Cancer Research in Switzerland

A publication of the Swiss Cancer Research foundation,
the Swiss Cancer League and the cantonal cancer leagues
on their funded research projects
Edition 2016

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Daniel Zahner (*1953 in St.Gallen), who gained his first design experience as an assistant stage designer, has now worked as an artist for over 30 years. He lives and works in Biel.

In his works featured in this report, Zahner highlights structures and patterns that he observed on the banks of Lake Biel and in a remote forest area in Sugiez. His photographs are snapshots of processes that are a part of growth and decay in nature.

The fact that these images are the result of Zahner's great patience and perseverance is something you only see at second glance. In that way they resemble the work of many cancer researchers.

danielzahner.ch

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Editorial

What once began as a letter asking for donations is today a foundation with a 25-year history – and an annual budget of almost 20 million francs. The unusual success story of the Swiss Cancer Research foundation begins in 1991. At that time, three million francs came together for research funding. That amount has since more than quintupled.

Because research embodies hope, cancer research is well suited for raising money through donations. And even if the increase in funding has grown constantly over the years, the goals of the foundation have remained unchanged: to use the monies collected to fund the best projects in all areas of cancer research.

Over the years, the number of grant applications submitted has risen. At first, about 50 applications were received each year. Today, researchers submit about 200 project proposals, which together would cost about 60 million francs. However, the Swiss Cancer Research foundation can fund only about one third of these projects. This makes it all the more important that the applications are evaluated carefully and only the most convincing proposals are funded. For the review of the project proposals the foundation relies on the Scientific Committee: Made up of recognized experts, it also regularly calls in international specialists for discussion and evaluation of the grant applications.

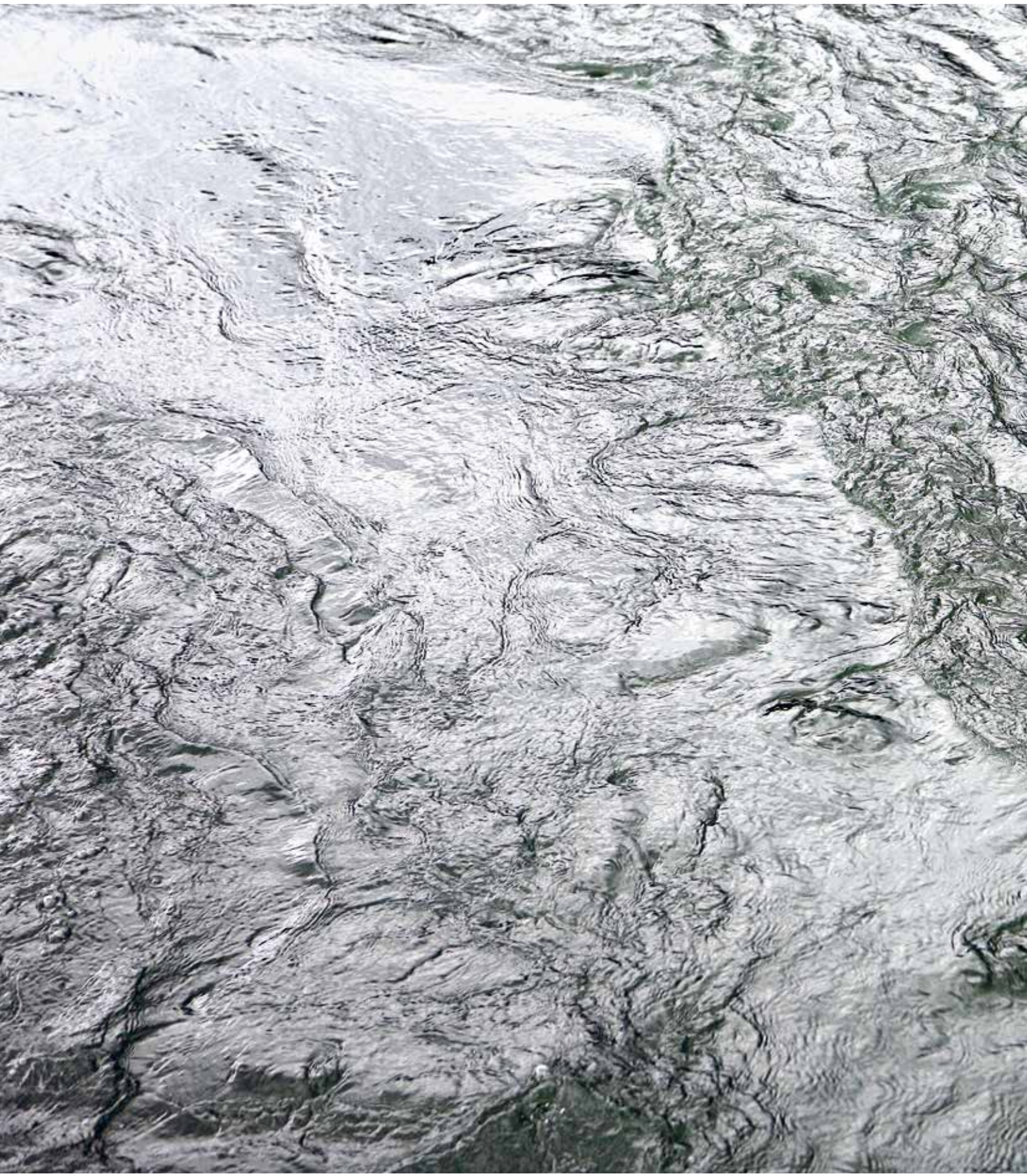
Thomas Cerny

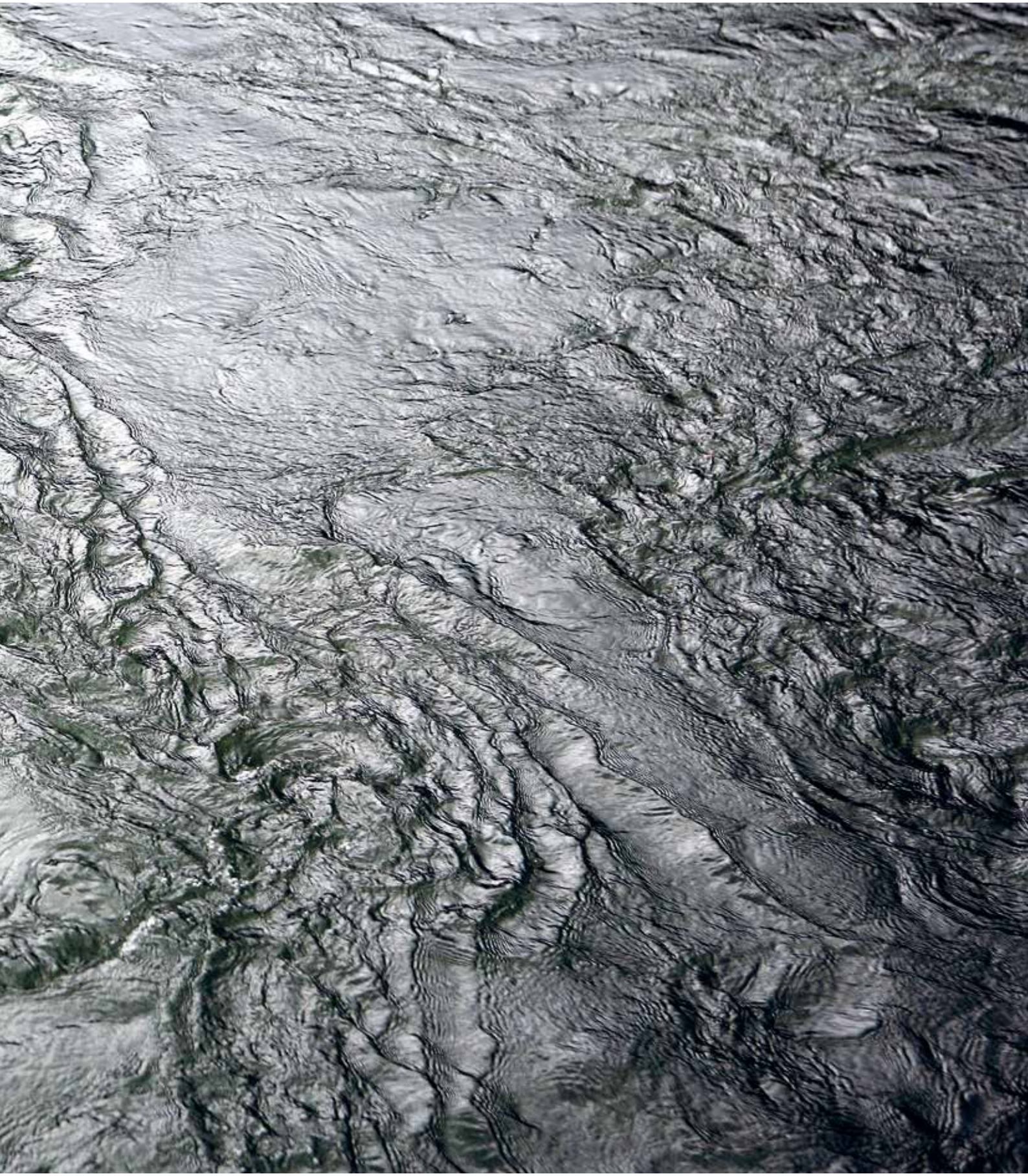
Jakob R. Passweg

In the past 25 years, the Swiss Cancer Research foundation has given a total of almost 200 million francs to approximately 1000 research projects. With this, it has contributed to countless research findings that have made numerous successes in the fight against cancer possible. Thanks to close cooperation with the partner organization Swiss Cancer League, which takes on some tasks compensated through service level agreements, the Swiss Cancer Research foundation makes do with very lean structures: This allows the foundation to steer an even greater percentage of the donations to research projects – and in this way to nourish the hope that important progress in treating and fighting cancer will continue to be made in the future.

Prof. Thomas Cerny, MD
President of the Swiss Cancer Research foundation

Prof. Jakob R. Passweg, MD
President of the Swiss Cancer League





Research: A beacon of hope

Together, the Swiss Cancer Research foundation (SCR), the Swiss Cancer League (SCL), and 10 cantonal cancer leagues (CCL) gave 22.6 million francs in funding to non-commercial cancer research in Switzerland in 2015. After careful review of all 191 research proposals submitted, the 56 best and most promising projects were funded. They raise hope that progress will continue to be made in treating and fighting cancer. We thank all of the charitable donors for their trust and support.

Despite worldwide and intensive research efforts, mankind has not yet conquered cancer. Although thanks to numerous discoveries and advances, for many persons cancer no longer ends in death and can be seen instead as a chronic illness, cancer is still the disease that in Switzerland takes the greatest toll on productive years of life. Continued efforts in oncology are therefore needed. Research is and remains the brightest beacon of hope in the fight against cancer. And even though the partner organizations support a great variety of different research projects, the goal of the funded projects can be brought down to a common denominator: the aim to improve survival rates and quality of life for patients with cancer.

Chain reaction

Funding research sets off a chain reaction: Research findings cross-fertilize and draw from each other. Newly gained insights mostly build on previously acquired knowledge. The metaphor of "dwarfs standing on the shoulders of giants" and discovering new horizons goes as far back as the Middle Ages. But it is all the more true today. Even if the advances achieved within single research studies are mostly only small, the successes become very visible when we see how far those many small steps have brought us over a longer period of time. One of the most impressive examples is leukaemia in children: Only 50 years ago, this cancer of the blood cells meant certain death; medicine was simply powerless against the disease. Today, approximately four out of five children with leukaemia can be saved. But for research, the story is not yet over. Are there ways to help the young patients for whom today's treatment methods fail? Several ongoing research studies, such as Jean-Pierre Bourquin's project at University Children's Hospital Zurich, are seeking answers to this question, and it is hoped that they will soon continue the success story.

But beyond generating new knowledge, the funding of research also plays an important role in the functioning of a high-quality research location: "I am very grateful to the Swiss Cancer Research foundation. By supporting high-quality research here in Switzerland, it contributes to a stimulating work environment with many curious and competent colleagues", says paediatric oncologist Jean-Pierre Bourquin. And the fact that a high-quality work environment also enables people to better help patients in need is just the last – but crucial – link in the chain reaction.

Rolf Marti, PhD
Head of Research, Innovation & Development department, Swiss Cancer League

Donors see for themselves

Interested charitable donors were invited to form a picture of this fruitful research-funding chain reaction with their own eyes. The Basel Cancer League, the Swiss Cancer League, and the Swiss Cancer Research foundation, in collaboration with University Hospital Basel, organized a visit to the Woman's Health Clinic of the hospital and showed vividly how donations are specifically put to work: After visiting the research laboratory of Viola Heinzelmann and Francis Jacob, where researchers are working to improve treatment of metastatic ovarian cancer, the donors got a close look at the da Vinci operation robots that surgeons use for precise procedures. Also on the programme was a presentation of a web-based program that helps patients manage stress. At the end, the listeners were given a raisin – with this sweet fruit in their mouths they were asked to savour the experience of "here and now". For the partner organizations, this event was also an opportunity to thank the donors for their loyal support. These thanks of course also go to everyone who could not attend the event: We are deeply grateful to all donors, whose generosity makes advances in the fight against cancer possible. Donations to cancer research lay the foundation for improvements in patients' survival rate and quality of life.

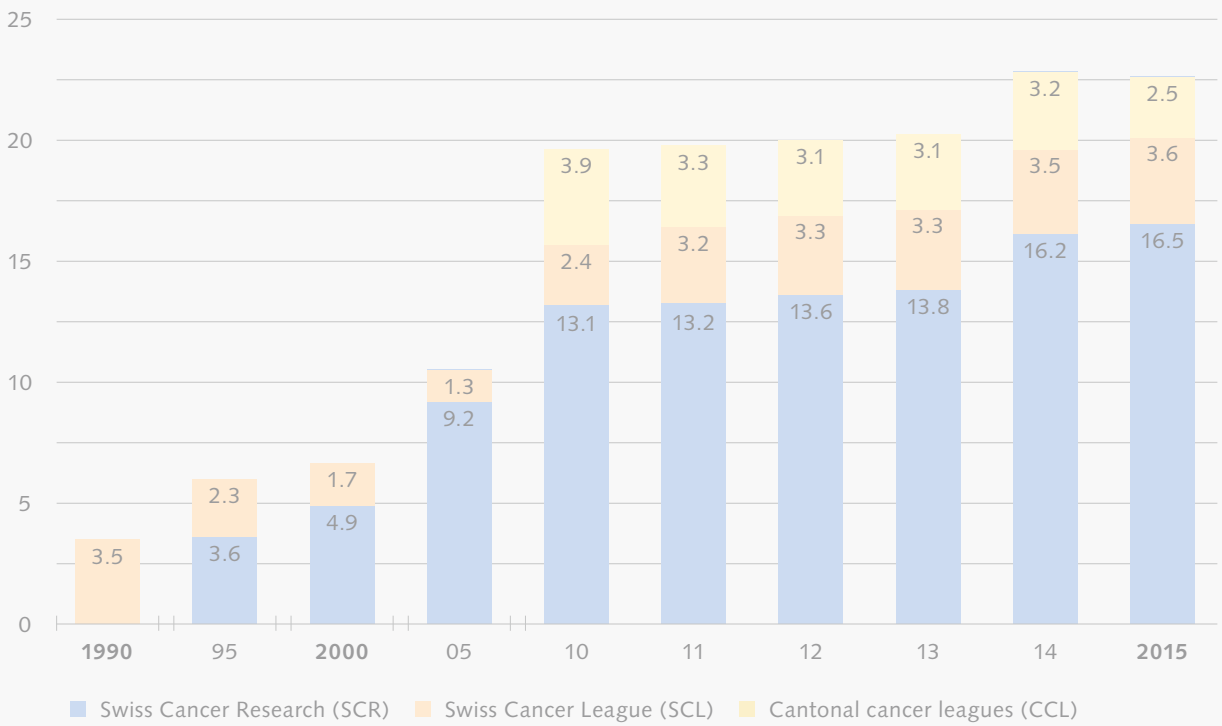
Donors of the Cancer League inspect the surgery robot.

Four main research areas

The SCR, SCL, and CCL support research projects across the entire broad range of cancer research, grouped in four central research areas: basic, clinical, psychosocial, and epidemiologic cancer research. Basic research studies how cancer cells develop, proliferate, and spread in the body. Clinical research works with cancer cells and tumour tissue, to identify new biomarkers or targets, for instance, so that better diagnostic methods or more effective drugs can be developed. Clinical research also conducts clinical trials with patients to establish new, improved treatments or to optimize existing treatments. Psychosocial research studies the mental and social effects of cancer. It aims to improve the quality of life of persons with cancer and their families. Epidemiologic

Figure 1
Cancer research funding by SCR, SCL, and CCL since the founding of SCR in 1990

Research funding by the CCL has been recorded centrally and published only since 2009.



research examines, for example, the rates of cancers in the population and the factors that have an effect on cancer risk, such as age, smoking, lack of exercise, one-sided diets, or unfavourable environmental factors. The SCR, SCL, and CCL also fund research projects in nursing sciences, prevention, public health, and health services research.

More than 20 million francs for over 150 research projects

In 2015 the SCR, SCL, and CCL provided a total of 22.6 million francs for 159 diverse research projects (Figure 1; Table 1). Just under three quarters of all-funds granted came from the SCR; the SCL contributed 16% and the CCL 11%.

In line with their funding strategy, the partner organizations supported mainly independent research projects: 18.3 million francs, or 81% of the total funding, went to projects on topics chosen by the researchers themselves. Just over 2.2 million francs, or about 10% of the total funding, went to six research organizations that provide elementary and indispensable basic services for clinical and epidemiologic research in Switzerland. The SCR and the SCL also supported international and national organizations and programmes like the Union for International Cancer Control, the European Organisation for Research and Treatment of Cancer, and the National Strategy Against Cancer with substantial amounts. Funding was also given to projects for the fight against cancer in Belarus, Nicaragua, and Cameroon.

