantity and homogeneity of the endogenous production of a particular photosensitizer in tumor cells by means of photobiomodulation (PBM). This consists in exposing the tumor tissues to specific doses of near infrared, non thermal radiation so as to stimulate the cell metabolism and correspondingly the production of photosensitizer.

The results are reported in an article submitted for publication.

## Project PEINCA (University of Basel (Institut für Pflegewissenschaft), Inselspital Bern, Triemlispital Zürich)

Studie zum Testen der Wirksamkeit des deutschsprachigen PRO-SELF© Plus Pain Control Program, einer Intervention für Patienten und Patientinnen mit fortgeschrittenen Krebserkrankungen und ihre Angehörigen zur Reduktion von Schmerzen und damit zusammenhängenden Beschwerden (E. Spichiger, R. Spirig, K. Zaugg)

(2015 - 2019)

Pain is unfortunately a continuous and often unbearable presence for patients with cancer in an advanced stage. It is a source of suffering for the patients and their relatives. To improve the quality of life, one needs an effective method to choose the type and dosage of the pain relief drugs.

The aim of the PEINCA project is to assess the efficacy of the PRO-SELF© Plus Pain Control Program in reducing pain and related symptoms, by adapting it to German-speaking cancer outpatients and their family caregivers.

The project has been completed in December 2019. The number of patients who participated was smaller than anticipated, but those patients engaged themselves actively in the study. One of the main results of the study was that the group of patients who applied the PRO-SELF Plus PCP method reported a substantial reduction of the pain on average. The daily logbook of the perceived pain was found to be very useful and effective for optimizing the treatment and the dosage under control of the medical and nursing staff. The authors of the study have recommended that the pain control program be adopted in the standard clinical praxis.

The study has been the subject of a doctoral thesis and of publications in scientific journals.

#### Project on prostate cancer (Department of clinical research (DKF), Uni Bern)

Towards a precision therapy for mutant prostate cancer (Mark A. Rubin) (2017 - 2018)

Certain forms of prostate cancer are defined through an early mutation in a gene called SPOP. These mutations enable the tumor cells to grow by activating two different critical pathways. The aim of the project is to investigate these processes.

The study will use cells from a mouse model system and the gene editing "scissors" CRISPR-cas9.

The researchers hope to obtain a deeper understanding of the SPOP mutant prostate cancer and to put forward a strategy for a precision therapy for the patients concerned.

This project is supported by Krebsforschung Schweiz (KLS-4102-02-17)

### Project RIPK3 (Institute of experimental immunology, University of Zurich)

The role of RIPK3 in tumor formation and metastasis (W. Wong) (2015 - 2017)

RIPK3 is a specific protein that influences the secretion of many cytokines, chemical messengers that can modify the immune system and the surrounding cells, facilitating the development of tumors and the formation of metastases.

The team of researchers at Uni Zurich investigates the role of the specific RIPK3 protein, which regulates the production of several cytokines. The study has in particular been focused on the role of RIPK3 on the formation of tumor nodules in the lungs.

The findings have been published in the scientific journal "Nature / Cell Death and Disease"

This research project was supported by Krebsforschung Schweiz (KFS 3386-02-2014).

#### Project at the Proton Therapy Center at Paul Scherrer Institut (PSI), Villigen

Development of a treatment verification system for continuous scanning in proton therapy (D. Meer, G. Klimpki) (2014 - 2018)

The Center for Proton Therapy at PSI is a long-standing leader in the field, having in particular developed the isocentric arm irradiation facility (Gantry) and pioneered the Spot-Scanning technique since the early 90's. This technique is used to irradiate with high precision deep-seated tumors that would otherwise be untreatable, while preserving at best the healthy areas at the boundary with the tumor.

Certain tumors are localized in organs that may move during the irradiation, because of breathing or muscular contractions, such as lungs, breast and liver for example. In order to assure the required precision in the proton beam position and delivered radiation dose in these cases, and reduce the irradiation times, the Proton therapy center at PSI developed the Continuous Scanning technique.

