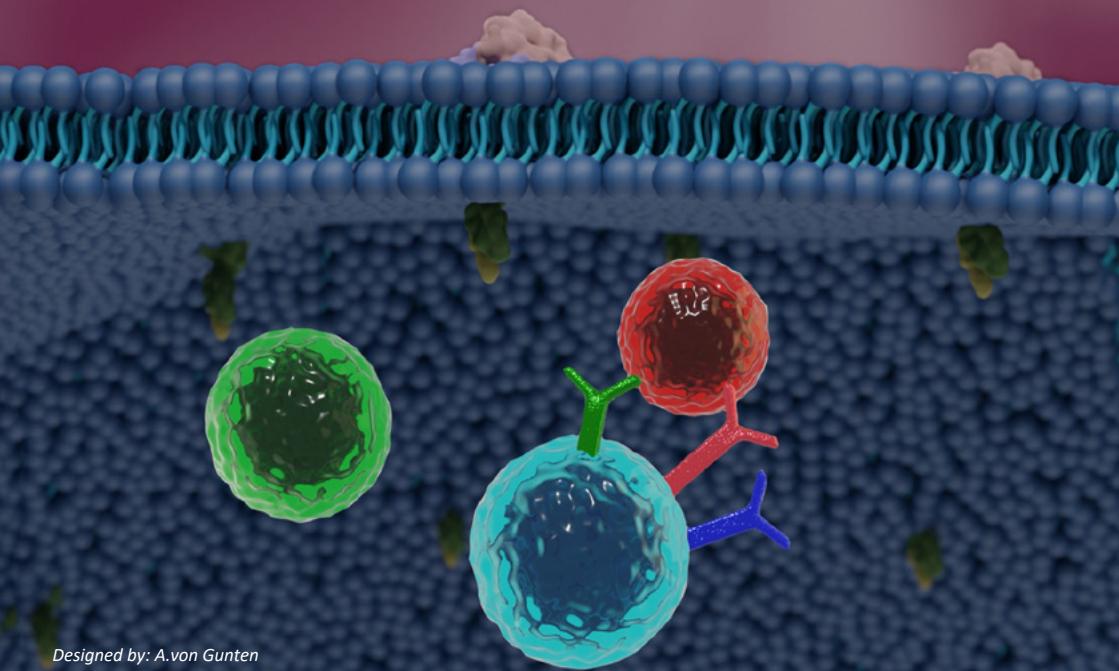


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Jahresbericht 2022



Annual Report 2022

**Institut für Pharmakologie (PKI)
der Universität Bern**

**Institute of Pharmacology
University of Bern**

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1. Introduction

1.1. Vorwort

Dies ist der zweiundzwanzigste umfassende Jahresbericht des Instituts für Pharmakologie (PKI) der Medizinischen Fakultät der Universität Bern. Auch im Jahr 2022 wurden die Arbeiten am PKI unter Einhaltung eines Schutzkonzeptes durchgeführt, ansonsten wurden alle Veranstaltungen, d.h. Seminare, Lehrveranstaltungen und Konferenzen, wieder in Präsenzform angeboten.

Nach unserem Umzug im Jahr 2015 bietet uns das INO-Gebäude des Inselspitals hervorragende Bedingungen für eine erfolgreiche Forschungstätigkeit. Mit dem Zentrum für Labormedizin teilen wir uns den Stock F und nutzen gemeinsam die vorhandene Infrastruktur. In Lehre und Forschung wurden inzwischen zahlreiche neue Projekte gestartet, mit dem Ziel die personalisierte Medizin weiterzuentwickeln. Das PKI arbeitet eng mit verschiedenen Kliniken des Inselspitals und mit anderen Forschungseinrichtungen der Universität Bern zusammen. Damit wollen wir helfen, die translationale Forschung sowie die Aus-, Weiter- und Fortbildung an der Medizinischen Fakultät zu stärken. Zum anderen sind wir an der Zusammenarbeit mit Firmen interessiert, wie die weiter hinten aufgeführten gegenwärtigen Kontakte der einzelnen Forschungsgruppen zeigen. Das PKI bietet ein breites Spektrum an Labormethoden an und kann Erfahrungen von der *biologischen Grundlagen-* bis zur *klinischen Forschung*, beides Kernaufgaben der Pharmakologie, in neue Forschungsprojekte einbringen.

Neben unserer regulären Lehrtätigkeit für Medizin-Studierende im 3. und 6. Studienjahr Medizin, sowie der Ausbildung der Zahnmediziner*innen, führen wir seit September 2019 die Pharmakologie-Ausbildung im 3. Studienjahr Pharmazie an unserer Universität durch. Zusätzlich sind einige Dozent*innen des Instituts in die Immunologieausbildung von Student*innen der Biologie (Naturwissenschaftliche Fakultät der Universität Bern) einbezogen. Weiterhin sind wir auch für die Pharmakologie-Ausbildung und M.Sc.-Kurse für Biomedizin der Universität Bern verantwortlich.

Die Dozent*innen des PKI sind außerdem innerhalb der interfakultären Graduate School for Cellular and Biomedical Sciences der Universität Bern aktiv tätig. Prof. Kaufmann, Prof. von Gunten und PD Dr. Konstantinidou sind Mitglieder einer Betreuungskommission innerhalb dieses Ausbildungsprogramms für Doktorierende. Dazu kommen zusätzliche Bildungsangebote in Form von Seminaren (Current Topics in Pharmacology and Theranostics; gemeinsam organisiert mit dem Zentrum für Labormedizin) und einer Summer

School, die durch Prof. von Gunten und Prof. Kaufmann organisiert wurden. Diese Bildungsangebote werden weitgehend aus eigenen finanziellen Mitteln und Sponsorengeldern bestritten.

Am Institut arbeiten gegenwärtig 19 Doktorand*innen. 3 Doktorand*innen (PhD) haben im Berichtsjahr 2022 ihre Promotion erfolgreich abgeschlossen.

Die Mitarbeiter*innen der Experimentellen und Klinischen Pharmakologie publizierten im Jahr 2022 insgesamt 39 Originalarbeiten sowie 15 Übersichtsartikel und 3 Fallberichte in internationalen Fachzeitschriften. Mehrere Mitarbeiter*innen des PKI wurden mit Forschungspreisen ausgezeichnet.

7 Mitarbeiter*innen der Experimentellen und Klinischen Pharmakologie wurden mit namhaften Beiträgen des Schweizerischen Nationalfonds unterstützt.

Diese Aufzählung belegt den hohen Stellenwert, den die Lehre und Forschung an unserem Institut besitzt.