Table 1
Research funding by SCR, SCL, and CCL in overview

Number of grants approved and amount granted in 2015 (all funding areas)

Total SCR, SCL, and CCL	Independent research projects	Bursaries	Research organizations	Programmes, organizations, and conferences	Total
Number of grants approved	101	10	7	41	**159**
Amount granted in kCHF	18 251	1164	2 250	921	**22 586**
Proportion of total funding in %	81	5	10	4	**100**
SCR					
Number of grants approved	44	8	6	20	**78**
Amount granted in kCHF	12 691	988	2 050	735	**16 464**
Proportion of total funding in %	77	6	12	4	**100**
SCL					
Number of grants approved	12	2	1	21	**36**
Amount granted in kCHF	3 039	176	200	186	**3 601**
Proportion of total funding in %	84	5	6	5	**100**
CCL					
Number of grants approved	45	–	–	–	**45**
Amount granted in kCHF	2 521	–	–	–	**2 521**

(percentage of funds)

Table 2
Distribution of cancer research funding by SCR and SCL to the research institutions in 2015

Research institutions	Number of projects	Amount in kCHF	Proportion in %
BITg Kreuzlingen	1	367	1.9
PSI Villigen	2	295	1.6
SAKK/IBCSG/SPOG/SCCR	5	1 750	9.2
University/Inselspital Bern	8	1 960	10.3
FMI Basel	2	572	3.0
University/University Hospital Basel	14	3 772	19.8
IELSG Bellinzona	1	250	1.3
Hospital San Giovanni Bellinzona	1	47	0.2
IOSI Bellinzona	3	694	3.6
IRB Bellinzona	2	598	3.1
University of Geneva/HUG	2	572	3.0
EPF Lausanne	4	1 428	7.5
University/CHUV Lausanne	6	1 628	8.6
Kantonsspital St. Gallen	2	605	3.2
NICER Zurich	1	250	1.3
ETH Zurich	1	374	2.0
University/University Hospital Zurich	17	3 852	20.3
Total	**72**	**19 014**	**100**

Abbreviations

BITg	Biotechnologie Institut Thurgau
CHUV	Centre Hospitalier Universitaire Vaudois
EPF	Ecole Polytechnique Fédérale
ETH	Eidgenössische Technische Hochschule
FMI	Friedrich-Miescher-Institut
HUG	Hôpitaux Universitaires de Genève
IBCSG	International Breast Cancer Study Group
IELSG	International Extranodal Lymphoma Study Group
IOSI	Istituto Oncologico della Svizzera Italiana
IRB	Institute for Research in Biomedicine
NICER	National Institute for Cancer Epidemiology and Registration
PSI	Paul Scherrer Institut
SAKK	Swiss Group for Clinical Cancer Research
SCCR	Swiss Childhood Cancer Registry
SPOG	Swiss Paediatric Oncology Group

The distribution of the funds (for independent research, bursaries, and research organizations) to academic institutions shows that in 2015, researchers at the universities and university hospitals of Zurich and Basel were the most successful in submitting research grant applications (Table 2): With 3.9 million francs (Zurich) and 3.8 million francs (Basel), researchers at each of these institutions received approximately one fifth of the total funding.

Stiffer competition

Compared to the previous year, in 2015 there was increased competition for the limited funding available for independent research projects (Table 3): More grant applications were submitted, but fewer projects could be funded than in 2014. Of the 191 grant applications submitted, the Scientific Committee of the SCR and the SCL recommended 103 projects for funding. Only 56 of these could be funded, however. And of the funds requested, only somewhat more than one quarter could be granted. The researchers requested nearly 57 million francs; just under 16 million could be granted to the approved projects.

In addition to the quality of the projects – which is the central criterion in funding – the funding strategy of the SCR and the SCL is to support research projects that it is hoped will produce results that benefit patients and their families. For this reason, 60 % of the funding is earmarked for what is called patient-centred research: 40 % for clinical research and 20 % for research studies in the psychosocial and epidemiologic areas. But again in 2015 the SCR and the SCL had to deviate from this ideal distribution rate: Even though all projects recommended for funding in psychosocial and epidemiologic research, for instance, were funded, only 4 % and 5 % of the total funding was granted to these research areas. Projects in basic research again received somewhat over half of the total funding, although 22 high-quality projects – recommended for funding by the Scientific Committee – in basic research could not be funded. The cut was the worst for research projects in clinical research: The Scientific Committee recommended 48 projects for funding, but only 23 of them (less than half of all recommended projects) could in fact be funded. But at least that number was four projects more than in the previous year.

Performance agreements in compensation for services

Patient-centred research is supported not only by funding independent research projects, however. The SCR and the SCL also compensate six research organizations for performing central and indispensable services for the benefit of clinical and epidemiologic research in Switzerland. In clinical research, these services include designing study protocols, coordinating national and international multicentre studies, and administrative tasks for the study approval process with the ethics committees and Swissmedic, the Swiss authorization authority. In the area of cancer epidemiology, the organizations supported by the SCR provide researchers with know-how and resources for collecting, managing, and analysing data in the cantonal and national cancer registries (see box).

Table 3
Distribution of funds by SCR and SCL and success rates within the amount granted to independent research projects

	2014		2015	
	Grant applications	Amount in kCHF	Grant applications	Amount in kCHF
All projects				
Received/applied for	167	47 956	191	56 960
Recommended	78		103	
Approved	60	16 057	56	15 730
Success rate	36 %	33 %	29 %	28 %
Basic research				
Received/applied for	85	26 133	95	30 217
Recommended	47		48	
Approved	29	8 708	26	8 122
Success rate	34 %	33 %	27 %	27 %
Clinical research				
Received/applied for	61	16 595	74	21 937
Recommended	19		48	
Approved	19	4 960	23	6 122
Success rate	31 %	30 %	31 %	28 %
Psychosocial research				
Received/applied for	9	2 013	9	2 107
Recommended	6		4	
Approved	6	1 139	4	624
Success rate	67 %	57 %	44 %	30 %
Epidemiologic research				
Received/applied for	12	3 215	13	2 699
Recommended	6		3	
Approved	6	1 250	3	862
Success rate	50 %	39 %	23 %	32 %

The research organizations supported in 2015, in brief

Swiss Group for Clinical Cancer Research (SAKK)
SAKK is a decentralized academic research institute that has conducted clinical studies on cancer treatment in all larger hospitals in Switzerland since 1965. SAKK encompasses a wide network of about 20 Swiss research groups and a coordination centre in Bern. For rare cancers SAKK works together with selected collaborative groups in other countries. SAKK aims to improve existing cancer treatments, study the effectiveness and tolerability of new treatments (radiotherapy, chemotherapy, surgery), and establish new treatment standards.

International Breast Cancer Study Group (IBCSG)
Since 1977 the IBCSG has conducted academic clinical trials with the aim to improve treatment of women with breast cancer. The IBCSG is a multicentre study group with a coordination centre located in Bern, a data management centre and a statistics centre in the United States, and a pathology reference laboratory in Italy that serves the entire organization. In Switzerland, all university clinics, numerous cantonal hospitals, and oncologists in private practices participate in IBCSG studies.

National Institute for Cancer Epidemiology and Registration (NICER)
As a national coordination centre, NICER harmonizes the work of the 14 cantonal and regional cancer registries. It compiles the cancer data collected in the cantons, assures the quality of the data, and analyses the data at the national level. These data collected in the network are utilized to determine national statistics on cancer incidence. For healthcare policy, the data enable evidence-based decision making that benefits the population as well as individual patients with cancer.

International Extranodal Lymphoma Study Group (IELSG)
The IELSG is a multicentre study group that was created in 1998 in Ascona, with a coordination and data management centre in Bellinzona. It aims to coordinate international research activities in the area of extranodal lymphomas. As these lymphomas develop in all organs in the body, different treatments are required. To test and optimize the effectiveness of treatments, more than 200 international institutes participate in this network.

Swiss Paediatric Oncology Group (SPOG)
SPOG has been conducting clinical cancer research in paediatric oncology/haematology since 1977, with the aim to improve treatment and quality of life of children and adolescents with cancer. SPOG is a national, independent association with its headquarters in Bern. Members are all paediatric oncology departments at Swiss hospitals and the Swiss Childhood Cancer Registry. As childhood cancers are relatively rare, research in childhood cancer is possible only in the framework of international collaborations. At present, SPOG is taking part in more than 20 clinical trials in which approximately 150 young patients in Switzerland are participating.

Swiss Childhood Cancer Registry (SCCR)
The SCCR is the national cancer registry for children and adolescents in Switzerland. Since 1976 it has captured all new cases of cancer in young persons up to the age of 20. It also documents treatments and conducts longitudinal studies on health and quality of life of childhood cancer survivors. In this way it contributes towards research on the causes of childhood cancer, improvement of cancer treatment, and prevention of late effects in cancer survivors. The SCCR, which is funded from several sources, is located at the Institute of Social and Preventive Medicine at the University of Bern.

Table 4
Supported research organizations

Funding by SCR, according to performance agreements in the years 2009–2015

Amount in kCHF

	2009	2010	2011	2012	2013	2014	2015
Swiss Group for Clinical Cancer Research (SAKK)	600	600	600	600	*900	*1 050	*1 100
International Breast Cancer Study Group (IBCSG)	560	560	560	560	500	450	400
National Institute for Cancer Epidemiology and Registration (NICER)	–	–	200	200	250	250	250
International Extranodal Lymphoma Study Group (IELSG)	–	–	–	200	200	200	250
Swiss Paediatric Oncology Group (SPOG)	100	100	100	150	150	150	150
Swiss Childhood Cancer Registry (SCCR)	–	–	50	50	75	75	100
Total	**1 260**	**1 260**	**1 510**	**1 760**	**2 075**	**2 175**	**2 250**

* of wich 200 000 CHF funded by SCL

Table 5
Research funding by the cantonal cancer leagues in overview

Number of research projects and institutions supported and amount granted

	Number of projects and institutions supported		Amount granted in kCHF	
Cancer league	2014	2015	2014	2015
Aargau	1	1	48	15
Basel	7	11	400	315
Bern	6	7	402	430
Central Switzerland	1	1	50	34
Eastern Switzerland	2	0	105	0
Geneva	16	9	1 305	945
Grisons	3	3	80	40
Neuchâtel	1	0	5	0
Schaffhausen	1	1	20	20
Ticino	4	2	250	175
Thurgau	1	2	33	48
Zurich	8	8	486	499
Total	**51**	**45**	**3 184**	**2 521**

For their expenditure, the research organizations receive compensation based on performance agreements that define in a clear and binding way the requirements with regard to reporting and evaluation and the objectives for research. In addition, there is the condition that the research organizations must secure independent and long-term financing that guarantees their continuing existence independently of contributions from the SCR. In 2015 the SCR supported the six research organizations with a total of 2.05 million francs. Another 200 000 francs were provided by the SCL (Table 4).

Research funding by the cantonal cancer leagues

Compared to the previous year, in 2015 the CCL supported a slightly lower number of research projects: Ten different cantonal and regional cancer leagues gave more than 2.5 million francs to 45 projects (Table 5). The largest sum was once again given by the Geneva Cancer League, followed by the Zurich, Bern, Basel, and Ticino Cancer Leagues. The research projects and institutions supported by the CCL are listed on pages 38 to 41.

Rolf Marti, PhD

Rolf Marti has headed the Research, Innovation & Development department (formerly: Scientific Office) at the Swiss Cancer League since 2003.
He is a member of the managing board of the Swiss Cancer League and director of the Swiss Cancer Research foundation office.
As a member of the core group of the National Strategy Against Cancer 2014–2017, he currently focuses his work on the fields of action "Research promotion" and "Epidemiology and monitoring".

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Partner organizations and committees

Swiss Cancer Research foundation (SCR)

In existence since 1990, the Swiss Cancer Research foundation, with the help of donations, provides funding for all areas of cancer research: basic, clinical, epidemiologic, and psychosocial research. A special focus is the funding of patient-centred research projects that result as far as possible in direct patient benefit. The SCR foundation board is responsible for distributing the funds to researchers. The board's funding decisions are based on the recommendations made by the Scientific Committee, which reviews the grant applications according to clearly defined criteria. The SCR also supports the development and implementation of measures to fight cancer in Switzerland – namely, the National Strategy Against Cancer 2014–2017.

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Swiss Cancer League (SCL)

The Swiss Cancer League (SCL) works towards a world where fewer persons get cancer, fewer persons suffer the consequences and die of cancer, more persons are cured of cancer, and persons with cancer and their families receive care and support in all phases of cancer and in dying. The Cancer League brings together the national umbrella organization headquartered in Bern and 19 cantonal and regional cancer leagues. The SCL supports the cantonal cancer leagues through knowledge transfer, provision of services, developments, and coordination at the national level. It provides information on risk factors and early detection measures and runs national cancer prevention programmes. It offers specific continuing education courses for a variety of occupational groups and funds cancer research.

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Cantonal cancer leagues (CCL)

The 19 cantonal and regional cancer leagues provide persons with cancer and their family members with individual advice from experts on treatment and financial and organizational questions. The CCL staff often advise persons over a longer time period and support them in difficult situations. They provide information on legal and insurance issues and help with the reorganization of the clients' social and financial situation. The CCL also provide contacts to other support institutions, such as home care organizations. If persons with cancer experience financial difficulties as a result of their illness, they can apply for support payments. The CCL organize group meetings and courses where persons with cancer can talk about their fears and experiences and learn ways to deal with their illness. Some cancer leagues offer specialized psycho-oncology support for children of adults with cancer. And in some cantons there are outpatient oncology care services that support persons with cancer at home.

The CCL are at work in Switzerland and in Liechtenstein. The CCL do not all offer the same services. The type and extent of services depends heavily on the financial and human resources of the individual cancer league as well as on the services made available by other providers.

Cantonal and regional cancer leagues in the German-speaking part of Switzerland and in Liechtenstein

- Aargau Cancer League
- Basel Cancer League
- Bern Cancer League
- Central Switzerland Cancer League
- Eastern Switzerland Cancer League
- Grisons Cancer League
- Liechtenstein Cancer League
- Schaffhausen Cancer League
- Solothurn Cancer League
- Thurgau Cancer League
- Zug Cancer League
- Zurich Cancer League

Cantonal cancer leagues in the French-speaking part of Switzerland and in Ticino

- Fribourg Cancer League
- Geneva Cancer League
- Jura Cancer League
- Neuchâtel Cancer League
- Ticino Cancer League
- Valais Cancer League
- Vaud Cancer League

The board of the Swiss Cancer Research foundation

The board is the highest body of the Swiss Cancer Research foundation (SCR).
It monitors adherence to the foundation goals and manages the foundation's assets.
The board of the SCR meets two to four times a year. It decides – based on the recommendations of the Scientific Committee – on the granting of funds to researchers.

The members of the SCR foundation board serve on a voluntary basis.
The eight members are:

President

Prof. Thomas Cerny, MD
Cantonal Hospital St. Gallen
Member of the board since 2009

Vice president

Prof. Richard Herrmann, MD
Basel University Hospital
Clinical cancer research representative
Member of the board since 2009

Prof. Matthias Egger, MD
University of Bern
Epidemiologic cancer research representative
Member of the board since 2009

Erika Forster-Vannini
Former member of the Swiss Council of States
St. Gallen
Member of the board since 2012

Prof. Nicolas von der Weid, MD
University Children's Hospital Basel (UKBB)
Paediatric cancer research representative
Member of the board since 2009

Eduard Holdener, MD
Therwil
Member of the board since 2009

Prof. Daniel E. Speiser, MD
University of Lausanne
Basic research representative
Member of the board since 2015

Treasurer

Gallus Mayer
Banking specialist
St. Gallen
Member of the board since 2006

The board of the Swiss Cancer League

The highest body of the Swiss Cancer League (SCL) is the delegates' assembly, to which the representatives of the cantonal and regional cancer leagues belong. Strategic management of the SCL is the responsibility of the board. Board members represent different specialties in the fight against cancer and also the different parts of Switzerland.

The eleven members of the board are:

President

Prof. Jakob R. Passweg, MD
Head physician of Haematology Clinic
Basel University Hospital
Member of the board since 2007

Vice president

PD Gilbert Bernard Zulian, MD
Head physician of Palliative Medicine
Hôpital de Bellerive
Geneva University Hospital
Member of the board since 2009

Prof. Thomas Cerny, MD
Head physician of Oncology/
Haematology
Cantonal Hospital St. Gallen
Member of the board since 1998

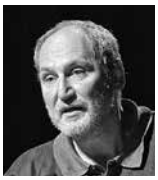
Prof. Daniel Betticher, MD
Head physician of Oncology
HFR Fribourg, Cantonal Hospital
Member of the board since 2006

Lucienne Bigler-Perrotin
Manager
Geneva Cancer League
Member of the board since 2009

Treasurer

Gallus Mayer
Banking specialist
St. Gallen
Member of the board since 2009

Hans Neuenschwander, MD
Head physician of Palliative Care
Regional Hospital of Lugano
Member of the board since 2010



Markus Notter, MD
Radio-Oncology
Lindenhof Hospital, Bern
Member of the board since 2013

Corinne Ullmann
Manager
Schaffhausen Cancer League
Member of the board since 2013

Brigitta Wössmer, PhD
Head psychologist of Psychosomatics
Basel University Hospital
Member of the board since 2011

Karin Zimmermann, PhD
Scientific staff member
Children's Hospital Zurich
Member of the board since 2014

The Scientific Committee

Members of the Scientific Committee in 2016 (from left to right): Kurt Fritzsche, Jürg Schwaller, Simone Benhamou, Emanuele Zucca, Maria Blettner, Silke Gillessen, Jörg Beyer, Pedro Romero, Rolf Marti (head of Research, Innovation & Development department of the Swiss Cancer League), Nancy Hynes (president), Aurel Perren, Curzio Rüegg, Beat Schäfer, Tatiana Petrova, Joerg Huelsken, Martin Pruschy, Hans-Uwe Simon, Peggy Janich (scientific collaborator at SCL). Not pictured: Primo Schär, Friedrich Stiefel.

Criteria for high-quality cancer research

The quality of research grant applications is evaluated according to the following criteria:

- Cancer relevance: Is the proposed research project expected to contribute important new observations or knowledge on the causes, prevention, or treatment of cancer?
- Originality or socioeconomic significance: Is the proposed research project original, innovative (basic research projects), or of socioeconomic importance (clinical or epidemiologic projects)?
- Choice of methodology: Have the most appropriate methods for realization of the project been chosen?
- Feasibility: Is the project feasible in terms of finances, human resources, and organization?
- Track record: What are the applicant's (or the project group's) previous research achievements?

The Scientific Committee reviews research grant applications according to clear criteria (see box, "Criteria for high-quality cancer research"). In the evaluation of research grant applications, the main criterion is always whether a research project can generate important new findings that will contribute towards improving the prevention or treatment of cancer. The Scientific Committee also rates the originality and feasibility of the research projects – and recommends only the best projects for funding approval. It attaches particular importance to patient-centred research.

The 18 members of the Scientific Committee are recognized experts with outstanding performance and achievements. Together they cover all areas relevant to cancer research.

Since 2015 the members of the Scientific Committee have represented the following disciplines:
– Basic research: 6 members
– Clinical cancer research: 8 members
– Epidemiology and cancer prevention: 2 members
– Psychosocial cancer research: 2 members

Each research grant application is reviewed carefully by several experts. In addition to two members of the Scientific Committee, also international reviewers evaluate the quality of the grant application (see box, "The research grant application review process"). At two meetings of the Scientific Committee per year, the grant applications are discussed in depth and ranked on a list. Based on the ranking list the boards of the SCR and SCL decide which projects will be approved for funding. Unfortunately, as the financial means are limited, not all high-quality grant applications can be funded. Funding goes exclusively to industry-independent research projects.

Operational support for the Scientific Committee's important tasks and responsibility is provided by the Research, Innovation & Development department of the SCL. It organizes the calls for and the peer review of research grant applications, makes the grant payments in annual increments, and receives the interim and final research reports.

The research grant application review process

The grant application is submitted online.
↓
The grant application is sent to two members of the Scientific Committee for review.
↓
The two Scientific Committee members recommend external reviewers.
↓
The Research, Innovation & Development department of the SCL asks the external reviewers to review the grant application.
↓
The grant application is reviewed. Four to six reviews are obtained for each grant application, two of which are by Scientific Committee members.
↓
The grant application and the reviews are discussed in detail at the biannual meeting of the Scientific Committee.
↓
After the meeting, the Research, Innovation & Development department writes up detailed minutes and creates a ranking list of all grant applications discussed, following the Scientific Committee's recommendations.
↓
The ranking list is forwarded to the boards of the SCR and SCL. The boards make the final funding decision.
↓
The grant applicant is informed of the decision by the Research, Innovation & Development department. Reviewer comments are fed back to the applicant anonymously.

