

# Projects

The projects supported financially by the foundation, in full or in co-funding, are outlined below. The outlines can be abstracts from the cover letter and/or from the proposal, or condensed summaries in plain, non-specialist language. A translation from the original language is provided when possible. Only the names of the institutes and the names of the project leaders are shown, the academic titles and other details are left out.

More information is available on request.

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## Cancer research and clinical studies on cancer

### *Liquid biopsy of CTCs on microchip (ETH Zurich)*

**Breast cancer - Circulating tumor cells (CTC) liquid biopsy on microchip (N. Aceto)**  
(2026 - 2028)

#### Abstract from the proposal

Metastases are responsible for more than 90% of cancer-related deaths. These metastases arise from so-called circulating tumor cells (CTCs), which spread through the body via the bloodstream. In breast cancer, a high number of CTCs is demonstrably associated with a worse prognosis. CTCs occur as single cells or as multicellular clusters, with the latter showing a heightened ability to successfully colonize other organs and form metastases. Multicellular clusters can be either homotypic—consisting exclusively of cancer cells—or heterotypic, in which cancer cells interact with CD45-positive immune cells.

Within this diversity of CTCs, only a small fraction can survive in the blood and form secondary tumors. The processes that regulate CTC survival and metastasis formation are still largely unclear.

Groundbreaking studies from Professor Nicola Aceto's laboratory at ETH Zurich demonstrated that the entry of CTCs into the bloodstream, so-called intravasation, depends on the circadian rhythm, which in turn is regulated by hormones such as melatonin or glucocorticoids. Accordingly, the highest release of CTCs occurs during sleep.

Other studies from different research groups have shown links between nutrition and both survival and quality of life in breast cancer patients and other cancer patients. For example, a meta-analysis revealed that a high-fat diet is a potential risk factor for breast cancer. Conversely, new evidence suggests that fasting could improve patients' quality of life through various biological mechanisms. Fasting is among the most extensively studied dietary interventions in oncology.

However, it remains unclear how fasting is linked to CTC intravasation and metastasis, and which factors play a key role in this relationship. What is known, however, is that fasting has a significant impact on the concentration of hormones, such as glucocorticoids, which rise strongly during fasting. Since glucocorticoids in turn suppress the release of CTCs, fasting could therefore reduce CTC intravasation.

The aim of this project is to establish a link between time-restricted dietary interventions and metastasis. As a result, dietary recommendations should be identified that reduce CTC formation in breast cancer and thereby improve the survival rate of breast cancer patients by delaying or even preventing metastasis.

In addition, molecular characterization and CRISPR-based interventions are planned to identify and validate the components responsible for the effectiveness of time-restricted fasting.

***ProBioCH - Clinical research project on prostate cancer in patients in Switzerland  
(Universitätsspital Zürich (USZ))***

**ProBioCH: An outcome-adaptive and randomized multi-arm biomarker driven study in patients with metastatic prostate cancer (A. Mortezaei)**  
(2026 - 2028)

Abstract from the cover letter

A wide range of new medications is now available for the treatment of metastatic prostate cancer. These therapies target the cancer in very different ways. However, it remains unclear which man will respond best—or not at all—to which drug, as this depends on the tumor's biology and cannot currently be predicted in advance. In approval trials, pharmaceutical companies typically do not conduct such detailed biological investigations or stratify patients accordingly. If a drug shows effectiveness in the general population, it is approved without restriction. We also lack reliable information about how each therapy affects patients' quality of life, as no comparative studies between individual treatments exist.

With ProBio—an investigator-initiated, academic study—we aim to address these important questions that matter greatly to clinicians and patients but have received low priority from the pharmaceutical industry.

To gain insights into tumor biology, we do not collect tissue samples from the tumor itself. Instead, we analyze fragments of cancer DNA (ctDNA) found in the blood of men with metastatic prostate cancer—a method known as liquid biopsy. This approach is not only less invasive and burdensome for patients (no need for needle biopsies), but also more representative of cancer cells that may be spread throughout the body. In preliminary studies, we have already demonstrated the validity of our method.

Based on the specific genetic alterations identified in a patient's cancer, we tailor the therapy accordingly. In the case of specific genetic alterations, we can use medications that target the tumor very precisely. Participants are followed over several years, during which we repeat tumor analyses and determine which combinations of tumor biology and therapy most effectively prolong life and best preserve quality of life.

The ProBio study was launched in Sweden in 2019. After a pause during the pandemic, it has now been active for about three years and has enrolled nearly 1000 patients. Following Belgium (2021) and Norway (2022), Switzerland joined the consortium in 2022, supported by the Cancer League of Basel, the Swiss Cancer League, and the University Hospital Basel. This initial funding enabled us to carry out the analyses at University Hospital Basel and Claraspital, and to include patients from these sites in the study. Soon, the Cantonal Hospital of Aarau will also join ProBio.

There are two compelling reasons why this study is especially significant to Switzerland. First, the frequency of genetic alterations may vary between populations. Including Swiss men in this study enables us to validate the concept directly within a Central European population, yielding valuable insights for future treatment strategies—even beyond the scope of this trial. Second, participants in the study benefit directly from the tumor analysis and adaptive treatment assignment (adaptive randomization, targeted therapies). ProBio has the potential to fundamentally improve the global standard of care for metastatic prostate cancer.

