

#### Imprint

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Swiss Cancer League
Effingerstrasse 40
P.O. Box 8219
CH-3001 Bern
Tel. +41 (0)31 389 91 16
scientific-office@swisscancer.ch
www.swisscancer.ch/research

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Responsible: Rolf Marti, PhD

Head of Research, Innovation & Development department,

Swiss Cancer League

Project management and editing:

Ori Schipper, PhD

Communication officer for Research, Innovation & Development

department, Swiss Cancer League

English translation: Ellen Russon, East Sandwich, Massachusetts, USA, www.ellenrusson.com

Images: Georg Aerni Design: atelierrichner.ch Print: Ast & Fischer AG, Wabern

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Georg Aerni (\*1959 in Winterthur) takes a sober look at the natural and built environment in his image series. He is interested in how objects – under the influence of time and nature – evade and resist the human drive to shape the environment.

This report presents a selection of architectural and vegetable finds that the Zurich photographer discovered in the province of Apulia in southern Italy for his work series "Plastiche" (2015/16).

The diptych "Blüemlisalpgletscher" (2006) on pages 6 and 7 is a part of his "Holozän" series.

georgaerni.ch

## Cancer Research in Switzerland

Edition 2018

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Research is the basis for medical progress, which – especially in the field of cancer – is also demonstrated by the fact that many cancers are more treatable than they were some decades ago. But concern about another development is noticeably dampening the joy over treatment successes: Switzerland's health care system, financed based on solidarity, is still one of the best in the world, but with the explosion in the prices of pharmaceutical products, it cannot keep up in the long term.

What is objectionable in today's system is that in negotiations with the authorities, the pharmaceutical industry is able to impose drug prices that are not justifiable, because they are less and less related to production costs. For although the pharmaceutical industry explains the high prices of medications with the high cost of research and development, it actually spends considerably more on marketing. That is how the industry ensures fat profits.

That these profits are unfair also has to do with the fact that many foundational discoveries are made at universities and research institutes. Taxpayers end up paying twice: First, they pay for the generation of ideas that pave the way for new treatments. And then they pay inflated prices for drugs that in most cases have been developed based on – publicly funded – basic research.







Gilbert Zulian

The ever-rising prices – especially for drugs in the field of cancer – are a threat: If this development undergoes no correction, soon only wealthy persons will be able to afford live-saving medications. But multi-class medical care is unacceptable; it contradicts the principles of Swiss society. Industry interests must not prevail over the interests of people. Affordable cancer drugs are needed today and in the future, and for this the Swiss Cancer Research foundation and the Swiss Cancer League will continue to advocate.

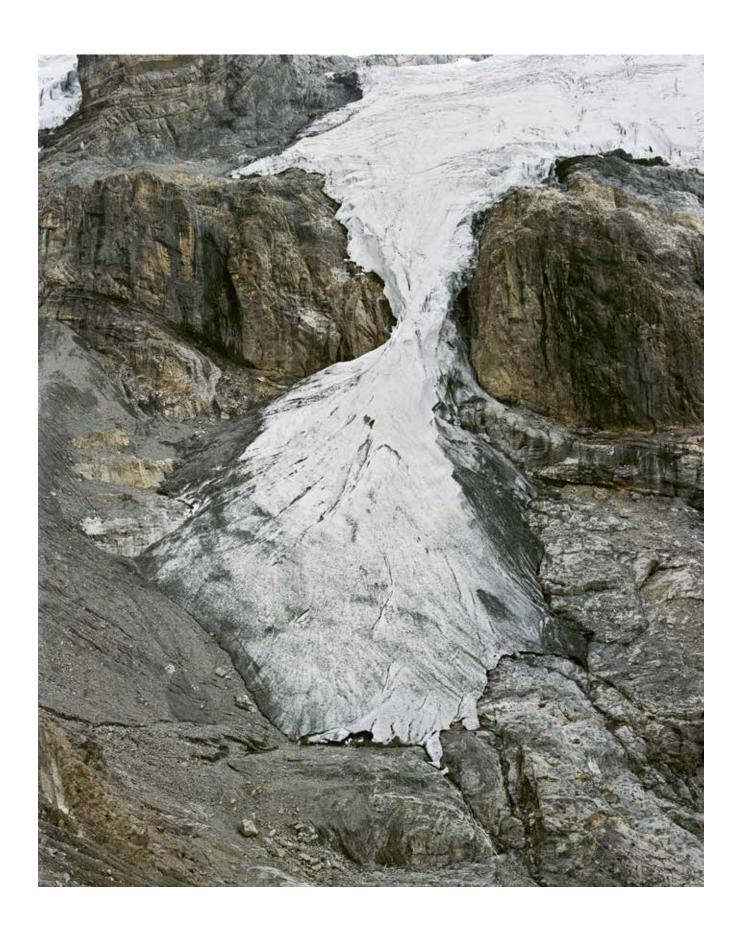
Prof. Thomas derny, MD

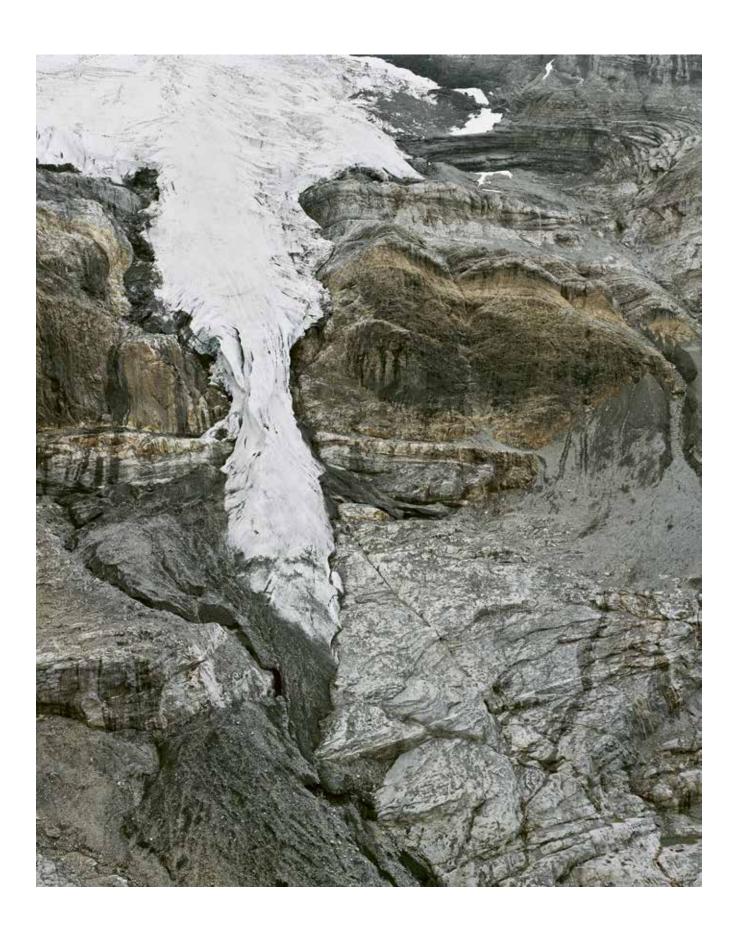
alley

President of the Swiss Cancer Research foundation

PD Gilbert Zulian, MD

President of the Swiss Cancer League





# Funding research – contributing to the good of patients

In 2017, 198 research proposals were submitted to the Swiss Cancer Research foundation and the Swiss Cancer League. After careful review, the 70 best projects could be funded with a total amount of 18.5 million francs. We thank all of the charitable donors for their trust and support.

PRO is one of the easily remembered acronyms, of which there are so many in English. PRO stands for patient-reported outcomes, a term that has become increasingly important and drawn more and more attention over the last 15 years. PRO are data that are directly reported by patients and that not only change the relationship between physicians and patients fundamentally but also can even prolong the life of cancer patients.

"We doctors assume that we know better about the side effects of a treatment than our patients do. But that's not true," says Ethan Basch. Basch, an oncologist at Memorial Sloan Kettering Cancer Center in New York and worldwide pioneer in research on PRO, spoke recently at the symposium 'Promoting Self-efficacy with Digital Tools' in Bern at the invitation of the Swiss Cancer League. As Basch and his colleagues have found in several studies, clinicians are unaware of nearly half of patient side-effects during cancer treatment.

#### Software solutions

There are many reasons for this. There is often not enough time during clinic visits to discuss all of the side effects. Or perhaps the patient has not had the sore throat for some time now and forgets to mention it when finally speaking to the doctor. Many studies have also shown that physicians tend to judge their patients' symptoms as less severe than they actually are. Fortunately, many of these problems can be solved today thanks to the use of the Internet and mobile devices such as tablets and smartphones.

There are software solutions that allow patients to record how they are feeling. They do not have to wait until their next visit to the clinic to describe symptoms that are bothering them. Instead, they can report the symptoms from home at any time. The system communicates the PRO to the treatment team, which in this way can assess the longitudinal development of the symptoms and in addition help their patients by responding with useful tips for symptom control. But perhaps even more importantly: If the team pays due attention to the PRO, it also intervenes early when a patient's symptom is severe or worsening. In many cases, the team in this way keeps the patients out of the hospital emergency room.

#### Survival benefit

This is how Basch explains the results of his most recent study. He and his research group compared two groups of patients with advanced cancer. The control group reported their symptoms to the oncologist during clinic visits. The second group, in addition to clinic visits, also self-reported their symptoms to the treatment team by computer from home.

Basch had expected that on average patients in the PRO group had better quality of life than patients in the control group. However, he was surprised to find that median survival among patients self-reporting their symptoms electronically was 31 months as opposed to 26 months for patients in the control group.

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.

Amount in million CHF

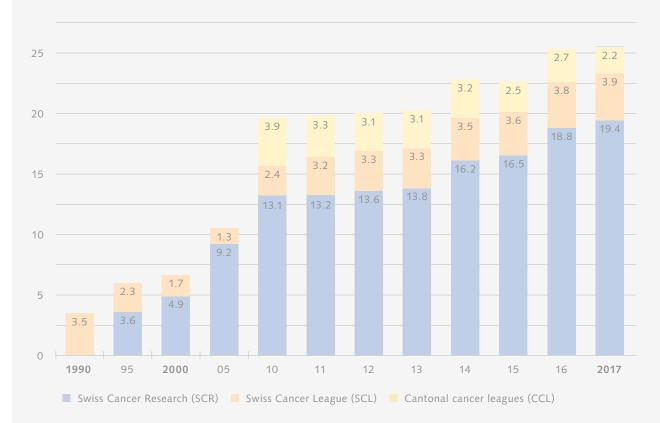


Table 1
Research funding by SCR, SCL, and CCL in overview
Number of grants approved and amount granted in 2017 (all funding areas)

	Number of grants approved	Amount granted in kCHF	Proportion of total funding in %
Total SCR, SCL, and CCL			
Independent research projects	99	19 810	80
Bursaries	7	1 057	4
Programme for health services research	7	942	4
Research organizations	7	2 600	10
Programmes, organizations and conferences	46	492	2
Total	166	25 433	100
SCR			
Independent research projects	52	14 586	77
Bursaries	5	746	4
Programme for health services research	7	942	5
Research organizations	6	2 400	13
Programmes, organizations and conferences	20	766	1
Total	90	19 440	100
SCL			
Independent research projects	11	3 016	80
Bursaries	2	311	8
Programme for health services research	-	-	-
Research organizations	1	200	5
Programmes, organizations and conferences	27	258	7
Total	41	3 785	100
CCL			
Independent research projects	36	2 208	
Bursaries	n.s.	n.s.	
Programme for health services research	-	-	
Research organizations	n.s.	n.s.	
Programmes, organizations and conferences	n.s.	n.s.	
Total	36	2 2 0 8	

n.s. = not specified



"The survival benefit of five months was greater than the survival benefit achieved by many cancer drugs that were approved in recent years," says Basch.

#### Experts on their own health

These results also mean that in the fight against cancer, it is not only about research on treatment options. Instead, medicine would be well advised to view patients as experts on their own health and to allow patients' expert knowledge to be taken into account in the treatment. Together with the cantonal and regional cancer leagues (CCL), the Swiss Cancer Research foundation (SCR) and the Swiss Cancer League (SCL) therefore support research projects across the whole spectrum of cancer research. In addition to the four traditional areas - basic, clinical, psychosocial, and epidemiological cancer research - health services research should be mentioned in particular, which, for example, compares the costs and benefits of medical care and studies care in real everyday life in clinic and treatment. Health services research is interested in the functioning of the health care system and is always on the lookout for possible concrete improvements.

# More than 25 million francs for over 160 different research projects

In 2017 the SCR, SCL, and the CCL together provided a total of 25.4 million francs for 166 different research institutions and research projects (Figure 1; Table 1). A good three quarters of all funds granted came from the SCR; the SCL contributed 15% and the CCL 9%.

The distribution of the funds from the two partner organizations SCR and SCL to research institutions in Switzerland shows that researchers at the university hospitals in Zurich, Bern, Lausanne, and Basel were the most successful with their research proposals; with contributions ranging between 4.8 million francs (Zurich) and 3.1 million francs (Basel), these research facilities received significant percentages of the total funding granted (Table 2). The academic research institutions in Zurich, Bern, and Lausanne stand out as centres of innovative cancer research in Switzerland. Each of them received approximately one fifth of the total funding in this highly competitive funding context.

In line with their funding strategy, the SCR and the SCL supported mainly independent research projects: In 2017, a total of 198 research proposals were submitted to the two partner organizations. Of these, after careful review, the 70 best and most promising research projects could be funded with 18.5 million francs (Table 3). Compared to the previous year, there was somewhat more competition for the limited

Table 2 Distribution of cancer research funding by SCR and SCL to the research institutions in 2017

Research institutions	Number of projects	Amount in kCHF	Proportion in%
Gastroenterologie Oberaargau Langenthal	1	340	1.7
University/Inselspital Bern	23	4 138	20.8
FMI Basel	2	284	1.4
University/University Hospital Basel	16	2 770	13.9
IOSI Bellinzona	4	654	3.3
IRB Bellinzona	3	813	4.1
Cardiocentro Ticino Lugano	1	95	0.5
University of Fribourg	1	152	0.8
University of Geneva/HUG	3	625	3.1
EPF Lausanne	4	827	4.2
University/CHUV Lausanne	15	2 936	14.8
Swiss Paraplegic Research Nottwil	1	184	0.9
University of Lucerne	1	168	0.8
Kantonsspital St. Gallen	4	900	4.5
HES-SO Valais-Wallis Leukerbad	1	119	0.6
ETH Zurich	1	228	1.1
University/University Hospital Zurich	19	4 514	22.7
Department of Health Sciences Helsana Group Zurio	ch 1	65	0.3
Stiftung Patientensicherheit Zurich	1	76	0.4
Total	102	19 888	100

#### Abbreviations

CHUV Centre Hospitalier Universitaire Vaudois

EPF Ecole Polytechnique Fédérale
ETH Eidgenössische Technische Hochschule
FMI Friedrich-Miescher-Institut

HES-SO Haute Ecole Spécialisée de Suisse Occidentale

HUG Hôpitaux Universitaires de Genève IOSI Istituto Oncologico della Svizzera Italiana

IRB Istituto di Ricerca in Biomedicina

funding available: Whereas in 2016 42% of all grant applications were approved, in 2017 the success rate decreased to 35%. Of the 198 grant applications submitted, the experts responsible for evaluating the quality of the proposals rated 89 projects as solid and promising and recommended them for funding. However, only 70 of the 89 projects recommended for support could be funded; for a further 19 high-quality research projects, there was unfortunately not enough funding available.

Compared to the previous year, it is noticeable that mainly the research projects in psychosocial research and epidemiological research had better success: In 2017 the Scientific Committee recommended two thirds of the research projects in these research areas for funding. Projects in health services research were reviewed by a specialized expert panel, the members of which include also persons with demonstrated expertise in, for example, health economics or nursing sciences.

The sum of all funds requested in competitive project research was 48.2 million francs, of which 18.5 million francs (or just under two fifths of the total funds requested) were granted to the approved projects. As in the previous year, somewhat more than one half of the funding total went to projects in basic research; 24% of the total went to projects in clinical research.

The remaining funds went to projects in psychosocial research and epidemiological research as well as to health services research. In these areas, the relatively small percentage of funding for projects is due, among other things, to the fact that only few high-quality research proposals were submitted. The SCR and the SCL were able to fund all research projects in these areas that were recommended for funding, but once again in 2017, the two partner organizations had to make difficult decisions in the other research areas and had to turn down 18 projects in basic research and one project in clinical research, even though they were rated highly in the evaluation by the Scientific Committee.

Table 3
Distribution of funds by SCR and SCL and success rates in the different research domains

All projects  Received/applied for  Recommended	Grant applications	Amount in kCHF	Grant applications	Amount in kCHF
Received/applied for Recommended	179			
Recommended	179			
	1/0	52 740	198	48 151
A	102		89	
Approved	74	18 746	70	18 544
Success rate	42 %	36%	35%	38%
Basic research				
Received/applied for	93	28 945	92	30 635
Recommended	53		51	
Approved	35	9 986	33	10 212
Success rate	38%	34%	36%	33%
Clinical research				
Received/applied for	66	19 144	44	11 666
Recommended	41			
Approved	31	7 308	18	4 495
Success rate	47 %	38%	41 %	31%
Psychosocial research Received/applied for	12	2 867	6	1 335
Recommended	4		4	
 Approved	4	438	4	829
Success rate	33%	15 %	67 %	62 %
Epidemiologic research				
Received/applied for	7	1 784	12	2 920
Recommended	4		8	
Approved	4	1 014	8	2 066
Success rate	57 %	57 %	67 %	71%
Health services research				
Received (letter of intent)/ap	onlied for		44	6 480
Invited (full proposal)/applie				1 595
Recommended	u 101		7	1 393
Recommended				
Approved			7	942

#### The research organizations supported, 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 network of about 20 Swiss research groups and a coordination centre in Bern. In particular 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.  $\rightarrow$  www.sakk.ch

#### 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.  $\rightarrow$  www.ibcsg.org

#### 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 health care policy, the data enable evidence-based decision making that benefits the population as well as individual patients with cancer.  $\rightarrow$  www.nicer.org

#### 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 are rare and moreover develop in all organs in the body, different treatments are required. To test and optimize the treatments, more than 200 international institutes participate in the IELSG network.  $\rightarrow$  www.ielsg.org

#### Swiss Paediatric Oncology Group (SPOG)

SPOG has been conducting clinical cancer research in paediatric oncology and 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 headquarters in Bern. The 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. → www.spog.ch

#### Swiss Childhood Cancer Registry (SKKR)

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. → www.kinderkrebsregister.ch

Table 4
Supported research organizations

Funding in the years 2010-2017

Amount in kCHF

7 11110 01111 11 11 11 11 11 11 11 11 11								
	2010	2011	2012	2013	2014	2015	2016	2017
Swiss Group for Clinical Cancer Research (SAKK)	600	600	600	*900	*1050	*1100	*1150	*1300
International Breast Cancer Study Group (IBCSG)	560	560	560	500	450	400	350	350
National Institute for Cancer Epidemiology and Registration (NICER)	-	200	200	250	250	250	250	250
International Extranodal Lymphoma Study Group (IELSG)	-	-	200	200	200	250	250	350
Swiss Paediatric Oncology Group (SPOG)	100	100	150	150	150	150	200	250
Swiss Childhood Cancer Registry (SCCR)	_	50	50	75	75	100	100	100
Total	1260	1 510	1760	2 075	2 175	2 250	2 300	2 600

<sup>\*</sup>of wich 200 000 CHF funded by SCL

#### Performance agreements for financing services

In the strategy of the two funding organizations SCR and SCL, approximately 60% of the funds is earmarked for what is called patient-centred research, the aim of which is to produce results that as far as possible directly benefit patients and their families. A look at the funding figures for independent research projects alone shows that this was not achieved. However, patient-centred research is supported not only by funding independent research projects. The SCR and the SCL also compensate six different research organizations for performing services for the benefit of clinical and epidemiological research in Switzerland.