The eighteen members are:

President

Prof. Nancy Hynes, PhD
Friedrich Miescher Institute for Biomedical Research (FMI)
Basel
Member since 2015

Basic research

Prof. Joerg Huelsken, PhD
Swiss Institute for Experimental Cancer Research (ISREC)
Swiss Federal Institute of Technology Lausanne (EPFL)
Lausanne
Member since 2016

Prof. Tatiana Petrova, PhD
Department of Fundamental Oncology
University of Lausanne
Epalinges
Member since 2016

Prof. Pedro Romero, MD
Ludwig Institute for Cancer Research
University of Lausanne
Epalinges
Member since 2015

Prof. Primo Schär, PhD
Department of Biomedicine
University of Basel
Basel
Member since 2010

Prof. Jürg Schwaller, MD
Department of Biomedicine
University Hospital Basel
Basel
Member since 2013

Up to 2015

Prof. Freddy Radtke, PhD
Swiss Institute for Experimental Cancer Research (ISREC)
Swiss Federal Institute of Technology Lausanne (EPFL)
Epalinges
Member since 2007

Clinical research

Prof. Jörg Beyer, MD
Department of Oncology
University of Zurich
Zurich
Member since 2015

Prof. Silke Gillessen, MD
Department of Oncology/Haematology
Cantonal Hospital St. Gallen
St. Gallen
Member since 2013

Prof. Aurel Perren, MD
Institute of Pathology
University of Bern
Bern
Member since 2016

Prof. Martin Pruschy, PhD
Department of Radiation Oncology
University Hospital Zurich
Zurich
Member since 2010

Prof. Curzio Rüegg, MD
Department of Medicine
University of Fribourg
Fribourg
Member since 2013

Prof. Beat W. Schäfer, PhD
Department of Oncology
Children's Hospital Zurich
Zurich
Member since 2012

Prof. Hans-Uwe Simon, MD
Institute of Pharmacology
University of Bern
Bern
Member since 2008

PD Emanuele Zucca, MD
Oncology Institute of Southern
Switzerland (IOSI)
Ospedale San Giovanni
Bellinzona
Member since 2013

Up to 2015

Prof. Holger Moch, MD
Institute of Surgical Pathology
University Hospital Zurich
Zurich
Member since 2006

Psychosocial research

Prof. Kurt Fritzsche, MD
Department of Psychosomatic
Medicine and Psychotherapy
Freiburg University Hospital
Freiburg im Breisgau, Germany
Member since 2009

Prof. Friedrich Stiefel, MD
Liaison Psychiatry Service
Lausanne University Hospital (CHUV)
Lausanne
Member since 2007

Epidemiologic research

Prof. Simone Benhamou, PhD
French National Institute of Health and
Medical Research (INSERM)
Paris, France
Member since 2011

Prof. Maria Blettner, PhD
Institute of Medical Biostatistics
Epidemiology and Informatics (IMBEI)
Johannes Gutenberg University Mainz
Mainz, Germany
Member since 2010

Prizes for outstanding achievements in cancer research and the fight against cancer

The Swiss Cancer League awarded the Cancer Prize 2015 to breast cancer specialist Monica Castiglione for her decades of committed work for the benefit of persons with cancer – both in scientific research and at the political level. The Recognition Award was given to Martin Rothenbühler for his great help and his selflessly given expertise in the development of a quality label for breast centres.
Finally, the Swiss Bridge Award was given to two research projects on stem cells and cancer: Sharing the 500 000 franc prize are the projects of Andreas Trumpp at the German Cancer Research Center in Heidelberg and Joerg Huelsken at the Swiss Federal Institute of Technology Lausanne.

The Cancer Prize 2015 was awarded to Prof. Monica Castiglione, MD, for her tireless commitment over decades as a breast cancer expert at the university hospitals of Bern and Geneva and as director of the International Breast Cancer Study Group (IBCSG) and of the Swiss Institute for Applied Cancer Research (SIAK).

Working for the goals of the Swiss Cancer League

Over several decades, Castiglione not only made an outstanding name for herself as a physician and researcher but also supported the Swiss Cancer League again and again with her vast expertise and her willingness to help. She served on the panel of experts, for instance, when the French-speaking part of Switzerland was introducing a mammography screening programme. As a breast cancer specialist she also

CEO Kathrin Kramis (left) and vice president Gilbert Zulian (right) of the Swiss Cancer League present the Cancer Prize to the laureate Monica Castiglione.

Ori Schipper, PhD
Communication officer for Research, Innovation & Development department, Swiss Cancer League

made a significant contribution in the development of patient brochures and fact sheets – on the topic of hormone therapy, for instance. And she also assisted the Swiss Cancer League as an auditor in the procedure for awarding the quality label for breast cancer centres. In summary, it can truly be said that Monica Castiglione has always done her utmost to further the goals of the Swiss Cancer League – politically, scientifically, and for the general public.

The Cancer Prize

With the Cancer Prize the Swiss Cancer League recognizes persons who have made outstanding contributions to cancer research or committed efforts to promote research activities in service of prevention, early detection, and treatment of cancer. The prize also serves as recognition for services to the Swiss Cancer League and its goals. The 10 000 franc prize is usually awarded each year.
www.krebsliga.ch/krebspreis

The Swiss Cancer League awarded the Recognition Award to Martin Rothenbühler in recognition of his important assistance in establishing the quality label for breast centres.

Significant regional differences

The story behind the quality label begins with a study conducted by the cancer registries of St. Gallen and Appenzell: The Pattern of Care study found not only significant regional differences in care of women with breast cancer in Switzerland but also that many women with breast cancer did not receive the treatment recommended by treatment guidelines. As a resource for persons with cancer, the Swiss Cancer League subsequently received a lot of inquiries that it could not answer, because the Swiss Cancer League does not speak in favour of or against any specific hospitals.

Assisting in the birth of a quality label for breast centres

To promote the quality of treatment and care of women with breast cancer, to issue the hospitals an impartial certification, and to provide patients with guidance, the Swiss Cancer League then brought a quality label for breast centres to life. Here the SCL was assisted by Martin Rothenbühler, founder and long-serving managing director of the SanaCERT foundation, who acted as the midwife, so to speak. With his expertise and selflessly offered know-how and experience, Martin Rothenbühler made a decisive contribution to the success of the quality label. Since it came into being five years ago, already 12 centres in Switzerland have earned the certification, so that today, about half of all women newly diagnosed with breast cancer each year – approximately 3000 of 5500, receive quality-controlled treatment and care.

The Recognition Award

With the Recognition Award the Swiss Cancer League honours persons or organizations for their committed work to improve the situation of patients. The award goes in particular to innovative projects or inventions that aid persons with cancer. The award comes with 5000 francs prize money.

Martin Rothenbühler (centre) receives the Recognition Award from CEO Kathrin Kramis (left) and the President of the Swiss Cancer League Jakob Passweg (right).

In 2015 the Swiss Bridge Award was reserved for research projects in the area of cancer stem cells. Stem cells reproduce themselves many times over and are more resistant than other cells. For this reason they are becoming more important in cancer research: They are often responsible for therapy failure, tumour recurrence, and metastasis.

A total of 45 researchers submitted research proposals to apply for the Swiss Bridge Award 2015. In a two-stage evaluation procedure, a jury of nine international experts then nominated a promising research proposal from Germany and one from Switzerland: Recipients of the 2015 Award were Prof. Andreas Trumpp, PhD, at the German Cancer Research Center in Heidelberg and Prof. Joerg Huelsken, PhD, at the Swiss Federal Institute of Technology Lausanne. The Research, Innovation & Development department of the Swiss Cancer League was once again responsible for the call for proposals and coordination of the project evaluation.

Metastases-forming cells in the blood

Andreas Trumpp heads the Division for Stem Cells and Cancer at the German Cancer Research Center in Heidelberg. His group recently found cells in the blood of patients with breast cancer that can form new secondary tumours, or metastases, on their own. In the project that is newly funded with 250 000 francs from the Swiss Bridge Award, Trumpp and his colleagues want to characterize the tumour cells circulating in the blood as completely as possible. They aim to find out what makes a normal circulating tumour cell different from a metastases-forming stem cell. These insights could not only provide the basis for new and better diagnostic methods but also reveal the weak points of these stem cells. Such possible points of attack could in the future perhaps even help to nip formation of deadly metastases in the bud.

Immunosuppressive characteristics

Joerg Huelsken's team at the Swiss Federal Institute of Technology Lausanne found recently that cancer stem cells are more resistant to chemotherapy and radiation therapy than other cancer cells and also that they play a crucial role in the body's own immune system. The immune system would actually be

Andreas Trumpp (left) thanks Thomas Hoepli (right).

Jakob Passweg (right) congratulates Joerg Huelsken (left).

able to recognize and kill cancer cells, but cancer stem cells escape its control: They apparently succeed at evading the immune system. In their new research study, also awarded 250 000 francs, Huelsken and his colleagues aim to decipher the immunosuppressive characteristics of cancer stem cells. If they succeed, the results could contribute towards providing the new immune therapy approaches with more powerful means.

Swiss Bridge Award
The Swiss Bridge Foundation was founded in 1997 at the initiative of Thomas Hoepli, foundation board member, with the support of the Swiss Cancer League. The aim of the foundation is to financially support high-quality cancer research projects in Switzerland and other countries with the help of charitable donors and foundations. Since its founding, the Swiss Bridge Foundation has awarded more than 25 million francs for research work in Belgium, Brazil, England, France, Germany, Israel, Italy, Norway, Spain, Sweden, and Switzerland.

Ori Schipper, PhD
Ori Schipper graduated in plant molecular biology and followed a postgraduate course in science journalism.
Since December 2014 he is communication officer of the Research, Innovation & Development department of the Swiss Cancer League and the Swiss Cancer Research foundation.
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Implementation of the National Strategy Against Cancer

The importance of research in the National Strategy Against Cancer

The Swiss health care system will be especially challenged in the coming years by cancer cases. Care provision for people with cancer that is oriented towards the principles of quality, efficiency, and social equality in health care services will become a reality only if all professional groups and organizations involved work together closely and in a coordinated way. For this reason, the Dialogue for National Health Policy, the joint platform of the federal government and the cantons, contracted Oncosuisse to develop, with the involvement of affected organizations, experts, professional associations, and the cantons a national strategy for improvements in preventing and combatting cancer. The result – based on the action areas, goals, and measures of the National Cancer Programme 2011–2015 – was the National Strategy Against Cancer 2014–2017. It divides the areas Prevention, Care, and Research into seven action fields and 15 projects (Table 6).

The National Strategy attaches very high importance to research: It is one of the three main areas. The area "Research" comprises two action fields. The action field "Research funding" aims mainly to strengthen research areas that are as yet little developed in Switzerland. The action field "Epidemiology and monitoring" focuses on further development of bases for full-coverage and uniform data registration.

Research funding

Switzerland holds a leading position internationally in basic research. But there are also research areas that still need to be developed. Health care research is still new in Switzerland and has little institutional anchoring. But current integrative procedures in health care also raise new research questions that demand a more interdisciplinary perspective and consideration of sociological, economic, and political science approaches. Development of integrative research approaches of that kind would also benefit projects in evaluation research.

There is also still a need for action in the funding of clinical and translational research in Switzerland. This is because besides the research interests of the pharmaceutical industry, which are also guided by the demands of the market, there are an increasing number of questions about clinical practice – namely, about optimizing treatment – that need to be studied in scientific research projects. In addition, translational research needs to be bolstered through setting up further coordinating networks and platforms. These platforms should allow targeted topics to become the subject of discussion in increased exchange between researchers and clinical practitioners. In this regard, the National Strategy seeks to further develop the activities to date, if possible, and set new initiatives so as to sustainably anchor and network high-quality translational, cross-area, and clinical research in Switzerland. In a first step, it is planned to create an overview of the most important research activities. They form the basis for the targeted research activities that are planned to follow.

Philippe Groux, PhD, MPH
Overall Project Manager National Strategy Against Cancer

Epidemiology and monitoring

Valid data adhering to international standards are indispensable for the planning, measurement of results, and coordination of a strategy against cancer. In paediatrics, the Swiss Childhood Cancer Registry has collected uniform and full-coverage data on childhood cancer, including data on treatment, care quality, and outcome research for years. But for adults the data collected are still not uniform and do not fully cover Switzerland. Data collection in the cantonal cancer registries and data analysis via the National Institute for Cancer Epidemiology and Registration (NICER) therefore need to be further developed, so that they are adequate for use in optimal planning of prevention (for example, screening programmes) and care (for example, treatment quality) and for studying specific research questions, especially in outcome research.

The aim of a national law on cancer registration is legal regulation of cancer registration at the national level, as opposed to the cantonal level. The law was passed in March by the National Council and the Council of States and should make possible nationwide, uniform collection of data on cancer incidence with a harmonized framework. If cancer registry data are collected uniformly, they are suitable for use in monitoring and providing scientific support for the success of health policy measures – such as prevention and screening programmes – and for the quality

Table 6
Overview of the action fields and projects of the National Strategy Against Cancer

3 Areas	7 Action Fields	15 Projects
Prevention	Prevention	– Improve structural measures and health literacy
	Screening	– Plan and implement colon cancer screening programmes
		– Introduce nationwide breast cancer screening programmes
		– Set up panel of experts in screening questions
Care	Clinical pathways/ quality development	– Clinical pathways
		– Guidelines and treatment guidelines
		– Tumour boards
	Health services	– Integrated health services organizations
	Education	– Promote patient self-efficacy
		– Competence building for experts
Research	Promotion of research	– Health services research
		– Clinical and translational research
	Epidemiology and monitoring	– Federal law on cancer registration
		– Registry data on treatment quality and data linking
		– Knowledge transfer to practice and policy

of treatments. There is currently still a lack of data on treatment quality in particular. The need for policy-relevant, reliable data will increase in the future. Well prepared data will be required as well as the transfer of the data into policy making.

Philippe Groux, PhD, MPH
After completing a PhD in biochemistry at the University of Bern, he worked for many years in the diagnostics and pharmaceutical field. He earned a Master of Public Health (MPH) degree at the Universities of Basel, Bern, and Zurich in 2012.
He took over as overall project manager for the National Strategy Against Cancer in January 2015.
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Launching health services research in oncology

The National Strategy against Cancer 2014–2017 aims to identify and sustainably anchor novel approaches for the prevention and care of cancer and promote areas of research in need of development. For implementation of these goals, one of the projects, Health Services Research, has taken a decisive step forward: The framework and objectives of a new funding programme to strengthen health services research in oncology in Switzerland have been created and defined. The first call for proposals was opened in 2016.

The main goal of most clinical research efforts in oncology is to improve treatment methods to save as many cancer patients as possible. However, apart from successful treatment, there are additional questions that have become more and more important for patients with cancer, their families, and the health care professionals providing care. Most of these questions relate to psychosocial, medical, or economic aspects, which can only be reasonably addressed using the methods of health services research.

In addition to basic and clinical research, health services research is considered the "third pillar" of health research. Whereas basic research studies cells, tissues, or animal models to gain new insights into biological processes, clinical research and health services research focus on the person. Clinical research examines the effectiveness of new treatments mostly only in clearly defined and selected patients (the study population). In contrast, health services research explores the effectiveness of treatment and care under real-life conditions and examines how to provide optimal access to the best possible medical treatment and how this can be developed and managed for the greatest benefit for all patients. Here, health services refers not only to patients but also to the healthy population (such as in prevention).

The first nationwide efforts to strengthen health services research were undertaken in 2012 by the Swiss Academy of Medical Sciences (SAMW) together with the Gottfried and Julia Bangerter-Rhyner Foundation with the creation of a four-year funding programme. Since 2015 there is also the National Research Programme 74 "Smarter Health Care" funded by the Swiss National Science Foundation (SNSF), which deals with urgent issues in overuse, underuse and misuse of health care services, coordination and collaboration among health care professionals, and caring for patients with multiple chronic conditions. These two funding programmes do not primarily extend to the field of oncology. But because of the worldwide reduced mortality rate with cancer and increased life expectancy, cancer poses a particular challenge, also in the future, for the health care system. Switzerland, too, has recognized the increased need for efficient and high-quality health services in the field of oncology. The goal of cancer-specific health services research is to demonstrate possible ways to achieve good cancer care provision and to master future challenges.

Based on the preliminary work of the SAMW and SNSF, the Swiss Cancer Research foundation (SCR) in connection with the National Strategy Against Cancer 2014-2017 has taken the lead in implementing a funding programme to strengthen cancer-specific health services research. With the support of the Accentus Foundation (Marlies-Engeler-Fonds), which to

Peggy Janich, PhD
Scientific collaborator, Innovation & Development department, Swiss Cancer League

date has supported more than 1000 not-for-profit projects worldwide, the SCR has issued a first call for proposals in 2016. Further calls for proposals are planned to be issued each year up to 2020.

Each year the programme will support two to four research projects and several small research studies in the form of Master's theses, literature reviews, pilot projects, or the like. Funds of a total of one million francs will be awarded each year. The grant applications will be evaluated by an independent committee of national and international experts in the most various areas of health services research. The programme is open to researchers at Swiss universities, hospitals, research and consulting institutes and health services providers.

Welcome are projects aimed at any point along the patient's path, which begins with prevention and early detection of cancer and continues on the long route through diagnosis, treatment, rehabilitation, and reintegration, and on to palliative care or survivorship. The goal of the health services research in oncology and cancer care programmes is to gain knowledge that will lead to optimization of health services in these areas or contribute towards improved quality of life for patients with cancer. The findings will serve not only patients, their families, and health care professionals but also decision makers in government and industry who can initiate possible necessary changes in the health care system.

Peggy Janich, PhD
After studying biotechnology at Brandenburg University of Technology Cottbus-Senftenberg and Technische Universität Dresden, Janich completed a PhD at the Centre for Genomic Regulation in Barcelona. She then worked as a researcher at the University of Lausanne before joining the Swiss Cancer League in February 2016.
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Research funding by the cantonal and regional cancer leagues

Promotion of cancer research in the Canton of Ticino

The Swiss Cancer League is organized as an association made up of 19 cantonal and regional cancer leagues and the umbrella organization, the Swiss Cancer League. In 2015, 10 cantonal cancer leagues, including the Ticino Cancer League, gave over 2.5 million francs to cancer research projects and institutes. To promote cancer research in the Italian-speaking part of Switzerland, the Ticino Cancer League relies on a foundation created specifically for research funding.

The Ticino Cancer League supports and promotes cancer research studies via the *Fondazione ticinese ricerca sul cancro* (Ticino Foundation for Cancer Research). The foundation was established in 1984 thanks to a private donation of approximately one million francs. The funds went first to the Oncology Institute of Southern Switzerland (*Istituto Oncologico della Svizzera Italiana,* IOSI), which then made the funds available for the creation of a new structure to fund research projects in the Italianspeaking part of Switzerland.

With this framework, the Ticino Cancer League decided that it would not engage directly in the evaluation of research proposals but would delegate this task to a structure that is specialized in this area and therefore especially effective. But the Cancer League holds the majority of the seats on the foundation board and ensures – with funding of differing amounts each year – the financing of the Ticino Foundation for Cancer Research. There are 11 members on the foundation board, which is currently chaired by Dick Marty, a lawyer and a representative of the Canton of Ticino in the Council of States. In addition, other (state and private) organizations are represented in the foundation that can bring in additional resources in the future. The Ticino Cancer League provides the foundation with financial means in varying amounts, on average 200 000 francs annually. Additionally, the foundation finances itself through private donations and through organization of various events, such as a public walk/run called *Corsa della speranza* (race of hope) benefitting cancer research that takes place in September of each year in Lugano.