Wir danken allen Mitarbeiter*innen für ihren Einsatz, welcher auch im Jahr 2022 zu einer Bilanz beitrug, die internationalen Massstäben gerecht wird. Ebenso danken wir allen Sponsor*innen, Kollaborationspartner*innen und Freund*innen des Instituts.



Prof. Dr. Andrea Huwiler
Direktorin

Bern, Februar 2023

1.2. Foreword

This is the twenty-second comprehensive annual report of the Institute of Pharmacology (PKI) of the Medical Faculty of the University of Bern. In 2022, work at the PKI was again carried out in compliance with a protection concept; otherwise, all events, i.e. seminars, courses and conferences, were again offered in attendance form.

After our move in 2015, the INO building of the Inselspital offers us excellent conditions for successful research activities. We share the floor F with the Centre for Laboratory Medicine and jointly use the existing infrastructure. Numerous new projects have been launched in teaching and research with the aim of further developing personalised medicine. The PKI collaborates with various clinics at Inselspital and with other research institutions at the University of Bern. In this way, we help to strengthen translational research as well as education, training and continuing education at the Faculty of Medicine. We are also collaborating with companies and offer a broad spectrum of laboratory methods and contribute expertise in basic biological assays and approaches for clinical research which are important for developing new research projects.

In addition to our regular teaching activities for medical students in the 3rd and 6th year of medicine, as well as the training of dentists, we have been conducting pharmacology training in the 3rd year of pharmacy at our university since September 2019. In addition, we are involved in the immunology training of biology students (Faculty of Natural Sciences of the University of Bern) and in the pharmacology training of biomedical science students at the University of Bern.

The PKI lecturers are also actively involved in the interfaculty Graduate School for Cellular and Biomedical Sciences at the University of Bern. Prof. Kaufmann, Prof. von Gunten and PD Dr. Konstantinidou are members of a supervisory committee within this training programme for doctoral students. In addition, there are additional educational offers in the form of seminars (Current Topics in Pharmacology and Theranostics; jointly organised with the Centre for Laboratory Medicine) and a Summer School organised by Profs von Gunten and Kaufmann. These educational programs are largely financed by the Institute's own financial resources and sponsorships.

The Institute currently employs 19 doctoral students. 3 doctoral students (PhD) successfully completed their doctorates in the reporting year 2022.

In 2022, the staff of the Experimental and Clinical Pharmacology published a total of 39 original papers, 15 review articles, and 3 case reports in international journals. Several PKI staff members were awarded research prizes. 7 Staff members of the Experimental and Clinical

Pharmacology were supported with considerable contributions from the Swiss National Science Foundation.

This list demonstrates the high value placed on teaching and research at our institute.

We would like to thank all our staff for their commitment, which also contributed to a balance sheet in 2022 that meets international standards. We would also like to thank all sponsors, collaborators and friends of the Institute.



Prof. Dr. Andrea Huwiler

Bern, February 2023

2. Staff 2022

Director

Prof. Dr. Huwiler, Andrea PhD (ad interim)

Deputy Director

Prof. Dr. Simon, Hans-Uwe MD, PhD, Dr. h.c. mult.

Principal Investigators

Prof. Dr.	Huwiler, Andrea	PhD
Prof. Dr.	Kaufmann, Thomas	PhD
SNF Prof.	Konstantinidou, Georgia	PhD* (until July 2022)
PD Dr.	Konstantinidou, Georgia	PhD (since Aug 2022)
Prof. Dr.	Simon, Hans-Uwe	MD, PhD, Dr. h.c
Prof. Dr.	von Gunten, Stephan	MD, PhD, MBA, MME
Prof. Dr.	Yousefi, Shida	PhD

Scientific Staff

Dr.	Bachmann, Daniel	Lab Technician
	Birkenfeld, Lena	Guest student (until Nov 2022)
	Boros-Majewska, Joanna	Lab Technician
	Chanwangpong, Apinya	M.Sc. student (until Jan 2022)
	Chen, Yihe	PhD student*
	Christen, Mira	Lab Technician*
	D'Agostino, Jessica	PhD student (since Oct 2022)
	Datismann, Sarah	B.Sc. student (until Oct 2022)
	Dutoit, Danielle	M.Sc. student (until June 2022)
	Falco, Simone	PhD student*
	Fettrelet, Timothée	PhD student
	Frei, Jöel	Assistant (until Aug 2022)
	Garczyk, Maciej	PhD student (since Nov 2022)
	Gigon, Lea	PhD student
	Glodjajic, Ella	M.Sc. student (since Oct 2022)
	Graber, Michelle	B.Sc. student (until May 2022)
	Gräub, Isabel	M.Sc. student (until Apr 2022)
	Hafizi, Redona	PhD student (until June 2022)
Dr.	He, Zhaoyue	Postdoctoral fellow
	Hevia Hernandez, Giselle	PhD student*
	Hosseini, Aref	PhD student
	Hugonnet Marjolaine, Claire	PhD student
	Jankovic, Jovana	M.Sc. student (until Aug 2022)
	Jazaeri, Ali	PhD student
	JeanRichard, Philippe	PhD student
	Khidr, Shaimaa	PhD student (since Nov 2022)
	Kozlowski, Evelyne	Lab Technician
	Kurbangaleeva, Sirina	Guest student (until Dec 2022)
	Lakomy Rebecca	M.Sc. student (until Feb 2022)
	Leroux, Cédric	PhD student (until Feb 2022)
	Manaila, Roxana	PhD student (since Feb 2022)

Dr.	Markov, Nikita Markov, Nikita Miholic, Marta Mürner, Lukas Nasser, Riim Oberson, Kevin Peng, Shuang Pozzato, Chiara Roos, Nadine	PhD student (until Apr 2022) Postdoctoral fellow (since May 2022) M.Sc. student (until July 2022) PhD student* Lab Technician Lab Technician PhD student* (until May 2022) PhD student* (until Oct 2022) B.Sc. student (until May 2022)
Dr.	Saliakoura, Maria Sharapova, Gulnaz	Postdoctoral fellow* (until Aug 2022) Gueststudent (until Dec 2022)
Dr.	Stepanovska Tanturovska, Bisera	Postdoctoral fellow
Dr.	Stojkov, Darko Toledo, Darien Verschoor, Daniëlle von Gunten, Aldona Wilhelm, Lea Wu, Liyang	Postdoctoral fellow PhD student PhD student (until Aug 2022) Technical Specialist M.Sc. student (until July 2022) PhD student* (since Dec 2022)