In clinical research, these central and indispensable 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 their resources for collecting, managing, and analysing data in the cantonal and national cancer registries (see box).

For their expenditure, these organizations receive compensation based on performance agreements that define in a clear and binding way the requirements regarding 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 the contributions from the SCR. In 2017, the SCR paid out a total of 2.4 million francs to the six research organizations. Another 200 000 francs were provided by the SCL (Table 4).



#### Rolf Marti, PhD

Rolf Marti has headed the Research, Innovation & Development department (formerly: Scientific Office) since 2003. He is a member of the managing board of the Swiss Cancer League and director of the Swiss Cancer Research foundation office.

Tel. +41 (0)31389 9145 rolf.marti@krebsliga.ch www.krebsliga.ch/forschung www.krebsforschung.ch

#### 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 2014–2020.

#### Contact

Swiss Cancer Research
Effingerstrasse 40
P. O. Box 7021
CH-3001 Bern
Tel. +41 (0)31 389 9116
info@krebsforschung.ch
www.krebsforschung.ch

#### Swiss Cancer League (SCL)

The Swiss Cancer League 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.

#### Contact

Swiss Cancer League
Effingerstrasse 40
P. O. Box 8219
CH-3001 Bern
Tel. +41 (0)31 389 91 00
info@krebsliga.ch
www.krebsliga.ch

#### 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 Frenchspeaking 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. Based on the recommendations of the Scientific Committee, it decides on the granting of funds to researchers.

20

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



President

Prof. Thomas Cerny, MD

Cantonal Hospital St. Gallen



Prof. Daniel E. Speiser, MD University of Lausanne Basic research representative



Prof. Nicolas von der Weid, MD University Children's Hospital Basel (UKBB) Paediatric research representative



Prof. Martin F. Fey, MD Inselspital Bern Clinical research representative



Christine Egerszegi-Obrist Former member of the Swiss Council of States Mellingen



Prof. Beat Thürlimann, MD Cantonal Hospital St. Gallen Clinical research representative



Silvio Inderbitzin, PhD St. Niklausen



Prof. Matthias Egger, MD University of Bern Epidemiologic research representative



Treasurer

Gallus Mayer

Banking specialist

St. Gallen

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 regions of Switzerland.

The members of the board are:



President

PD Gilbert Bernard Zulian, MD

Head physician of Palliative Medicine

Hôpital de Bellerive

Geneva University Hospital (HUG)



Treasurer

Gallus Mayer

Banking specialist
St. Gallen



Vice president

PD Georg Stüssi, MD

Head, Department of Haematology
Oncology Institute of Southern

Switzerland (IOSI)



Hans Neuenschwander, MD Former head physician of Palliative Care Regional Hospital of Lugano



Prof. Daniel Betticher, MD Head physician of Oncology HFR Fribourg, Cantonal Hospital



Markus Notter, MD Radio-Oncology Lindenhof Hospital, Bern



Lucienne Bigler-Perrotin Manager Geneva Cancer League



**Brigitta Wössmer, PhD**Head psychologist of Psychosomatics
Basel University Hospital



Christoph Kurze Managing director Grisons Cancer League



Karin Zimmermann, PhD Registered nurse/scientific staff member Inselspital Bern



Members of the Scientific Committee in April 2018 (from left to right): Pedro Romero, Sarah Dauchy, Jürg Schwaller, Mark Rubin, Primo Schär, Joerg Huelsken, Maria Blettner, Andrea Alimonti, Simone Benhamou, Aurel Perren, Emanuele Zucca, Jörg Beyer, Nancy Hynes (president), Beat Schäfer, Martin Pruschy, Sabine Werner, Silke Gillessen, Rolf Marti (head of Research, Innovation & Development department), Tatiana Petrova, Peggy Janich (head of Research Funding), Sophie Pautex.

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

- Basic research: 6 members

- Clinical research: 8 members

- Psychosocial research: 2 members

- Epidemiologic research: 2 members

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 approval. It attaches particular importance to patient-centred research.

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. As the financial means are limited, not all high-quality grant applications can be funded, unfortunately. Funding goes exclusively to industry-independent research projects.

The Scientific Committee receives operational support from the Research, Innovation & Development department of the SCL. The department 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 members of the Scientific Committee are:

#### Basic research



Prof. Andrea Alimonti, MD Oncology Institute of Southern Switzerland (IOSI) Bellinzona



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



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



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



Prof. Pedro Romero, MD Department of Oncology University of Lausanne Epalinges



Prof. Primo Schär, PhD
Department of Biomedicine
University of Basel
Basel



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

#### Clinical research



Prof. Jörg Beyer, MD
Department of Oncology
University of Zurich
Zurich



Prof. Emanuele Zucca, MD Oncology Institute of Southern Switzerland (IOSI) Ospedale San Giovanni Bellinzona



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



Psychosocial research

Sarah Dauchy, MD
Department of Supportive Care
Gustave Roussy
Villejuif, France



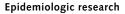
Prof. Aurel Perren, MD Institute of Pathology University of Bern Bern



Prof. Sophie Pautex, MD
Geriatric and Community Palliative
Care Unit
Geneva University Hospitals (HUG)
Chêne-Bougeries



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





Prof. Mark A. Rubin, MD
Department for Biomedical
Research (DBMR)
University of Bern
Bern



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



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



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



Prof. Sabine Werner, MD Institute of Molecular Health Sciences ETH Zurich Zurich

# Prizes for outstanding achievements

# in cancer research and the fight against cancer

In 2017, the Swiss Cancer League awarded the Robert Wenner Prize to Michele De Palma for his work investigating the complex interactions in the microenvironment of tumours. Friedrich Stiefel was awarded the Cancer Prize in recognition of his contributions to the development and conducting of communication courses for oncologists. Honouring a pioneer of the cancer helpline, the Cancer Medal was given to Irma Boving. Thomas Hoepli received the Recognition Award for founding the Swiss Bridge foundation. And finally, the 2017 Swiss Bridge Award for Cancer Research was awarded to dual recipients, a researcher in Israel and a researcher in Switzerland.

The 2017 Robert Wenner Prize of 100 000 francs for researchers under the age of 45 was awarded to biologist Michele De Palma at the Swiss Federal Institute of Technology Lausanne (EPFL). His investigations have contributed towards a better understanding of the interactions between the tumour cells and the cells in their direct environment.

Whether a tumour can be held in check by the body's immune system and rendered harmless or whether it grows and metastasizes depends not only on cancer cells themselves but also to a significant extent on cells in the environment of the tumour. Nearby healthy cells can form new blood vessels that can supply tumours with the blood they need and the nutrients required for the rapid division of hungry cancer cells. The neighbouring cells are also able to create what is called an immunosuppressive zone, in which the cancer cells are protected against attacks by the immune system.

#### A new class of immune cells

De Palma's research results show that these two aspects – blood supply and protection from the immune response – are more closely linked than previously assumed. Already during his dissertation, De Palma discovered a new class of immune cells, which are called TIE2-expressing macrophages or TEMs, which express substances that promote the formation of new blood vessels. Because TEMs at the same time have an immunosuppressive effect, they are important new points of attack in the fight against cancer.



Michele De Palma receives the 2017 Robert Wenner Prize.

# The interplay between formation of blood vessels and the immune response

The De Palma team has recently published findings on another functional connection between blood vessel formation and the immune response. In experiments with mice, the researchers found that when they suppressed the new formation of blood vessels by means of special antibodies, they observed more and more immune cells migrating into the tumour. And because the extent of this infiltration is decisive for the effectiveness of new immunotherapies – called immune checkpoint inhibitors – combinations of substances will now be tested in clinical studies that should inhibit the formation of new blood vessels as well as activate immune cells.

For his extraordinary research achievements, the Swiss Cancer League awarded De Palma the 2017 Robert Wenner Prize. The award ceremony was held in a worthy setting in the Empire Room of "zum Äusseren Stand", a restaurant in Bern.

#### **Robert Wenner Prize**

Thanks to the bequest of Robert Wenner, a gynaecologist from Basel who died in 1979, the Swiss Cancer League awards the Robert Wenner Prize of 100 000 francs to recognize outstanding research work by young researchers under the age of 45. The prize is given to research work conducted in Switzerland and from the entire range of cancer research. The first Robert Wenner Prize was awarded in 1983.

The Scientific Committee is responsible for evaluation of the candidates and selection of the prize winner. The prize winners receive 100 000 francs, with 80 000 francs earmarked for an ongoing research project and 20 000 francs as discretionary funds.

→ www.krebsliga.ch/rwp



Friedrich Stiefel, winner of the Cancer Prize, with Gilbert Zulian, president of the Swiss Cancer League, and Kathrin Kramis-Aebischer, CEO of the Swiss Cancer League.

The 10 000-franc Cancer Prize was awarded to Prof. Friedrich Stiefel, MD, head of the Service of Liaison Psychiatry, University Hospital of Lausanne, in gratitude for his valuable contributions as initiator and organizer of courses for improving the communication abilities of oncologists. In addition, Stiefel was vice president of the Swiss Cancer League from 2004 to 2007 and a member of the Scientific Committee from 2007 to 2016.

#### Beneficial effects of good communication

Communication is a central element in cancer care. The better the communication, the better that patients take their medications regularly and the more closely they follow their physicians' advice. In addition, good communication ensures less stress and greater work satisfaction for physicians and nursing staff. To allow

for and promote these beneficial effects, the Swiss Cancer League commissioned a working group just before the turn of the century with the development of a communication course. Stiefel and other experts were members of the group.

They put together a curriculum, which starts with a two-day block course in which the participants discuss difficult cases and reflect upon their own communication behaviour by means of video recordings of simulated conversations with patients. Course participants also have four to six supervisions in the following six months and then a final training. Introduced in 2000, the course was made a mandatory part of the training of prospective oncologists in Switzerland in 2005 by the professional association after successful evaluation. More than 600 persons have now completed the communication skills training. As a direct result, patients with cancer on average are experiencing better conversations today than they did 20 years ago.

Stiefel has played an essential role in this success story, as he not only contributed to the planning and development of the communication skills training but also ensured international exchange and alignment – for instance by organizing consensus conferences – and in this way paved the way for widespread incorporation and continuous further development and improvement of communication courses. Stiefel and his team have also conducted scientific studies on the effectiveness of the course, which also for the first time examined the clinicians' defence mechanisms in oncology.



Award winner Thomas Hoepli gives his thank-you speech.

#### **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 honoured Thomas Hoepli with the 2017 Recognition Award. Hoepli, a former financial expert, was recognized for his establishment of the Swiss Bridge foundation and for over 20 years of successful collaboration in the field of cancer research funding. Thanks to Hoepli's tireless efforts, the Swiss Bridge Award has become well established as a valuable funding instrument for competitive cancer research at the European level.

#### **Recognition Award**

With the Recognition Award the Swiss Cancer League honours persons or organizations for their committed work towards improving 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.

→ www.krebsliga.ch/anerkennungspreis

Irma Boving, registered nurse and qualified psychooncology advisor, is one of the pioneers of the cancer helpline. After establishing the advice and information services in 1995, Boving worked for decades as a qualified specialist, helping thousands of persons seeking advice. After 22 years, she retired in May 2017. But she still performs a small workload for Swiss Cancer League, which awarded her the Cancer Medal in gratitude for her loyal and valuable services.

#### Cancer Medal

The Cancer Medal was designed by iron sculptor Bernhard Luginbühl. It is awarded by the Swiss Cancer League every one to two years and recognizes outstanding services in the areas of prevention, early detection, and the fight against cancer and its consequences.

→ www.krebsliga.ch/krebsmedaille



Irma Boving received the 2017 Cancer Medal



Swiss Bridge Award ceremony (from left to right):
Philipp Lücke (CEO of the Swiss Bridge Foundation),
Johanna Joyce, Yaron Carmi, Jakob Passweg (president of
the Swiss Bridge Foundation).

The 2017 Swiss Bridge Award went to a research group from Israel and to a research group from Switzerland. With the 250 000 francs awarded to each, the researchers aim to investigate interactions between cancer cells and the cells in their immediate environment.

The 2017 Swiss Bridge Award was presented to researchers under the age of 45 years who are pursuing the investigation of the complex interactions by which tumour cells and cells in their immediate environment influence each other. These interactions are not only of theoretical interest but also have practical implications, since more and more treatment approaches are not directed at cancer cells but instead attempt to cut off blood supply to tumours or stimulate immune cells to fight cancer cells.

For the 2017 award, the Swiss Bridge Foundation received applications from 59 researchers. In a two-step evaluation process, an 11-member jury selected the projects of two researchers: Yaron Carmi at Tel Aviv University, Israel, and Johanna Joyce at the University of Lausanne, Switzerland, each received 250 000 francs for realization of their research projects.

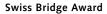
#### Interaction of different immune cells

In the project conducted by Yaron Carmi and his team, the researchers want to find out what prevents cytotoxic T-cells from penetrating into the area occupied by the tumour. In the immediate environment of most tumours, there are many other immune cells, such as dendritic cells. They play an important role in the maturation and activation of cytotoxic T-cells. By closely examining the interaction among different classes of

immune cells, Carmi's research team hopes for new insights and ideas about possible ways to improve immunotherapies, which unfortunately are currently only effective in a small percentage of patients.

#### New points of attack against brain metastases

Johanna Joyce's project investigates the role of immune cells in the environment of metastases in the brain. For a long time, it was assumed that the bloodbrain barrier prevents immune cells from entering the brain. However, more and more evidence showed that the blood-brain barrier becomes increasingly leaky in advanced cancers and lets tumour cells as well as immune cells through. For this reason, immune cells can often be found in biopsy samples of brain metastases from patients with breast and lung cancers. The majority of these immune cells are neutrophilic cells. Joyce and her team aim to decipher the role of this class of immune cells and hope to identify new therapeutic targets.



The Swiss Bridge Foundation was founded in 1997 at the initiative of Thomas Hoepli, foundation board member, and 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. Since its beginnings, 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.

 $\rightarrow www.krebsliga.ch/swissbridgeaward$ 



#### 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.

Tel. +41 (0)31389 9331 ori.schipper@krebsliga.ch www.krebsliga.ch/forschung www.krebsforschung.ch

# Continuation of the National Strategy

# **Against Cancer**

The National Strategy Against Cancer has been extended up to the end of 2020. The decision was made in October 2017 by the federal government and the cantons in the coordination platform Dialogue National Health Policy (Dialog Nationale Gesundheitspolitik). This sends out a clear signal that Switzerland continues to need a broadly-based alliance against cancer.

In the last years, the National Strategy Against Cancer (NSC) has made important advances in its three areas, seven action fields, and 15 implementation projects. For this reason, the NSC will adhere to its vision and its objectives also for the continuation phase. The NSC will continue to be an important and widely appreciated instrument in fighting cancer in Switzerland and will play a decisive role in the bundling and focusing of the various activities.

In the continuation phase the NSC seeks to ensure continuity and coherence – while at the same time also choosing to engage in new developments. The diversity of the action fields will remain unchanged, for instance. At the level of the areas, action fields, and projects, there are only minor modifications. At the same time, however, there is a focus on three new priorities: quality, innovation, and coordination. Focusing on these areas means not only that the activities in the continuation phase are to be innovative, quality assured, and coordinated among each other but also that the NSC overall should contribute towards high-quality cancer prevention, cancer treatment, and cancer aftercare – and in this way create added value for the Swiss health care system.

The added value of networking the different organizations and action fields has a decades-long tradition in the field of cancer. In view of the fact that overlaps between the NSC organizations and its projects are increasing, the plan is to take measures to further intensify the networking and targeted exchange of information in the next three years. The aim is to build a cancer community: to be committed together – and as free as possible of individual interests – to a Switzerland where fewer persons are diagnosed with cancer and suffer from the consequences of cancer and where all persons with cancer and their families receive attention and help.



#### Kathrin Kramis-Aebischer, PhD

After working as a teacher and special education teacher, Kathrin Kramis-Aebischer studied clinical psychology and education sciences at the University of Fribourg. She earned a doctorate in educational psychology and trained as a psychotherapist. She has several years of experience in research

and teaching, management and consulting, and organizational consulting and development. For about nine years she was the director of the Institute for Continuing Education in Bern and member of the executive board of the teacher training college. She joined the Swiss Cancer League/Oncosuisse as CEO in 2011 and is head of operations for the implementation of the National Strategy Against Cancer.

Tel. +41 (0)31 389 91 23 kathrin.kramis@krebsliga.ch

Figure

Overview over the continuation of the National Strategy Against Cancer 2017-2020 In the coming years three focal points will shape the continuation: quality, innovation and coordination.

Quality, innovation, coordination					
Prevention	Care and Aftercare	Bases			
<b>1</b> Prevention	3 Clinical pathways, criteria and certifications	<b>6</b> Research			
<b>2</b> Screening	4 Health services	7 Data and registries	ds		
	<b>5</b> Competencies		Action fields		
Communication, stakeholder management and knowledge transfer					
Networking with other strategies					
Building a cancer community					

# Programme for strengthening oncological health services research

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Incorporated in the National Strategy Against Cancer 2014–2020, the Swiss Cancer Research foundation announces – with the support of the Accentus Foundation – a research programme that grants one million francs per year to studies in health services research in the years 2016 to 2020. In the previous two calls for proposals, a total of 14 projects were funded.

How high are the costs of a medical service compared to the benefits? And does utilization of this medical service vary across the different regions of Switzerland? Unlike basic research, which studies the molecular causes of cancer, and clinical research, which examines new treatment options in certain groups of patients, health services research deals with medical care in the clinical routine: It is interested in the effectiveness of therapies in daily practice and looks out for possible concrete improvements. It is hoped that the findings of oncological health services research will pave the way towards equitable access to high-quality services for all patients with cancer.



The panel of experts (from left to right): Rolf Marti (head of Research, Innovation & Development department), Isabelle Peytremann-Bridevaux, Urs Brügger, Corinna Bergelt, Thomas Perneger, Marcel Zwahlen, Sabina De Geest, Cinzia Brunelli, Oliver Gautschi, Thomas Rosemann, Thomas Ruhstaller, Peggy Janich (head of Research Funding).