Research grant applications can be submitted using the templates and electronic application forms of the Swiss Cancer League and Oncosuisse. Applications are accepted each year up to the end of September. They are then reviewed by national and international experts. Based on the experts' evaluations, the foundation board makes the decision on what projects will be funded. The foundation usually funds three to four projects per year: In the 32 years of its existence, the Ticino Foundation for Cancer Research has in this way provided over 10 million francs for research. In addition, in memory of the first head of the foundation, lawyer Mario Luvini, a scholarship in his name in the amount of 30 000 francs was established that is used to finance stays abroad for oncologists and researchers from the Italian-speaking part of Switzerland.

The foundation considers only research projects that are conducted in the Canton of Ticino, or the Italian-speaking part of Switzerland. They are often research projects that were rated promising by the funding programme of the Swiss Cancer League but

Prof. Franco Cavalli, MD
Member of the Executive Committee of the Ticino Cancer League

could not be funded due to lack of monies (projects falling in the category "approved but not funded", or ABNF). The main recipients of the grants are the IOSI (including its research laboratories) and the groups working at the Institute of Oncology Research (IOR), the Ticino Cantonal Institute of Pathology, and the Institute for Research in Biomedicine (IRB) in Bellinzona.

In 2015, for instance, in addition to the Mario Luvini Scholarship, the foundation funded a clinical study and two laboratory studies. The clinical study is investigating the extent to which the introduction of a tumour board can improve the choice of an appropriate treatment for patients with prostate cancer. To find the answer, the current situation is being compared to older data from the IOSI. The two laboratory studies relate to two projects that are studying the role of some new oncogenes in the pathogenesis of prostate cancer. Here the two studies are examining, among other things, the possibility that new treatments can be developed based on the newly gained knowledge.

For grant applications there are no restrictions regarding the topic of research: Proposals in the most various research areas may be submitted. But because the research foci at the IOSI include prostate cancer and lymphoma, it is not surprising that a great many of the projects focus on these areas. It is difficult to assess which projects were the most successful, not least because the Ticino Foundation for Cancer Research has funded more than 100 research projects up to now. But worthy of mention in this connection is the funding of a number of projects studying lymphomas that resulted in a new classification of malignant lymphoma. Today, what is known as the Lugano Classification is used worldwide for staging and treatment response assessment in patients with lymphoma.

Prof. Franco Cavalli, MD
Oncologist Franco Cavalli was president of the Swiss Cancer League from 2001 to 2004. He has been the director of the Oncology Institute of Southern Switzerland (IOSI) in Bellinzona since 2003. He is one of the most highly regarded cancer researchers of Switzerland, and he is also active in the international fight against cancer – such as through the International Union Against Cancer (UICC), of which he has served as president in the years 2006 to 2008.

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List of funded research projects and institutions

The list shows the financial contributions granted in 2015.

Aargau Cancer League

Weber Damien Charles | RiSK data analysis
Zentrum für Protonentherapie, Paul Scherrer Institut, Villigen
CHF 14 800.– | Duration: 1. 3. 2015 – 30. 6. 2015

Basel Cancer League

Aceto Nicola | shRNA Screening of cell-cell junction components implicated in breast cancer metastasis
Departement Biomedizin, Universitätsspital Basel, Basel
CHF 60 000.– | Duration: 1. 4. 2015 – 31. 3. 2016

Conen Katrin | Costs and benefits in glioblastoma patients – A retrospective single centre quality adjusted survival analysis (EVALUATE-study)
Medizinische Onkologie, Universitätsspital Basel, Basel
CHF 5000.– | Duration: 1. 5. 2015 – 31. 3. 2016

Ebbing Jan | Urinary calprotectin: a new diagnostic marker in urothelial carcinoma of the bladder
Klinik für Urologie, Universitätsspital Basel, Basel
CHF 20 000.– | Duration: 15. 1. 2014 – 31. 12. 2018

Jacob Francis | Modelling the globoside-ecadherin axis in ovarian cancer metastasis using genome-engineered cells
Departement Biomedizin, Universitätsspital Basel, Basel
CHF 17 000.– | Duration: 1. 8. 2015 – 29. 2. 2016

Läubli Heinz | In vivo investigations of Siglec-9 function on T cells in anti-tumour immune responses
Medizinische Onkologie, Universitätsspital Basel, Basel
CHF 25 000.– | Duration: 1. 9. 2015 – 31. 8. 2016

Manegold-Brauer Gwendolin | Prenatal prediction of total nucleated cell count in the umbilical cord blood (UCB) as a tool for optimized donor selection for public UCB donations
Frauenklinik, Universitätsspital Basel, Basel
CHF 10 500.– | Duration: 1. 5. 2015 – 31. 12. 2016

Münst Simone | Genetic alterations in benign breast biopsies of subsequent breast cancer patients
Institut für Pathologie, Universitätsspital Basel, Basel
CHF 57 200.– | Duration: 1. 9. 2015 – 31. 8. 2016

Ruiz Christian | Deciphering the clonal evolution in malignant melanoma
Institut für Pathologie, Universitätsspital Basel, Basel
CHF 60 000.– | Duration: 1. 10. 2015 – 30. 6. 2017

Ruppen Wilhelm | Comparison of oral morphine versus nasal ketamine spray with chitosan in cancer pain outpatients
Departement für Anästhesie, Universitätsspital Basel, Basel
CHF 30 000.– | Duration: 1. 1. 2015 – 31. 12. 2017

Spichiger Elisabeth | Mixed methods study to test the efficacy of the adapted German PRO-SELF© Plus Pain Control Program, an intervention directed at outpatients with cancer and their family caregivers to reduce pain and related symptoms (PEINCA)
Departement Public Health, Medizinische Fakultät, Universität Basel, Basel
CHF 20 000.– | Duration: 1. 6. 2015 – 1. 10. 2018

Zajac Paul | Anti-tumour potential of a recombinant vaccinia virus encoding CD40 ligand: a preclinical study
Departement für Biomedizin, Universitätsspital Basel, Basel
CHF 10 000.– | Duration: 1. 9. 2015 – 1. 9. 2016

Bern Cancer League

Dal Pra Alan | PROMET: multicentre, randomized, double blind, placebo controlled phase II trial of salvage radiotherapy +/- metformin HCL after prostatectomy failure
Universitätsklinik für Radioonkologie, Inselspital Bern, Bern
CHF 70 000.– | Duration: 1. 3. 2016 – 1. 8. 2017

Dislich Bastian | The role of autophagy for resistance to Her2 directed therapy in adenocarcinomas of the upper gastrointestinal tract
Institut für Pathologie, Universität Bern, Bern
CHF 60 000.– | Duration: 1. 10. 2015 – 1. 10. 2016

Hlushchuk Ruslan | Novel microangio-CT contrast agent enables 3D visualization and quantitative evaluation of the tumour vasculature down to the capillary level with the subsequent histological investigation
Institut für Anatomie, Universität Bern, Bern
CHF 60 000.– | Duration: 1. 9. 2015 – 1. 9. 2017

Medovà Michaela | Impact of PI3K mutations on MET receptor tyrosine kinase targeting in head and neck cancer
Departement Klinische Forschung, Universität Bern, Bern
CHF 60 000.– | Duration: 1. 10. 2015 – 1. 3. 2017

Schardt Julian | Identification of genetic alterations in circulating tumour cells associated with the development of resistance to targeted therapies in kidney cancer
Klinik für medizinische Onkologie, Inselspital Bern, Bern
CHF 60 000.– | Duration: 1. 1. 2016 – 1. 7. 2017

Schläfli Anna | Improving retinoic acid therapy in breast cancer by autophagy modulation
Institut für Pathologie, Universität Bern, Bern
CHF 80 000.– | Duration: 1. 3. 2016 – 1. 9. 2017

Weber Benedikt | Correlation of different Vascular Endothelial Growth Factor (VEGF) subtypes and their respective receptors (VEGFRs) with malignant melanoma disease progression
Klinik für Dermatologie, Inselspital Bern, Bern
CHF 40 000.– | Duration: 1. 1. 2016 – 1. 7. 2017

Central Switzerland Cancer League

Günthert Andreas | Vulvar prevalence of human papilloma viruses in patients with cervical intraepithelial neoplasia
Neue Frauenklinik, Kantonsspital, Luzern
CHF 34 000.– | Duration: 1. 1. 2015 – 31. 12. 2016

Geneva Cancer League

Bounameaux Henri | Support to create a translational research centre in onco-haematology
Centre de recherche translationnelle en onco-hématologie, Université de Genève, Genève
CHF 200 000.– | Duration: 1. 1. 2015 – 31. 12. 2019

Curran Joseph | The 5'UTR fingerprint: A new diagnostic marker for breast cancer
Département de Microbiologie et Médecine Moléculaire, Université de Genève, Genève
CHF 106 909.– | Duration: 1. 1. 2013 – 31. 12. 2015

Farina Annarita | Identification and quantification of clinically relevant biomarkers for difficult-to-diagnose digestive malignancies
Département de science des protéines humaines, Faculté de Médecine, Université de Genève, Genève
CHF 101 584.– | Duration: 1. 1. 2014 – 31. 12. 2015

Le Gal Frédérique | Melanoma: role of beta-adrenergic signalling
Service de Dermatologie, Hôpitaux universitaires de Genève, Genève
CHF 113 179.– | Duration: 1.1.2014 – 31.12.2015

Petignat Patrick | «DEPIST»: Randomized clinical trial to evaluate whether self-sampling for HPV could improve screening for women who do not attend cervical cancer screening
Département de Gynécologie et Obstétrique, Hôpitaux universitaires de Genève, Genève
CHF 79 750.– | Duration: 1.1.2015 – 31.12.2015

Preynat-Seauve Olivier | Identification of miRNA targets for glioblastoma using a novel in vitro model
Laboratoire d'immuno-hématologie transfusionnelle, Hôpitaux universitaires de Genève, Genève
CHF 99 986.– | Duration: 1.1.2013 – 31.12.2015

Serre-Beinier Véronique | Study of the role of the MIF/CD74 pathway in mesothelioma development
Département de chirurgie, Université de Genève, Genève
CHF 85 082.– | Duration: 1.1.2015 – 31.12.2015

Walker Paul | Improving the efficacy of glioma immunotherapy
Service d'Oncologie, Hôpitaux universitaires de Genève, Genève
CHF 88 054.– | Duration: 1.1.2014 – 31.12.2016

Wehrle-Haller Bernard | Kinase-Independent functions of the receptor tyrosine kinase, c-kit in the persistence and adhesion of cancer stem cells to their environmental niche
Département de Physiologie Cellulaire et Métabolisme, Université de Genève, Genève
CHF 70 500.– | Duration: 1.1.2013 – 31.12.2015

Grisons Cancer League

Cathomas Richard | Clinical research for the long-term follow-up of patients
Onkologie/Hämatologie, Kantonsspital Graubünden, Chur
CHF 20 000.– | Duration: 1.9.2014 – 31.12.2016

Cathomas Richard | Project on testicular cancer
Onkologie/Hämatologie, Kantonsspital Graubünden, Chur
CHF 10 000.– | Duration: 1.9.2014 – 31.12.2016

Zwahlen Daniel | 3D in vitro tumour model using a self-developed microfluidic chip for spheroids of bladder cancer cells
Radio-Onkologie, Kantonsspital Graubünden, Chur
CHF 10 000.– | Duration: 1.9.2014 – 31.12.2015

Schaffhausen Cancer League

Albisser Heidi | Day to day ethics in out-of-hospital health care services: development of an ethical decision-making model
Institut für Pflegewissenschaft, Universität Basel, Basel
CHF 20 000.– | Duration: 1.1.2014 – 31.12.2016

Thurgau Cancer League

Benz Rudolf | Long term follow-up of hairy cell leukaemia patients treated with subcutaneous Cladribine in SAKK trials
Klinik für Hämatologie, Kantonsspital Münsterlingen, Münsterlingen
CHF 15 000.– | Duration: 1.1.2015 – 31.12.2015

Legler Daniel | Breast cancer project
Biotechnologie Institut Thurgau, Kreuzlingen
CHF 33 333.– | Duration: 1.1.2013 – 31.12.2015

Ticino Cancer League

Catapano Carlo | Biological and genetic determinants of sensibility and resistance to small molecule inhibitors of STAT3 in human cancer
Istituto Oncologico della Svizzera Italiana (IOSI), Bellinzona
CHF 125 000.– | Duration: 1.1.2015 – 31.12.2015

Roggero Enrico | Comparison study to evaluate the impact of a multi-disciplinary board on the treatment of patients with prostate cancer
Istituto Oncologico della Svizzera Italiana (IOSI), Bellinzona
CHF 50 000.– | Duration: 1.1.2015 – 31.12.2015

Zurich Cancer League

Chijioke Obinna | Role of activating receptor-ligand interactions in natural killer cell mediated immune control of lytic infection by the oncogenic Epstein-Barr virus
Institut für Experimentelle Immunologie, Universität Zürich, Zürich
CHF 65 625.– | Duration: 1.1.2013 – 31.12.2015

Müller Anne | Epigenetic silencing of tumour suppressor genes in the pathogenesis of diffuse large B-cell lymphoma
Institut für Molekulare Krebsforschung, Universität Zürich, Zürich
CHF 77 215.– | Duration: 1.1.2013 – 31.12.2015

Santoro Raffaela | Therapeutic targeting of TIP5 in aggressive prostate cancer
Institut für molekulare Mechanismen bei Krankheiten, Universität Zürich, Zürich
CHF 95 000.– | Duration: 1.1.2015 – 31.12.2015

Schäfer Beat | Therapeutic targeting of oncogenic fusion proteins by transcriptional repression
Abteilung Onkologie, Universitäts-Kinderspital Zürich, Zürich
CHF 55 335.– | Duration: 1.1.2014 – 31.12.2016

Spirig Rebecca | Mixed methods study to test the efficacy of the adapted German PRO-SELF© Plus Pain Control Program, an intervention directed at outpatients with cancer and their family caregivers to reduce pain and related symptoms (PEINCA)
Pflegedirektion, Universitätsspital Zürich, Zürich
CHF 20 211.– | Duration: 1.1.2015 – 31.12.2015

van den Broek Maries | Tertiary lymphoid structures in lung cancer
Institut für Experimentelle Immunologie, Universität Zürich, Zürich
CHF 108 639.– | Duration: 1.1.2015 – 31.12.2015

Vees Hansjörg | SAKK 15/12, Early prophylactic cranial irradiation with hippocampal avoidance in patients with limited disease small-cell lung cancer. A multicentre phase II trial
Institut für Radiotherapie, Klinik Hirslanden, Zürich
CHF 20 000.– | Duration: 1.1.2015 – 31.12.2015

Wong Wei-Lynn | The role of inhibitors of apoptosis proteins in the tumour microenvironment
Institut für Experimentelle Immunologie, Universität Zürich, Zürich
CHF 56 866.– | Duration: 1.1.2015 – 31.12.2015

Cancer epigenetics and new biomarkers

What is epigenetics? The term describes heritable changes in gene expression (active versus inactive genes) that direct the programs in cells without changes to the actual DNA sequence. This regulation of how the genes are read defines the phenotype without altering the genotype; the metamorphosis of caterpillars into butterflies is a beautiful example[1].

Epigenetic changes in cancer

It has been recognized over the last two decades that alterations of gene regulation are an important aspect of cancer development. Key elements associated with deregulation of gene expression in cancer have been associated with epigenetic reprogramming, comprising epigenetic silencing of key genes mediated by DNA methylation and modification of histone proteins that package DNA into a higher order of structure called chromatin. Cancer-related epigenetic deregulations go hand in hand with gene mutations and other physical alterations of DNA, comprising gene deletions, amplifications, and rearrangements, all characteristic features of cancer cells. The dynamics of the interaction of these alterations lead to the gene expression patterns that actually drive the cancer process. Currently, research efforts are aiming at deciphering the underlying mechanisms that lead to these cancer-associated epigenetic changes. This could lead to the development of clinically relevant biomarkers. In addition, understanding these underlying processes should point to potential druggable targets and thus eventually allow the devising of new strategies for cancer treatment.

Aberrant DNA methylation

The epigenetic modification of DNA comprises the enzymatic addition of methyl groups at regulatory regions of genes, which also include "CpG islands" commonly located in gene promoters that regulate gene expression[1]. Methylation of these CpG islands silences the respective genes and leads to loss of ex-

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pression of these genes. In tumours, silencing is often observed at tumour suppressor genes. The aberrant DNA methylation can be measured at individual genes of interest or genome-wide using several types of high throughput technologies that allow determination of the "methylome" of tumours. The methylome is quite characteristic for a given tumour type. Besides the tumour-associated methylation changes, the methylome still holds information about the cell of origin. The methylome has thus provided insights into the aetiology of different types of tumours that arise at specific ages in life and may affect specific locations (e.g. for certain types of brain tumours, as we will see below).

Since aberrant DNA methylation is an early event in many tumour types, this can also be used as a biomarker for the presence of rare cancer cells in small biopsies. For instance, in prostate cancer, needle biopsies are epigenetically profiled for aberrant DNA methylation of a set of three key genes (GSTP1, APC and RASSF1) that are suited for early disease detection. This improves the exclusion of false negative histology results, thereby reducing the need for further biopsies[2].

Mutations in epigenetic modifiers

On the histone level, alterations in gene regulation are brought about by chromatin modifiers that comprise epigenetic "writers", which add different types of modifications (methylation, acetylation, etc.) to the histone tails. The modified histone tails constitute an epigenetic regulatory code that is recognized by specific proteins, the chromatin "readers". Depending on the specific modification, the "readers" can either activate or inactivate subsequent processes affecting gene expression. Finally, there are "erasers" that remove the modifications added by the "writers". Hence, histone modifications are highly complex, and it is not surprising that these processes are deregulated during cancer development.

For example, our research laboratory focuses on human gliomas, the most common brain tumours. More than 50% of gliomas carry mutations in at least one of a set of 36 chromatin modifier genes. Moreover, mutations are also found in histone *H3F3A*, affecting one third of paediatric glioblastomas[3]. Glioblastomas are the most aggressive form of gliomas and have a dismal prognosis. There are two recurrent mutations, both of which are located in the histone tail, near (G34) or at a position (K27) subject to regulatory modifications impacting gene expression. Hence, either of the two mutations will affect the regulatory function of the histone. Consequently, these tumours are epigenetically profoundly deranged, which is also reflected in characteristically altered patterns of genome-wide DNA methylation. The glioblastomas with the K27 mutation are mostly located in midline structures of the brain, e.g. in the brain stem, which is not the case for the G34 mutant glioblastomas. Furthermore, glioblastoma patients with a K27 mutation have a particularly bad prognosis when compared to all other glioblastoma patients. Thus, the K27 and G34 mutations have become important biomarkers for diagnostic and prognostic purposes in gliomas in children and also young adults.