*at least partially paid from external sources, often research grants

Principal Investigators – Clinical Pharmacology

Prof. Dr.	Haschke, Manuel	MD
PD Dr.	Liakoni, Evangelia	MD
PD Dr.	Hammann, Felix	MD, PhD

Scientific Staff – Clinical Pharmacology

Dr.	van der Velpen, Vera Hirt, Mats	PhD, Scientist and Lead LC-MS lab Lab technician
Dr.	Schöning Verena	PhD, Postdoctoral fellow
PD Dr.	Weiler, Stefan	MD
Dr.	Bekka, Elias	MD, Study physician by CPT specialty trainee
Dr.	Hermann, Laura Kern, Charlotte Christen, Samuel	MD, Study physician by CPT specialty trainee PhD student PhD student
	Pahud de Mortanges, Aurélie	PhD student

External University Teachers

Dr.	Bürgi, Sibylle	PhD
PD Dr.	Cachelin, Armand	MD, PhD

Guest Scientists

Prof. Dr.	Simon, Dagmar	MD, Dept. Dermatology, Inselspital, Univ. Bern
Prof. Dr.	Spirk, David	MD, MMD, Sanofi-Aventis AG

Office

Joray, Celine	Secretary,
Opitz, Krystyna	Secretary, (since Feb 2022)
Scherrer, Debora	Secretary, (until Apr 2022)
Sutovska, Vanda	Secretary, (since Aug 2022)
Wettstein, Valentina	Secretary, (until June 2022)
Conforti, Isa	Workshop / House Keeping

Meeting of the Swiss Society of Pharmacology and Toxicology (SSPT)

Progress in Pharmacology-
Pharmacotherapies of pain and
pharmacology of cannabinoids.
Bern, January 25th, 2022

Summer School

Members of the Institute of Pharmacology of the University of Bern together with participants of our International Summer School in Bönigen; August 21 - 23th, 2022

3. Teaching Activities

3.1. Lectures

Lectures for Medical Students: Pharmacology

Date	Lecturer	Titel of the lecture
Mar 08, 2022	Prof. Stephan von Gunten	Hormone aus pharmakol. Sicht 1 (1h)
Mar 08, 2022	Prof. Stephan von Gunten	Hormone aus pharmakol. Sicht 2 (1h)
Mar 14, 2022	Prof. Stephan von Gunten	Antidiabetika (1h)
Mar 14, 2022	Prof. Stephan von Gunten	Lipide, Urikostatika (1h)
Mar 21, 2022	Prof. Andrea Huwiler	Anti- Parkinson, Antidementiva (1h)
Mar 22, 2022	Prof. Andrea Huwiler	Lokalanästhetika (1h)
Apr 04, 2022	Prof. Andrea Huwiler	Antiepileptika (1h)
Apr 05, 2022	Prof. Andrea Huwiler	Allgemeinanästhetika (1h)
Apr 11, 2022	Prof. Andrea Huwiler	Psychopharmakologie (1h)
Apr 12, 2022	Prof. Andrea Huwiler	Anxiolytika und Hypnotika (1h)
Apr 12, 2022	Prof. Andrea Huwiler	Antipsychotika (1h)
Apr 25, 2022	Prof. Andrea Huwiler	Antidepressiva (1h)
May 09, 2022	Prof. Thomas Kaufmann	Immunmodulation (1h)
Sep 26, 2022	Prof. Hans-Uwe Simon	Pharmakodynamik 1 (1h)
Sep 26, 2022	Prof. Hans-Uwe Simon	Pharmakodynamik 2 (1h)
Oct 04, 2022	Prof. Hans-Uwe Simon	Entzündungshemmung TB1 (1h)
Oct 04, 2022	Prof. Hans-Uwe Simon	Toxikologie TB1 (1h)
Oct 10, 2022	Prof. Hans-Uwe Simon	Pharmakotherapie bei Lungenerkrankungen (1h)
Oct 25, 2022	Prof. David Spirk	Pharmakologie der Hämostase (1h)
Nov 01, 2022	Prof. Thomas Kaufmann	Pharmakologie des vegetativen Nervensystems (1h)
Nov 08, 2022	Prof. Stephan von Gunten	Antihypertensiva (1h)
Nov 08, 2022	Prof. Stephan von Gunten	Antiarrhythmika (1h)
Nov 08, 2022	Prof. David Spirk	Behandlung der Angina pectoris und Herzinsuffizienz (1h)
Dec 12, 2022	Prof. Stephan von Gunten	Diuretika 1 (1h)
Dec 12, 2022	Prof. Stephan von Gunten	Diuretika 2 (1h)

All lecturers additionally participated in the “Wochensynthese” and “Blocksynthese”.

All lectures were recorded as a podcast.

Lectures for Medical Students: Cell Biology

Date	Lecturer	Titel of the lecture
Sep 29, 2022	Prof. Thomas Kaufmann	Entwicklung des Lebens (2h)
Oct 17, 2022	Prof. Thomas Kaufmann	Zellstoffwechsel (1h)
Nov 03, 2022	Prof. Thomas Kaufmann	Zelltod 2 (1h)

Special seminars for Medical Students: Grundprinzipien lebender Systeme / Zellen und Organismen

Date	Lecturer	Titel of the lecture
Mar 13, 2022	Prof. Stephan von Gunten	Immunpharmakologie PHA1 (2h)
Mar 14, 2022	Prof. Thomas Kaufmann	Modulation des Zelltodes - aktueller Stand und neue Entwicklungen (2h)
Mar 21, 2022	PD Dr. Georgia Konstantinidou	Tumorpharmakologie (2h)
Mar 26, 2022	Prof. Manuel Haschke	Personalisierte Arzneimitteltherapie (2h)

Lectures for Dental Medicine Students: Pharmacology (Coordinator: Prof. Thomas Kaufmann)

Date	Lecturer	Title of the lecture
Feb 07, 2022	Prof. Hans-Uwe Simon	Rezeptoren, Dosis-Wirkungskurven Antagonisten, Applikationsarten
Feb 16, 2022	Prof. Thomas Kaufmann	Vegetatives Nervensystem
Feb 23, 2022	Prof. Thomas Kaufmann	Interaktionen & Pharmakogenetik
Mar 07, 2022	Prof. David Spirk	Herz-Kreislauf Medikamente Antithrombotika
Mar 09, 2022	Prof. Andrea Huwiler	Pharmakologie der Atemwege
Mar 21, 2022	Prof. Stephan von Gunten	Pharmakologie des Knochens
Mar 23, 2022	Prof. Stephan von Gunten	Magensaurehemmung
Mar 30, 2022	Prof. Andrea Huwiler	Narkose, Beruhigungsmittel
Apr 04, 2022	PD Dr. Armand Cachelin	Analgetika
Apr 13, 2022	Dr. Sibylle Bürgi	Antidiabetika
Apr 27, 2022	Dr. Sibylle Bürgi	Lokalanästhetika
May 02, 2022	Dr. Sibylle Bürgi	Antibiotika