The research programme 'Health Services Research in Oncology and Cancer Care' issued a second call for proposals in July 2017: Once again, one million francs were available to support the research projects. By mid-September 2017, 29 project outlines had been submitted to the Swiss Cancer Research foundation. A panel of 10 experts rated the research project outlines according to the following criteria:

- 1. Importance of the project in view of improving oncological care
- 2. Scientific quality and appropriateness of the chosen methods
- 3. Feasibility of the project
- 4. Applicants' previous scientific track record

# Another seven health services research projects funded

After careful consideration, the panel of experts asked 14 researchers to further develop their project outlines and submit a detailed research proposal. By mid-January 2018, 13 complete research proposals had been submitted, which were evaluated by members of the panel and by other experts in Switzerland and other countries. At the end of March 2018, the panel of experts recommended one smaller and six larger research projects for funding. The board of the Swiss Cancer Research foundation followed the recommendations and approved funding the seven projects to the total amount of just under 1.4 million francs. The increased amount of the funding was made possible by taking additional monies from a project-specific fund.



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.
She has been the head of Research
Funding since January 2017.

Tel. +41 (0)31389 9363 peggy.janich@krebsliga.ch www.krebsliga.ch/forschung

# What is 'community building' in health services research?

The social sciences define community building as "activities pursued by a community in order to increase the social capacity of its members". 1 By analogy, we view community building in health services research as a pool of measures that promotes social cohesion in the research community and at the same time strengthens the research capacities of the individual members.

To build a strong research community, the following elements and principles are needed:

- A common research culture and common values
- Trust, mutual respect, and teamwork
- The principle of unity in diversity
- Good internal communication
- Participation as the fundamental principle
- Collaboration with other research groups

When building a community of researchers, the building of trust plays a central role. The community is built step by step, entailing the following steps:

- a) Exchange of information and mutual learning
- b) Development of common strategies, aims, methods, and instruments
- c) Conducting of joint projects

# Where do health services research and NRP 74 stand in Switzerland?

Health services research is a young science in Switzerland. However, it has gained a lot more visibility in the last five years. Significantly contributing to that were research funding and symposia by the Gottfried and Julia Bangerter-Rhyner-Stiftung and the Swiss Academy of Medical Sciences, research funding by the Swiss Cancer Research foundation, and the funding of the Swiss National Science Foundation's NRP 74. The federal government, the cantons, patient organizations, professional associations and societies, insurance companies, and other actors in the health care system are interested in learning more about health care provision in Switzerland in order to ensure the best possible access to care as well as the best possible quality and efficiency.

Since starting in 2017, NRP 74 (www.nrp74.ch) is supporting 29 research projects. In addition, there is currently a second, targeted call for proposals for projects that will fill some gaps. Already now, the projects cover a wide and diverse range of topics (Figure): They cover a variety of aspects from patient care (microlevel) to the organization of care (mesolevel) and to the political level (macrolevel). Many projects are positioned at the interfaces between inpatient care, outpatient care, and care at home as well as at the interfaces between the micro-, meso-, and macrolevel. This shows that numerous challenges and issues in health care provision lie in these transition areas.

Figure
The projects of NRP 74 (as of June 2018)



1 Abel Learning from migrant women's experiences and improving healthcare services | 2 Auer Promoting participatory medicine in colorectal cancer screening | 3 Aujesky What factors affect the performance of elective interventions in Switzerland? | 4 Bayer-Oglesby Social inequalities in the provision of in-patient healthcare in Switzerland | 5 Bodenmann Using case management to remove burden on emergency departments | 6 Bugnon Optimising the medication of elderly persons living in nursing homes | 7 Chmiel Improving the data situation in out-patient healthcare | 8 Crivelli Cost-effectiveness of home treatment for acute mental illness | 9 Csajka Automatic detection of adverse drug events in the geriatric care | 10 Elger Promoting the merging of health data in Switzerland | 11 Eychmüller End of life: more quality and less suffering through better planning and coordination? | 12 Felder Less fee-for-services, more flat reimbursement: Does it work in the out-patient sector? | 13 Gerfin What effects does the closure of general practices have on patients and the health service? | 14 Huttner Reliably determining optimal antibiotic durations | 15 Jenni Provision of care for children with developmental disorders in the canton of Zurich | 16 Liebig Successful models of palliative care in Switzerland | 17 Lucas Diagnosing dementia: cantonal policies and ethical issues | 18 Müller Does systematic interprofessional collaboration shorten the length of hospital stays? | 19 Neuner-Jehle Optimised medication and communication at discharge | 20 Peng-Keller The spiritual dimension of pain therapy | 21 Stucki Standardised reporting of functioning of people with chronic diseases | 22 Streit Optimising medication with electronic decision-making assistants in patients with multiple chronical illnesses | 23 Rosemann Do financial incentives improve the treatment of diabetes? | 24 Dratva Better data on the quality of home care | 25 Santos-Eggimann What are long-term care choices in the older population? | 26 Schwenkglenks How do guidelines and recommendations influence medical treatment? | 27 Simon Development of a nurse-led care model for nursing homes | 28 Tarr Vaccine-sceptical patients and doctors in Switzerland | 29 Watzke Better identification and treatment of mental disorders in primary care

# Who belongs to the health services research community?

In the preparatory stage of NRP 74, it was not very easy to estimate how many researchers in Switzerland are working in health services research. An important reason for this was that previously, health services research was not visible as a whole field but only in individual areas (for example, general practice/primary care). In addition, before the launching of NRP 74, only few researchers defined themselves explicitly as health services researchers.

The large number of 173 grant applications submitted during the first NRP 74 call for proposals then showed the whole spectrum of health services research. The applicants were not only from the medical field – such as human medicine, nursing sciences, physiotherapy, ethics, epidemiology, or biostatistics - but also from economics, the political sciences, computer sciences, sociology, or theology. And finally, researchers in most of the projects work together with employees of the federal government (for example, the Federal Statistical Office or the Federal Office of Public Health), the cantons (departments of health, cantonal hospitals), patient organizations, professional associations and societies, or insurance companies, which is highly relevant regarding the research projects, knowledge transfer, and community building.

NRP 74 undertakes activities that for resource-related reasons are confined to the funded research projects. However, with a view to sustainably anchoring health services research in Switzerland, NRP 74 wants the activities to be as broadly based as possible. For this reason, community building goes beyond the projects of NRP 74, as the research programme is limited in time and not everyone working in health services research in Switzerland is involved in an NRP 74 project. That is why NRP 74 is in contact with, among others, the national initiative Swiss Learning Health System, which is building an infrastructure for health services research and exchange between research, policy, and practice (www.slhs.ch). The majority of the persons participating in this initiative are also working on an NRP 74 project, which facilitates coordination of the activities. NRP 74 is also seeking contact with other institutions, organizations, and initiatives, so as to bundle the forces in the field of health services research as effectively as possible.

# What community building measures is NRP 74 implementing?

The community is being built step by step, following the three steps mentioned above:

- a) Exchange of information and mutual learning:
  - Provision of information material (www.nrp74.ch)
  - Annual Programme Conference NRP 74
     (for the researchers conducting the currently 29 projects)
  - Annual conference on health services research (not limited to NRP 74)
  - NRP 74 knowledge transfer: exchange and collaboration with stakeholders
  - Exchange with the international research community (Wennberg International Collaborative)
- b) Development of common strategies, aims, methods, and instruments:
  - Building of project clusters in NRP 74:
     cooperation between projects with related
     content or methodology
  - Collaboration with the Swiss Learning Health
     System and the Swiss School of Public Health
     in the training of the early career researchers,
     the events, and the exchange with stakeholders
  - NRP 74 knowledge transfer: systematically developed methodological concept for the exchange between research, policy, and practice
- c) Conducting of joint projects:
  - Emerging Health Care Leaders (EHCL) programme: promoting the early career researchers in NRP 74
  - TO REACH Initiative (to-reach.eu) in cooperation with the Federal Office of Public Health and international partners

## How does the Emerging Health Care Leaders (EHCL) programme promote community building?

The EHCL programme serves promotion of early career scientists in health services research. It aims to build a strong future research community in health services research in Switzerland, to foster robust networking, and to support the young researchers in their careers also in their acquisition of non-academic competencies. The programme was developed according to the needs of young researchers, and parts of the programme are also open to young researchers not participating in NRP 74. The programme comprises six elements: career coaching, workshops for training social and personal skills, courses promoting professional skills, workshops on soft skills, knowledge transfer activities (contacts between the young researchers and stakeholders in policy and practice), and community building activities, such as retreats for EHCL participants but also project discussions in content clusters, meetings with Swiss and international experts in their research areas, dialogue rounds with external stakeholders. Social events and incentives for joint projects should ensure that over the course of the NRP 74 project duration, the participating young researchers build the necessary trust in one another, develop a good feeling of community, and go on in the future to tackle health services research in a united way and equipped with international competitiveness.

#### Conclusion and outlook

Several health services research meetings and symposia - such as the ones organized by the Gottfried and Julia Bangerter-Rhyner-Stiftung, the SAMS, and the Swiss School of Public Health (SSPH+) in March 2017, the First Programme Conference of NRP 74 in August 2017, and the Wennberg International Collaborative Spring Policy Meeting in April 2018 (www.wennbergzurich.org) - have successfully laid foundations for a health services research community in Switzerland. It must be emphasized, however, that it is still too soon to evaluate the measures taken up to now and that the community building efforts can only be conclusively assessed in two to three years from now. The currently positive situation should also not blind us to the fact that for consolidation of the research community after the end of NRP 74, the course must be set now. For this, new financial resources are required. Especially for promotion of early career researchers, opportunities for exchange among researchers, and project funding, a solid financial basis needs to be pursued. In the framework of NRP 74, as many activities as possible are being planned with a view to continuation after 2022 to strengthen health services research in the long term. However, for a successful future of health services research and its research community, it is important that the Swiss National Science Foundation, the federal government, the cantons, non-profit organizations like the Swiss Cancer League and the Swiss Lung League, and professional associations, insurance companies, and industry together, or at least in a coordinated way, find ways to finance health services research in the long term.



#### Prof. Milo Puhan, MD, PhD

Milo Puhan studied medicine at the University of Zurich and completed a PhD in epidemiology at the University of Amsterdam in 2006. From 2008 to 2012, he was an associate professor in the Department of Epidemiology at the Johns Hopkins Bloomberg School of Public Health in Bal-

timore, Maryland (USA). He has been full professor of Epidemiology and Public Health and director of the Epidemiology, Biostatistics and Prevention Institute at the University of Zurich since 2013. He is currently the president of the National Research Programme 'Smarter Health Care' (NRP 74) of the Swiss National Science Foundation. His main research interests are prevention and management of chronic diseases.

Tel. +41 (0)44 634 46 10 miloalan.puhan@uzh.ch www.ebpi.uzh.ch/en/aboutus/director.html

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# Research funding by the cantonal and regional cancer leagues

# Many-sided commitment at the cantonal and regional level

The Cancer League is organized as a federation and unites 19 cantonal and regional leagues as well as the national umbrella organization, the Swiss Cancer League. Progress through research and innovation – of that the cantonal and regional cancer leagues are sure: They are committed to supporting research in their canton.

In 2017, nine cantonal and regional cancer leagues gave over 2.2 million francs to a total of 36 different cancer research projects and institutes. Compared to the previous year, the cantonal and regional cancer leagues thus supported nine fewer research projects (Table). The largest sum was invested by the Basel Cancer League, followed by the cancer leagues of Geneva, Bern, Zurich, and Ticino. Over the last five years, the cantonal and regional cancer leagues have given between 2 and 3 million francs to cancer research annually. With this, their contribution each year made up about 10% to 15% of the total funding; the remaining 85 % to 90 % was provided by the Swiss Cancer League (SCL) and the Swiss Cancer Research foundation (SCR). When granting these considerable funds, the cantonal cancer leagues rely on various committees of experts. Through their expertise and experience, the committees ensure that the funded research projects are of high quality.

The Basel Cancer League and the Bern Cancer League each have their own independent scientific committee. The committee members come from all specialist areas in clinical and experimental cancer research, and they mainly work at the university or the university hospital in the canton. For evaluation of research grant applications, the Ticino Cancer League relies on

a foundation created expressly for research funding the Fondazione ticinese ricerca sul cancro (Ticino Foundation for Cancer Research). The majority of seats on the foundation board are held by members of the Ticino Cancer League; among them are also oncology experts. At the Zurich Cancer League, the Canton of Zurich Cancer Committee is responsible for the allocation of funds; this expert committee is composed of equal numbers of representatives of the Zurich Cancer League and the Canton of Zurich. In addition to the research funding activities of the Zurich Cancer League, the Cancer Committee is mainly also responsible for the coordination of research activities and representation of research activities in the Canton of Zurich. For cantonal cancer leagues that do not have their own committee of experts, such as for example the Geneva Cancer League, individual members of the board who have a background in biology/medicine take over the evaluation of research proposals.

Depending on the league, research grant applications are submitted one to two times per year by a certain submission deadline. Smaller cantonal and regional cancer leagues also accept applications throughout the year. Each grant application is reviewed by two members of the particular committee of experts (or the board). In part, further national and international experts are included in the evaluation process. Funding is granted to research projects in all areas of cancer research: basic research, clinical research, cancer epidemiology and cancer prevention, and research in the areas of psycho-oncology and palliative medicine.

Projects pursuing commercial goals or interests are excluded from funding. The main recipients of research funds are established researchers at the universities and hospitals in the canton. But the leagues also support early career researchers, who receive start-up financing for the implementation of their research ideas. To be mentioned here above all is the Bern Cancer League, which has set as its primary task the promotion of young researchers.

Also contributing to research funding are those cantonal and regional cancer leagues that support, for instance, the cancer registry in their canton, such as the Eastern Switzerland Cancer League and the Fribourg Cancer League. With this, they not only contribute towards recording and ensuring high-quality data on cancer cases but also make possible the provision of these data for diverse research purposes.

The data can be used, for example, to investigate the effect of screening programmes on cancer mortality or to study the causes of different cancers.

The cantonal and regional cancer leagues also receive regular information on research projects that are evaluated by the SCL and the SCR and rated as eligible for funding. Unfortunately, due to limited funds, it is never possible to fund all of the high-quality research projects. Cantonal cancer leagues without their own research funding programmes have the opportunity to participate financially in SCL and SCR research projects. In this way, they can co-fund already evaluated research projects in their canton in a targeted manner. This was done last year by the Aargau Cancer League; it is co-funding a research project for three years that

Table
Research funding by the cantonal cancer leagues in overview

	Number of projects and institutions supported		Amount granted in kCHF	
Cancer league	2016	2017	2016	2017
Aargau	0	1	0	40
Basel	9	11	450	560
Bern	10	6	550	400
Central Switzerland	2	2	66	65
Eastern Switzerland	1	1	100	100
Fribourg	1	0	4	0
Geneva	9	7	785	534
Grisons	2	0	30	0
Thurgau	1	1	10	10
Ticino	4	3	285	228
Zurich	8	4	453	271
Total	47	36	2 733	2 208

is testing a new imaging technique to support proton therapy for uveal melanoma. The goal is to make the treatment for this common tumour of the eye more efficient and safer. The project is being conducted at the Paul Scherrer Institute in Villigen, one of the leading research institutes worldwide in the area of proton therapy.

Cantonal cancer leagues that do not have their own committee of experts for the evaluation of grant applications can, when needed, rely on the experience and expertise of the SCL and the SCR. But the umbrella organization also offers support in the grant application evaluation process to cantonal cancer leagues that have their own committee of experts. In the context of a pilot project, in 2017 the Basel Cancer League handled the submission and evaluation of its research projects paperless via the Grant Application Portal of the SCL and the SCR. This online portal allows transparent and efficient administration of grant applications from submission to evaluation and reporting. The portal also guarantees secure exchange of information between applicants, reviewers, and the Swiss Cancer League. As the pilot project was a success, it will be continued and expanded in 2018. Upon request, other cantonal and regional cancer leagues can join the online portal.

Even though there are differences among the cantonal and regional cancer leagues in their research project evaluation procedures, they all have a common goal: to fund the best cancer research projects and institutes. With this, the cantonal and regional cancer leagues make possible the realization of innovative and promising ideas about treatment and investigation of cancer. This knowledge benefits patients with cancer not only today but also in the future.



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. She has been the head of Research Funding since January 2017.

Tel. +41 (0)31389 9363 peggy.janich@krebsliga.ch www.krebsliga.ch/forschung

## List of funded research projects

The list shows the financial contributions granted in 2017.