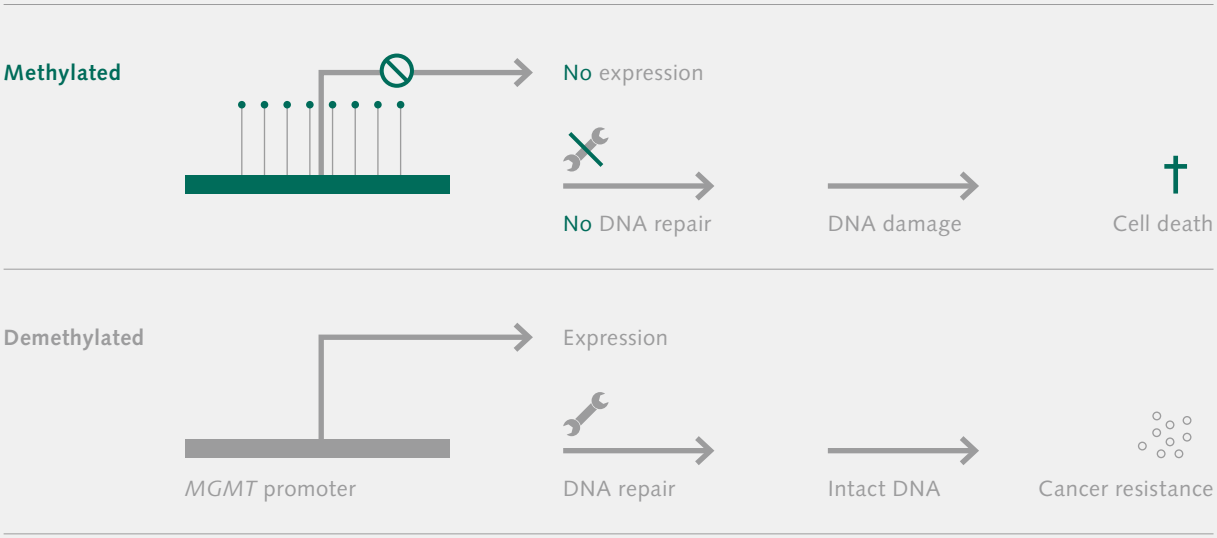
IDH mutations are characteristic for glioma in young adults associated with a good prognosis

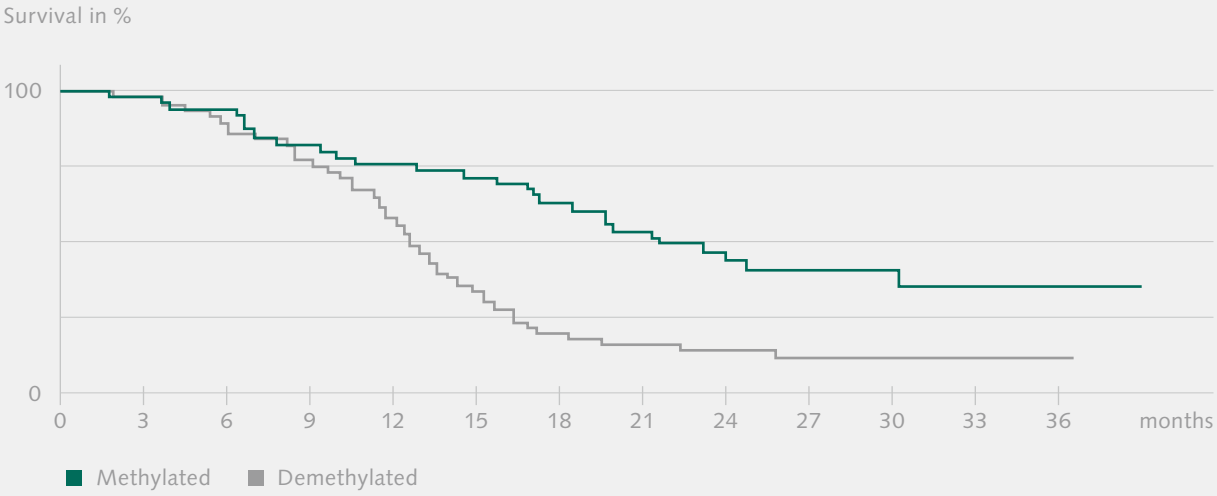
Mutations in the isocitrate dehydrogenase genes 1 or 2 (*IDH1* or *IDH2*) are characteristic for lower grade gliomas, which constitute a subtype of glioblastomas affecting predominantly young adults[4]. Interestingly, the occurrence of an IDH-mutation in a tumour indirectly induces a CpG Island Methylator Phenotype (CIMP), where a large characteristic set of genes is unduly methylated and thereby inactivated. The mechanism is quite astounding: The mutated IDH-proteins produce an oncometabolite (2-hydroxy glutarate) that does not normally exist in the body and accumulates in high concentrations.

Figure

Promoter methylation of the DNA repair gene *MGMT* in glioblastomas sensitizes to temozolomide chemotherapy

In tumour cells with a methylated *MGMT* promoter, the repair gene *MGMT* is turned off, and DNA lesions induced by alkylating agent therapy such as temozolomide are not repaired. The cells therefore die. In contrast, in tumours with an unmethylated *MGMT* promoter, the *MGMT* gene is expressed, the DNA damages are repaired, and the cancer cells survive.
The survival curves from a clinical trial[8] indicate that chemoradiotherapy with temozolomide yields better results in patients with a methylated *MGMT*.





This oncometabolite has an inhibitory effect on epigenetic modifiers, e. g. those responsible for demethylating DNA – hence resulting in CIMP[5]. Young patients with this tumour characteristic have a better prognosis and respond fairly well to radio- and chemotherapy[6]. The same mutations associated with CIMP are also found in a subset of leukaemia and some other tumour types. The mutation status of *IDH1* and *IDH2* has therefore become a clinically important biomarker that is now determined in routine diagnostics for these tumour types. In addition, there are efforts aiming at devising therapies specifically targeting tumours with IDH-mutations[7].

Epigenetic silencing of the repair gene MGMT is predictive for benefit from alkylating agent therapy in glioblastomas

Aberrant DNA methylation in tumours targets a wide range of genes that may impede tumour growth. However, these epigenetically inactive genes may become the "Achilles heel" of a tumour when treated with certain drugs. In almost 50 % of glioblastomas, the repair gene *MGMT* (O6-methylguanine DNA methyl transferase) has a methylated promoter and is therefore turned off (see Figure). This repair protein is normally expressed in all cells and efficiently repairs lesions set by alkylating agent therapy such as temozolomide. We found in several clinical trials that patients whose tumours harbour a methylated *MGMT* may benefit from temozolomide treatment, whereas this is not the case in patients with an unmethylated *MGMT*[8,9]. Therefore, separate trials are devised for glioblastoma patients with an unmethylated *MGMT* in which new drugs with other modes of action are tested in order to improve outcomes in these patients[10].

In conclusion

These recent discoveries have identified a number of new biologically and clinically relevant epigenetic biomarkers that have greatly improved our understanding, here exemplified mostly for brain tumours. Some of these biomarkers are relevant for more accurate tumour diagnosis and prognosis. The first epigenetic biomarkers have already been integrated into the newly updated WHO 2016 classification for brain tumours[11]. Other epigenetic alterations, such as the methylation status of *MGMT,* have a predictive value and allow biomarker-driven treatment decisions. However, there are large gene sets that are epigenetically inactivated and still await discovery. They will inform us about new potential "Achilles heel(s)" of these tumours that may be targeted by specific treatments.

Monika Hegi, PhD

Prof. Monika Hegi completed her PhD at the Federal Institute of Technology (ETH) in Zurich, and she joined the National Institute of Environmental Health Sciences in North Carolina (United States) for her postdoctoral training. Since 1998 she has directed the Laboratory of Brain Tumor Biology and Genetics in the Department of Clinical Neurosciences at Lausanne University Hospital (CHUV). Her research aims at identifying new molecular targets and predictive factors for response to therapy and outcome in patients with brain tumours, with a special interest in cancer epigenomics. Her research efforts are undertaken in close collaboration with clinicians and international cooperative groups for clinical trials.

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4. Yan H, Parsons DW, Jin G, McLendon R, Rasheed BA, Yuan W, et al. IDH1 and IDH2 mutations in gliomas. *N Engl J Med.* 2009;360:765-73.
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9. Hegi ME, Stupp R. Withholding temozolomide in glioblastoma patients with unmethylated *MGMT* promoter – still a dilemma? *Neuro Oncol.* 2015;17:1425-7.
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11. Louis DN, Perry A, Reifenberger G, von Deimling A, Figarella-Branger D, Cavenee WK, et al. The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary. *Acta Neuropathol.* 2016;131:803-20.

Selected results

Project
Telomere instability and the DNA damage response in cancer: a proteomic approach
Institut Suisse de Recherche Expérimentale sur le Cancer, EPF de Lausanne, Lausanne
CHF 347 200.– | Duration: 1. 4. 2012 – 31. 7. 2015 | KFS 2810-08-2011

Project coordinator
Prof. Joachim Lingner, PhD | joachim.lingner@epfl.ch

New Achilles heel of cancer cells

The reproduction potential of cells is limited, because the ends of the chromosomes shorten with each cell division. To grow unchecked, cancer cells depend on the lengthening of their chromosome ends. Based on studies supported by the Swiss Cancer Research foundation, Joachim Lingner's research group presents a strategy to prevent this lengthening – and thus to stop the proliferation of cancer cells.

For a cell to be able to divide, it must first replicate its DNA. But the molecular machinery responsible for this fails to replicate a small amount of DNA at the chromosome end. For this reason, chromosome ends, or telomeres, shorten with every round of cell division. This begins a natural maturation and aging process that ultimately leads to senescent cells, with telomeres that are so short that the cells can no longer divide.

Cancer cells have to overcome this limitation in order to be capable of unchecked proliferation. For this they make use of an enzyme called telomerase, which is normally activated only during embryonic development and in stem cells, where the telomerase turns back the biological clock of the cells, so to speak, by lengthening the chromosome ends. As after birth it is mainly cancer cells that depend on the activity of telomerase, this enzyme is actually an ideal target for anti-cancer therapy. "The problem is that the telomerase inhibitors developed up to now are not efficient enough and have therefore not achieved good clinical results", says Joachim Lingner, a biologist heading a research lab in Lausanne.

In studies supported by the Swiss Cancer Research foundation, Lingner's team has taken a closer look at the aging process at the telomeres. They have found senescence factors that accumulate when telomere length shortens. But the Lingner lab has also found a protein called peroxiredoxin 1 (PRDX1) that protects telomeres from oxidation. Like iron, which increasingly rusts, cell components are also affected by chemical breakdown over time. In studies with cell cultures, oxidative damage occurred at the telomeres when the researchers removed the PRDX1 enzyme.

This is significant, because telomerase can counteract telomere shortening only at undamaged telomeres. Therefore, an important aim of future research studies at the Lingner lab will be to find substances that can inhibit or even block PRDX1. For if it were possible to break through the protective shield that saves telomeres from oxidative stress, the rejuvenating activity of telomerase could be indirectly prevented and thus the proliferation of cancer cells kept within bounds.

Reference

Grolimund L, Aeby E, Hamelin R, Armand F, Chiappe D, Moniatte M, et al. A quantitative telomeric chromatin isolation protocol identifies different telomeric states. *Nat Commun.* 2013;4:2848.

Project
Enhancing anti-cancer immunity through sequential stimulation of innate immune pathways
Departement Medizin, Universität Freiburg, Freiburg
CHF 109 700.– | Duration: 1. 8. 2012 – 31. 1. 2015 | KFS 2910-02-2012

Project coordinator
Prof. Carole Bourquin, MD | carole.bourquin@unifr.ch

Giving the immune system a helping hand – at the right time

Immunomodulators can activate the body's own immune system and thus make it able to fight and destroy cancer cells. But the effect of the modulators is dependent upon the time point at which they are administered, as Carole Bourquin and her team of researchers show in mice studies supported by the Swiss Cancer League.

Immunotherapies are among the most promising approaches in the fight against cancer. They are not acting on the cancer cells directly but instead redirect the body's existing defence system against cancer cells. But up to now, there is only a limited understanding of how to best and the most effectively activate the immune system, which is a highly complex interplay of many different cells.

Mice studies conducted by Carole Bourquin and her research group at the University of Fribourg have now brought an important new aspect to light: For the stimulation of the immune system it not only matters what substances are used but also at what time point they are administered. In their studies, the researchers have activated the immune system in mice using a combination of two different immunomodulators. The two modulators are synthetically produced molecules that resemble components of viruses – and thus appear to the immune system to indicate viral infection.

"The immune response to a viral infection can be divided into two phases", explains Bourquin. First, the immune cells have to detect the antigens in the body. If immune cells, for instance in the lung, meet with viral RNA (or the first immunomodulator, which resembles viral RNA), they sound the alarm: They send out messenger substances that circulate throughout the body and enhance the readiness of all other immune cells. In the second phase, when also the alarmed cells meet with virus components (or the second immunomodulator), the immune response is much stronger than without the previous alarm.

That the immune cells go into a state of emergency, in that they respond very strongly to the administration of a second immunomodulator but no longer respond at all to another administration of the first immunomodulator – and that they show a completely different sensitivity, was something that Bourquin did not expect. To Bourquin, this dynamic adaptation of these cells also explains why the combination of the two modulators – administered at staggered intervals – led to much better results in the mice studies.

Further studies are needed to show that also the human immune system has this two-phase response to viruses. If that should be the case, it would become necessary based on Bourquin's findings to optimize the administration methods for immunotherapeutics. With correctly timed, increased activation of the immune system, there are better chances that the great hopes now being placed in immunotherapies can in fact be fulfilled.

Reference

Hotz C, Roetzer LC, Huber T, Sailer A, Oberson A, Treinies M, et al. TLR and RLR Signaling Are Reprogrammed in Opposite Directions after Detection of Viral Infection. *J Immunol.* 2015;195:4387-95.

List of approved research projects in 2015

More information about the funded projects can be found on www.krebsliga.ch/researchprojects

Total funds allocated: CHF 8 006 200.–

Ballmer-Hofer Kurt | Role of VEGF receptor signalling in primary and metastatic tumour growth and preclinical evaluation of novel allosteric VEGFR-2 inhibitors
Forschungsbereich Biologie und Chemie, Paul Scherrer Institut, Villigen
CHF 76 550.– | Duration: 1. 9. 2015 – 29. 2. 2016 | KLS 3569-02-2015

Basler Konrad | Assessment of the therapeutic potential of targeting Wnt ligand production and ß-catenin activity in treating colon cancer
Institut für Molekulare Biologie, Universität Zürich, Zürich
CHF 360 350.– | Duration: 1. 8. 2015 – 31. 7. 2018 | KFS 3572-02-2015

Bentires-Alj Mohamed | Targeting the phosphatase SHP2 and blocking macrophages in metastatic breast cancer
Friedrich-Miescher-Institut für biomedizinische Forschung (FMI), Basel
CHF 357 150.– | Duration: 1. 3. 2016 – 1. 3. 2019 | KFS 3571-02-2015

Bertoni Francesco | Characterization of FLI1 as an oncogene and therapeutic target in diffuse large B-cell lymphomas
Istituto Oncologico di Ricerca (IOR), Bellinzona
CHF 359 800.– | Duration: 2. 8. 2015 – 1. 8. 2018 | KLS 3580-02-2015

De Libero Gennaro | A novel population of human MR1-restricted T-cells in anti-tumour immunity
Departement Biomedizin, Universität Basel, Basel
CHF 365 100.– | Duration: 1. 1. 2016 – 31. 12. 2018 | KFS 3730-08-2015

Frew Ian | Development of mouse models and identification of therapies for renal angiomyolipoma
Physiologisches Institut, Universität Zürich, Zürich
CHF 375 000.– | Duration: 1. 12. 2015 – 30. 11. 2018 | KFS 3693-08-2015

Giachino Claudio | A novel tumour suppressor function of Notch receptors in glioma
Departement Biomedizin, Universität Basel, Basel
CHF 351 250.– | Duration: 1. 3. 2016 – 1. 3. 2019 | KFS 3600-02-2015

Gilliet Michel | Spontaneous and therapeutic STING activation in the tumour microenvironment of melanoma
Service de dermatologie, Centre hospitalier universitaire vaudois (CHUV), Lausanne
CHF 370 800.– | Duration: 1. 8. 2015 – 31. 7. 2018 | KFS 3652-02-2015

Gorr Thomas | Role of myoglobin in the tumourigenesis of p53 wild type and deficient breast cancers
Institut für Veterinärphysiologie, Universität Zürich, Zürich
CHF 242 450.– | Duration: 1. 3. 2016 – 28. 2. 2019 | KFS 3692-08-2015

Groettrup Marcus | Investigating immunoproteasome inhibition as a new approach to colorectal cancer therapy
Biotechnologie Institut Thurgau, Kreuzlingen
CHF 367 300.– | Duration: 1. 2. 2016 – 31. 1. 2019 | KFS 3687-08-2015

Grzesiek Stephan | Structural and dynamical basis of allosteric regulation and inhibition of abelson tyrosine kinase, a drug target in the treatment of chronic myelogeneous leukaemia
Biozentrum, Universität Basel, Basel
CHF 329 950.– | Duration: 1. 9. 2015 – 31. 8. 2018 | KFS 3603-02-2015

Handschin Christoph | Effect of exercise and exercise factors on cancer cachexia
Biozentrum, Universität Basel, Basel
CHF 255 500.– | Duration: 1.1.2016 – 31.12.2018 | KFS 3733-08-2015

Hantschel Oliver | Identification and targeting of allosteric regulatory sites in oncogenic cytoplasmic tyrosine kinases
Institut suisse de recherche expérimentale sur le cancer (ISREC), EPF de Lausanne, Lausanne
CHF 374 750.– | Duration: 1.10.2015 – 30.9.2018 | KLS 3595-02-2015

Held Werner | Memory-like CD8 T-cells in tumour immune responses
Centre Ludwig pour la recherche sur le cancer, Université de Lausanne, Epalinges
CHF 356 850.– | Duration: 1.7.2015 – 30.6.2018 | KFS 3601-02-2015

Hottiger Michael O. | Dissecting the molecular mechanisms of PARP inhibitor synthetic lethality in breast cancer cells
Institut für Veterinärbiochemie und Molekularbiologie, Universität Zürich, Zürich
CHF 370 900.– | Duration: 1.2.2016 – 31.1.2019 | KFS 3740-08-2015-R

Krek Wilhelm | Hypoxia-driven Sf3b1-dependent splicing in pancreatic cancer growth
Institut für Molekulare Gesundheitswissenschaften, ETH Zürich, Zürich
CHF 373 900.– | Duration: 1.7.2015 – 30.6.2018 | KFS 3651-02-2015

Müller Anne | The haematopoietic oncoprotein FoxP1 promotes tumour cell survival in diffuse large B-cell lymphoma: identification of FoxP1 target genes and their relevance for patient stratification and prognostication
Institut für Molekulare Krebsforschung, Universität Zürich, Zürich
CHF 164 900.– | Duration: 1.7.2015 – 30.6.2018 | KLS 3612-02-2015

Nigg Erich A. | Bacterial vector-mediated cancer therapy: increased tumour specificity with enhanced cytotoxicity
Biozentrum, Universität Basel, Basel
CHF 119 750.– | Duration: 1.8.2015 – 31.12.2017 | KFS 3579-02-2015

Pertz Olivier | A tumour on a chip approach to understand signalling networks mediating melanoma drug resistance at the single-cell level
Institut für Zellbiologie, Universität Bern, Bern
CHF 363 200.– | Duration: 1.6.2016 – 1.6.2019 | KFS 3727-08-2015