Oral examinations: Prof. Huwiler, Prof. von Gunten,
Prof. Simon, Prof. Kaufmann, Prof. Spirk

Lectures for Pharmacy Students: Pharmacology (Coordinators: Prof. Hans-Uwe Simon, Prof. Manuel Haschke)

Mar 04, 2022	Prof. Andrea Huwiler	Depressionen (2h)
Mar 10, 2022	Prof. Andrea Huwiler	Schlaf- und Angststörungen (2h)
Mar 11, 2022	Prof. Andrea Huwiler	Psychostimulanten, Antipsychotika und Stimmungsstabilisatoren (2h)
Mar 17, 2022	Prof. Andrea Huwiler	Demenz (2h)
Mar 18, 2022	Prof. Andrea Huwiler	Nozizeption, Allgemein- und Lokal-Anästhesie (2h)
Apr 01, 2022	Prof. Stephan von Gunten	Knochenkrankheiten, Osteoporose, Gicht (2h)
Apr 07, 2022	Prof. Stephan von Gunten	Knochenkrankheiten, Osteoporose, Gicht (2h)
Apr 08, 2022	Prof. Stephan von Gunten	Gelenkkrankheiten, Arthrose, Arthritis (2h)
May 12, 2022	Prof. Andrea Huwiler	Epilepsie (2h)
May 13, 2022	Prof. Andrea Huwiler	Parkinson (2h)
May 19, 2022	PD Dr. Georgia Konstantinidou	Prostataerkrankungen (2h)
May 20, 2022	Prof. Thomas Kaufmann	Krankheiten des Immunsystems, Transplantation (2h)
May 27, 2022	Prof. Thomas Kaufmann	Krankheiten des Immunsystems, Transplantation (2h)
Jun 02, 2022	PD Dr. Georgia Konstantinidou	Tumormunologie (2h)
Sep 19, 2022	Prof. Hans-Uwe Simon	Grundlagen/ Pharmakodynamik (3h)
Sep 19, 2022	Prof. Hans-Uwe Simon	Arzneimittelallergien (1h)
Sep 27, 2022	Prof. Hans-Uwe Simon	Experimentelle Toxikologie (2h)
Nov 17, 2022	Prof. Stephan von Gunten	Säureassoziierte KH / Erbrechen (2h)
Nov 22, 2022	Prof. Stephan von Gunten	Motilitätsstörungen / Entzündliche Darmerkrankungen (2h)
Nov 29, 2022	PD Dr. Georgia Konstantinidou	Tumor Innerer Organe, part 1 (2h)
Dec 01, 2022	PD Dr. Georgia Konstantinidou	Tumor Innerer Organe, part 2 (2h)
Dec 06, 2022	PD Dr. Georgia Konstantinidou	Tumormunologie (2h)
Dec 08, 2022	Prof. Thomas Kaufmann	Krankheiten des Immunsystems, Transplantation (2h)
Dec 13, 2022	Prof. Thomas Kaufmann	Krankheiten des Immunsystems, Transplantation (2h)
Dec 15, 2022	Prof. Thomas Kaufmann	Anämien (2h)
Dec 20, 2022	Prof. Thomas Kaufmann	Leukämien (2h)
Dec 22, 2022	Prof. Thomas Kaufmann	Lymphome (2h)

Written examinations: Prof. Huwiler, Prof. von Gunten,
Prof. Simon, Prof. Kaufmann

**Lectures for Natural Sciences Faculty and Biomedical Sciences students:
Clinical Immunology (Coordinator: Prof. Stephan von Gunten)**

Date	Lecturer	Title of the lecture
Feb 24, 2022	Prof. Stephan von Gunten	Introduction to Clinical Immunology (1h)
Feb 24, 2022	Prof. Stephan von Gunten	Glycoimmunology (1h)
Apr 28, 2022	PD Dr. Georgia Konstantinidou	Immunopharmacology (1h)

Written examination and oral tests: Prof. Stephan von Gunten

Lecture for Natural Sciences Faculty: Cellular and Molecular Immunology (Coordinator: Prof. Christoph Müller)

Date	Lecturer	Title of the lecture
Sep 22, 2022	Prof. Thomas Kaufmann	Cell death in the immune system

Lectures for Biomedical Sciences students (M.Sc. program, Bern) and Natural Sciences Faculty: Molecular Biology of Inflammation (Coordinator: Prof. Britta Engelhardt)

Date	Lecturer	Title of the lecture
Apr 07, 2022	PD Dr. Georgia Konstantinidou	Lipid mediators in inflammation (2h)
May 12, 2022	Dr. Darko Stojkov	Inflammation - good or bad?
		Resolution of inflammation – apoptosis (2h)

**Practical work for Natural Science Faculty: Immunology II
(Coordinator: Prof. Andreas Marti)**

This 6-day practical course organized by the Faculty of Natural Sciences was supported by the groups of Prof. von Gunten and Prof. Kaufmann.

**Lectures for Biomedical Sciences Students (M.Sc. program, Bern) and Graduate School for Cellular and Biomedical Sciences:
Pharmacology of Major Organ Systems (Coordinator: Prof. Thomas Kaufmann)**

Date	Lecturer	Title of the lecture
Sep 23, 2022	Prof. Stephan von Gunten	Gastrointestinal tract (2h)
Sep 23, 2022	Prof. David Spirk	Haemopoietic system and haemostasis (2h)

Oct 07, 2022	Prof. Stephan von Gunten	Heart and vascular system (2h)
Oct 14, 2022	Prof. Stephan von Gunten	Endocrine and reproductive system (2h)
Oct 21, 2022	PD Dr. Georgia Konstantinidou	Immune system (2h)
Oct 28, 2022	Dr. Darko Stojkov	Antiiinfectious therapy (2h)
Nov 04, 2022	Dr. Darko Stojkov	Lungs and kidneys (2h)
Nov 11, 2022	Dr. Bisera Stepanovska	Nervous system (2h)