Aargau Cancer League

Pica Alessia | High-resolution ophthalmic magnetic resonance imaging at 1.5T: towards a non-invasive method to assist proton therapy planning for uveal melanoma Paul Scherrer Institut (PSI), Villigen

CHF 40 000.- | Duration: 16. 1. 2017 - 15. 1. 2020

**Basel Cancer League** 

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Aceto Nicola | Computational analysis of single cell transcriptome and exome profiling of human circulating tumour cells

Departement Biomedizin, Universitätsspital Basel, Basel

CHF 63 600.- | Duration: 1. 8. 2017 - 31.7. 2018

**Bentires-Alj Mohamed** | Reactivation of estrogen receptor signalling in triple negative breast cancer

Departement Biomedizin, Universitätsspital Basel, Basel

CHF 100 000.- | Duration: 1.7. 2017 - 30. 6. 2019

**Läubli Heinz** | Combination of siglec-targeting with checkpoint inhibition for cancer immunotherapy

Medizinische Onkologie, Universitätsspital Basel, Basel

CHF 67 045.- | Duration: 1.9. 2017 - 31. 8. 2018

**Lengerke Claudia** | Investigation of homing capacity as prognostic marker and stemness property in human acute myeloid leukaemia

Klinik für Hämatologie und Departement Biomedizin, Universitätsspital Basel, Basel

CHF 14 000.- | Duration: 1.5. 2017 - 30. 4. 2018

Matter Matthias | Mutational landscape of primary hepatocellular carcinoma and matched metastases

Institut für Pathologie, Universitätsspital Basel, Basel CHF 24 488.- | Duration: 1.10. 2017 - 30. 9. 2018

**Medinger Michael** | Protocol SAKK 16/1 - Anti-PD-L1 antibody MEDI4736 in addition to neoadjuvant chemotherapy in patients with stage IIIA(N2) non-small cell lung cancer (NSCLC). A multicentre single-arm phase II trial

Klinik für Hämatologie und Klinik für Innere Medizin, Universitätsspital Basel, Basel

CHF 14 000.- | Duration: 1.7. 2017 - 31.1. 2020

Mertz Kirsten | STING immunoprofiling as a predictor of responses to immune checkpoint inhibitors – towards personalized cancer immunotherapy

Institut für Pathologie, Kantonsspital Baselland, Liestal

CHF 52 372.- | Duration: 1. 6. 2017 - 31. 5. 2018

Ng Kiu Yan Charlotte | The feasibility of genetic profiling using plasma-derived cell-free DNA in therapy-naïve hepatocellular carcinoma patients

Departement Biomedizin, Universität Basel, Basel CHF 46 012.- | Duration: 1.9.2017 - 31.8.2018

**Schwaller Jürg** Characterization of the anti-leukaemic immune response in a conditional transgenic mouse model of acute myeloid leukaemia (AML)

Departement Biomedizin, Universitäts-Kinderspital beider Basel, Basel

CHF 60 000.- | Duration: 1.10.2017 - 30.9.2018

Weber Walter Paul | Taxis: targeted axillary dissection and radiotherapy in breast cancer with high-volume nodal disease or residual nodal disease after neoadjuvant chemotherapy

Brustzentrum, Universitätsspital Basel, Basel
CHF 100 000.- | Duration: 1.10.2017 - 30.9.2020

Zanetti Dällenbach Rosanna | Comparison of accuracy and reproducibility of breast lesion characterization between real time elastography and shear wave elastography

Gynäkologische Onkologie, St. Claraspital, Basel CHF 18 435.- | Duration: 1.9.2017 - 31.8.2020

Bern Cancer League

**Banz Yara** | The role of interleukin-33/ST2 signaling in the pathogenesis of malignant lymphomas Institut für Pathologie, Universität Bern, Bern

CHF 65 000.- | Duration: 1. 6. 2017 - 30. 11. 2018

Dorn Patrick | Targeting mitochondrial activity to enhance lung cancer therapy

Klinik für Thoraxchirurgie, Inselspital Bern, Bern CHF 90 000.- | Duration: 1.10.2017 - 31.3.2019

Fernandez Palomo Christian | Combining microbeam synchrotron radiotherapy and gold-nanoparticles: A novel anti-cancer approach to treat melanoma

Institut für Anatomie, Universität Bern, Bern
CHF 70 000.- | Duration: 1.4.2018 - 30.9.2019

 $\textbf{Humbert Magali} \hspace{0.2cm} | \hspace{0.2cm} \textbf{Understanding the role of macro- and chaperone-mediated autophagy} \\ \text{in leukaemia development and sustainment} \\$ 

Institut für Pathologie, Universität Bern, Bern CHF 85 000.- | Duration: 1.9.2017 - 28.2.2019

 $\label{lem:lemboden} \textbf{Sara} \hspace{0.2cm} \mid \hspace{0.2cm} \textbf{Moving towards personalized medicine in endometrial cancer: classification of endometrial cancer according to TCGA subgroups - a clinic orientated, multicentre cohort study and the study of the study$ 

Klinik für Frauenheilkunde, Inselspital Bern, Bern CHF 10 000. – | Duration: 1.8.2017 – 31.1.2018

**Kocher Gregor** | Identify therapeutic targets to promote chemotherapy efficacy in KRAS-mutant lung cancer by CRISPR screen

Klinik für Thoraxchirurgie, Inselspital Bern, Bern CHF 80 000.- | Duration: 1. 4. 2018 - 30. 9. 2019

Central Switzerland Cancer League

**Michel Gisela** | Psychological late effects in long-term childhood cancer survivors - Development of guidelines for follow-up care

Health Sciences and Health Policy, Universität Luzern, Luzern

CHF 35 000.- | Duration: 1.1.2016 - 31.12.2018

 $\label{lem:with_alder_Ralph} \begin{tabular}{ll} SAKK 24/14: Anti-EGFR-immunoliposomes loaded with doxorubic in patients with advanced triple negative EGFR positive breast cancer – a multicentre single arm phase II trial$ 

Medizinische Onkologie, Luzerner Kantonsspital, Luzern

CHF 30 000.- | Duration: 1.1.2017 - 31.12.2018

Ludewig Burkhard | Targeting breast cancer through manipulation of IL-7 producing tumour fibroblasts

Institut für Immunbiologie, Kantonsspital St. Gallen, St. Gallen

CHF 99 980.- | Duration: 1.1.2016 - 31.12.2017

Geneva Cancer League

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Farina Annarita | Extracellular vesicles released in proximal fluids by pancreatic biliary cancers:

characterization and evaluation of their role in biology and diagnosis of cancer

Département de science des protéines humaines, Université de Genève, Genève

CHF 99 272.- | Duration: 1.7. 2016 - 30. 6. 2017

Foti Michelangelo | Role of proteins binding to adenine-uridine-rich elements and P-bodies in hepatocellular carcinoma

Département de physiologie cellulaire et métabolisme, Université de Genève, Genève

CHF 88 622.- | Duration: 1.7. 2016 - 30. 6. 2017

**Hibaoui Youssef** | Study of the molecular mechanisms of leukemia associated with Down syndrome using a new model based on induced pluripotent stem cells (iPSCs generated from monozygotic twins discordant for trisomy 21)

Département de médecine génétique et développement, Université de Genève, Genève

CHF 87 092.- | Duration: 1.7. 2016 - 30. 6. 2017

Mandriota Stefano | Role of aluminium in the development of breast cancer

Clinique des Grangettes, Genève

CHF 60 000.- | Duration: 1.7. 2016 - 30. 6. 2018

Mary Camille | Characterization of the protein THEM6: a thioesterase potentially involved in cancer

Département de science des protéines humaines, Université de Genève, Genève

CHF 4000.- | Duration: 1.7. 2016 - 30. 6. 2017

 $\textbf{Serre-Beinier V\'eronique} \hspace{0.2cm} | \hspace{0.2cm} \textbf{Study of the role of the MIF/CD74 pathway in mesothelioma development} \hspace{0.2cm}$ 

Département de chirurgie, Université de Genève, Genève

CHF 85 081.- | Duration: 1.1.2015 - 31.12.2017

Toso Christian | Surgical treatment of patients with hepatocellular carcinoma

Service de chirurgie viscérale, Hôpitaux universitaires de Genève, Genève

CHF 109 675.- | Duration: 1.7. 2016 - 30. 6. 2018

Thurgau Cancer League

Schmidt Anne | Support Cancer Registry Thurgau

Krebsregister Thurgau, Kreuzlingen

CHF 10 000.- | Duration: 1.1.2017 - 31.12.2017

Ticino Cancer League

Catapano Carlo | Preclinical modelling of cancer stem cells directed therapies

Institute of Oncology Research, Università della Svizzera Italiana, Bellinzona

CHF 100 000.- | Duration: 1.1. 2018 - 31.12.2018

Rossi Davide | Development of biomarkers for treatment tailoring in splenic marginal zone lymphoma

Institute of Oncology Research (IOR), Università della Svizzera Italiana, Bellinzona

CHF 88 000.- | Duration: 1.1. 2017 - 31. 12. 2019

**Theurillat Jean-Philippe** | Oncogenic aversion: a concept towards new therapeutic avenues in prostate cancer

Institute of Oncology Research, Università della Svizzera Italiana, Bellinzona

CHF 40 000.- | Duration: 1.7. 2017 - 31. 12. 2018

**Bourquin Jean-Pierre** | Exploring the genomic landscape of myeloid and stem cell marker VNN2 positive unfavorable acute lymphoblastic leukemia

Abteilung Onkologie, Universitäts-Kinderspital Zürich, Zürich

CHF 65 821.- | Duration: 1.1. 2016 - 31. 12. 2017

**Dieterich Lothar** | Tumor-derived extracellular vesicles – messengers that shape the lymph node microenvironment and control tumour immunity in melanoma

Pharmazeutische Wissenschaften, ETH Zürich, Zürich CHF 49 963.- | Duration: 1.1. 2017 - 31.12. 2017

 $\textbf{Sch\"{a}fer Beat} \hspace{0.2cm} \mid \hspace{0.2cm} \textbf{The rapeutic targeting of oncogenic fusion proteins by transcriptional repression}$ 

Abteilung Onkologie, Universitäts-Kinderspital Zürich, Zürich

CHF 58 050.- | Duration: 1.1. 2014 - 31. 12. 2017

 $\textbf{Wong Wei-Lynn} \hspace{0.2cm} | \hspace{0.2cm} \textbf{The role of inhibitors of apoptosis proteins in the tumour microenvironment} \\$ 

Institut für experimentelle Immunologie, Universität Zürich, Zürich

CHF 77 546.- | Duration: 1.1.2015 - 31.12.2017







# Towards a Swiss Personalized Health Network: Lessons from precision oncology

Mira Lund\* was the newly named CEO of a biotechnology company known for innovation and stellar record for their social commitment to improving health care. In 2016 at a New York fundraising event, I was introduced to her, and we managed to exchange a few words despite a time conscious organizer trying to move her along to the podium. Mira's eyes beamed as I gave her the elevator pitch about the new Englander Institute for Precision Medicine, a burgeoning effort in precision medicine to align the right therapy with the right patient at the right time. Our goal, I explained, is to improve patient care<sup>1</sup> by investing in infrastructure and linking hospital clinical patient records (the electronic health record) to large genomic data sets2. She nodded as the event organizer escorted her to the podium. She glanced at her prepared notes and began in a soft, confident, and enthusiastic voice to describe the cause for which the event was raising money. She pleaded with the assembled crowd of New York City social luminaries to donate help and support to cancer research.

In the fall of 2012, precision medicine was an abstract, evolving term in the United States. It came to my attention when I was preparing a grant application for a 10-million-dollar grant from Stand Up to Cancer and the Prostate Cancer Foundation (SU2C-PCF). Charles Sawyers, one of our team leaders and chair of the group that penned a White Paper for the Institute of Medicine on precision medicine<sup>3</sup>, suggested we focus on the feasibility of a precision medicine trial. And so we wrote an outline for a prospective clinical trial aiming to better understand why anti-androgen therapy often fails with men with advanced prostate cancer. This treatment is standard of care, but we asked whether better results could be achieved – and achieved not necessarily with new

<sup>\*</sup> Name and circumstances have been changed to protect privacy.

drugs but with existing drugs. For every patient enrolled in the study, biopsies of prostate cancer metastases would be performed; the intention was not to diagnose their cancer again (we already knew that the patients had advanced prostate cancer) but instead to find out what newly acquired mutations their tumours had developed since the start of therapy. We proposed performing whole exome sequencing and whole transcript sequencing with the goal of discovering novel mechanisms of resistance. At the time, this was at the least a logarithmic leap compared to what was being done for genomic testing of prostate cancer; we were going from one to five genes to 20 000. We would link clinical and pathology data from all six clinical sites (the Fred Hutch Cancer Center, Memorial Sloan Kettering Cancer Center, Weill Cornell Medicine, Dana Farber Cancer Center, the University of Michigan Cancer Center, and the Royal Marsden in England) with the so-called Big Data - the large genomic datasets generated at the Broad Institute, Weill Cornell Medicine, and the University of Michigan.

This was all new at the time. Our first study on prostate cancer had attributes of a clinical trial as well as of genome research. But unlike research, we needed to move the genomics to a clinically relevant level. Could we do this in real time, so that our findings could play a direct role in patient care? Could we meet the regulatory requirements for this study? Over the next five years, we enrolled over 500 men with advanced prostate cancer. At first, obtaining metastatic biopsies from each patient seemed like an unreachable goal due to the requirements of coordinating biopsies with interventional radiologists, oncologists, pathologists, and clinical laboratories. However, after a slow start and rumblings about the costs and the increased time required, and once we

developed and established work routines (standard operating procedures)<sup>4</sup>, we managed more and more to obtain high-quality biopsies and to process the tiny tumour samples for genomic and transcriptomic analyses. We began to see phenomenal results, and not just from one institution; all six sites working together could achieve inclusion rates in the 90% range. This experience confirmed that patients with advanced cancer and their families participate in research enthusiastically, even if the projects will help to save only few patients and will more likely help improve the treatment methods of the future.

Observations made at all six centres led one of our team members, Johann de Bono at the Royal Marsden, to an important finding: As many as 20% of our patients with advanced prostate cancer had a mutation in one of the many DNA repair genes. Genes called PARP are responsible for maintaining the integrity of the genome. We became interested in these mutations, because de Bono was already using PARP inhibitors in one of his clinical trials. The PARP inhibitors disarm the alternate way that the tumour cells repair their DNA. This leads to what is called synthetic lethality - basically a one-two punch that results in the death of the tumour cells. When de Bono and his group examined the genomic features of the 30% of men who had long-term responses to PARP inhibition therapy, there was a preponderance of DNA repair gene mutations in contrast to men who did not respond to the therapy<sup>5</sup>. The study allowed our group to perform a larger study, which

confirmed that 10% to 20% of men with advanced prostate cancer had a DNA repair gene mutation – often from birth<sup>6</sup>. These findings will change the treatment of men with advanced prostate cancer. In the future, men will have genetic testing and counselling and will be informed of their genetic risk. This was our first special moment in precision medicine.

As oncologists and researchers at my former institutions learned about our work, they asked us to apply our methods also to other cancers. The same tools and concepts established in the SU2C-PCF funded trial could now be applied more broadly<sup>1</sup>. Lessons learned about sharing data through genomic sequencing portals also gave our researchers an opportunity to develop hypotheses for new research studies by posting them on cBioportal – a Google-like webbased application for researchers to explore the land-scape of cancer mutations and posit new questions.

One innovation of our programme was a living tumour bank. We began to culture patients' tumour cells using methods developed by Hans Clevers' group in the Netherlands for examining colon cells. Culturing the cells in a three-dimensional scaffold or matrix promotes the formation of tumour cell spheroids or organoids. Could these patient-derived organoids be used as avatars aiding quick selection of available drugs? Could the organoids in this way help to avoid adverse side effects and save valuable time? The precision medicine approach would be to identify the right drug and thus to create a new standard of care. In the lab, we saw success<sup>7</sup>. We and others<sup>8</sup> can now show which drugs or drug combinations can optimally kill tumour cells and thus can predict the best drugs for individual patients. This is precision oncology.

The real challenges of precision medicine hit home for us when Mira Lund's doctor asked us to help her. Mira, the wiry, energetic entrepreneur – an industry leader – had widespread metastases. She wanted us to try everything and anything. Her consulting oncologists from across the United States told her that there were no more options for her. We organized a biopsy of the metastases and performed all the genomic tests that we had developed in the SU2C-PCF study. We were able to obtain enough tumour cells to culture organoids. A screening of all FDA-approved drugs revealed a combination of therapies that worked astonishingly well on her tumour cells (but not on

other tumour cells from the same type of cancer taken from other patients). From this, we knew which two drugs to give her, even though we did not understand why. But Mira's fight against cancer was now fatiguing her more and more. By the time we were able to do additional testing in xenograft models to confirm our findings, she was too sick for therapy of any sort, and she died shortly after our discovery. What a loss for our community. We grieved for her. We also grieved for our inability to help her in time despite coming to the right conclusion.

Both Mira's story and the DNA repair mutation story belong to precision medicine reality. As we succeed at becoming better, smarter, and more efficient, we may have the chance to get patients like Mira into the right trial or to treat them with the right drugs – and thus to make a difference. The more studies that we conduct and especially the more data that we share, the better the biomedical community will understand why some patients respond and others do not. Researchers, too, will later benefit from these findings and, it is hoped, the findings will contribute towards development of urgently needed future classes of drugs.

But first it was important to demonstrate that this work added to the quality of clinical care. In precision tumour boards, we discussed all the findings of patients on the trial. However, only anecdotally did we find a better treatment for a patient. Of course, our starting point put us in a challenging position – our patients had already failed the typical therapies or standard of care. Currently, these results are not particular to prostate cancer. In a recent large trial

with over 10 000 comprehensively sequenced tumours from the Memorial Sloan Kettering Cancer Center, the investigators were able to find a genomically matched novel therapy at a rate of only 10% of the cases that did not respond to standard of care<sup>9</sup>. We need to find innovative ways to propose new therapies and new trials. And we need to do this in a timely manner.

As I now begin working with my new colleagues in Switzerland at the Inselspital and the University of Bern to set up precision medicine for cardiology, neurology, oncology and other areas where help is needed, I am more aware than ever that we have a lot of hard work ahead of us. The findings of our prostate cancer study and experiences with patients like Mira remind me what we need to do. We need to work closely in Switzerland and also at the international level and utilize the chances to improve health care. With its well-functioning health care system, highly educated population, and high availability of technology in the health care system, Switzerland is well positioned to make important advances in precision medicine - and this particularly as there is significant support for the national development of precision medicine from two national programmes.

This earmarked support from the Swiss Personalized Health Network (SPHN) and Personalized Health and Related Technologies (PHRT) should allow us to ask bold research questions and to dissolve the boundaries between clinical care and basic research. We need to find ways to share data freely, responsibly, and swiftly to gain the knowledge that will save the next Mira that comes to us asking for help. Finally, we need to make this knowledge available to each and every patient, whether the patient is the head of the company that makes trains and buses or the person who drives the number 10 bus in Bern.

I think of Mira every day. I shook her hand, looked into her eyes. We almost had something to offer her – we saw the drugs work on her tumour cells growing in a dish – but we were too late. And that is just not good enough. We must work together for the Swiss Personalized Health Network, so that we can be right on time. And punctuality, as I have learned over the past year, is a very Swiss characteristic.



Prof. Mark A. Rubin, MD
Mark Rubin was born in Riverside, California, and studied at
Mount Sinai School of Medicine,
New York (USA). After completing his clinical training at the
Deutsches Herzzentrum Berlin
(Germany), Georgetown University
Medical Center in Washington,
DC, and Johns Hopkins Hospital

in Baltimore, he specialized in urology and pathology and worked as an assistant professor at the University of Michigan in Ann Arbor. In 2002, he moved to Brigham and Women's Hospital in Boston. Rubin joined Weill Cornell Medicine in New York as a full professor in 2007 and became the director of the Englander Institute for Precision Medicine in 2013. Since February 2017 he is also director of the department of clinical research at Inselspital in Bern.

His research endeavors mainly focus on the genomic changes accompanying and driving the progression of prostate cancer. His research teams in New York and Bern are also developing novel treatment strategies to treat advanced prostate cancer.

Tel. +41 (0)31 632 88 65 mark.rubin@dbmr.unibe.ch www.dbmr.unibe.ch

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### Selected results

Project

Targeting the tumour immune system for pro-senescence therapy for cancer Istituto Oncologico della Svizzera Italiana (IOSI), Bellinzona CHF 299 400.- | Duration: 1.1. 2015 - 31. 12. 2017 | KFS-3505-08-2014

Project coordinator

Prof. Andrea Alimonti, MD | andrea.alimonti@ior.iosi.ch

#### Camplan

#### Counteracting the schemes of prostate cancer cells

The body's own immune system can either fight a tumour of the prostate or protect the cancer cells. But this protection can be halted, as researchers show in one of the projects supported by the Swiss Cancer Research foundation.

It is increasingly evident that tumour development depends not only on what happens within the cancer cells but also on the interactions between the cancer cells and the healthy cells in the direct microenvironment of the tumour. Here, a decisive role is played by immune cells: Macrophages can infiltrate into the tumour tissue, but they often appear to come under the control of the cancer cells.