The aim of this project, for which the Foundation has co-funded a PhD researcher, is to develop a verification system to monitor the proton beam in continuous scanning mode (energy, intensity, position). Precision, speed, safety and reliability are key issues.

The development of the new system has been completed in the first half of 2018. The system has been installed and tested and is now ready to become operational in Gantry 2.

The PhD thesis report is available at the link:

https://www.research-collection.ethz.ch/handle/20.500.11850/258251

### **Project at the Institute for Molecular Cancer Research (IMCR, University of Zurich)**

*Identification of germline mutations in families with predisposition to prostate cancer (J. Jiricny, G. Marra)* (2013 - 2021)

The aim of this research project is to investigate the heritable mutations that might cause the predisposition to prostate cancer in two families with twins. The identification of the mutations would be of great importance in the planning of preventive strategies in the offspring and, hopefully, also in many other families in the future.

The genetic samples from different members in the family pedigrees were analyzed using the next generation DNA sequencing of exome and genome. Following a preliminary data analysis at IMCR, a collaboration was established in 2015 with the project IMPACT in the UK which is active in this field and disposes of a much larger number of bioinformaticians.

The in-depth analysis showed the presence, in one family pedigree and through all generations, of a variant of a little known mutation that could be the cause, or one of the causes, of the predisposition to prostate cancer.

This finding was inserted in the international reference databases in order to determine if other occurrences of this mutation were observed and reported.

In October 2016 a collaboration was established with a research laboratory in the Netherlands with acknowledged expertise in studies in vitro of this type of cell samples. In 2017 the results of the study confirmed that this mutation variant is indeed pathogenic.

In 2018 the study was extended to tumor cell samples under paraffin of some family members deceased since about a decade. These studies have been found to be technically very challenging and have been continued in 2019 and 2020. The final results have been reported in an article published in February 2022 that can be found at the link:

https://aacrjournals.org/cancerres/article/82/4/615/678076/Functional-Analysis-Identifies-Damaging-CHEK2

The main finding of this investigation, namely that the specific mutation variant is indeed pathogenic, has been conveyed through the appropriate channels to the members of the family, whose identity is of course unknown to the foundation.

### **B) Visual Arts**

### Project "Maria Netter" - Swiss Institute for Art Research (SIK-ISEA, Zurich)

Übernahme des fotografischen Nachlasses der Basler Kunstkritikerin Maria Netter (1917-1982) (M. Oberlin, S. Noseda)

(2014 - 2017)

Maria Netter was a prominent Swiss art critic in the years 1944 to 1982. Her photographic archive is of exceptional interest for the knowledge of the artistic activities and its protagonists in Switzerland in that period. The collection consists of about 1'500 b/w negative films for a total of more than 50'000 pictures as well as excerpts from magazines.

This material has been processed following a scientific methodology (protection, inventarisation, digitalisation and conservation).

An inventory has been made. Individual films have been entered in the general database of SIK-ISEA with meta-data, i.e. date, people, places etc. A selection of 600 pictures has been analysed and the corresponding negatives have been digitized at high resolution. A dedicated domain has been reserved and a dedicated website with many interactive features has been developed.

On 01.03.2017 SIK-ISEA organised a podium panel to present the project to the researchers and the public and opened the access to the website.

The link to the website is:

https://www.maria-netter.ch/content.aspx

## C) Classical Music

Grants to students of Swiss Conservatories and Academies of Music (Conservatoires, Hautes écoles de musique, Musikhochschulen)

(2014 - ongoing)

The foundation supports talented students at Master level in the Conservatories and Academies with grants that cover the cost of tuition fees for one or two semesters (based on the current tariffs in Switzerland).

# Piano competition for the students of the "Confédération des écoles genevoises de musique (CEGM)"

(2013 - 2015)

The CEGM consists of two conservatories and one institute. The Foundation has organized this competition in three successive years. The auditions and the concerts of the prize winners have been hosted in turn by the three music schools.