Lectures for Biomedical Sciences students (M.Sc. Program, Fribourg): Ethics

Date	Lecturer	Title of the lecture
Nov 16, 2022	Prof. Stephan von Gunten	Ethics and its governance in the 21 st century (2h)

Lecture for Biomedical Sciences Students (M.Sc. program, Bern) and Graduate School for Cellular and Biomedical Sciences: Topics in Tumor Biology (Coordinator: Prof. Deborah Stroka)

Date	Lecturer	Title of the lecture
Feb 02, 2022	PD Dr. Georgia Konstantinidou	Oncogenes – how to target them (1h)

Lecture for Natural Sciences Faculty and Biomedical Sciences students (M.Sc. program, Cell Biology, Bern) and Graduate School for Cellular and Biomedical Sciences: General Pathology & Histology (Coordinator: Prof. Dr. Philippe Krebs)

Date	Lecturer	Title of the lecture
Oct 11, 2022	Prof. Thomas Kaufmann	Cell damage (1h)

Lecture for Biomedical Sciences students (M.Sc. program, Bern): Cutting Edge Laser Scanning Microscopy (Coordinator: Prof. Britta Engelhardt)

Date	Lecturer	Title of the lecture
Oct 28, 2022	Prof. Shida Yousefi	Laser scanning microscopy and specific applications (FRET, FRAP, spectral unmixing) and digital image restoration (Huygen and Imaris software)

Cell Biology tutorial “Happy Cell” 2022 (5.0 ECTS), CTS/KSL 7606”

Date	Lecturer	Title of the lecture
Oct 19, 2022	Prof. Thomas Kaufmann	Chapter 15 (Cell signaling) (2h)
Jan 12, 2022	Prof. Shida Yousefi	Chapters 20 (Cancer), and Chapter 22 (Stem cells and Tissue Renewal) (2h)

Lectures for Medical Students: Clinical Pharmacology

Date	Lecturer	Title of the lecture
Feb 07, 2022	Prof. Manuel Haschke	Pharmakologie GIT
Feb 09, 2022	Prof. Manuel Haschke	Säuresekretion
Feb 15, 2022	PD Felix Hammann	Pharmakokinetik 3&4 (2 Lekt.)
Mar 08, 2022	PD Evangelia Liakoni	Analgetika
Mar 10, 2022	PD Evangelia Liakoni	Antikoagulantien & Thrombozytenhemmer
Mar 10, 2022	PD Stefan Weiler	Notfall-Medikamente
Mar 28, 2022	PD Stefan Weiler	Arterielle Hypertonie u. Herzinsuffizienz
Mar 28, 2022	PD Stefan Weiler	Diabetes u. Dyslipidämie
Mar 28, 2022	Prof. Manuel Haschke	Antibiotika
Apr 26, 2022	Prof. Manuel Haschke	Schmerzmittel 1&2 (2 Lekt.)
Sep 22, 2022	Prof. Manuel Haschke	Pharmakokinetik 1&2 (2 Lekt.)
Sep 26, 2022	PD Felix Hammann	Wochensynthese
Oct 10, 2022	PD Evangelia Liakoni	Interaktionen
Oct 10, 2022	PD Evangelia Liakoni	Unerwünschte Wirkungen

Online Lectures for Dental Medicine Students: Clinical Pharmacology

Date	Lecturer	Title of the lecture
Feb 21, 2022	PD Stefan Weiler	Einführung in die Pharmakokinetik
Mar 21, 2022	Prof. Manuel Haschke	Personalisierte Medizin
Oct 26, 2022	PD Felix Hammann	Pat. mit akuten med. Problemen
Nov 02, 2022	Dr. Elias Bekka	Antikoagulation
Nov 09, 2022	PD Felix Hammann	Pat. mit chronischen med. Problem
Nov 16, 2022	Prof. Manuel Haschke	Antibiotika1
Nov 23, 2022	Prof. Manuel Haschke	Antibiotika 2
Nov 30, 2022	Dr. Laura Hermann	UAW im Mund
Dec 07, 2022	PD Evangelia Liakoni	Analgetika 1
Dec 14, 2022	PD Evangelia Liakoni	Analgetika 2

Lectures for Pharmacy Students (Bachelor): Clinical Pharmacology

Date	Lecturer	Titel of the lecture
Feb 22, 2022	PD Felix Hammann	Biopharmazie
Feb 24, 2022	PD Evangelia Liakoni	Asthma, COPD, Pneumonien
Feb 25, 2022	PD Evangelia Liakoni	Asthma, COPD, Pneumonien
Mar 01, 2022	PD Evangelia Liakoni	Biopharmazie
Mar 08, 2022	Prof. Manuel Haschke	Biopharmazie
Mar 15, 2022	Dr. Verena Schöning	Biopharmazie
Mar 18, 2022	PD Felix Hammann	Einführung Pharmazeutische Wissenschaft
Mar 22, 2022	PD Felix Hammann	Biopharmazie
Mar 24, 2022	Prof. Manuel Haschke	Opioidanalgetika
Mar 25, 2022	PD Evangelia Liakoni	Nicht-opioid Analgetika
Mar 29, 2022	PD Felix Hammann	Biopharmazie
Mar 31, 2022	PD Evangelia Liakoni	Schmerz, neuropathisch
Mar 31, 2022	Prof. Manuel Haschke	Kopfschmerzen, Migräne
Apr 05, 2022	PD Felix Hammann	Biopharmazie
Apr 12, 2022	Dr. Vera van der Velpen	Biopharmazie
Apr 14, 2022	Prof. Stephan Krähenbühl	Schilddrüsenkrankheiten
Apr 26, 2022	PD Felix Hammann	Biopharmazie
Apr 28, 2022	Prof. Manuel Haschke	Hypophysäre Störungen
Apr 29, 2022	PD Evangelia Liakoni	Dyslipidämie
May 03, 2022	PD Felix Hammann	Biopharmazie
May 05, 2022	PD Stefan Weiler	Diabetes
May 10, 2022	Prof. Carlo Largiadèr	Biopharmazie
May 17, 2022	Prof. Carlo Largiadèr	Biopharmazie
May 19, 2022	PD Stefan Weiler	Polypharmazie
May 24, 2022	Prof. Manuel Haschke	Biopharmazie
June 03, 2022	Prof. Stephan Krähenbühl	Geschlechtshormone, Kontrazeptiva
Sep 29, 2022	PD Stefan Weiler	Pharmakokinetik I & II
Oct 04, 2022	PD Stefan Weiler	Pharmakokinetik III
Oct 13, 2022	Sarah Banholzer	Arzneimittelsicherheit/unerwünschte Ereignisse/ Pharmakovigilanz
Oct 18, 2022	Prof. Stephan Krähenbühl	Venöse KH
Oct 20, 2022	Prof. Stephan Krähenbühl	Arterielle KH
Oct 25, 2022	PD Felix Hammann	Hypertonie
Oct 27, 2022	PD Felix Hammann	Herzinsuffizienz, Rhythmusstörungen
Nov 01, 2022	Prof. Manuel Haschke	Bakterielle Infektionen I & II
Nov 03, 2022	Prof. Manuel Haschke	Bakterielle Infektionen III & IV
Nov 08, 2022	PD Stefan Weiler	Virale und retrovirale KH
Nov 10, 2022	PD Stefan Weiler	Pilzerkrankungen Mycobacterielle KH
Nov 15, 2022	PD Stefan Weiler	Parasiten / Malaria