Andrea Alimonti and his team, with the support of the Swiss Cancer Research foundation, have now discovered the molecular signals that prostate cancer cells use for their schemes: They secrete a chemical messenger (a cytokine) named CXCL2. When it is recognized by specific CXCR2 receptors on the surface of the macrophages, the behaviour of the immune cells changes: Like defectors, they change sides – and provide for a growth-friendly climate in the microenvironment of the tumour, in that the macrophages secrete substances that lead to the development of new blood vessels and thus to an improved supply of nutrients to the cancer cells.

Alimonti's research team has found this kind of renegade macrophages in much greater numbers in aggressive forms of prostate cancer than in slower-growing forms. And what is more: The researchers have tested a substance that binds to the CXCR2 receptors and in this way can block the CXCL2 signal of the prostate cancer cells. The treatment prevented

the macrophages from changing sides – the macrophages maintained their immune function and thus reduced the power of the cancer cells to divide by promoting cellular senescence and growth arrest in the tumour.

In experiments with mice, the Alimonti team was able to reduce the growth of aggressive forms of prostate cancer by more than one half. The researchers are now working together with researchers in Ireland and Great Britain to investigate whether the substance also works in humans.

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Project

Dose-rate effect of novel radiation technologies: relevance for the clinical use Klinik für Radio-Onkologie, Stadtspital Triemli, Zürich

CHF 211 885.- | Duration: 1.8. 2014 - 31. 7. 2017 | KFS-2901-02-2012

Project coordinator

PD Kathrin Zaugg, MD | kathrin.zaugg@triemli.zuerich.ch

#### Shorter but more intensive radiation

The goal of radiation therapy is to damage and kill as many cancer cells as possible. Decisive is not only the dose but also the intensity, as researchers have discovered in a project supported by the Swiss Cancer Research foundation.

When radioactive beams or rays enter into cells, they can cause considerable damage, because their energy is sufficient to destroy the structure of the vulnerable biological molecules inside the cell. Radiation thus can lead to breaks in the DNA inside cells. For rapidly dividing cancer cells, these breaks are a problem: If the damage is not quickly repaired, the cells cannot copy their genetic material and distribute it to the daughter cells. The cells are threatened with cell death.

In a research project supported by the Swiss Cancer Research foundation, radiation-oncologist Kathrin Zaugg and her team broke down in detail how the radiation effects colon cancer cells. They treated cell cultures with different radiation doses and different radiation intensities. They found considerable differences between cells that grew two-dimensionally (as a single layer) in the culture dish and cells that could multiply three-dimensionally in small spheroids.

The cells on the surface of the spheroids were just as sensitive to the radiation as the cells in the single layer were, but the cells inside the spheroids were much more resistant. Zaugg traces this radiation resistance back to the low oxygen inside the cluster of cells: Because the cells on the surface use the oxygen, only a small remainder gets to the centre of the spheroid. The cells on the inside of the cell clusters adapt – and slow their metabolism and their growth. Through this, they have more time to repair the damage in the DNA before they again divide.

As expected, stronger radiation doses cause greater damage. But in addition, the researchers discovered that when the dose remains the same, radiation intensity is also important: Faster and more intensive delivery of the radiation seemed to cause more damage to the cancer cells than a radiation dose delivered over a longer time period. However, further investigations are necessary before these findings can be applied clinically to radiation therapy with real patients, says Zaugg.

## List of approved research projects in 2017

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

Total funds allocated: CHF 10 212 300.-

Aceto Nicola | The role of hypoxia in the generation of circulating tumour cell clusters

Departement Biomedizin, Universität Basel, Basel

CHF 168 100.- | Duration: 1. 5. 2018 - 31. 10. 2019 | KLS-4222-08-2017

Alimonti Andrea | Development of senolytic therapies for chemotherapy-treated prostate cancers

Istituto Oncologico della Svizzera Italiana (IOSI), Bellinzona

CHF 312 500.- | Duration: 1.1. 2018 - 30. 6. 2020 | KFS-4267-08-2017

**Bachmann Martin** | Development and exploration of a novel personalized cancer vaccine based on virus-like particles incorporating patient-specific melanoma T-cell epitopes

Department for Biomedical Research, Universität Bern, Bern

CHF 340 650.- | Duration: 1.1.2018 - 31.12.2020 | KFS-4291-08-2017

Bourquin Jean-Pierre | Modelling and targeting critical oncogenic determinants driven by

the TCF3-HLF translocation in high risk ALL

Abteilung Onkologie, Kinderspital Zürich, Zürich

CHF 375 000.- | Duration: 1.9.2018 - 31.8.2021 | KLS-4237-08-2017

**Boyman Onur** | In vivo characterization of anti-tumour properties and tumour immune landscape of different interleukin-2 complexes

Klinik für Immunologie, Universitätsspital Zürich, Zürich

CHF 375 000.- | Duration: 1. 8. 2017 - 31. 7. 2020 | KFS-4136-02-2017

Christofori Gerhard | Is an EMT really responsible for therapy resistance and metastasis?

Departement Biomedizin, Universität Basel, Basel

CHF 358 500.- | Duration: 1. 3. 2018 - 28. 2. 2021 | KFS-4229-08-2017

**Deplancke Bart** | Characterizing the regulatory role of a novel non-coding variant in modulating the pathology of chronic lymphocytic leukaemia

Laboratory of Systems Biology and Genetics, Ecole Polytechnique Fédérale de Lausanne (EPFL), Lausanne

CHF 347 400.- | Duration: 1.1. 2018 - 31.12. 2020 | KFS-4275-08-2017

**Djonov Valentin** | Microbeam irradiation – innovative vascular disruptive approach for lung cancer treatment

Institut für Anatomie, Universität Bern, Bern

CHF 337 000.- | Duration: 1.5. 2018 - 30. 4. 2022 | KFS-4281-08-2017

**Dormond Olivier** | Serotonin-mediated angiogenesis as a resistance mechanism to anti-VEGF therapies

Service de chirurgie viscérale, Centre hospitalier universitaire vaudois (CHUV), Lausanne

CHF 250 000.- | Duration: 1.2.2018 - 31.1.2020 | KFS-4128-02-2017

in breast cancer

Klinik für Reproduktions-Endokrinologie, Universitätsspital Zürich, Schlieren

CHF 325 000.- | Duration: 1.5. 2017 - 30. 4. 2021 | KFS-4125-02-2017

Fernandez Gonzalez Santiago | In vivo characterization of melanoma dissemination through the lymphatic system

Istituto di Ricerca in Biomedicina (IRB), Bellinzona

CHF 249 900.- | Duration: 1.1. 2018 - 31.12. 2020 | KFS-4274-08-2017

Foti Michelangelo | Molecular mechanisms of microRNA-22 tumour suppressive activity in liver cancer

Département de physiologie cellulaire et métabolisme, Université de Genève, Genève

CHF 375 000.- | Duration: 1.3.2018 - 28.2.2021 | KFS-4094-02-2017

Gasser Susan M. | DNA polymerase delta in cancer: targeting the fragile fork

Friedrich Miescher Institute for Biomedical Research, Basel

CHF 281 150.- | Duration: 1.7.2017 - 30.6.2020 | KFS-4167-02-2017

Gfeller David | Expanding (neo-)antigen predictions in tumours using in-depth HLA peptidomics data:

an opportunity for investigating cancer-immune cell interactions in human

Ludwig Center of Cancer Research at the University of Lausanne, Epalinges

CHF 259 800.- | Duration: 1.12.2017 - 30.11.2020 | KFS-4104-02-2017

Grassi Fabio | The ATP-gated ionotropic P2X7 receptor as a possible target to enhance the efficacy

of cancer immunotherapy

Istituto di Ricerca in Biomedicina (IRB), Bellinzona

CHF 235 600.- | Duration: 1.7.2017 - 31.10.2019 | KFS-4110-02-2017

Holland Jason P. | Harnessing androgen receptor signalling for imaging protein degradation therapy

in prostate cancer

Institut für Chemie, Universität Zürich, Zürich

CHF 330 000.- | Duration: 1.8.2018 - 31.7.2022 | KFS-4257-08-2017

Martinon Fabio | Deciphering the anti-tumoural properties of IRE1 in diffuse large B-cell lymphoma

Département de biochimie, Université de Lausanne, Epalinges

CHF 244 300.- | Duration: 1. 2. 2018 - 31. 1. 2021 | KFS-4230-08-2017

Müller Anne | The sphingosine-1-receptor 2 is a novel tumour suppressor in diffuse large B-cell lymphoma:

investigating its regulation, mode of action and clinical relevance

Institut für molekulare Krebsforschung, Universität Zürich, Zürich

CHF 219 850.- | Duration: 1.7. 2017 - 30. 6. 2019 | KFS-4120-02-2017

Münz Christian | Biology and therapy of primary effusion lymphoma (PEL) like tumours that are caused by double-infection with the Epstein Barr virus (EBV) and the Kaposi sarcoma associated herpes

virus (KSHV) in vivo

Institut für experimentelle Immunologie, Universität Zürich, Zürich

CHF 369 000.- | Duration: 1.9.2017 - 31.8.2020 | KFS-4091-02-2017

Nardelli Haefliger Denise | Local immunostimulation with bacterial vaccines for combination therapies against human papillomavirus-associated cancers

Service d'urologie, Centre hospitalier universitaire vaudois (CHUV), Lausanne

CHF 361 350.- | Duration: 1.9.2017 - 31.8.2020 | KFS-4103-02-2017

Plückthun Andreas | Novel approaches of targeting the RAS subfamily of small GTPases in human cancer

Biochemisches Institut, Universität Zürich, Zürich

CHF 339 000.- | Duration: 1. 7. 2017 - 30. 6. 2020 | KFS-4147-02-2017

Rottenberg Sven | Understanding the role of the CST complex in the synthetic lethal interaction between BRCA1 deficiency and PARP inhibition

Departement für Infektionskrankheiten und Pathobiologie, Universität Bern, Bern

CHF 330 000.- | Duration: 1. 2. 2018 - 31. 1. 2022 | KLS-4282-08-2017

Rubin Mark A. | Towards a precision therapy for SPOP mutant prostate cancer

Department for BioMedical Research (DBMR), Universität Bern, Bern CHF 369 400.- | Duration: 1.7. 2017 - 30. 6. 2020 | KFS-4102-02-2017

Santamaria-Martinez Albert | Role of TGFBI in breast cancer stem cells and potential therapeutic applications

Département de médicine, Université de Fribourg, Fribourg

CHF 152 350.- | Duration: 1.1.2018 - 30.6.2019 | KLS-4121-02-2017

Sauer Uwe | Finding common metabolic programmes in quiescent cancer cells using high-throughput metabolomics

Departement Biologie, ETH Zürich, Zürich

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CHF 228 200.- | Duration: 1.1. 2018 - 31. 12. 2019 | KLS-4124-02-2017

Schoonjans Kristina | Anatomical and molecular exploration of the role of the adrenergic system on liver cancer

Laboratory of Metabolic Signaling, Ecole Polytechnique Fédérale de Lausanne (EPFL), Lausanne

CHF 375 000.- | Duration: 1. 2. 2018 - 31. 1. 2022 | KFS-4226-08-2017

Schwaller Jürg | Genomics, models and mechanisms of human acute erythroleukaemia

Departement Biomedizin, Universitäts-Kinderspital beider Basel, Basel CHF 375 000.- | Duration: 1.5. 2018 - 30. 4. 2021 | KFS-4258-08-2017

Stamenkovic Ivan | Analysis of the molecular mechanisms underlying the pathogenesis of Ewing family tumours

Institut universitaire de pathologie, Centre hospitalier universitaire vaudois (CHUV), Lausanne

CHF 360 350.- | Duration: 1.7. 2018 - 30. 6. 2021 | KLS-4249-08-2017

**Thelen Marcus** | The function of ACKR3 in B-cell lymphoma tissue invasion

Istituto di Ricerca in Biomedicina (IRB), Bellinzona

CHF 326 950.- | Duration: 1.1. 2018 - 31.12. 2021 | KFS-4223-08-2017

Theurillat Jean-Philippe | URB5 - A driver of lethal prostate cancer?

Institute of Oncology Research, Bellinzona

CHF 316 300.- | Duration: 1. 3. 2018 - 28. 2. 2021 | KFS-4248-08-2017

Thome-Miazza Margot | Analysis of the role of a novel MALT1 substrate in lymphoma development

Département de biochimie, Université de Lausanne, Epalinges

CHF 314 950.- | Duration: 1. 8. 2017 - 31. 7. 2021 | KFS-4095-02-2017

van den Broek Maries | The role of NK and NKT cells in development and progression of liver metastasis

Institut für experimentelle Immunologie, Universität Zürich, Zürich

CHF 242 450.- | Duration: 1. 7. 2017 - 30. 6. 2021 | KLS-4098-02-2017

vom Berg Johannes | Local immunotherapy of brain cancer using an Interleukin-12 Fc fusion cytokine -

in vitro refinement, dose escalation and interventional study in spontaneous canine brain tumours

Institut für Labortierkunde, Universität Zürich, Zürich

CHF 367 250.- | Duration: 1. 9. 2017 - 31. 8. 2020 | KFS-4146-02-2017

Approved bursaries in 2017

Total funds allocated: CHF 107 950.-

Leiser Dominic | Protection of neuronal stem cells and neurocognitive function in brain radiation therapy

Destination: Division of Translational Radiation Sciences, University of Maryland, USA

CHF 107 950.- | Duration: 1.12.2017 - 30.11.2019 | BIL KFS-4127-02-2017







## A registry for immune-oncology drugs

At this year's meeting of the American Society of Clinical Oncology, ASCO 2018, it was confirmed again: For many cancers, tumour immunology and the possibilities of cancer immunotherapy are the driver of advances in oncological treatment. Since the first report on the efficacy of immune checkpoint inhibitors in the treatment of metastatic melanoma in 2010, there has been an avalanche of new treatment options. Today, representatives of the new class of drugs are clinically tested in almost all cancers, and in many areas they have already been approved for use.

Approval is most often based on Phase 2 and Phase 3 trials that tested the use of a checkpoint inhibitor as a first-line or second-line treatment for metastasizing cancers. A resulting problem is how the immunotherapy affects the subsequent therapy algorithm, for there is no knowledge of how a prior immunotherapy

affects subsequent therapies such as chemotherapy or radiation therapy. This question concerning the sequencing of therapies is usually not answered by clinical trials, as there is limited commercial interest in clarifying such complex questions. This problem gets worse, as the checkpoint inhibitors are also used already prior to surgery (that is, they are already being used in the neo-adjuvant setting), and the question arises as to how to proceed if there is metastasis or recurrence.

In addition, immunotherapy drugs are tested in combination with chemotherapy and further new substances, which makes the issue of the right sequencing of therapies even more urgent. With this, in my opinion, oncology is faced with the massive problem of knowledge processing for optimal clinical care of patients. In lectures and in discussions, I hear again and again that the best way to solve this problem is to enrol patients in trials, because the situation at the moment is so unclear and complex and a clinical trial

would help answer at least one more clearly formulated question. But this argument overlooks the reality of the oncology care landscape in Switzerland, where only a minority of patients are treated in clinical trials. Also, inclusion in a trial does not solve the problem but merely postpones it, for after the trial, the patient needs further oncology care.

Clinical trials, as at ASCO 2018 this year, are of elemental importance in further developing treatment for patient benefit, in that new drugs are tested in a targeted manner. But they are a poor instrument for evaluating sequencing of therapy, as they frequently examine and evaluate only one part of a care algorithm. Although there is an attempt in trials to capture the entire case history after the intervention by means of endpoints, such as overall survival and disease- or progression-free survival, this does not achieve high data accuracy. This holds especially for clinical trials that clearly focus on product placement.

Consequently, in my view there is a need for action when the treatment options of many oncology patients are changing so rapidly and radically. We need to know how the advent of immunotherapy changes care in daily clinical practice and what events and consequences this has for the patients being treated. For this, registries are a possible tool: They can map the temporal progression of a treatment and record the care reality. To meet this challenge as comprehensively as possible, a registry could be established as in the following.

#### Aim

A tumour immunology registry must capture data by means of a standardized procedure on all patients who receive immune modulating therapy for the treatment of a malignant tumour outside of clinical trials. Here, the focus must go beyond today's checkpoint inhibitors. All immune modulating oncology treatments must be recorded, for the future will see vaccines against cancer, cellular therapies, or treatments changing the gut microbiome. The data recorded should be utilized to gain a better understanding of the effectiveness, side effects, quality of life, and economic aspects of immune modulating oncology therapies. A registry of this kind should also make research possible. For instance, the registry could aid identification of 'premium responders' who show complete remission or whose cancer can be controlled successfully by means of immunotherapy for more than 12 months. This leads to interesting translational research questions, such as what the underlying immunological mechanisms of a premium response are.

#### Data and functions

The registry must primarily contain the clinical data on the person, the malignant tumour, and the clinical results of the treatment. These data are particularly valuable if the use of immune oncology drugs is recorded in the clinical context and if, in addition, safety data (side effects and adverse events) are included. The registry provides more in-depth and more comprehensive data than a clinical trial, because it could contain also information on the utilization of immune oncology drugs, particularly also on off-label use of the drugs (a different use than that specified in the approved packaging label) and on use of a combination of drugs. Important for successful data collection is that the data can be recorded reliably, without extra work on the part of the treatment team. A study

team that visits centres and collects the data is a possible solution to avoiding extra work. In addition to the main clinical questions, questions on health economics could be asked and answered based on the registry data. This is of special interest, as the therapies generate high costs and there are strong cost pressures on the health care system. The registry data could be utilized for the development of innovative remuneration models, which for example could be based more on what are called 'pay-for-performance' models.

#### Linking

To avoid duplications and for optimal use of synergies, a tumour immunology registry would have to be planned such that it falls within the scope of developments in connection with the national law on cancer registration that will soon enter into force and in the best case can complement and support the cancer registry. At present, it is still being decided what data from the cantonal epidemiological cancer registries will be collected (and aggregated nationally by NICER). The development of a tumour immunology registry is favoured not only by current policy dynamics and existing interest on the part of key opinion leaders but also by several in part datadriven academic initiatives. These are mainly the initiatives on health services research (NRP, SAMS, SCR), the Swiss Personalized Health Network Initiative (SAMS, SNSF), the setting up of a Swiss Biobanking Platform, the Data Science Initiative, the ETH Domain focus on personalized medicine, and the Immuno-Oncology Working Group of the Swiss Group for Clinical Cancer Research (SAKK).

#### Challenges

I am aware that establishing a registry with the necessary wide anchoring in the Swiss oncology care landscape will pose great challenges. The registry must fulfil data needs comprehensively, so as to prevent the setting up of parallel registry structures. For this, it is very important that the handling of the data and the work involved be done in a manner based on partnership. It must also have interface compatibility, so that collaborations are possible, for only an exchange of the data increases its scientific value. To be able to exchange data, the data must first be aggregated and anonymized. Furthermore, patients must be informed of utilization of the data, and studies must be approved by cantonal ethics committees. Another complex task is the financing of the registry. All partners involved should participate in the financing. This includes insurance companies, the pharmaceutical industry, and the society, which can participate in the form of public research funds.