***Project on treatment of acute lymphoblastic leukemia (ALL) - Phase 2 (Children's Research Center - Kinderspital Zürich)***

**Leveraging necroptosis to augment immunotherapy (B. Bornhauser)**  
(2025 - 2027)

Acute lymphoblastic leukemia (ALL) is the most common childhood malignancy. Current treatment mainly relies on multiagent chemotherapy with an overall survival rate of almost 90% in children. However, 15-20% of pediatric patients and around 30-40% of young adult patients respond poorly to initial chemotherapy, will relapse or remain refractory to primary treatment. The outcome for these patients is poor.

One of the important contributing factors is the failure to mount a decent programmed cell death (apoptosis) response in leukemia cells. On the basis of our earlier identification of a specific vulnerability of leukemia cells to undergo necroptosis, an alternative cell death mechanism, we formulate that due to the potential immunogenic nature of this cell death response we may be able to increase immune responses by activation of this recently identified pathway. In the previous funding period, we could identify the role of transcriptional regulation in this necroptosis response, which identifies among others also secreted factors to be potentially relevant for such an immune system triggering response.

In this project we aim to identify the immunogenic potential of necroptosis and to derive strategies to prime leukemia cells for programmed cell death upon CAR T-cell therapy. The idea is to construct therapy combinations that eliminate residual leukemia cells to avoid relapse and increase therapeutic efficiency.

We estimate that findings that we will gain in this project will also be of relevance for other tumor entities (expanding towards solid tumors), which can also be driven into non-apoptotic but necroptotic cell death phenotypes.

***In vivo study of a therapeutic target for preventing aging-related diseases and cancer (Hôpitaux Universitaires de Genève (HUG))***

**In Vivo Validation of a hairpin structure within HuR mRNA as a Therapeutic Target to Prevent Aging and Cancer (R. Mérat)**

(2025 - 2027)

The accumulation of senescent cells in the body is increasingly seen as one of the tissue-level mechanisms linking aging and cancer. These senescent cells, durably arrested in their cell-division cycle, no longer contribute optimally to tissue repair. They can also disrupt the tissue microenvironment by making it inflammatory, which promotes the emergence of cancers. By contrast, cells that are able to “reset” support tissue regeneration and are less likely to become cancerous.

Our project tests a strategy aimed at limiting the accumulation of senescent cells by preventing, within senescent cells, the deregulation of a key protein called HuR. HuR acts as a central regulator coordinating many processes closely linked to senescence, including cell proliferation, DNA repair, the inflammatory response, and tissue regeneration. In preliminary work using cells grown in the laboratory, we used gene editing to target a regulatory structure located at one end of HuR messenger RNA (mRNA). Eliminating this structure made it possible to maintain the “youthful” regulation of HuR and thereby delay cellular senescence while improving essential cellular functions such as DNA repair.

We are now evaluating this potential therapeutic approach in vivo in mice. In genetically modified mice designed to mimic the regulatory effect that could potentially be achieved with drugs, we either abolished or enhanced the formation of the candidate mRNA structure. In this way, we will be able to test whether preventing HuR deregulation, as it occurs in senescent cells, can slow biological aging and reduce associated pathologies, notably cancer, which is a major cause of mortality in the chosen mouse model. The study has been approved by the Geneva ethics committee for animal experimentation and could help develop new preventive strategies for aging-related diseases, particularly malignancies.

***RNA Therapeutic in colorectal cancer - Study with patient derived organoids (Unispital and Inselspital Bern)***

**RCALI-RNATX: CASC19 and LINC00460 as Emerging RNA Therapeutics in Advanced Colorectal Cancer Therapy (R. Esposito)**

(2025 - 2027)

Colorectal cancer (CRC) remains the third leading cause of cancer deaths worldwide. In the advanced stages of the disease, KRAS- and BRAF-mutations, in particular, correlate with a poorer prognosis. Current therapeutic strategies offer limited benefits for CRC patients with these mutations.

RNA therapeutics offer a route to effective, low-toxicity precision medicine, employing antisense oligonucleotide (ASO) inhibitors. Previous cancer research has mainly focused on protein coding gene networks. This project aims at designing new ASOs targeting long non-coding RNAs classes, where promising new RNA-based targets for CRC therapies have been found.

In view of the importance of developing therapies within an environment mirroring the in vivo disease, the project will leverage patient-derived tumor organoids, which offer a unique and clinically relevant platform for pre-clinical drug testing.

The methods developed in this project have also the potential to reveal novel RNA therapeutics against advanced CRC, that can be explored also in other cancer types.

***Tumor Profiler Center - Clinical study on ovarian cancer (ETH Zürich, University Zürich (UZH), University Hospital Basel (USB))***

**Tumor Profiler Center: Klinische Studie zu Eierstockkrebs (B. Bodenmiller, V. Heinzelmann-Schwarz, A. Wicki)**

(2022 - 2025)

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 - 2024)

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 - 2023)

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 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 - 2022)

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.

***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.

# Visual Arts

*Project “Maria Netter” - Swiss Institute for Art Research (SIK-ISEA, Zurich)*

**Übernahme des fotografischen Nachlasses der Basler Kunstkritikerin Maria Netter (1917-1982) (S. Nosedà)**

(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.sik-isea.ch/en-us/Art-Archives-Library/Art-Archives/Fonds-Collection/Virtual-Showcases/Detail/content/2586>