Lectures for Pharmacy Students (Master): Clinical Pharmacology

Date	Lecturer	Titel of the lecture
Mar 24, 2022	PD Stefan Weiler	Antibiotika - Auswahl (Interaktionen), (Resistenzen), UAWs
Apr 07, 2022	PD Stefan Weiler	Antikoagulantien – Bridging
May 12, 2022	PD Stefan Weiler	Geriatrie / Niereninsuffizienz
May 12, 2022	PD Evangelia Liakoni	Beurteilung von Labor-Parametern (TDM)
Sep 29, 2022	PD Stefan Weiler	Antibiotika-Auswahl
Oct 18, 2022	Sarah Banholzer	Unerwünschte Wirkungen, Interaktionen, Safety, Pharmakovigilanz II

Master of Advanced Studies in Orthodontics and Dentofacial Orthopedics, University of Bern (MAS ORTHO Unibe)

Date	Lecturer	Titel of the lecture
Feb 23, 2022	Prof. Stephan von Gunten	Pharmacology (2h)
Apr 6, 2022	Prof. Stephan von Gunten	Pharmacology (2h)

3.2. Coordination PBL Medical Students 3rd year (2022/2023)

Core group member:

Prof. Andrea Huwiler

Representatives of Pharmacology for teaching blocks:

Prof. Hans-Uwe Simon (blocks I and II)

Prof. Thomas Kaufmann (blocks III and X)

Prof. Stephan von Gunten (block IV and VIII)

Prof. Andrea Huwiler (blocks VII and IX)

3.3. Tutorials (study year 2022/2023)

For Medical Students 3rd year:

PD Dr. Georgia Konstantinidou

Dr. Zhaoyue He

Dr. Bisera Stepanovska Tanturovska

Philippe Jean-Richard

Prof. Thomas Kaufmann

Marjolaine Claire Hugonnet

Dr. Darko Stojkov

Roxana Manaila

For PhD students,***Graduate School for Cellular and Biomedical Sciences, course “Happy Cell”:***

Prof. Shida Yousefi

Prof. Thomas Kaufmann

Graduate School for Cellular and Biomedical Sciences, Training course on “Concepts and Methods in Programmed Cell Death and Autophagy”

Prof. Thomas Kaufmann

3.4. Seminars of Invited Speakers

Date	Teacher	Title of the seminar	Host
Jan 19, 2022	Prof. Dr. Sebastian Leidel, Department of Chemistry, Biochemistry and Pharmaceutical Sciences, University of Bern	RNA modifications and disease: Cause or cure?	A. Huwiler
Apr 13, 2022	Dr. Michaela Medova, Department for BioMedical Research, University of Bern	METworks - at the interface between radioresistance and behavior	G. Konstantinidou
July 6, 2022	Priv. Doz. Dr. Gabriele Weitz-Schmidt, AlloCyte Pharmaceuticals AG, Basel	Integrin targeting pharmacology – The mechanism of action matter	A. Huwiler
Sep 21, 2022	Prof. Dr. Britta Maurer, Universitätsklinik für Rheumatologie und Immunologie, Inselspital, Bern	Predictive potential of the integration of multi-source molecular data and imaging-based radiomic data in (experimental) fibrosing ILD	S. von Gunten
Oct 12, 2022	Prof. Dr. Wolfgang Eberhardt, Pharmazentrum Frankfurt/ZAFES, Goethe University Frankfurt am Main	Multifaceted roles of the E3 Ligase TRIM25 in colorectal cancer	A. Huwiler
Dec 19, 2022	Dr. Anna Brichkina, Center for Tumor Biology and Immunology, Philipps University of Marburg, Germany	Targeting the tumor stroma: new concepts and potential approaches	H.-U. Simon

Academic Degrees

Markov Nikita, PhD, University of Bern

Thesis: "The functional and metabolic consequences of mitochondrial dysfunction in macrophages" (April 2022)
 Supervisor: Prof. Hans-Uwe Simon

Pozzato Chiara, PhD, University of Bern

Thesis: "The role of focal adhesion kinase in lung cancer progression" (May 2022)
 Supervisor: PD Dr. Georgia Konstantinidou

Redona Hafizi, PhD, University of Bern

Thesis: "The role of Sphingosine-1-phosphate on fibrotic processes and erythropoietin production in renal cells" (June 2022)
 Supervisor: Prof. Andrea Huwiler

Wenger Nicolas, MD, University of Bern

Thesis: "Differences in duration of anticoagulation after pulmonary embolism and deep vein thrombosis: Findings from the SWISS Venous ThromboEmbolism Registry (SWIVTER)" (December 2022)
 Supervisor: Prof. David Spirk

Chanwangpong Apinya, M.Sc., University of Basel

Thesis: "Eosinophil biomarkers in eosinophilic diseases" (Jan 2022)
 Supervisor: Prof. Dagmar Simon, Prof. Hans-Uwe Simon

Dutoit Danielle, M.Sc., University of Basel

Thesis: "Novel Players in the Pathogenesis of Atopic Dermatitis" (June 2022)
 Supervisor: Prof. Dagmar Simon, Prof. Hans-Uwe Simon

Fleisch Silvan Christian, M.Sc. med., University of Bern

Thesis: "Siglec Ligands in Tumor- NK cell interaction and fatty acid metabolism"
 (July 2022)
 Supervisor: Prof. Stephan von Gunten

Jankovic Jovana, M.Sc., University of Bern

Thesis: "Characterization of Siglec-7 expression on CD8⁺ T cells" (Aug 2022)
 Supervisor: Prof. Stephan von Gunten