Rass Ulrich | Assessment of nuclease/helicase DNA2 and holliday junction resolvase GEN1 as potential targets for cancer therapy
Friedrich-Miescher-Institut für biomedizinische Forschung (FMI), Basel
CHF 215 250.– | Duration: 1.2.2016 – 3.3.2018 | KFS 3754-08-2015

Shakhova Olga | Unravelling the molecular mechanisms of Sox10-dependent melanoma progression
Klinik für Onkologie, Universitätsspital Zürich, Schlieren
CHF 364 900.– | Duration: 1.7.2015 – 30.6.2018 | KFS 3607-02-2015-R

Simon Hans-Uwe | Methylation of ATG genes and melanoma metastasis
Institut für Pharmakologie, Universität Bern, Bern
CHF 366 950.– | Duration: 1.1.2016 – 31.12.2018 | KFS 3703-08-2015

Sommer Lukas | Cellular and molecular mechanisms governing melanoma initiation, growth, and metastasis formation in vivo
Anatomisches Institut, Universität Zürich, Zürich
CHF 375 000.– | Duration: 1.1.2016 – 31.12.2018 | KFS 3682-08-2015

Theurillat Jean-Philippe | Role of TRIM24 in prostate cancer initiation and progression
Istituto Oncologico di Ricerca (IOR), Bellinzona
CHF 247 200.– | Duration: 1.9.2015 – 31.8.2017 | KLS 3654-02-2015

Varani Luca | Targeted delivery of chemotherapy agents to acute myeloid leukaemia cells by antibody-nanoparticle conjugates
Istituto di ricerca in biomedicina (IRB), Bellinzona
CHF 237 900.– | Duration: 1. 2. 2016 – 31. 1. 2018 | KFS 3728-08-2015

Zippelius Alfred | Development of novel targeted immunotherapies for the treatment of non-small cell lung cancer
Departement Biomedizin, Universitätsspital Basel, Basel
CHF 263 550.– | Duration: 1. 9. 2016 – 1. 9. 2019 | KFS 3394-02-2014

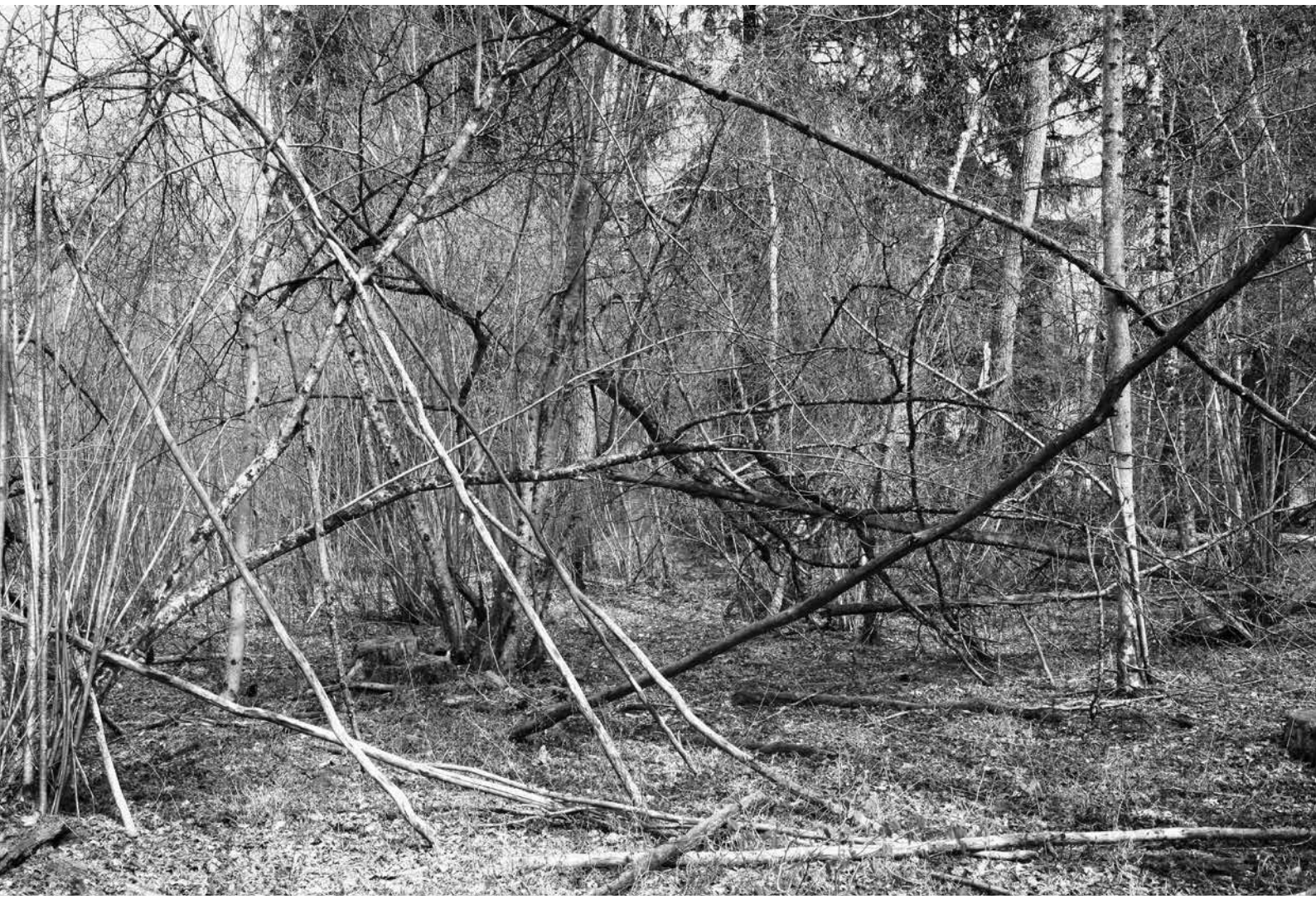
Approved bursaries in 2015

Total funds allocated: CHF 455 000.–

Gschwend Thomas | TNFR and TNIK signalling in colon cancer stem cells
Destination: Universitätsklinik für medizinische Onkologie, Inselspital Bern, Bern
CHF 180 000.– | Duration: 1. 9. 2015 – 31. 8. 2018 | MD-PhD 3559-06-2015

Räber Miro Emanuel | Immune response to abdominal tumours and their metastases
Destination: Klinik für Immunologie, Universitätsspital Zürich, Zürich
CHF 180 000.– | Duration: 1. 9. 2015 – 31. 8. 2018 | MD-PhD 3557-06-2015

Weiss Tobias | Vaccination against glioblastoma with tumour antigen-derived designer peptides
Destination: Labor für Molekulare Neuro-Onkologie, Universitätsspital Zürich, Zürich
CHF 180 000.– | Duration: 1. 9. 2015 – 31. 8. 2018 | MD-PhD 3558-06-2015



Exercise and cancer

The male mouse runs an average 6.8 km per day on the running wheel. In contrast to a sedentary mouse, which dies within a short time from implanted tumours, tumour growth is suppressed in wheel-running tumour-bearing mice, as a recently published study found[1]. Spectacular! If the running wheel was a drug, we would immediately find it in multimillion clinical research programmes at all large pharmaceutical companies. Why are things different in the field of exercise research? And where do we currently stand?

Do we need clinical cancer research in the area of physical activity?

Don't we all know that exercise is healthy? Then "just do it"! From a pragmatic point of view, we would endorse that statement in the areas of primary and secondary prevention. Multiple epidemiological studies, such as a recently published study on leisure-time physical activity and reduced risk of cancer[2], have found an association between lack of exercise and both cancer incidence and cancer mortality. Together with the known benefits for metabolism and for cardiovascular, mental, and probably also brain health (memory!), the recommendation is clear: "Just do it!" Research questions focus here on the underlying mechanisms, knowledge of which may possibly lead to targeted non-drug interventions for prevention and early detection in risk populations. Another focus would be in the area of societal and behavioural research: How do people in the industrialized countries regain motivation for daily physical activity?

Exercise and established cancer

Can implementation of structured physical activity play a role in the prognosis and quality of life of cancer patients? This question is a hot topic worldwide and is also being studied by our research group in Basel, supported by a Swiss National Science Foundation research professorship. So far, we know that exercise programmes are possible and safe during chemotherapy treatment. Controlled studies have also shown that the exercise is efficient – that is, also

Prof. Viviane Hess, MD
Senior physician of oncology and head of the Clinical Cancer Research Center at University Hospital Basel

patients with cancer can increase their fitness level through exercise. A classical measurement parameter for this is an increase in aerobic capacity or strength[3].

When we compare an exercise programme with a new medication, it has passed Phase I testing regarding feasibility, safety, and meeting the goal (increase in physical fitness). In the next step, evidence of efficacy must be found. But what does efficacy mean in the context of exercise research? A look at the current research literature shows that decisions vary widely across studies on what the main result should be to see if exercise works, and thus on what should be measured as the primary endpoint. In my opinion, there is no reason why for the intervention "exercise" we should use different criteria for effectiveness than for other interventions, such as drug interventions: In a clearly defined population of patients with cancer, a clearly defined intervention should result in significantly longer survival time and/or better quality of life.

That is precisely what is being tested in the large-scale ACTIVE-2 (SAKK 41/14) study, which is being conducted at 17 Swiss hospitals. Patients with inoperable colon cancer are treated with standard chemotherapy. One half of the patients, randomly selected, remain neither more nor less physically active in their daily lives than beforehand (control group). But the other half of the patients (intervention group) takes part during chemotherapy treatment in a physical activity programme with physiotherapy (interval training on a bicycle ergometer, twice a week for 12 weeks). With a total of 524 planned participants, this study will provide a definitive answer on whether patient survival (primary endpoint: progression-free survival as a surrogate for overall survival) and/or quality of life (measured using the established questionnaire of the Edmonton Symptom Assessment System[4]) can be improved through this combination of chemotherapy and exercise. Internationally there is only one comparable study, which is investigating whether the combination of exercise training and drug therapy as compared to drug therapy alone affects the survival rate of patients with breast cancer at the Memorial Sloan Kettering Cancer Center in New York. However, currently ongoing is only the preparatory Phase II trial (NCT01725633).

Why should exercise have an effect on cancer prognosis?

The short answer: We do not know the exact mechanisms. But we do know that exercise affects many cellular processes that are also important in cancer progression. It is also likely that there are several mechanisms involved. Exercise is not only one intervention but instead probably has very different effects depending on the population and situation. Intervention studies should take this into account and select and define the intervention and the population carefully: In this connection, Lee W. Jones at Memorial Sloan Kettering Cancer Center, who is one of the leading exercise researchers worldwide, uses the term "precision medicine"[5].

The following is an incomplete list of possible mechanisms[6]:

- Cellular metabolism: Exercise has an effect on the mTor/PI3K signalling pathway, which is important in cancer progression – via insulin and insulin-like growth factors as well as indirectly via energy balance (AMP kinase).
- Immune system: NK cells, the natural killer cells essential for tumour control, are recruited in the blood and to tumours through exercise, both in human beings and also in the mouse experiment mentioned above.
- Interaction with chemotherapy: For one, it has been shown that women with breast cancer who exercise during chemotherapy experience fewer side effects (including nausea) and thus tolerate a higher dose overall, which can improve the effectiveness of the treatment per se[7]. For another, it is conceivable that in "the physically active body" chemotherapy is differently distributed and metabolized (pharmacokinetics) and as a result works differently.
- Stress reduction: Changes in the body in response to acute stress are essential for survival, but the persistent hormonal changes in response to chronic stress (cortisol, adrenalin) are not healthy and are associated – directly or indirectly via changes in the immune system (NK cells) – with processes that promote cancer growth[8]. In reverse, regular physical activity leads to stress reduction. This means that chronic stress and physical activity are two interdependent factors that can both play a role in the course of cancer. In this complex research area we find ourselves only at the beginning, especially when we leave animal experiments and attempt clinical research with patients. In two clinical studies supported by the Swiss Cancer Research foundation, we are investigating some first aspects of these connections.

In the TOGETHER study, we are measuring longitudinally mental (Distress Thermometer) and physical stress (daily time course of cortisol) in patients with newly diagnosed Glioblastoma multiforme (GBM). The primary analysis examines whether measurable stress at diagnosis has an effect on prognosis. At the same time, and also studied longitudinally, we are measuring physical activity and physical fitness in the six-minute walk test as a stress-modulating factor. We are particularly interested in another, as yet little studied, possible stress-modulating factor: stress level in the person closest to the patient. Who those persons are, is defined by the patients themselves and may be a partner/spouse, parent, adult child, or a person close to the patient outside the family who has daily contact with the patient. With their consent, their stress levels (Distress Thermometer and daily course of cortisol in saliva) are also measured at the same time points. We expect that next year we will be able to describe, for the first time, how the stress levels in this close relationship system behave over time, how they are dependent on one another, and whether there are possibly any indications that they may affect the prognosis of the illness.

In the STREAM study, psychological stress is being charted prospectively, longitudinally also in a broader collective of newly diagnosed cancer patients. At the same time, we are investigating the feasibility, acceptance, and efficacy of a new online stress management programme that we have developed specifically for patients with cancer (www.stress-aktiv-mindern.ch).

Challenges in conducting exercise studies

There are numerous indications from preclinical, epidemiological, and observational studies that physical activity can play a role in prognosis also for established cancer. However, there is a lack of large randomized intervention studies that provide definitive evidence and are needed to make interventions a standard of clinical care. The ACTIVE-2 (SAKK 41/14) study is one such study, and in developing it, we have experienced many of the challenges in planning and conducting exercise studies. In the very first place we should mention the main difference from large drug studies: There is no backing from an industry supplying funds to the tune of millions of francs, which are required for the conducting of sound, well-conceived, large, and multicentre studies. Flagship projects of that kind cannot be conducted with enthusiasm alone. We are still seeking additional financial support.

A second challenge worth noting is the problem of preconceived opinions in this area: Patients, physiotherapists, and physicians often have a firm opinion on whether exercise is beneficial or not. Although it is completely self-understood that, for example, after heart attacks patients are enrolled in physical activity programmes (also for patients with a predisposition to cardiovascular disease, which often does not apply for patients with colon cancer), some physicians find it difficult to send patients to the physiotherapist in addition to chemotherapy. On the other hand, precisely studies of this kind provide an opportunity for rethinking our customary reflexes. The participation of 17 hospitals in this study shows that we are capable of doing so.

Prof. Viviane Hess, MD

Viviane Hess studied medicine at the University of Lausanne and University of Zurich and then specialized in internal medicine and oncology. After research fellowships at Royal Marsden Hospital in London and the Dana Farber Cancer Institute in Boston she joined University Hospital Basel, where she has been head of clinical cancer research since 2011. In 2012 she was also awarded an SNSF professorship by the Swiss National Science Foundation. Her main research interests are drug development studies for gastrointestinal tumours and investigation of the impact of non-drug interventions – such as physical activity – on the effect of systemic cancer treatment.

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8. Reiche EM, Nunes SO, Morimoto HK. Stress, depression, the immune system, and cancer. *Lancet Oncol.* 2004;5:617-25.

Selected results

Project
Characterization of ATG5 as a tumour suppressor in cutaneous melanoma
Institut für Pharmakologie, Universität Bern, Bern
CHF 264 300.– | Duration: 1.7.2013 – 30.6.2015 | KFS 3099-02-2013

Project coordinator
Prof. Hans-Uwe Simon, MD, PhD | hans-uwe.simon@pki.unibe.ch

Examining self-renewal of cells

Cancer cells survive even under adverse conditions, because they have efficient recycling activities. However, these activities are reduced in the early stage, thus promoting the formation of a tumour. This has been found by Hans-Uwe Simon and his team in studies supported by the Swiss Cancer Research foundation.

As unbelievably complex molecular wonder machines, cells also possess a disposal system that degrades defective cell components and breaks them down into individual parts that the cell can then utilize again to build new components. Biologists call this recycling and renewal taking place inside the cell "autophagy", a term derived from Greek meaning roughly "self-eating".

These self-cleaning processes play an important role in maintaining cellular balance, or homeostasis. It has also been known for some time that tumour cells often show high levels of autophagy. Thanks to this high activity they can also survive under stress conditions – such as under the low oxygen levels typical of tumours or the toxic effects of chemotherapy. For this reason, researchers worldwide are studying substances that inhibit autophagy and can thus improve the effectiveness of cancer treatment.

However, that is only one side of the story: "Depending on the time point in the course of the disease, autophagy can not only promote tumour growth but also suppress it", says Hans-Uwe Simon, director of the Institute of Pharmacology at the University of Bern. In studies supported by the Swiss Cancer Research foundation, Simon's group has demonstrated that low levels of autophagy can promote the formation of cutaneous melanoma. They found that various autophagy-related genes are active in the cells of benign moles on the skin but are reduced in malignant melanomas. Based on these astonishing findings, Simon and his colleagues concluded that "neither too much nor too little autophagy is good".

The regulation of the genes involved in the self-renewal of the cells is probably a dynamic process, according to Simon: In early stages, the inactivation of these genes allows the degenerated cells to proliferate unchecked. But later, when the tumour has been established and disseminates metastases, it is dependent on increased activity of the autophagy-related genes: "This confuses laymen but also confuses us specialists", says Simon. In view of substances that can intervene in autophagy, it will be important in the future to consider not only what patients can benefit from these substances but also in what stage they should be administered.

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Liu H, He Z, Simon HU. Autophagy suppresses melanoma tumorigenesis by inducing senescence. *Autophagy.* 2014;10:372-3.
Liu H, He Z, Simon HU. Protective role of autophagy and autophagy-related protein 5 in early tumorigenesis. *J Mol Med (Berl).* 2015;93:159-64.

Project
Medical image analysis for brain tumour studies
Institut für chirurgische Technologien und Biomechanik, Universität Bern, Bern
CHF 228 300.– | Duration: 1. 8. 2013 – 31. 7. 2015 | KLS 3167-02-2013

Project coordinator
Prof. Mauricio Reyes, PhD | mauricio.reyes@istb.unibe.ch

When computers learn to read images of the brain

Radiologists have to have a good eye and a lot of experience to interpret the black, white and many shades of grey in magnetic resonance imaging (MRI) images to determine the volume of a tumour. Now, in cooperation with physicians, computer scientists supported by the Swiss Cancer League have developed software that can teach itself image analysis. The software is expected to support – and relieve – radiologists in the future.

Computers are better at the board games chess or Go than human players due not only to the ever increasing capacity of computer hardware but also to advances in the programming of machine learning: the algorithms that computers use to teach themselves how to solve a task. In research studies supported by the Swiss Cancer League, an interdisciplinary team of physicians and computer scientists led by Mauricio Reyes at the University of Bern have developed software that can analyse MRI scans and identify and measure brain tumours. And it can do so at least as well as experienced neuroradiologists can.

To the untrained eye, often not much more than the skull and the brain are identifiable in the grey-scale images. And also the software program developed by Reyes' group has to first train its analytical skills using images manually rated by human experts; this teaches it how to distinguish between healthy brain tissue and brain tumours. From the training data, the program – called BraTumIA ("Brain Tumor Image Analyzer") – derives decision rules that it then applies to new images. In this way the software decides for every voxel on a grid in three-dimensional space whether it belongs to the healthy white or grey matter in the brain – or to a cancerous lesion and the bleeding surrounding the tumour.