#### Swiss Tumor Immunology Registry (SwissTIR)

The members of the Swiss Tumor Immunology Institute have risen to these challenges by founding an association and in this way laying the foundation for the establishment of the Swiss Tumor Immunology Registry (SwissTIR). The aims and the challenges mentioned above are already being addressed through starting the recording of patient data in SwissTIR, and initial experience has been gained. After data have been collected for the first 300 patients, the first evaluation of data quality will be conducted. With this, a first, practical approach to health services research will have been carried out for immune modulating oncology therapy, and we hope that the findings will contribute towards a better understanding of the care of patients in the new era of immunotherapy to treat cancer.



#### PD Ulf Petrausch, MD

Ulf Petrausch studied medicine in Mainz and Berlin and then specialized as an oncologist and subsequently immunologist and allergist at University Hospital Zurich. In Zurich he also became an FMH-certified specialist in internal medicine before completing a habilitation in clinical

tumour immunology and T-cell therapy. Since 2015 he has headed the immune-oncology section at Onkozentrum Zurich. He also serves as president of the Swiss Tumor Immunology Institute, which he co-founded in 2016.

Tel. +41 (0)43 344 33 33 ulf.petrausch@swisstii.ch swisstii.ch

## Selected results

#### Project

Improving clinical interpretation of genetic variations underlying common cancers Département de science des protéines humaines, Université de Genève, Genève CHF 231 200.- | Duration: 1.2.2014 - 30.4.2017 | KFS-3297-08-2013

Project coordinator

Prof. Amos Bairoch, PhD | amos.bairoch@unige.ch

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#### Useful store of knowledge

Development of cancer is in most cases a result of mutations. Knowledge of these mutations provides important indications for how the cancer can be treated successfully. In a project supported by the Swiss Cancer Research foundation, researchers are bringing the dispersed data on cancer-specific mutations together in a knowledge base.

The more advances that are made in science, the more knowledge is generated on cancer. However, as research results are mostly published in pieces and in different journals, it is becoming increasingly difficult to manage the ever-growing flood of information and maintain an overview. For instance, there are thousands upon thousands of different genetic variants or mutations. Most of them are neither beneficial nor detrimental (and are called 'neutral' mutations), but some of them change the structure of proteins. Mutations of that kind can affect the metabolism of the cells, lead to more rapid cell division, or diminish the ability of the cells to repair arising damage to the genetic material. Mutations are often a causal factor in the emergence of cancer.

For this reason, more and more frequently, tumour samples from patients are examined not only under the microscope but also genetically. To help physicians interpret this genetic information, a team of bioinformaticians headed by Amos Bairoch at the University of Geneva is developing a large database called neXtProt, a comprehensive knowledge platform on human proteins, with support from the Swiss Cancer Research foundation.

"The human protein knowledgebase integrates data to provide comprehensive, up-to-date, high quality information," the researchers report in a journal article. The collection and systematic organization of research findings requires a great deal of patience and persistence, as indicated by the quotation attributed to the

Chinese philosopher Lao Tzu that Bairoch and his colleagues chose for the neXtProt website: "A journey of a thousand miles begins with a single step."

After three years of work, the researchers have viewed, collected, and categorized the findings in research literature on more than 4000 variations in a number of important genes involved in cancers. In this way Bairoch and his team have increased a store of knowledge that is becoming ever more useful as they continue to make progress on their journey.

#### References

Gaudet P, Michel PA, Zahn-Zabal M, Britan A, Cusin I, Domagalski M, et al. The neXtProt knowledgebase on human proteins: 2017 update. *Nucleic Acids Res.* 2017;45:D177-82.

Gaudet P, Michel PA, Zahn-Zabal M, Cusin I, Duek PD, Evalet O, et al. The neXtProt knowledgebase on human proteins: current status. *Nucleic Acids Res.* 2015;43:D764-70.

Lane L, Argoud-Puy G, Britan A, Cusin I, Duek PD, Evalet O, et al. neXtProt: a knowledge platform for human proteins. *Nucleic Acids Res.* 2012;40:D76-83.

Project

Development of chimeric antigen receptor T-cells for immunotherapy of glioma Service d'oncologie, Hôpitaux universitaires de Genève (HUG), Genève CHF 248 000.- | Duration: 1.1.2014 - 30. 9. 2017 | KFS-3270-08-2013

Project coordinator

Prof. Pierre-Yves Dietrich, MD | pierre-yves.dietrich@hcuge.ch

## Development of immunotherapy for deadly brain tumours

Gliomas are still very difficult to treat, and for this reason are one of the most frequent causes of death due to cancer in children. In a research project supported by the Swiss Cancer Research foundation, researchers are modifying immune cells genetically to arm them for the fight against the tumour cells.

Gliomas are rare but very malignant tumours, as they grow aggressively, spread rapidly, and destroy healthy brain tissue. If not treated, highly malignant gliomas lead to death within months. But even with treatment, there is little chance of a cure. For treatment often proves to be difficult: Due to the rapid and invasive growth, surgeons cannot remove the tumour completely, and also chemotherapy and radiation therapy have only very limited effects.

Pierre-Yves Dietrich and his research team in the Tumor Immunology Laboratory at Geneva University Hospitals (HUG) have committed themselves to the goal of improving the bleak prospects of young patients. The researchers are following several approaches that all have one thing in common: It is always about increasing the power of the body's own immune system in fighting the glioma.

With financial support from the Swiss Cancer Research foundation, Dietrich and his team have equipped a certain class of immune cells called T-cells with an additional receptor created in the laboratory by genetic engineering. The receptor is a mixed creature (chimera) that is composed of a part within the cell that can boost the metabolism of the cell and put the cell on alert and also of a part that protrudes from the immune cell and binds to molecules that only lie on the surface of tumour cells (and not on healthy cells). With this, the chimeric antigen receptor (CAR) tells the immune cells what cells to attack.

The CAR T-cell therapy approach has been shown to be successful with leukaemia, and in the United States the first such therapies were approved last year. Dietrich and his research team are not yet that far; they are working with cell cultures. But their results are encouraging and give grounds for hope that the CAR T-cells will soon be tested in animal experiments – and perhaps also in some years will help patients.

#### References

Dietrich PY, Dutoit V, Walker PR. Immunotherapy for glioma: from illusion to realistic prospects? *Am Soc Clin Oncol Educ Book*. 2014:51-9.

Dutoit V, Herold-Mende C, Hilf N, Schoor O, Beckhove P, Bucher J, et al. Exploiting the glioblastoma peptidome to discover novel tumour-associated antigens for immunotherapy. *Brain.* 2012;135:1042-54.

Dutoit V, Migliorini D, Ranzanici G, Marinari E, Widmer V, Lobrinus JA, et al. Antigenic expression and spontaneous immune responses support the use of a selected peptide set from the IMA950 glioblastoma vaccine for immunotherapy of grade II and III glioma. *Oncoimmunology*. 2017;7:e1391972.

Dutoit V, Migliorini D, Walker PR, Dietrich PY. Immunotherapy of brain tumors. Prog Tumor Res. 2015;42:11-21. Migliorini D, Dietrich PY, Stupp R, Linette GP, Posey AD Jr, June CH. CAR T-Cell Therapies in Glioblastoma: A First Look. *Clin Cancer Res.* 2018 24(3):535-540.

## List of approved research projects in 2017

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

Total funds allocated: CHF 4 495 050.-

Beyer Jörg | miRNAs in testicular cancer patient surveillance

Medizinische Onkologie, Inselspital Bern, Bern

CHF 362 800.- | Duration: 1.1. 2018 - 31.12. 2021 | KFS-4297-08-2017

**de Leval Laurence** | Deciphering the heterogeneity and multistep molecular pathogenesis of intestinal T-cell lymphomas

Institut universitaire de pathologie, Centre hospitalier universitaire vaudois (CHUV), Lausanne CHF 250 000.- | Duration: 1.1.2018 - 31.12.2019 | KLS-4293-08-2017

**Derré Laurent** | Characterization of myeloid suppressive cells and innate lymphoid cells involved in BCG treatment failure to define novel prognostic marker and treatment for urothelial cancer Service d'urologie, Centre hospitalier universitaire vaudois (CHUV), Lausanne CHF 243 900.- | Duration: 1.10.2017 - 30.9.2020 | KFS-4101-02-2017

**Grouzmann Eric** | Proneuropeptide Y, neuropeptide Y and their fragments as biomarkers for the diagnosis and prognosis of prostate cancer

Laboratoire des catécholamines et peptides, Centre hospitalier universitaire vaudois (CHUV), Lausanne CHF 364 700.- | Duration: 1.1.2018 - 31.12.2020 | KLS-4283-08-2017

**Guenova Emmanuella** | Defining tumour progression & immune modulation in the management of cutaneous T-cell lymphoma

Dermatologische Klinik, Universitätsspital Zürich, Zürich

CHF 375 000.- | Duration: 1.5. 2018 - 30. 4. 2022 | KFS-4243-08-2017

Hilfiker Roger | Interventions for persons with cancer related fatigue during and after cancer treatment. Living systematic review with a network meta-analysis and meta-regression on exercises characteristics. Continuously updated results on a free website with an interactive visualization tool

Haute Ecole de Santé Valais, Leukerbad

CHF 119 200.- | Duration: 31.1.2018 - 30.1.2019 | KFS-4286-08-2017

**Honecker Friedemann** | WISE STUDY: walking intervention for symptom elimination under aromatase inhibitor therapy. The preventive effect of a 24 week home-based walking programme on symptom burden among breast cancer survivors receiving aromatase inhibitor therapy

Onkologisches Zentrum, Tumor- und Brustzentrum ZeTuP, St. Gallen

CHF 356 200.- | Duration: 1. 3. 2018 - 28. 2. 2021 | KFS-4268-08-2017

**Knauer Michael** | TAXIS: targeted axillary dissection and radiotherapy in breast cancer with high-volume nodal disease or residual nodal disease after neoadjuvant chemotherapy

Brustzentrum, Kantonsspital St. Gallen, St. Gallen

CHF 364 050.- | Duration: 1.7.2017 - 30.6.2020 | KFS-4105-02-2017

Krebs Philippe | Role of IL-33 signalling for the progression of myeloproliferative neoplasms

Institut für Pathologie, Universität Bern, Bern

CHF 312 500.- | Duration: 1.10.2017 - 31.3.2020 | KFS-4162-02-2017

**Läubli Heinz** | EGFR-targeted immunoliposomes for recurrent glioblastoma multiforme: a phase I pharmacokinetic study

Medizinische Onkologie, Universitätsspital Basel, Basel

CHF 152 800.- | Duration: 1.9. 2017 - 31. 8. 2019 | KFS-4129-02-2017

**Lugli Alessandro** | The tumour microenvironment score: a novel biomarker in risk assessment of nodal metastases in pT1 colorectal cancer

Institut für Pathologie, Universität Bern, Bern

CHF 139 450.- | Duration: 2.10.2017 - 1.4.2019 | KFS-4108-02-2017

Marti Thomas | Targeting tumour initiating cells in lung cancer

Universitätsklinik für Thoraxchirurgie, Inselspital Bern, Bern

CHF 242 450.- | Duration: 1. 3. 2018 - 28. 2. 2021 | KFS-4265-08-2017

Matter Matthias | The role of "phosphoprotein enriched in diabetes" in liver cancer development and disease

Institut für Pathologie, Universitätsspital Basel, Basel

CHF 185 100. - | Duration: 1.8.2017 - 31.1.2020 | KFS-4168-02-2017

Perren Aurel | Precision medicine approach for novel epigenetic pancreatic neuroendocrine tumour (PanNET) treatment

Institut für Pathologie, Universität Bern, Bern

CHF 359 450.- | Duration: 1.5.2018 - 30.4.2022 | KFS-4227-08-2017

Richter Andre | A multicentre study observing relations between white matter, affective symptoms and social support in adults with cerebral glioma before and after surgery

Klinik für Konsiliarpsychiatrie und Psychosomatik, Universitätsspital Zürich, Zürich

CHF 108 050.- | Duration: 1.1. 2018 - 31.12. 2019 | KFS-4270-08-2017

Truninger Kaspar | DNA methylation in early detection and prevention of colorectal cancer

Gastroenterologie Oberaargau, Langenthal

CHF 339 600.- | Duration: 1. 2. 2018 - 31.1. 2021 | KFS-4301-08-2017

**Vassalli Giuseppe** | Role of Notch signalling and therapeutic potential of exosomes in doxorubicine/ trastuzumab-induced cardiomyopathy

Cardiocentro Ticino, Lugano

CHF 94 800.- | Duration: 1. 8. 2017 - 31. 7. 2018 | KFS-4111-02-2017

Wild Peter Johannes | Genetic fingerprinting of uterine cancer

Institut für Pathologie und Molekularpathologie, Universitätsspital Zürich, Zürich

CHF 125 000.- | Duration: 1.1. 2018 - 31. 12. 2018 | KFS-4245-08-2017

Approved bursaries in 2017

Total funds allocated: CHF 433 300.-

**Ackermann Christoph** | Realising the potential of liquid biopsies to understand tumour evolution, treatment resistance and tailor precision medicines for improved outcomes in patients with lung cancer

Destination: Christie Hospital in Manchester, GB

CHF 198 000.- | Duration: 1.5. 2018 - 30. 4. 2020 | BIL KLS-4244-08-2017

**Biskup Ewelina Maria** | Cancer in the oldest old – a prospective multicentre cohort and randomized controlled study on decisions, treatment patterns and prognosis

Destination: Fudan University Cancer Center Shanghai, CHN

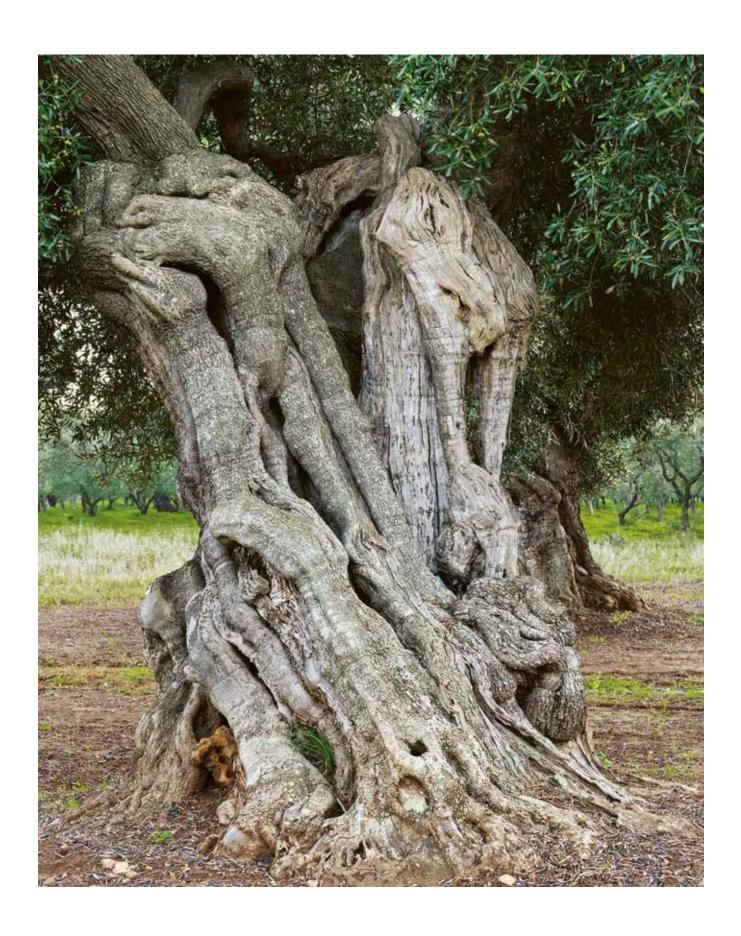
CHF 98 500.- | Duration: 2.4.2018 - 1.4.2020 | BIL KFS-4261-08-2017

**Stieb Sonja** | Assessment of magnetic resonance imaging biomarkers in patients with oropharyngeal cancer to predict radiation-induced normal tissue toxicity

Destination: MD Anderson Cancer Center, The University of Texas, USA CHF 136 800.- | Duration: 1.4.2018 - 31.3.2020 | BIL KLS-4300-08-2017







# Making better use of patient experience

#### What are patient-reported outcomes (PRO)?

According to estimates, as of the end of 2015 the number of persons living in Switzerland with at least one past diagnosis of cancer in their lifetime was more than 3160001. This group is expected to increase in size in coming years because of demographic ageing, better prognoses due to more effective treatments, and improved diagnostics. The survival of patients with cancer is naturally an important goal in cancer research. But beyond that, their experience of their cancer is also crucial for the patients. This is also true of patients with cancer who have to adjust to the fact that they cannot be cured. For this reason, for the further development of treatment and care of patients with cancer, there must also be a focus on how well patients with cancer can deal with a cancer diagnosis and the necessary therapies and on how the diagnosis and treatment place restrictions on patients' everyday life.

This question can be answered if patients can provide regular information on the status of their health, such as when they report their blood pressure or temperature, for example. To learn about patient experience also when investigating the effectiveness of therapies, concepts such as health-related quality of life became established in the last decades. These concepts then paved the way for patient-reported outcome (PRO) measures<sup>2-4</sup>. PRO concern any area related to health as assessed by the patients themselves. The U.S. Department of Health and Human Services defines PRO as "a measurement based on a report that comes directly from the patient about the status of a patient's health condition without amendment or interpretation of the patient's response by a clinician or anyone else"5. Today, the drug authorities in the United States and Europe call for the use of PRO in clinical trials<sup>5,6</sup>. PRO can concern symptoms or side effects but also general health status, quality of life, patient

#### Prof. Manuela Eicher, PhD

Professor at the Institute of Higher Education and Research in Health Care of the University of Lausanne

#### Karin Ribi, PhD, MPH

satisfaction with treatment, and possible treatment preferences<sup>7</sup>. PRO data are collected by patients or their relatives by filling out paper-and-pencil or (more and more frequently) electronic surveys (electronic patient-reported outcome, ePRO).

# The introduction of PRO and ePRO in clinical practice

Although the importance of PRO in pharmacological cancer trials is undisputed, their use in routine clinical practice is still hotly debated. Several studies have shown that health care professionals frequently underestimate the extent and severity of the symptoms<sup>8,9</sup> and that patients classify symptoms like nausea and vomiting, fatigue, and pain as more severe than physicians and nurses do <sup>10</sup>. Consequently, it is now considered that quality of life, symptoms, and patient burden can be best captured through direct self-assessments.