Lakomy Rebecca, M.Sc., Pharm, University of Basel

Thesis: "The role of intracellular sphingosine 1-phosphate in the pathogenesis of chronic kidney disease by using the cellular model of renal fibroblasts."
 (Jan 2022)
 Supervisor: Prof. Andrea Huwiler, Dr. Bisera Stepanovska-Tanturovska

Miholic Marta, M.Sc., University of Ljubljana

Thesis: "Novel pharmacological approaches to block neutrophil extracellular trap formation" (July 2022)
Supervisor: Prof. Hans-Uwe Simon

Wilhelm Lea, M.Sc.pharm., University of Bern

Thesis: "Development of a novel functional mast cell assay to diagnose allergies" (Aug 2022)
Supervisor: Prof. Thomas Kaufmann

Graber Michelle Lorraine, B.Sc., University of Bern

Thesis: "Expression of PILR α ligands and PILR β ligands on human myelogenous leukaemia cancer cells" (May 2022)
Supervisor: Prof. Stephan von Gunten

Roos Nadine, B.Sc., University of Bern

Thesis: "Evaluation of the interaction between Neu5GcGM3 and Siglec 7/9" (June 2022)
Supervisor: Prof. Stephan von Gunten

4. Research Activities

4.1. Research Projects and Publications

Group Prof. Andrea Huwiler



Photo: Group Huwiler

Group members:

- Riim Nasser, Lab Technician
- Dr. Bisera Stepanovska Tanturovska, postdoctoral fellow
- Redona Hafizi, PhD student (until June 2022)
- Roxana Manaila, PhD student (since Feb 2022)
- Jessica D'Agostino, PhD student (since Oct 2022)
- Shaimaa Khidr, PhD student (since Nov 2022)
- Lakomy Rebecca, M.Sc. pharm. student (until Feb 2022)
- Helen Broughton, MD student
- Datismann Sarah, B.Sc. student (Oct 2022)

Our research is focused on sphingolipids and their contribution to physiological and pathophysiological processes and how they regulate diseases such as cancer, inflammation and fibrosis. A special focus we have put on those sphingolipid species that build the cellular “rheostat”, i.e. ceramide, sphingosine, sphingosine 1-phosphate (S1P), and ceramide 1-phosphate (C1P). We are studying the regulation of the critical sphingolipid-generating and -degrading enzymes including ceramidases, sphingosine kinases, and the ceramide kinase to

understand under which conditions a certain sphingolipid is accumulating in the cell to exert a function. The major goal is it to identify novel therapeutic targets within the sphingolipid cascades which may turn useful in the treatment of diseases characterized by abnormal cell growth.

In an ongoing collaboration with the group of Prof. Manuel Haschke, Clinical Pharmacology, we are analyzing and quantifying sphingolipid species from cells, tissues and plasma by LC-MS/MS.

Sphk1 and Sphk2 Differentially Regulate Erythropoietin Synthesis in Mouse Renal Interstitial Fibroblast-like Cells

Hafizi R, Imeri F, Stepanovska Tanturovska B, Manaila R, Schwalm S, Trautmann S, Wenger RH, Pfeilschifter J, Huwiler A

Erythropoietin (Epo) is a crucial hormone regulating red blood cell number and consequently the hematocrit. Epo is mainly produced in the kidney by interstitial fibroblast-like cells. Previously, we have shown that in cultures of the immortalized mouse renal fibroblast-like cell line FAIK F3-5, sphingosine 1-phosphate (S1P), by activating S1P₁ and S1P₃ receptors, can stabilize hypoxia-inducible factor (HIF)-2α and upregulate Epo mRNA and protein synthesis. In this study, we have addressed the role of intracellular iS1P derived from sphingosine kinases (Sphk) 1 and 2 on Epo synthesis in F3-5 cells and in mouse primary cultures of renal fibroblasts. We show that stable knockdown of Sphk2 in F3-5 cells increases HIF-2α protein and Epo mRNA and protein levels, while Sphk1 knockdown leads to a reduction of hypoxia-stimulated HIF-2α and Epo protein. A similar effect was obtained using primary cultures of renal fibroblasts isolated from wildtype mice, *Sphk1*-/-, or *Sphk2*-/- mice. Furthermore, selective Sphk2 inhibitors mimicked the effect of genetic *Sphk2* depletion and also upregulated HIF-2α and Epo protein levels. The combined blockade of Sphk1 and Sphk2, using *Sphk2*-/- renal fibroblasts treated with the Sphk1 inhibitor PF543, resulted in reduced HIF-2α and Epo compared to the untreated *Sphk2*-/- cells. Exogenous sphingosine (Sph) enhanced HIF-2α and Epo, and this was abolished by the combined treatment with the selective S1P₁ and S1P₃ antagonists NIBR-0213 and TY52156, suggesting that Sph was taken up by cells and converted to iS1P and exported to then act in an autocrine manner through S1P₁ and S1P₃. The upregulation of HIF-2α and Epo synthesis by Sphk2 knockdown was confirmed in the human hepatoma cell line Hep3B, which is well-established to upregulate Epo production under hypoxia. In summary, these data show that sphingolipids have diverse effects on Epo synthesis. While accumulation of intracellular Sph reduces Epo synthesis, iS1P will be exported to act through S1P₁₊₃ to enhance Epo synthesis. Furthermore, these data suggest that selective inhibition of Sphk2 is an attractive new option to enhance Epo synthesis and thereby to reduce anemia development in chronic kidney disease.

See original publication No 1

Original publications

1. Hafizi R, Imeri F, Stepanovska Tanturovska B, Manaila R, Schwalm S, Trautmann S, Wenger RH, Pfeilschifter J, **Huwiler A**: Sphk1 and Sphk2 Differentially Regulate Erythropoietin Synthesis in Mouse Renal Interstitial Fibroblast-like Cells. *Int J Mol Sci.* 23 (2022), 1-16.
2. Theodoropoulou MA, Psarra A, Erhardt M, Nikolaou A, Gerogiannopoulou AD, Hadjipav-lou-Litina D, Hayashi D, Dennis EA, **Huwiler A**, Kokotos G: N-Acylated and N-Alkylated 2-Aminobenzothiazoles Are Novel Agents That Suppress the Generation of Prostaglandin E2. *Biomolecules.* 12 (2022), 1-23.