In a study conducted at Bern University Hospital, the BraTumIA program estimated tumour volumes as well as two human raters did. Experts' estimations of the localization and the volume of the tumour serve as the basis for radiation treatment planning and should therefore concur. In fact, however, there are often considerable differences. Reyes speaks of "a subjective component that is inherent in manual analysis". Fully-automated image analysis could limit the effect of inter-rater disagreement. Beyond that, it could also be a time saver for radiologists: They would only have to check whether they agree with the classification made by the BraTumIA program instead of having to measure brain tumours manually in a time-consuming procedure in front of the screen.

In the meanwhile, Reyes and his colleagues are already thinking ahead: As their program can analyse all types of imaging data, the software – once it learns what it needs to, based on imaging training data – could simplify analysis also in other medical areas such as diagnosis of multiple sclerosis or acute stroke.

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List of approved research projects in 2015

More information about the funded projects can be found on www.krebsliga.ch/researchprojects

Total funds allocated: CHF 6 121 750.–

Ammann Roland A. | SPOG – multicentre trial comparing high versus low temperature limit defining fever in paediatric patients with cancer in chemotherapy-induced neutropenia (FN)
Hämatologie und Onkologie, Universitätsklinik für Kinderheilkunde, Inselspital, Bern
CHF 327 800.– | Duration: 1.10.2015 – 30.9.2019 | KLS 3645-02-2015

Bornhauser Beat | Exploiting alternative cell death mechanisms to fight drug resistance in childhood leukaemia
Abteilung Onkologie, Universitäts-Kinderspital Zürich, Zürich
CHF 364 950.– | Duration: 1.7.2015 – 30.6.2018 | KFS 3609-02-2015

Brisken Cathrin | Lobular carcinoma of the breast: insights from a new PDX model
Institut suisse de recherche expérimentale sur le cancer (ISREC), EPF de Lausanne, Lausanne
CHF 357 750.– | Duration: 1.5.2016 – 30.4.2019 | KFS 3701-08-2015

Cordier Dominik | Treatment of recurrent or progressive meningiomas with the radiolabelled somatostatin antagonist Lu-177-DOTA-OPS201
Neurochirurgie, Universitätsspital Basel, Basel
CHF 122 800.– | Duration: 1.1.2017 – 31.12.2020 | KFS 3712-08-2015

Dal Pra Alan | PROMET: multicentre, randomized, double blind, placebo controlled phase II trial of salvage radiotherapy +/- metformin HCL after prostatectomy failure
Universitätsklinik für Radio-Onkologie, Inselspital, Bern
CHF 356 950.– | Duration: 1.7.2016 – 30.6.2019 | KFS 3742-08-2015

De Palma Michele | Targeting angiogenesis to enhance the efficacy of lung cancer immunotherapy
Institut suisse de recherche expérimentale sur le cancer (ISREC), EPF de Lausanne, Lausanne
CHF 368 700.– | Duration: 1.2.2016 – 3.3.2019 | KFS 3759-08-2015

Driessen Christoph | Preclinical assessment of next-generation, subunit-selective proteasome inhibitors for cancer therapy
Abteilung Onkologie und Hämatologie, Kantonsspital St. Gallen, St. Gallen
CHF 253 250.– | Duration: 1.5.2015 – 31.10.2017 | KFS 3567-02-2015

Eychmüller Steffen | Is early palliative care associated with a reduction in intensity and costs of care at the end of life in patients with advanced cancer? A randomized trial
Universitäres Zentrum für Palliative Care, Inselspital, Bern
CHF 192 600.– | Duration: 1.11.2016 – 30.4.2019 | KFS 3725-08-2015

Grünberg Jürgen | Ovarian cancer stem cells: radioimmunodiagnosis and -therapy using radiolanthanide coupled monoclonal antibodies
Zentrum für Radiopharmazeutische Wissenschaften, Paul Scherrer Institut, Villigen
CHF 218 000.– | Duration: 1.7.2015 – 30.6.2018 | KFS 3585-02-2015-R

Güller Ulrich | SAKK 41/13 adjuvant aspirin treatment in PIK3CA mutated colon cancer patients. A randomized, double-blinded, placebo-controlled, phase III trial
Klinik für Onkologie und Hämatologie, Kantonsspital St. Gallen, St. Gallen
CHF 351 650.– | Duration: 1.9.2015 – 31.8.2018 | KLS 3596-02-2015-R

Hemkens Lars | Clinical decision-making with novel cancer treatments: a meta-epidemiological study on the post-approval generation of clinical evidence
Institut für Klinische Epidemiologie und Biostatistik, Universitätsspital Basel, Basel
CHF 166 000.– | Duration: 1.10.2015 – 30.9.2018 | KLS 3587-02-2015

Hess Christoph | B-cell transformation and PTLD – investigating virus-mediated metabolic dysregulation in EBV infected cells
Departement Biomedizin, Universität Basel, Basel
CHF 373 850.– | Duration: 1.1.2016 – 31.12.2018 | KFS 3773-08-2015

Jandus Camilla | Harnessing the new family of innate lymphoid cells for immunotherapy of cancer
Centre Ludwig pour la recherche sur le cancer, Université de Lausanne, Epalinges
CHF 243 450.– | Duration: 1.7.2016 – 1.7.2018 | KFS 3710-08-2015-R

Karlo Christoph | Texture analysis of diagnostic imaging data in patients with renal neoplasms
Institut für diagnostische und interventionelle Radiologie, Universitätsspital Zürich, Zürich
CHF 49 250.– | Duration: 1.1.2016 – 31.12.2016 | KFS 3769-08-2015

Langer Rupert | Interaction of HER2 and molecular chaperones in gastroesophageal adenocarcinomas – biologic significance and therapeutic impact
Institut für Pathologie, Universität Bern, Bern
CHF 214 250.– | Duration: 1.4.2016 – 30.4.2018 | KFS 3700-08-2015

Meylan Etienne | Expression and functional characterization of glucose transporter GLUT1 in lung adenocarcinoma
Institut suisse de recherche expérimentale sur le cancer (ISREC), EPF de Lausanne, Lausanne
CHF 326 950.– | Duration: 1.2.2016 – 31.1.2020 | KFS 3681-08-2015-R

Rinaldi Andrea | Towards personalized medicine for patients affected by mantle cell lymphoma: Identification of genetic and epigenetic lesions within a large prospective phase III clinical trial
Istituto Oncologico di Ricerca (IOR), Bellinzona
CHF 115 800.– | Duration: 2.8.2015 – 1.8.2018 | KLS-3636-02-2015

Rossi Davide | Analysis of circulating tumour DNA to inform lymphoma management
Istituto Oncologico di Ricerca (IOR), Bellinzona
CHF 330 800.– | Duration: 1.2.2016 – 31.1.2019 | KFS 3746-08-2015

Schmitt-Opitz Isabelle | Mesoscape 001 – pS6: construction of a multi-institutional European tissue bank
Klinik für Thoraxchirurgie, Universitätsspital Zürich, Zürich
CHF 235 650.– | Duration: 1.4.2015 – 31.3.2018 | KFS 3626-02-2015-R

Skoda Radek C. | The pathogenesis of myeloproliferative neoplasms
Departement Biomedizin, Universitätsspital Basel, Basel
CHF 374 950.– | Duration: 1.10.2015 – 30.9.2018 | KFS-3655-02-2015

Terracciano Luigi M. | Genetic determinants for progression from cirrhosis to hepatocellular carcinoma
Institut für Pathologie, Universität Basel, Basel
CHF 365 000.– | Duration: 1.3.2016 – 28.2.2019 | KLS 3639-02-2015

Verdeil Gregory | Finding new targets to overcome T-cell exhaustion for immunotherapy of melanoma
Centre Ludwig pour la recherche sur le cancer, Université de Lausanne, Epalinges
CHF 243 900.– | Duration: 1.3.2016 – 28.2.2019 | KFS 3679-08-2015

Wolf Martin | Tumour oxygenation measured quantitatively and non-invasively by near-infrared optical tomography
Klinik für Neonatologie, Universitätsspital Zürich, Zürich
CHF 167 450.– | Duration: 1.4.2016 – 31.3.2019 | KFS 3732-08-2015

Approved bursaries in 2015

Total funds allocated: CHF 494 500.–

Berger Nicole Alexandra | Radiologic characterization of breast lesions with uncertain malignant potential (B3 lesions)
Destination: Dipartimento di Scienze Biomediche per la Salute, Università degli Studi di Milano, Milano, Italia
CHF 58 700.– | Duration: 1.1.2016 – 31.12.2016 | BIL KFS 3684-08-2015

Böttcher Steffen | Generation of mouse models of acute myeloid leukaemia for the identification of genotype-specific therapeutic targets
Destination: Brigham and Women's Hospital, Harvard Medical School, Dana-Farber Cancer Institute, Boston, USA
CHF 80 800.– | Duration: 1.1.2016 – 31.12.2017 | BIL KLS 3625-02-2015

Oriani Anna | Optimizing palliative care for elderly people in community settings: development and evaluation of a new short-term integrated service
Destination: Department of Palliative Care, Policy and Rehabilitation, King's College London, London, United Kingdom
CHF 46 900.– | Duration: 1.1.2016 – 31.12.2016 | BIL KFS 3709-08-2015

Schubert Adrian Daniel | A prospective study evaluating clinical outcomes using plasma and salivary ctDNA in HNSCC
Destination: Division of Head and Neck Cancer Research, Department of Otolaryngology, Johns Hopkins Medicine, Baltimore, USA
CHF 95 050.– | Duration: 1.10.2015 – 2.4.2017 | BIL KLS 3649-02-2015

Selby Kevin | Optimizing colorectal cancer screening in the general population
Destination: Kaiser Permanente Division of Research, University of California, Oakland, USA
CHF 122 800.– | Duration: 20.7.2016 – 19.7.2018 | BIL KFS 3720-08-2015

Tschan-Plessl Astrid | Integrative cellular profiling of NK cell repertoires in malignant lymphoma
Destination: Institute for Cancer Research, Oslo universitetssykehus, Norge
CHF 90 250.– | Duration: 1.5.2016 – 3.10.2017 | BIL KFS 3745-08-2015

Palliative care in transition

Modern medicine aims primarily to prevent and cure disease and prevent death. Accordingly, training and research focus mainly on these goals. The successes are impressive: In the last 60 years, life expectancy has increased by about 20 years. In a parallel development, there has been a change from acute illnesses to chronic health conditions. This has made palliative care ever more important. A considerable part of the growing need for palliative care can therefore be seen as an undesired, and especially unplanned, by-product of the success of modern medicine. In a visionary way, Aldous Huxley (1894–1963) put it like this over 60 years ago: "Medical science has made such tremendous progress that there is hardly a healthy human left."

Despite this societal change in disease presentations and progressions, in Switzerland, as in most non-Anglo-American countries, palliative care was put on the national agenda relatively late. Still, some regions, like the Canton of Geneva and Canton of Vaud and later also St. Gallen and Ticino, developed quite respectable palliative care services – primarily due to great efforts by a few pioneers. All of these local and regional offerings were created and implemented from the basis, bottom-up. For this reason, they always carried the risk of lack of sustainability.

In our alpine republic Switzerland, with its long-standing democratic tradition and especially its federalism, decision processes advance slowly, because political, geographical and cultural compromises always have to be worked out. What emerges from originally creative ideas, after a lengthy process, are majority-consensus projects with all rough edges rounded out. Unfortunately, the initial originality often falls by the wayside. Over time this mechanism practically won a place in the collective Swiss

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Member of the board of the Swiss Cancer League; former head physician of palliative care at the public cantonal hospitals of Ticino

genome. Great advances are therefore not the order of the day in our country. They arise at most from private initiatives of highly motivated-to-dogged persons or groups. All the more gratifying is the success story of the National Strategy for Palliative Care.

The National Strategy was initiated and published by the Dialogue on National Health Policy (a body that serves cooperation between the Federal Office of Public Health (FOPH) and the Swiss Conference of the Cantonal Ministers of Public Health (GDK)) in 2010, as commissioned by the head of the Federal Department of Home Affairs (FDHA) at the time, Federal Councillor Pascal Couchepin. The National Strategy was first developed for the years 2010–2012. Under Federal Councillor Burkhalter, who had since taken over the FDHA, it was renewed up to 2015 – and implemented in a number of core areas, such as the action areas of purely medical competencies and of care. But the National Strategy invested also in care structures and quality, tariff structures, and especially in education, training, and research.

The National Strategy is now concluded, but the issue of palliative care gained a lot of momentum from it, both among the public and in the professional area, so that it still has high priority on the social and political agenda of the FOPH. In fact, the FOPH and the GDK turned the National Strategy into the "Plattform Palliative Care", which continues to pursue the goal of ensuring that all persons in the country have low-threshold access to solid-quality palliative care. Without any doubt, the National Strategy's contribution was considerable in transforming a languishing wallflower into a strong and resilient plant, about whose future we no longer need to worry. In this sense, the National Strategy serves as a model and has an exemplary function for the National Dementia Strategy and the National Cancer Strategy. The momentum that the issue of palliative care has retained in the last years and decades was created by both the basis – that is, the public and the providers – and, increasingly, by the political and institutional decision makers. From a subjective viewpoint, I will describe and comment here on some of the important reasons for this.

The public

There have been enormous medical advances in the last decades. In the last 20 years especially, the development in diagnostics and treatment has been so fast that increasingly, it is economic considerations that limit the medical services on offer. The new challenge will thus no longer be, "What more can we do?" but instead, "What can we forgo – and soon: what must we forgo?" And equitable distribution will no longer be only an issue in the North-South divide but rather will move into the foreground also within our national social framework.

The undisputed progress has in part aroused unrealistic expectations. Our lifespan according to the statistics has almost eclipsed consciousness of our finite nature. But certain sober realizations regarding the omnipotence of medicine in the last 15 years have led many people to again put a priority on quality of life (above quantity of life). As a result, on the part of the (potential) "consumers" there has been an increasing demand for good palliative care in health care provision. This motivation is user driven and bottom-up.

Assisted suicide

Many classical definitions of palliative care state, among other things, that it respects life and its finite nature (in the wording of the European Association for Palliative Care: "Palliative care affirms life and regards dying as a normal process; it neither hastens nor postpones death"). But does this still hold? Is dying really still a "normal process" today? For decades modern medicine has no longer permitted natural death. It intervenes in nature at the end of life (and also at the start of life), certainly with the noble intention of having a positive effect perhaps not on life per se but at least on length of life and quality of life.

Assisted suicide is a perennial discussion issue on the political, social, ethical, and also medical levels. Switzerland is unique in that the law limits the circumstances in which assisted suicide is a crime, decriminalizing it in other cases (Article 115 of the Swiss penal code); the organizations offering suicide assistance refer to the law, and it ensures that the debate is not over. This has helped the development of palliative care in Switzerland. Opponents of euthanasia, and especially assisted suicide, argue that with good palliative care, the question of assisted suicide is unnecessary. The Federal Council, too, drove the development of the National Strategy forward using this argumentation.

But palliative care should not be declared and offered as an alternative to assisted suicide. Palliative care should be offered to everyone, in good and controlled quality – and that's that! Good palliative care means also that I, as a specialist in palliative care, can hear the question concerning assisted suicide and deal with it and do so unconstrained, without prejudice, and especially nonjudgmentally. Consequently, this also means that a person who wishes to die is not actively prevented, that I lend him a hand in his search for support or even support him myself, after having cared for the patient for perhaps weeks, months, or years, instead of referring the person wishing to die to a more or less anonymous instance/organization. However, this requires that the palliative care specialist must be specifically and comprehensively educated and trained in this area (that is not the case today!).

Swiss Cancer League

The Swiss Cancer League (SCL) played a leading role as a midwife to palliative care. In the early 1990s the SCL offered a multidisciplinary continuing education course in palliative care, which was pioneering for the time. Further, with the programme "Gemeinsam gegen Schmerzen" (together against pain) the SCL made successful efforts to implement pain and symptom management for patients with cancer. Many supporters of palliative care were sensitized by this programme. The SCL also gave decisive support to palliative ch, the Swiss Society for Palliative Medicine, Care and Support, for example in organizing large national events. Necessarily, however, the target public of the SCL was limited to patients with cancer. For this reason, and so as not to stand in the way of palliative ch in the framework of the National Strategy, the SCL withdrew somewhat but not without continuing to support palliative care in the background. In the context of the National Strategy Against Cancer and after the completed restructuring of the SCL, it makes sense to expand palliative care offerings, such as in the areas of sensitization, continuing education, and research.

Swiss Academy of Medical Sciences

The Swiss Academy of Medical Sciences (SAMS) took notice of the little seedling "palliative care" relatively early. It published the first ethical guidelines on palliative care in 2006 (and revised them in 2012). SAMS also recognized, for example, the role model character of the interprofessionalism that is well developed in palliative care. In the framework of projects under the National Strategy for Palliative Care, SAMS is mainly committed to supporting the fifth field of action, research, and has established a research funding programme in palliative care.

National Research Programme 67

In 2011 the Swiss National Science Foundation announced its National Research Programme "End of Life" (NRP 67), with the aim to gain knowledge useful to guiding decisions and practices at the end of life and to make this knowledge available to decision makers in the health care system, as well as to politicians and professionals involved in the care of persons at the end of life. NRP 67 approved 33 projects for funding. The studies deal with mainly health policy topics but also topics in the psychosocial area dealing with autonomy, decision making, and assisted suicide. Medical research questions in the narrower sense are not covered, however. Still, it can be expected that the results of the research programme on palliative care will provide an additional boost within the political and public discourse. Recent research has found that integration of palliative care in the entire cancer patient path has a positive effect on quality of life and quantity of life. The New England Journal of Medicine published Temel's[1] pioneering study on this in 2010, and Temel's findings have been confirmed by several studies since[2–4].

Swiss Medical Association (FMH)

With the interdisciplinary subspecialty "palliative medicine" that is new this year, physicians with various specialties can document that they have acquired in-depth knowledge in palliative medicine through completing targeted continuing medical education. The requirements to be fulfilled for earning the certification are quite demanding (www.palliative.ch/de/fachbereich/fachgruppe-aerzte/interdisziplinaerer-schwerpunkt).

Outlook, opportunities, and risks

What can we wish for the present and the future? Palliative care fills a real and increasing need of all people who have chronic progressive illness. The development of recent years is gratifyingly targeted and enlightened. However, this should not blind us to the fact that also the palliative movement offers room for fundamentalist attitudes. Fortunately, this risk is decreasing, but it remains important to make sure that palliative care is not misused as a vehicle against curative medicine or assisted suicide.

Merging the bottom-up development with the top-down development is strenuous (as is also the interprofessional and interdisciplinary work). Regarding sustainability, however, bringing them together turns out to be the model for success: It rids palliative care of the decades-old fug of "common or garden-variety medicine", but without becoming out of touch with reality and moving away into an ivory tower. What is needed now is more serious, comprehensible research that will be a key driver for recognition of the discipline. Cooperative research platforms have also taken up their work. This encouraging development received additional impetus with the creation of a chair/professorship at the University of Bern, University of Lausanne, and University of Zurich (where it is located within the faculty of theology!).

Modern palliative care entered our awareness due to the growing needs of patients with incurable cancer. But in the future that patient group will probably make up only a small part of those potentially benefitting from palliative care. The demographic development will ensure exponentially increasing demand for palliative care services. In the forefront here will be diseases such as chronic heart failure, chronic respiratory diseases, progressive neurological conditions, dementia, and – especially – multimorbidity and vulnerability/fragility in the elderly.