Advances in technological information processing open new possibilities of electronic data collection, which has some important advantages over paperand-pencil instruments: Patients do not have to remember their complaints and symptoms until their next appointment with the physician; instead, they can enter their symptoms as they occur. This systematic self-assessment of symptoms or quality of life and reporting it to health care professionals can not only improve communication regarding patient-relevant concerns. When health care personnel know more about the patient's symptoms, unmet needs, and changes in quality of life, they can initiate supporting measures sooner and more frequently - and in this way often control the effects of the treatment better. In addition, patients who have better communication with their physicians and nurses through electronic self-report assessment have on average greater patient satisfaction <sup>11-13</sup>. Patients with advanced cancer possibly even live longer when PRO are collected systematically and treatment teams, especially nurses, respond promptly <sup>14</sup>.

In Switzerland, the first projects using ePRO in clinical practice are being conducted <sup>15-17</sup>. Recently, a symposium was held at which experts reported on international developments and on some selected noncommercial aids or tools that are being developed in Switzerland. The 'Promoting Self-efficacy with Digital Tools' symposium was organized by the Swiss Cancer League as part of the National Strategy Against Cancer; the symposium presentations and further information are available at digiself2018.ch.

#### From PRO to ePRO to digital health

However, the development of digital possibilities goes far beyond the electronic collection of PRO data. The broad spectrum of what is called 'digital health' encompasses mobile health applications (mHealth), information technology in health (health IT), wearable measurement instruments (wearables), telemedicine, and personalized medicine<sup>18</sup>. The development of the digital health market is being driven by the information technology sector especially and is proceeding at breathtaking speed. Overall, this development is promising: If various health data can be brought together and correctly interpreted, this will open up opportunities for medicine to make enormous advances.

At the individual level, health data can help people to monitor their health status. The data entry and targeted feedback can also support patients and their family members in dealing with risks or complaints. Together, patients and health professionals can detect problems and changes for the worse sooner and therefore take measures and adjust the treatment to individual characteristics of the patient.

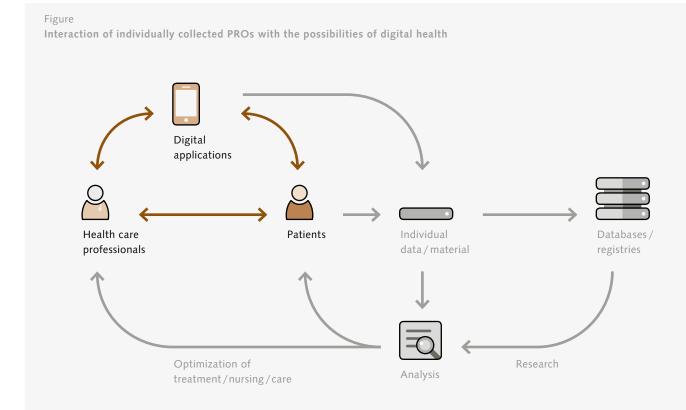
At the population level, aggregated data can help to improve outcomes for specific patient or risk groups. Researchers hope that large health care databases and big data analytics will foster medical innovations and speed up therapy development - and this especially in oncology, where personalized medicine has already become a part of clinical practice and where today we are already able to aim therapy at individual molecular targets. Digital health care data can also be of interest from an economic perspective: They can lead to more targeted use of interventions and therefore reduce the costs of health care. In addition, aggregated patient data can be utilized for continuous development of the quality and safety of the health care system (Figure). However, this rapid development of digital health also raises numerous ethical and political questions.

# PRO, digital health: many questions - what are the answers?

The critical issues in connection with the collection of PRO and the development of digital health can be classified as belonging to the following areas: data access, data protection, accountability, evidence base, and trust<sup>19</sup>. The promises of digital health can probably only be realized if at the same time it is assured that individuals have access to their data but also

that their data is protected. Initiatives of personalized therapies and of public health that are being developed in the wake of digital health must be held accountable to the public law authorities. In addition, medical services must be based on evidence, which cannot be supported by observational data alone. To guarantee security and trustworthiness for everyone affected, developments in digital health must also continue to meet the established standards of ethics in medical research <sup>19</sup>.

ePRO and other tools of digital health are therefore only useful if they also in the future aim for added, verifiable benefit for patients. For the development of useful tools, multidisciplinary approaches are not sufficient. Rather, transdisciplinary teams are required,



made up of experts in various disciplines (such as oncology, biomedicine, information technology, and bioinformatics) but also with the participation of persons affected or users in all phases of development and research. For this reason, our team in Lausanne works in various projects with the persons affected and their family members. Together we develop PRO, for instance for patients with immune-oncology therapy, and test their use in clinical practice in combination with other data (such as biomarkers). Further, in programmes we investigate how self-management of symptoms can be fostered – and here, too, we include patients and family members in the development and research phases.



Prof. Manuela Eicher, PhD
Originally trained as a registered
nurse in 1994, Manuela Eicher
completed her doctorate at
Witten/Herdecke University in
Germany in 2008. Since 2016
she is a professor at the Institute
of Higher Education and Research
in Health Care at the University
of Lausanne. This includes an

appointment as research consultant in the Department of Oncology at University Hospital Lausanne (CHUV). With her research team she studies how to enhance supportive care services in oncology, particularly through nurse-led interventions

Tel. +41 (0)21 314 87 60 manuela.eicher@chuv.ch www.unil.ch/sciences-infirmieres/home/menuinst/ recherche/manuela-eicher.html



Karin Ribi, PhD, MPH

Karin Ribi is a psychologist, and she earned a doctoral degree at the University of Zurich in 2003 with a research project that she conducted at University Children's Hospital Zurich. During that time, she also provided psycho-oncology care to children with cancer and their families. Since 2004 she has

worked in quality of life research in the context of clinical cancer trials for the International Breast Cancer Study Group and the Swiss Group for Clinical Cancer Research. In addition, she became a member of Manuela Eicher's research team in 2017.

karin.ribi@chuv.ch

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#### Selected results

#### Project

Dignity therapy+: a brief psychological and existential intervention for dying patients and their families – a pilot study

Klinik für Konsiliarpsychiatrie und Psychosomatik, Universitätsspital Zürich, Zürich

CHF 81 800.- | Duration: 1.7. 2015 - 30. 9. 2017 | KFS-3637-02-2015

Project coordinator

Prof. Josef Jenewein, MD | josef.jenewein@usz.ch

#### Being able to leave the world with dignity

At the end of life, many patients with cancer experience anxiety and depression. Despite good palliative care, there is still a lack of psychotherapeutic concepts for mitigating this psychological distress. With support from the Swiss Cancer Research foundation, researchers tested a psychotherapy approach and, in the process, held moving conversations.

Although palliative care has made significant progress in symptom management and pain relief in patients nearing death, the end of life - the so-called terminal phase - is a time of increased psychological distress. It is distressing for the patients, for their families, and also for the treatment team. "In this very difficult phase, of all phases, we are often helpless and can offer little," says Josef Jenewein of the Department of Consultation-Liaison Psychiatry and Psychosomatic Medicine at University Hospital Zurich. In a pilot study supported by the Swiss Cancer Research foundation, Jenewein and his colleagues tested whether a standardized psychotherapy approach could give back to dying patients a feeling of dignity and selfdetermination and in this way reduce their psychological distress.

The study participants, who had a life expectancy of only a few weeks, were randomly assigned to one of three groups. The first group received standard palliative care. Patients in the second and third groups in addition had the psychotherapy. Patients in the second group met with the therapist alone; in the third group, a partner or family member was included in the psychotherapy with the patient.

The psychotherapy gave patients the opportunity to talk about their lives and to respond to questions like, "When did you feel the most alive?", "What are you particularly proud of?", "What would you most want remembered?", or "What did life teach you?".

The therapists audiotaped the sessions and then prepared a transcribed and edited document with a short biography of the patients and their wishes for the future. "The conversations triggered a lot of emotions," says Jenewein.

All of the participants filled out a survey after the psychotherapy. Their feedback indicates that thanks to the psychotherapy, patients experience less distress and that especially also their family members have fewer symptoms of anxiety and depression. Jenewein's team now wants to confirm the promising results of the pilot study in a larger, statistically sound study.

# List of approved research projects in 2017

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

Total funds allocated: CHF 828 350.-

**Rubinelli Sara** | The discourse around the role and services of specialized palliative care in oncology and haemato-oncology. An evaluation of health care professionals' and public views in the Italian-speaking part of Switzerland.

Schweizer Paraplegiker-Forschung, Nottwil

CHF 184 450.- | Duration: 1.11. 2017 - 31.10. 2020 | KFS-4163-02-2017

**Schaefert Rainer Michael** | A clinical trial of group-based body psychotherapy to improve bodily disturbances in posttreatment cancer patients, in combination with randomized controlled smartphone-triggered bodily interventions

Psychosomatik, Universitätsspital Basel, Basel

CHF 188 500.- | Duration: 1. 3. 2018 - 28. 2. 2021 | KLS-4304-08-2017

**Tschudin Sibil** | Fertility preservation in men affected by cancer: assessment of patients' needs and development of an online decision-aid

Frauenklinik, Universitätsspital Basel, Basel

CHF 80 400.- | Duration: 1.7. 2017 - 31. 12. 2019 | KFS-4122-02-2017

**Wolf Ursula** | Eurythmy therapy as treatment option for fatigue in metastatic breast cancer patients – a prospective, randomized, controlled, multi-centre trial

Institut für Komplementärmedizin, Universität Bern, Bern

CHF 375 000.- | Duration: 1. 2. 2018 - 31. 1. 2022 | KFS-4259-08-2017







# Use of microsimulation models to optimize colon cancer screening

Colorectal cancer, cancer of the colon and the rectum, is the third most common cancer in industrialized countries – and is the second most deadly (after lung cancer)<sup>1</sup>. Fortunately, colon cancer incidence and mortality can be reduced by screening. Two screening methods have been demonstrated to have benefits for cancer prevention: 1) detection of occult blood in the stool as a biological marker for cancer (faecal occult blood test, FOBT)<sup>2-5</sup>, and 2) endoscopy<sup>6-9</sup>, which visualizes the lining of the colon and rectum.

There are screening tests for several types of cancer, but colon cancer screening methods are especially effective because the tumour develops slowly and stepwise from benign precancerous lesions, which can not only be discovered but also often immediately removed during the intervention. In the colon, at first small, or early, polyps (adenomas) with a benign (tubular) histology and with a size of 2 to 9 mm develop. They can grow into advanced adenomas that are either larger than 10 mm in size or display an

advanced villous or serrated histology. Cancer then develops from one of these advanced adenomas. How long this process takes is not yet clear, but estimates range from seven to twenty years 10. During this period, it is possible, through screening, to discover an existing adenoma and remove it, thus effectively preventing colorectal cancer.

Screening can save lives: The faecal occult blood test (FOBT) reduces colorectal cancer mortality by 30% with tests every year and by 20% with tests every two years<sup>2-5</sup>. In addition, several large randomized studies have shown that a once-only flexible sigmoidoscopy screening (a smaller variant of a full colonoscopy that examines the lower 30 to 50 cm of the colon) can prevent 20% to 30% of new carci-

nomas<sup>6-9</sup>. The effectiveness of colonoscopy, which visualizes the whole colon, has been demonstrated in many observation studies<sup>11-13</sup>. But there is as yet no ultimate evidence of the effectiveness of colonoscopy from a large, longitudinal randomized controlled trial. Nevertheless, many gastroenterologists and patients prefer colonoscopy, as with colonoscopy adenomas and carcinomas can be detected the most reliably <sup>11</sup>.

In Switzerland, health insurance companies have covered the costs of colon cancer screening since 1 July 2013. For all persons 50 to 69 years of age, they cover either two colonoscopies 10 years apart or one FOBT every two years. In the U.S. health care system, coverage is quite a bit more generous: Health insurance companies cover the costs of up to three screening colonoscopies.

For colorectal cancer prevention, there are still a number of open questions, concerning both matters of principle and practical issues. Many of these questions cannot be answered through high-quality randomized studies: To demonstrate the effectiveness of colon cancer screening, you would have to compare patients with screening to a control group with no screening – which in view of the current state of knowledge would be ethically questionable at the least. For this reason, the questions are increasingly being studied through analyses using computer models.

Of particular interest here are microsimulations. Microsimulations are detailed models that follow the temporal course of a virtual population with a number of single, different individuals (for example, different in gender, risk for adenomas). In microsimulations for colon cancer, some virtual patients develop adenomas that can then progress to advanced adenomas and carcinomas 10,14.

Microsimulations also have to account for the variation in individual risk for adenomas and cancer and for the fact that adenomas progress only very slowly or not at all but can also be very aggressive. With so many parameters, simpler methods (for example, Markov models) reach their limits. Microsimulations, however, can incorporate this complexity of patients with differing risks, adenomas with different progressions, and other variations.

With support from the Swiss Cancer Research foundation, we developed the microsimulation model 'Colon Modeling Open Source Tool' (CMOST)<sup>14</sup>. One of the particular challenges was calibration of the model. For this, epidemiological data, such as from a cancer registry or from large studies, is utilized. Using mathematical methods, the optimal setting of the internal parameters of the model must be found in order to depict the behaviour of the cancer and its precursor stages with maximal precision. Not all parameters are known. For example, the average time from the appearance of adenoma to the appearance of carcinoma (called 'adenoma dwell time') is completely unknown. For ethical and practical reasons, this adenoma dwell time can also not be determined in observational studies. For this reason, for our microsimulation model we used three different adenoma dwell times of 8, 13, and 19 years. Practical questions can be studied using all three adenoma dwell times; the results calculated appear to be all the more relevant, the better that the predictions of all three adenoma dwell times agree.

CMOST is not the first or the only microsimulation model for colorectal cancer. In past years, epidemiologists in the United States and the Netherlands developed three microsimulation models: MISCAN, SimCRC, and CRCSpin 10. However, the program codes and exact structures of the models are not publicly available, and hence the predictions of these models cannot be independently reproduced or further developed. CMOST, however, is an open source tool; the model and program code are publicly available. This will enable any interested epidemiologists to advance the model. Further, predictions of our microsimulation were compared to the published results on MISCAN, SimCRC, and CRCSpin, and great similarities were found 14.

A first simple and practice-relevant use of our model is assessment of the benefit and cost-effectiveness of screening by colonoscopy. Based on the predictions of CMOST, three screening colonoscopies performed between the ages of 50 and 75 years can reduce the incidence of a colorectal carcinoma by 55% and mortality by as much as 60%. To prevent one colorectal cancer 135 colonoscopies are needed ('colonoscopies per case prevented'), and 26 colonoscopies are needed per one life year gained. Very similar figures were published for the MISCAN model.

In health economics discussions today, cost-efficiency analyses are becoming more and more important. For non-economists, cost-efficiency analyses often appear bizarre, as putting a price on a life year gained seems ethically questionable. Nevertheless, the calculated cost efficiencies enable comparison of various interventions (for example, colonoscopy screening versus reimbursement for extremely expensive modern cancer drugs versus public health campaigns for stopping smoking, healthy nutrition, and physical exercise). Because the financial means are limited, their use in the health care system should be well thought out and based on rational considerations.

To calculate cost efficiency, the costs of colorectal cancer screening and treatment of colorectal cancer must be estimated in the various stages. Following practice in health economics, the costs incurred or saved and the benefit (life years gained) of each intervention are discounted by 3% per year. Thus, in the first year the value of costs and benefits of a screening colonoscopy is 100%, in the second year 97%, in the third year 94%, and so on. According to these calculations then, costs or benefit of the screening (such as the first screening colonoscopy at age 50) are the full 100%; a possible benefit due to, for example, no need for treatment of a prevented colorectal carcinoma in 10 years is then adjusted to only 76%. Thus, discounting is a conservative estimation that prevents overly optimistic expectations. The disadvantage is that the results of discounted calculations are not very easily understood. Most often, interventions with costs less than 100 000 U.S. dollars per life year gained are considered cost-effective. Based on calculations using CMOST, colorectal cancer screening with three colonoscopies is cost-effective: Compared to a scenario without colon cancer screening, about 37500 (discounted) U.S. dollars must be spent to gain one (discounted) life year gained 14.

Microsimulation models can now be applied to optimize the use of colonoscopy further. For example, it is unclear whether older or very elderly patients benefit from this test: For one, colon cancer is the most frequent in this age group, but for another, the rates of complications of colonoscopy also increase in old age. In addition, the treatment options for carcinoma are limited, because many elderly patients do not tolerate chemotherapy. With the MISCAN model, various scenarios were calculated for colorectal cancer screening in old age. The results speak for a personalized approach to screening that considers individual risk for

colorectal cancer as well as comorbidities. A colonoscopy for a patient with a low risk for carcinoma (for example, a 74-year-old woman with negative results 10 years previously and no risk factors) but with existing comorbidities is not cost-effective. In contrast, a colonoscopy for a patient with a high risk (for example, an 81-year-old man with no previous colonoscopy and no comorbidities) is highly cost-effective.

There are other possible uses of microsimulation models with concrete practical problems in gastroenterology: For instance, despite preparation for the colonoscopy with laxatives, the colon is not clear of waste in approximately 10% to 20% of all patients undergoing the procedure. In this situation, many but not all adenomas can be found 15. However, repeating the colonoscopy immediately is very likely not cost-effective. The optimal interval between colonoscopies is not clear, but it can be calculated using microsimulation models. Another potential use concerns surveillance of adenomas or carcinomas. Detailed recommendations on surveillance intervals exist, but they have not been validated through randomized studies. Microsimulation models can help to find the most efficient and cost-effective surveillance strategy. Finally, there are no limits to the possible uses, and any practical question that can be described mathematically can be answered by a calculation. Clinicians and biostatisticians must of course be always aware that these are calculations in silico that always have to be validated through observational studies or, better yet, randomized studies.



PD Benjamin Misselwitz, MD
Benjamin Misselwitz studied medicine at the University of Erlangen and the University of Leipzig.
He trained in internal medicine at Münsterlingen Cantonal Hospital and University Hospital Zurich.
He interrupted his studies and clinical work twice for research stays of several years at Harvard

University and at ETH Zurich, during which, among other things, he studied the pathogenesis of Salmonella infections. Misselwitz then completed training in gastroenterology. Since 2012 he has worked as attending physician at University Hospital Zurich. His current research interests are colon cancer and inflammation mechanisms in chronic inflammatory bowel diseases.

Tel. +41 (0)44 255 85 48 benjamin.misselwitz@usz.ch

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### Selected results

Project

Ototoxicity, pulmonary outcomes and quality of life in Swiss childhood cancer survivors Institut für Sozial- und Präventivmedizin, Universität Bern, Bern CHF 364 000.- | Duration: 1.7. 2014 - 30. 6. 2017 | KLS-3412-02-2014

Project coordinator

Prof. Claudia E. Kuehni, MD | claudia.kuehni@ispm.unibe.ch

### Cancer survivors earn less than their siblings

Compared to their siblings, cancer survivors have an increased risk of not only hearing loss and other late effects of cancer and cancer treatment; on average, they also have lower incomes. This was the finding of a research study supported by the Swiss Cancer League.

Between 1976 and 2005, over 4000 children and young adults were diagnosed with cancer. Fortunately, most of them (more than 80%) survived the disease and the treatment. To find out more about the lives of survivors of childhood cancer, the Swiss Childhood Cancer Registry (SCCR) sends questionnaires to the survivors themselves and to their siblings - to enable comparisons of long-term data.