Hans Neuenschwander, MD
After studying medicine at the University of Bern, Hans Neuenschwander worked for some years as a cancer specialist at the Istituto Oncologico della Svizzera Italiana (IOSI) and then founded Hospice Ticino, a palliative homecare service for patients with cancer. After a stay in Canada, Neuenschwander also started the palliative care unit at the IOSI. In addition, Neuenschwander is the author of a standard reference work, "Handbuch Palliativmedizin", which was published in a third, completely revised edition in 2015.
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Selected results

Project
An interview study on Swiss palliative care physicians' opinions concerning hastened death practices
Servizio Cure Palliative, IOSI, Ospedale S. Giovanni, Bellinzona
CHF 58 700.– | Duration: 2. 6. 2014 – 1. 6. 2015 | KFS 3347-02-2014

Project coordinator
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Palliative care physicians' position on assisted suicide

Specialists in palliative medicine are regularly asked about assisted suicide, even though it is not a part of their education and training. Most palliative care physicians exercise great caution when dealing with these inquiries, but many still wish for better cooperation with assisted suicide organizations. These are the findings of a study supported by the Swiss Cancer Research foundation.

In Switzerland, actively helping someone to die with euthanasia is forbidden by law, but assisting in suicide is allowed under specific circumstances. Here, the role foreseen for physicians is limited to certifying that a person wishing to die is terminally ill and mentally competent. For the actual assistance in suicide – being present at the moment when the person seeking death takes the lethal drug – the assisted suicide organizations therefore usually rely on volunteers. How do palliative care physicians deal with assisted suicide requests, how do they cooperate with these organizations, and what are their experiences in this ethically delicate, legal grey area?

Claudia Gamondi and her team examined these questions in depth in a study supported by the Swiss Cancer Research foundation. Gamondi conducted qualitative interviews with 23 Swiss palliative care physicians and found that all of the specialists interviewed care for several patients each year that wish to die, but that only few of those patients finally die of assisted suicide. In conversations with their patients most of the palliative care physicians make it clear from the start that they do not see it as their role to prescribe the lethal drug but rather to support the patients in their decision making – by examining together the reasons for the patient's wish for assisted suicide, presenting alternatives, or involving family members.

"Many participants were faced with an ethical dilemma", Gamondi says. "They want to respect the patient's self-determination, but their own personal convictions and professional expectations speak against participating in assisted suicide." For Gamondi, this explains some of the physicians' reluctance in dealing with inquiries about assisted suicide. Only few of the physicians interviewed had contacted assisted suicide organizations, even though many palliative care physicians basically want better cooperation with these organizations. Compared to Belgium or the Netherlands, for instance, where the medical profession has developed specific medical education courses and support systems and the physicians' tasks are more clearly legally defined, in Switzerland palliative care physicians take on a more passive role probably out of caution. Gamondi thinks that Switzerland would do well to close the gaps in the law and eliminate ambiguities regarding physicians' responsibility; this would reduce physicians' uncertainty and more clearly structure the process of assisted suicide.

Reference

Gamondi C, Borasio GD, Oliver P, Preston NJ, Payne S. Palliative care physicians' experiences of the Swiss model of assisted suicide: a qualitative interview study. (in preparation)

List of approved research projects in 2015

More information about the funded projects can be found on www.krebsliga.ch/researchprojects

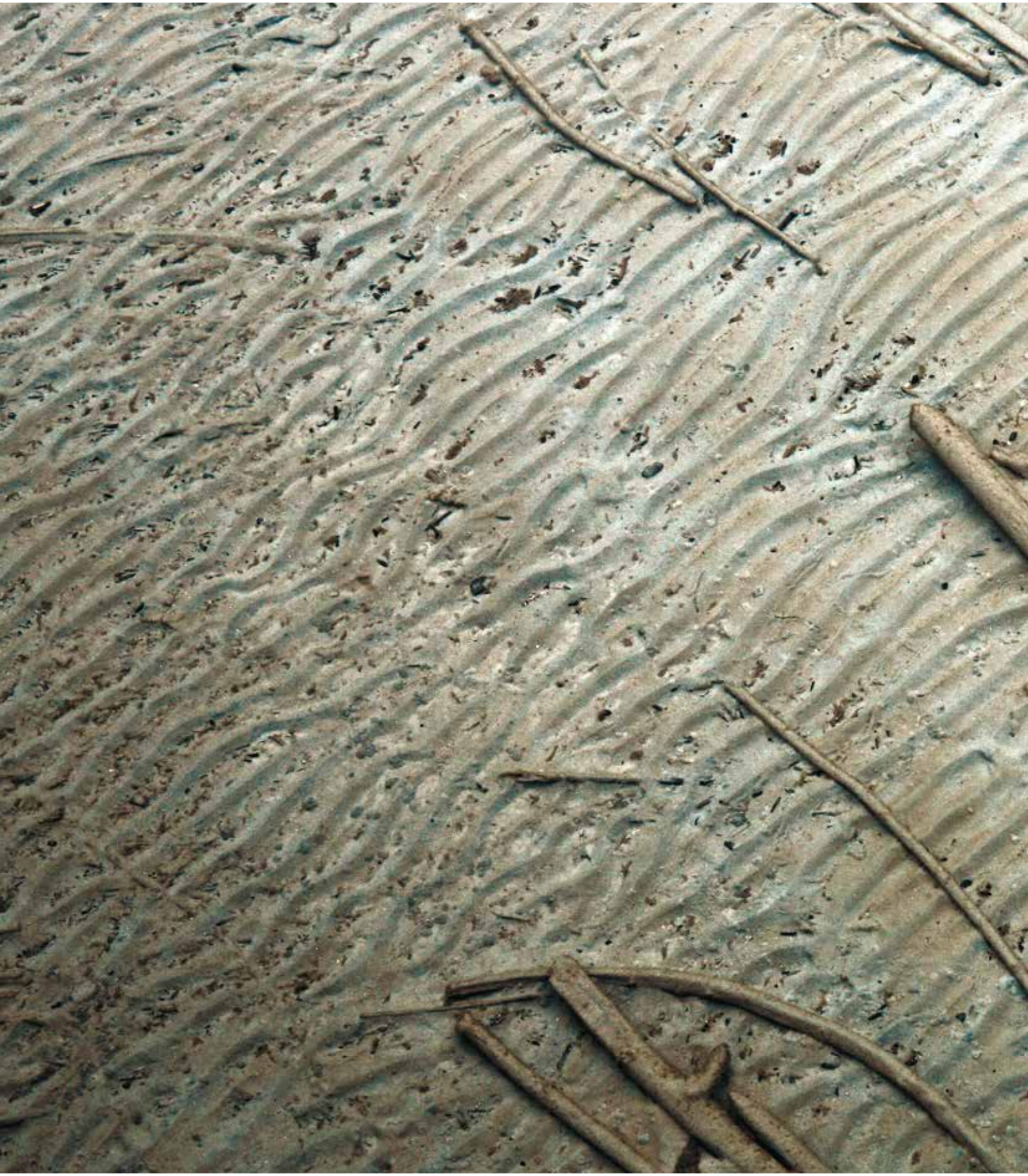
Total funds allocated: CHF 608 250.–

Barth Jürgen | Feasibility of a mind-body medicine mobile app for cancer patients
Institut für komplementäre und integrative Medizin, Universitätsspital Zürich, Zürich
CHF 199 550.– | Duration: 1. 8. 2015 – 31. 7. 2018 | KLS 3564-02-2015

Jenewein Josef | Dignity therapy+: a brief psychological and existential intervention for dying patients and their families – a pilot study
Klinik für Psychiatrie und Psychotherapie, Universitätsspital Zürich, Zürich
CHF 81 800.– | Duration: 1. 7. 2015 – 30. 6. 2016 | KFS 3637-02-2015

Leibundgut Kurt | Efficacy of cognitive and physical remediation trainings in paediatric cancer survivors
Universitätsklinik für Kinderheilkunde, Inselspital Bern, Bern
CHF 226 750.– | Duration: 1. 1. 2016 – 31. 12. 2017 | KFS 3705-08-2015

Tschudin Sibil | Decisional conflict of young cancer patients with regard to fertility preservation – effects of an online decision-aid tool
Abteilung für gynäkologische Sozialmedizin und Psychosomatik, Frauenklinik, Universitätsspital Basel, Basel
CHF 100 150.– | Duration: 1. 7. 2014 – 30. 6. 2017 | KFS 3584-02-2015



Cancer epidemiology in HIV-positive populations

"Rare cancer seen in 41 homosexuals": This article, published on July 3, 1981, in the New York Times, was one of the first reports on a disease that was defined a few months later as Acquired Immune Deficiency Syndrome (AIDS)[1]. Since its first description by dermatologist Moritz Kaposi in 1872, the classical Kaposi sarcoma had been known in Europe and the United States as a rare cancer[2]. But with the outbreak of the HIV/AIDS epidemic, the rate of this cancer greatly increased: Kaposi sarcoma is one of the most common cancers in persons with HIV. In addition, non-Hodgkin lymphoma and cervical cancer are also among the diseases called AIDS-defining illnesses. In the early 1990s patients with AIDS in the United States had an age-standardized incidence rate of more than 3500 per 100 000 person-years for Kaposi sarcoma, more than 2000 per 100 000 person-years for non-Hodgkin lymphoma, and more than 600 per 100 000 person-years for cervical cancer[3].

There are other cancers that are not classified as AIDS-defining illnesses but that also more commonly occur in persons with HIV than in the general population. These cancers include, for example, Hodgkin lymphoma, which occurs 11 times more often than in the general population (standardized incidence ratio (SIR): 11; 95 % confidence level (CL): 9 to 15), anal cancer (SIR: 28; 95 % CL: 21 to 35), and liver cancer (SIR: 6; 95 % CL: 4 to 8)[4]. Risk of developing other cancers is not higher than in the general population, such as colon cancer (SIR: 1.1; 95 % CL: 0.7 to 1.7), or is even reduced, such as prostate cancer (SIR: 0.7; 95 % CL: 0.6 to 0.9) and breast cancer (SIR: 0.7; 95 % CL: 0.6 to 0.97)[4].

Association with oncogenic pathogens

With few exceptions, cancers that more commonly occur in persons with HIV are associated with infection with an oncogenic pathogen. Tumorigenesis in persons with HIV is a multifactor process. Replication of the HI virus results in suppression of the immune system, which in turn leads to reduced con-

PD Julia Bohlius, MD
Head of research group at the Institute of Social and Preventive Medicine (ISPM) at the University of Bern

trol of pathogens, such as oncogenic viruses, and of malignant cells. In patients with HIV, approximately 40 % of cancers are associated with infections, whereas in the general population, only 4 % of cancers are associated with infections[5]. Among the most common cancers in patients with HIV are human herpesvirus-8-associated Kaposi sarcoma, Epstein-Barr virus-associated lymphoma, and human papillomavirus-associated anal and genital cancers. The association between the degree of immunodeficiency and risk of cancers has been shown for several AIDS-defining cancers and non-AIDS-defining cancers. The association is particularly strong for Kaposi sarcoma and non-Hodgkin lymphoma[6].

Lifestyle factors such as smoking also contribute towards a higher risk of cancer in persons with HIV. Studies have found that the percentage of smokers in the HIV-positive population in Europe and the United States is higher than in the general population[7]. With the increasing life expectancy of persons with HIV, the average age of the HIV-positive population has risen as well, which in turn facilitates cancer development.

AIDS therapy also reduces cancer incidence

The introduction of highly active antiretroviral therapy (HAART) in 1996 led to a great decrease in the incidence of AIDS-defining diseases. The Swiss HIV Cohort Study found that HAART has reduced the risk of Kaposi sarcoma by 90 % and non-Hodgkin lymphoma by 70 %[8,9]. However, most observational studies up to now have not been able to show that HAART also reduces the incidence of other cancers. Both in the United States and in Europe, the incidence rates for Hodgkin lymphoma, for example, have not decreased with the use of HAART[10,11]. The incidence of non-AIDS-defining cancers has remained largely constant, which has led to an overall relative increase in the incidence of non-AIDS-defining cancers in persons with HIV. Data from European HIV cohorts show that in the years 1999 and 2000, about 9 % of all deaths were caused by non-AIDS-defining cancers. From 2009 to 2011, this increased to 23 %[12].

A randomized trial published in 2015 found that early initiation of HAART considerably reduced the incidence of non-AIDS-defining cancers[13]. Compared to asymptomatic persons with HIV, who were started on HAART after the $CD4^+$-T-cell-count decreased to 350 cells per cubic millimetre, the group that was immediately treated with HAART with a $CD4^+$-count of more than 500 cells per cubic millimetre had a 40 % lower risk of non-AIDS-defining cancers (hazard ratio 0.61; 95 % CL: 0.38 to 0.97). This result seems to contradict the findings of earlier observational studies. However, it should be borne in mind that the data in the observational studies were collected under the treatment guidelines prevailing at the time, meaning that back then, patients with asymptomatic HIV were started on HAART after the $CD4^+$-count had dropped considerably lower than in the study cited here.

Positive effect of early initiation of therapy

In patients with symptomatic HIV infection, HAART is initiated immediately, but for patients with asymptomatic HIV the criteria for starting the therapy have changed since HAART was introduced. At first, HAART was initiated in asymptomatic patients only after the $CD4^+$-count had declined to below 200 $CD4^+$ cells per cubic millimetre. In 2011 the European guidelines raised that threshold value to 350 $CD4^+$ cells per cubic millimetre (http://www.eacsociety.org). Since 2015 the World Health Organization has recommended starting HAART as soon as possible after diagnosis of HIV and not waiting until the $CD4^+$ cells decline. For one, the hope is to reduce transmission of HIV to other persons. For another, it is expected that with this strategy a further reduction in HIV-related morbidity and mortality can be achieved. If the risk of non-AIDS-defining cancers is significantly affected by the HI-virus load and the status of the immune system prior to beginning antiretroviral therapy, very early initiation of HAART could definitely have a positive effect on cancer in persons with HIV. Evidence from further studies is needed.

To counter the increased risk of cancers in persons with HIV, preventive measures and screening tests are indispensable. Hepatitis B and human papillomavirus vaccinations and regular screening for cervical cancer are recommended in European guidelines (http://www.eacsociety.org). Whether or not it makes sense to screen for anal cancer in selected risk groups is under discussion. Screening recommendations for breast cancer, prostate cancer, and colon cancer are based on the recommendations for the general population.

Summary

Compared to the general population, persons with HIV have a considerably higher risk of cancers. HAART has increased the life expectancy of persons with HIV significantly. As HAART has thus far been able to reduce new occurrence of AIDS-defining illnesses but not of non-AIDS-defining cancers, cancers are an increasing problem in the HIV-positive population. Further studies are needed so that preventive measures can be developed and optimized.

PD Julia Bohlius, MD
Julia Bohlius studied medicine at the University of Hamburg and also completed a Master of Science in Public Health in London. After a number of years as a medical resident and research fellow at the University of Cologne and the Cochrane Haematological Malignancies Group located there, she joined the Institute of Social and Preventive Medicine at the University of Bern in 2007, where she heads the research group HIV-related Cancers. In 2011 she received the Robert Wenner Award given by the Swiss Cancer League for her work. In her research she is currently focusing the situation of HIV-positive patients in Europe and Africa. Her research studies are supported by the Swiss Cancer League and the Swiss National Science Foundation (Ambizione-PROSPER grant).
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Selected results

Project
Late mortality, second primary cancers and cardiovascular late effects in childhood cancer survivors
Institut für Sozial- und Präventivmedizin, Universität Bern, Bern
CHF 270 000.– | Duration: 1. 7. 2011 – 30. 6. 2014 | KFS 2783-02-2011

Project coordinator
Prof. Claudia Kühni, MD | claudia.kuehni@ispm.unibe.ch

When treatment touches our hearts

Thanks to spectacular advances, today more than 80 % of children with cancer are treated successfully. But chemotherapy and radiation therapy often leave their mark: Survivors of childhood cancer have a higher risk of cardiovascular disease in adulthood. Unfortunately, even the newer treatment protocols have not changed this, as Claudia Kühni and her research team found in a study supported by the Swiss Cancer Research foundation.

Just 50 years ago, doctors were simply powerless against cancer in children. Today, thanks to impressive advances in medicine, four out of five children can be treated successfully. This means that the number of childhood cancer survivors is growing rapidly; in Switzerland it is estimated to be 10 000 persons. Because the methods used to fight cancer – mainly the anthracycline family of chemotherapy drugs and radiation therapy – not only kill cancer cells but can also damage healthy tissue, they lead to side effects in many patients.

In that regard, topping the list of concerns is cardiovascular disease, which can often appear only decades after the cancer treatment. To estimate the extent of these late effects in Switzerland, Claudia Kühni and her team at the Swiss Childhood Cancer Registry in Bern asked survivors – and their siblings who had not had cancer – to fill out a questionnaire asking whether they had had cardiovascular problems. The researchers were interested in the entire spectrum of possible problems, from high blood pressure and arrhythmias to heart failure and strokes.

They found that childhood cancer survivors are affected about twice as often: Approximately 15 % of childhood cancer survivors – and only 8 % of their siblings – reported at least one cardiovascular problem on the questionnaire. And although treatment methods have changed a lot in the last 30 years (for instance, children used to receive whole chest radiation much more often than they do today), the risk of cardiovascular disease has not dropped noticeably.

What is more, the actual risk is probably higher than the survey indicates: "We think that the questionnaires show us only the tip of the iceberg", says Kühni. That is because cardiovascular problems usually begin slowly via subclinical pre-stages. For example, a reduced force of contraction of the heart can indicate the beginning of heart failure. But because people have no symptoms in these very early stages, they are usually not aware of them. For this reason, Kühni and her colleagues are planning a follow-up study in which they will use new methods that can identify these early stages. They aim to capture the late effects of cancer therapies in an early stage – that is, at a point in time when patients still can gain optimal benefit from treatment.

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Caccia JN, Hau-Grosch EM, Kasteler R, Spycher B, Suter T, Ammann RA, et al. Time trends and risk factors of cardiovascular disease after childhood acute lymphoblastic leukemia: report from the Swiss Childhood Cancer Survivor Study. (in preparation)

List of approved research projects in 2015

More information about the funded projects can be found on www.krebsliga.ch/researchprojects

Total funds allocated: CHF 862 100.–

Bochud Murielle | Dietary habits, nutrition and risk of late effects after childhood cancer
Institut Universitaire de Médecine Sociale et Préventive, Centre hospitalier universitaire vaudois (CHUV), Lausanne
CHF 290 200.– | Duration: 1. 7. 2015 – 30. 6. 2018 | KLS 3644-02-2015

Bouchardy Christine | Breast cancer and young women: tumour profile, treatment, outcome and effect on pregnancies
Registre genevois des tumeurs, Genève
CHF 268 650.– | Duration: 1.1.2016 – 30. 6. 2018 | KFS 3713-08-2015

Chappuis Pierre Olivier | Identification of new early-onset colorectal cancer susceptibility genes
Unité d'oncogénétique et de prévention des cancers, Hôpitaux universitaires de Genève, Genève
CHF 303 250.– | Duration: 4.1.2016 – 1.3.2019 | KFS 3753-08-2015

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