Claudia Kuehni and her colleagues at the Swiss Pediatric Oncology Group (SPOG) are interested in possible late effects of cancer or cancer treatment. One of the researchers' recent findings is that approximately 10% of childhood cancer survivors had hearing loss later in life, whereas only about 3% of siblings reported hearing loss.

The questionnaire also contained questions about the social and economic consequences of the disease. Kuehni's team thus got to know about the education and income of cancer survivors and their siblings. The fact that women on average earn less than men was found by Kuehni and her team also for cancer survivors. In addition, cancer survivors had lower incomes than siblings: Of cancer survivors, 41% reported a monthly income of less than 3000 francs per month; among healthy siblings that was the case for only 36%. More siblings than survivors reported a monthly income of 4500 to 9000 francs: 38% of siblings versus 28% of survivors.

The responses on the questionnaires do not allow conclusions to be drawn about whether the underlying reason for the difference in income is that cancer survivors choose different (and less well paid) jobs and occupations than their siblings. Or whether possible long-term effects - such as fatigue or problems to concentrate - have a negative impact on educational outcomes and consequently, on income. These are questions that should be investigated in followup studies, Kuehni and her team conclude in their report.

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# List of approved research projects in 2017

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

Total funds allocated: CHF 2 065 700.-

Berzigotti Annalisa | Effect of direct acting antiviral drugs on the occurrence and recurrence of intra- and extra-hepatic malignancies in patients with chronic hepatitis C Universitätsklinik für viszerale Chirurgie und Medizin, Inselspital Bern, Bern CHF 198 000.- | Duration: 1.6. 2017 - 31.5. 2020 | KFS-4131-02-2017

**Bohlius Julia** | Improving cervical cancer screening among HIV-positive women in Southern Africa *Institut für Sozial- und Präventivmedizin, Universität Bern, Bern* CHF 272 050.- | Duration: 3.7.2017 - 2.7.2020 | KFS-4156-02-2017

**Bucher Heiner C.** | Risk of non-AIDS defining and AIDS defining malignancies with early versus delayed initiation of antiretroviral therapy: an international multicohort study *Institut für klinische Epidemiologie und Biostatistik, Universität Basel, Basel* CHF 99 400.- | Duration: 1.7. 2017 - 31.12. 2018 | KFS-4106-02-2017

Kasenda Benjamin | Comparative effectiveness of treatments for cancer in off-label indications – contrasting evidence to reimbursement reality

Klinik für Onkologie, Universitätsspital Basel, Basel

CHF 318 000.- | Duration: 2.1.2018 – 1.1.2021 | KFS-4262-08-2017

**Katapodi Maria** | The CASCADE cohort: a family-based cohort for investigating the use and impact of genetic testing, and the development of comprehensive interventions for hereditary breast/ovarian and lynch syndromes in Switzerland

\*Institut für Pflegewissenschaft, Universität Basel, Basel

CHF 356 300.- | Duration: 1.1. 2018 - 31. 12. 2020 | KLS-4294-08-2017

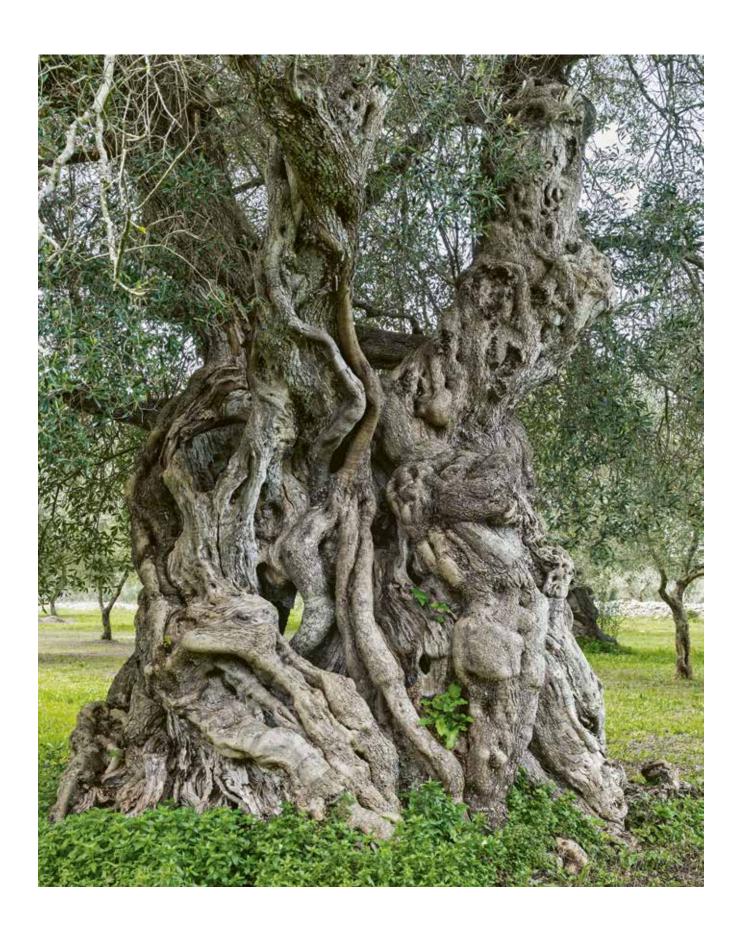
**Kuehni Claudia E.** | Pulmonary dysfunction after childhood cancer: diagnosing early stage disease *Institut für Sozial- und Präventivmedizin, Universität Bern, Bern*CHF 263 800.- | Duration: 1.9.2017 - 31.8.2020 | KFS-4157-02-2017

Rohrmann Sabine | Epidemiology of in situ breast cancer and subsequent risk of invasive breast cancer in the canton of Zurich – results from a 35-year observation period Institut für Epidemiologie, Biostatistik und Prävention, Universität Zürich, Zürich CHF 185 850.- | Duration: 1.12.2017 – 30.11.2020 | KFS-4114-02-2017

**Röösli Martin** | Prospective cohort study on skin cancer and residential radon exposure Schweizerisches Tropen- und Public Health-Institut, Basel
CHF 372 300.- | Duration: 1.9.2017 - 31.8.2021 | KFS-4116-02-2017







# Health services research using insurance data

Health services research is indisputably a necessary complement to clinical trials1. Routine data from health insurance companies are an extremely valuable data base here. Health insurance companies, as the only source of these data in the health care system, have at their disposal all information on the insurance benefits paid out to an individual patient - regardless of the sector in which the patient received care - and this also over longer time intervals. Naturally, health insurance data contain billing-relevant data and no clinical data. Since the introduction of the SwissDRG tariff system, information is available on diagnoses in inpatient care in hospitals. In outpatient care, patients' conditions can be identified based on pharmacy data - namely, the validated and established pharmacy-based cost groups (PCG)2. Billing data can also be analysed with a focus on service providers.

#### Helsana's engagement in research

The Health Sciences department at Helsana, established in 2011, is a company-internal research centre that conducts projects and analyses in the context of health services research. With this, Helsana is the only health insurance company in Switzerland to have established itself in this area. With numerous publications by the department, Helsana contributes to transparency regarding effectiveness, economic efficiency, and treatment quality in the Swiss health care system, which benefits not least also the company's own insured persons. The department's research activities are complemented by the annual publication of the Helsana Arzneimittelreport (Helsana drug report)<sup>3</sup>. In addition, Helsana health care sector reports take a look at the development of expenditure and costs in health care4 or the premium situation in Switzerland<sup>5</sup>.

The prerequisites for credibility of data generated in the insurance sector are high quality requirements regarding data preparation and data analysis, close collaboration with academic institutions, publications in peer-reviewed journals, and, of course first and foremost, adherence to scientific independence and good scientific practice<sup>6</sup>.

# Examples of previous research studies and conclusions derived from them

Polypharmacy and potentially inappropriate medication: from description to potential quality indicator

Taking five or more medications is called polypharmacy. Polypharmacy increases the risk of adverse drug reactions and hospitalizations. Potentially inappropriate medication refers to the prescribing of medications that according to interdisciplinary expert consensus often lead to adverse drug reactions in patients older than 65 years of age and therefore should be replaced by alternative substances whenever possible.

Harm caused by the prescribing of inappropriate therapies is avoidable in principle. A first descriptive study using claims data from basic policy holders insured by Helsana quantified the problem among community-dwelling persons and found polypharmacy and potentially inappropriate medication to be high in the Swiss population<sup>7</sup>. In addition, various initiatives were launched, such as the project 'assistance pharmaceutique', where pharmacists systematically assist Swiss nursing homes with medications. To emphasize the topic and to generate new ideas on how medication

quality in nursing homes can be improved, the Helsana drug report 2017 contains a special chapter on the supply of medicinal products in nursing homes. As polypharmacy and potentially inappropriate medication continue to be indicators of poor quality in the provision of medications to older persons, future studies will investigate how great the differences in these two criteria are across Switzerland.

# Adherence to guidelines with Diabetes mellitus: from patient care study to implementation of pay-for-performance

Based on recommendations by the American Diabetes Association, the Health Sciences department formulated four quality indicators for care of patients with diabetes: at least two measurements of long-term blood sugar levels (HbA1c measurements) per year; at least one lipid (cholesterol) profile per year; at least one measurement of nephropathy status per year; and one ophthalmologist visit per year. The analysis of insured persons' data revealed that only 5% of patients with diabetes were monitored by means of all four recommended measures. However, the better the adherence was to the diabetes care guidelines for a particular patient, the lower the probability that the patient would have hospitalizations in two consecutive years. If all care guidelines were followed for a specific patient, the risk of hospitalization was reduced by up to 29 %8. This was proof that it is possible to calculate patient-relevant indicators of health services quality on the basis of data from the mandatory basic insurance.

For quite some time now, the managed care scene has been calling for quality-dependent remuneration models. But up to now, no concrete suggestions for implementation could be contributed to the debate. Based on its own research activity, Helsana - as the first health insurance company to do so - developed an evidence- and data-based approach. As of 2018, Helsana has implemented this approach in the framework of managed care contracts with over 60 networks of physicians. These contractual partnerships are the basis of the primary care physician/HMO model. They regulate patient care in these models, and the contracts also determine the remuneration of the physicians' network involved, whereby the networks receive a payment per number of patients, the amount of which also depends on the percentage of patients with diabetes treated with adherence to the guidelines.

It is being shown that implementation of more performance-based remuneration models is not only possible but is also accepted by the contract partners. We will learn whether or not remuneration models of this kind can additionally also drive developments in the desired direction once we have evaluated the measure scientifically.

#### Smarter medicine: preoperative chest radiography

Preoperative chest radiography for patients with no clinical suspicion of respiratory or cardiovascular diseases is - according to the top five list in the Swiss Smarter Medicine campaign - one of the top five unnecessary tests and treatments in outpatient care. However, analysis of claims data from hospitalized patients revealed that only 9% of the insured had an ambulatory preoperative chest radiography in the two months prior to the hospitalization. There was considerable variation across the cantons, but overall there was no indication of excessive use of this preoperative chest imaging procedure in Switzerland9. Even though these lists are based on widely accepted international sources, consideration of health services data when creating or updating the lists could be helpful in identifying the most important unnecessary tests and treatments - that is, those that are the most significant in terms of quantity or costs or harm.

## Studies with insurance data in the 'Health Services Research in Oncology and Cancer Care' funding programme

#### Continuity of care in Swiss cancer patients

Continuity of care is an important quality characteristic for the care of patients with cancer. In our research project supported by the Swiss Cancer Research foundation, 'Continuity of care in Swiss cancer patients' (HSR-4083-11-2016), we are evaluating four different scores that measure the continuity of care using routine data. We want to find out to what extent these scores correlate with the use of health services and with mortality. The further development potential in patient care lies mainly in stronger networking of the various specialties and sectors. For this reason, we believe that gaining scientific knowledge and developing methods in the area of continuity of care and avoiding problems at the interface of different care providers are of central importance. Such knowledge can in principle be useful also in other contexts, such as when comparing health care models or when measuring the effects of interventions that aim at improving continuity of care.

#### Use of colorectal cancer screening

Opinions differ widely in Switzerland about the use of cancer screening programmes. Some cantons are convinced that they save lives and offer their residents screening programmes not subject to deductible. Other cantons opt not to offer them. In turn, payment by the insurance companies for the screening is regulated nationally in the Health Insurance Benefits Ordinance. In an ongoing study, we are examining how this political heterogeneity affects utilization of colon cancer screening. The study should aid better estimation of the effects of future changes in the regulations on screening.

#### Summary

For several years, both descriptive reports and analytical studies based on health insurance data have been conducted successfully. These studies support the data-based discussion on health policies. Scientific evaluation of these data makes an important contribution to the development of useful concepts for necessary structural adjustments in the health care system.

Previously, the use of health insurance data focused on the analysis of morbidity, utilization of health services, and costs. In this connection, if well-supported expertise (for example, guidelines) are taken as a yardstick, conclusions can be drawn regarding overuse, underuse, or misuse. These analyses are usually of patient-related variables, over time or by region. Other topics are the evaluation of health policy measures, the efficiency effects, and effectiveness and safety of new types of care as well as assessment of the quality of care.

Especially for studies that require indications, severity, symptoms, or clinical outcomes, routine data are of only limited value. But when these data are linked with primary data, they are important also here <sup>10</sup>.

Also when health insurance data are collected and processed for accounting purposes and thus are simply 'available', the effort required to use them in the context of health services research is not insignificant. Moreover, that effort rises steeply with the increasing degree of complexity of the desired investigations. The analyses of these data therefore require special competencies, good knowledge of pitfalls, and close collaborations.

In health service research in the insurance sector, the framework conditions for reimbursement of services through the mandatory basic health insurance must naturally be considered. For this reason, it is important for the researchers to be familiar with current health policy developments, so that the research findings can aid health policy. For instance, health services research based on insurance data can always help to estimate the effects of changes in the regulation of the health care system.



PD Eva Blozik, MD, MPH
Eva Blozik is a specialist in prevention and public health (FMH).
She worked at several institutions in the health care system (academic institutes, public authorities, health services) in Germany and Switzerland. She completed a habilitation in health services research and public health at

the University of Lübeck in Germany. She has headed Health Sciences at the Helsana Group since 2017. Tel. +41 (0)58 340 71 01 eva.blozik@helsana.ch www.helsana.ch/de/helsana-gruppe/unternehmen/gesundheitswissenschaften

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#### Selected results

Project

Patient safety issues in health information technology use in clinical cancer care: an information flow perspective

Stiftung für Patientensicherheit, Zürich

CHF 75 750.- | Duration: 1. 5. 2017 - 31. 7. 2018 | HSR-4074-11-2016

Project coordinator

Prof. David Schwappach, PhD | schwappach@patientensicherheit.ch

#### On risks and side effects of electronic patient data

Paper-based patient records in hospitals are outdated. Increasingly, complex computer systems are being used. What is the impact of this on patient safety?

There are great hopes resting on the electronic health record: Ideally, it ensures that the relevant patient data are available to the entire treatment team at all times. The information technology systems required for this, called health information technology (HIT) systems, are now in use at practically all hospitals in Switzerland. They not only manage patient data but also, if needed, can send out notices and reminder messages (such as reminders about upcoming appointments and tests). But up to now, it has not been known whether these systems represent a risk for patient safety.

In a study supported by the Swiss Cancer Research foundation, David Schwappach and his colleagues at the Swiss Patient Safety Foundation have now examined the use of HIT systems based on interview and observation methods. Schwappach's team spoke with physicians and nurses in three different oncology outpatient clinics. "Some of the interviewees criticized that the information in the HIT system is not always reliable," says Schwappach. And this makes hospital staff uncomfortable.

The interviews revealed also numerous other problems: The systems sometimes take a long time to load a patient's data. Some nurses work with printouts of a patient's electronic health records, but if they note their entries on paper, the other treatment team members know nothing about them. And there are physicians that write their reports as 'Word' documents, because the word processing functions in their HIT system are too cumbersome.

To validate the problems reported in the interviews, the researchers working with Schwappach plan to accompany a number of physicians and nurses during their daily routine and to observe their every use of the HIT system. The next step will be to bring all of these anecdotal descriptions into a systematic order and, in a few months' time, to publish the final results. However, already now the findings indicate that especially the incompatibility of various HIT systems and copy/paste functions represent a risk for patient safety. "The fundamental problem is that hospital staff must frequently adapt to the particular HIT system – instead of the other way around," says Schwappach.

# List of approved research projects in 2017

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

Total funds allocated: CHF 1392 600.-

**Auer Reto** | Changes in colorectal cancer testing rates and method for testing in Switzerland 2012-2017: evidence from claims data

Berner Institut für Hausarztmedizin, Universität Bern, Bern CHF 166 600.- | Duration: 1. 6. 2018 - 30. 11. 2019 | HSR-4366-11-2017

**De Clercq Eva** | Harnessing social media in adolescent and young adult (AYA) oncology. The views of AYA and healthcare providers: an exploratory study

Institut für Bio- und Medizinethik, Universität Basel, Basel CHF 74 750.- | Duration: 1.1. 2019 – 1.5. 2020 | HSR-4361-11-2017

De Geest Sabina M. | Towards implementation of an integrated model of care in long-term follow-up after allogeneic hematopoietic stem cell transplantation facilitated by e-Health technology in Switzerland: the SMILe project Institut für Pflegewissenschaft, Universität Basel, Basel

CHF 242 250.- | Duration: 1.7. 2018 - 30. 6. 2022 | HSR-4362-11-2017

Giger Roland | Impact of two different follow-up strategies on overall survival, oncological outcome, quality of life and economics in head and neck cancer patients after clinical complete remission – a randomized controlled prospective trial

Universitätsklinik für Hals-, Nasen- und Ohrenkrankheiten, Inselspital Bern, Bern CHF 249 900.- | Duration: 1.1.2019 - 31.12.2022 | HSR-4356-11-2017

Peytremann-Bridevaux Isabelle | The Swiss cancer patient experiences (SCAPE) study: a multicentre cross-sectional survey of patient experiences with cancer care in French-speaking Switzerland

Institut universitaire de médecine sociale et préventive, Université de Lausanne, Lausanne CHF 226 000.- | Duration: 1.5.2018 - 30.4.2020 | HSR-4354-11-2017

Scheinemann Katrin | Aftercare of childhood cancer survivors in Switzerland – the ACCS Switzerland project Onkologie/Hämatologie, Universitäts-Kinderspital beider Basel, Basel CHF 183 100. – | Duration: 1.7.2018 – 30.6.2020 | HSR-4359-11-2017

Wilhelm Matthias | Importance of exercise training therapy timing with regard to cardiotoxicity and patient preference in early breast cancer patients undergoing adjuvant chemotherapy

Universitätsklinik für Kardiologie, Inselspital Bern, Bern

CHF 250 000.- | Duration: 1.1.2019 - 31.12.2022 | HSR-4360-11-2017

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