Group Prof. Thomas Kaufmann

Photo: Group Kaufmann

Group members: Philippe JeanRichard, PhD student
Ali Jazaeri, PhD student
Liyang Wu, PhD student (since Dec 2022)
Daniel Bachmann, Lab Technician
Frei Jöel, Support Assistant (June - Aug 2022)
Wilhelm Lea, M.Sc. pharm. student (until July 2022)

Our group is interested in the molecular mechanisms of programmed cell death (PCD), in particular apoptosis and necroptosis, and the link between cell death and innate immune signaling. A focus in the latter lies on myeloid cells, in particular granulocytes (neutrophils and basophils) and mast cells, which are central players of innate immunity. Apoptosis is recognized as the most relevant (patho-) physiological form of PCD, whereas the physiological role of necroptosis is less well understood. Given the fact that apoptosis suppresses necroptosis, the latter is hypothesized to serve as a backup, proinflammatory form of PCD upon infection with pathogens that actively block apoptosis.

Granulocytes isolated from mice can only be obtained in low numbers, which makes biochemical analyses difficult, and – in the case of basophils – almost impossible. We have established a protocol to generate conditionally immortalized progenitor cells (“Hoxb8 cells”) that are committed to the macrophage/neutrophil- or the basophil lineages. Those cells can

be differentiated in vitro into mature granulocytes in nearly unlimited numbers. An advantage of "Hoxb8" cells over primary granulocytes lies in the straightforward possibility of further genetic manipulation, such as overexpression of genes of interest reconstitution of gene deficient cells lines with particular mutants of that same gene. Regarding basophils and mast cells, we are interested how cytokines, such as IL-3, or binding of IgE and subsequent cross-linking of the high affinity IgE receptor by antigen, activate these cells, and if/how those stimuli increase cellular viability. On the other hand, selective killing of activated basophils or mast cells (or activated immune cells in general) is an intriguing concept to target immunological disorders, including allergies. Newly developed drugs aiming at inducing apoptosis in cancer cells (so called BH3-mimetics) are tested in our lab for their potential to kill activated leukocyte populations selectively.

Currently of great interest to our group is the pro-apoptotic family member BOK. BOK has raised much interest recently, as it is deleted in human cancers with surprisingly high frequency. Several cancer models with our newly developed Bok-deficient mouse strain are ongoing in our lab and in collaboration with others to test the potential tumour suppressor potential of BOK. Our recent data indicate that BOK may have a previously non-recognized tumor-suppressor function in non-small-cell lung cancer and that BOK is a crucial mediator of liver damage and carcinogenesis induced by chemical carcinogens. Other BOK related projects focus on the molecular function of this still rather enigmatic protein, as well as its role in cancer development and maintenance. Regarding the latter, we have recently identified a novel function of BOK, linking this cell death regulator to nucleotide metabolism.

Original publications

1. Seiler K, Humbert M, Minder P, Mashimo I, Schläfli AM, Krauer D, Federzoni EA, Vu B, Moresco JJ, Yates JR 3rd, Sadowski MC, Radpour R, **Kaufmann T**, Sarry JE, Dengjel J, Tschan MP, Torbett BE: Hexokinase 3 enhances myeloid cell survival via non-glycolytic functions. *Cell Death Dis.* 13 (2022), 1-14.
2. Zbären N, Brigger D, Bachmann D, Helbling A, Jörg L, Horn MP, Schmid JM, Hoffmann HJ, Kinet JP, **Kaufmann T**, Eggel A: A novel functional mast cell assay for the detection of allergies. *J Allergy Clin Immunol.* 149 (2022), 1018-1030.
3. Meinhardt AL, Munkhbaatar E, Höckendorf U, Dietzen M, Dechant M, Anton M, Jacob A, Steiger K, Weichert W, Brücke L, McGranahan N, Branca C, **Kaufmann T**, Dengler M, Jost P: The BCL-2 family member BOK promotes KRAS-driven lung cancer progression in a p53-dependent manner. *Oncogene* 41 (2022), 1376-1382.

Review article

1. **Kaufmann T**, Simon HU: Pharmacological Induction of Granulocyte Cell Death As Therapeutic Strategy. *Annu Rev Pharmacol Toxicol.* (2022), 1-17.

Group PD Dr. Georgia Konstantinidou*Photo: Group Konstantinidou***Group members:**

Chiara Pozzato, PhD student (until Oct 2022)
Maria Saliakoura, postdoctoral fellow (until Aug 2022)
Ioanna Nikdima, PhD student
Cédric Leroux, PhD student (until Feb 2022)
Simone Falco, PhD student
Maciej Garczyk, PhD student (since Nov 2022)

Cancer cells undergo oncogene-directed reprogramming to meet the energetic and biosynthetic challenges of cell survival, growth and proliferation. Our lab aims at identifying vulnerabilities of cancer cells in order to reveal targets for the development of innovative therapeutic strategies. We focus on the signaling and lipid metabolic alterations in KRAS-induced lung and pancreatic cancer. We work on cell lines (using a combination of techniques in molecular biology, cell biology and biochemistry), mouse models of lung and pancreatic cancer and human specimens

Restriction of extracellular lipids renders pancreatic cancer dependent on autophagy

Saliakoura M, Rossi Sebastiano M, Nikdima I, Pozzato C, Konstantinidou G

Background: KRAS is the predominant oncogene mutated in pancreatic ductal adenocarcinoma (PDAC), the fourth cause of cancer-related deaths worldwide. Mutant KRAS-driven tumors are metabolically programmed to support their growth and survival, which can be used to identify metabolic vulnerabilities. In the present study, we aimed to understand the role of extracellularly derived fatty acids in KRAS-driven pancreatic cancer.

Methods: To assess the dependence of PDAC cells on extracellular fatty acids we employed delipidated serum or RNAi-mediated suppression of ACSL3 (to inhibit the activation and cellular retention of extracellular fatty acids) followed by cell proliferation assays, qPCR, apoptosis assays, immunoblots and fluorescence microscopy experiments. To assess autophagy *in vivo*, we employed the *Kras^{G12D/+};Trp53^{flox/flox};Pdx1-CreERT2* (KPC) mice crossed with *Acs3* knockout mice, and to assess the efficacy of the combination therapy of ACSL3 and autophagy inhibition we used xenografted human cancer cell-derived tumors in immunocompromised mice.

Results: Here we show that depletion of extracellularly derived lipids either by serum lipid restriction or suppression of ACSL3, triggers autophagy, a process that protects PDAC cells from the reduction of bioenergetic intermediates. Combined extracellular lipid deprivation and autophagy inhibition exhibits anti-proliferative and pro-apoptotic effects against PDAC cell lines *in vitro* and promotes suppression of xenografted human pancreatic cancer cell-derived tumors in mice. Therefore, we propose lipid deprivation and autophagy blockade as a potential co-targeting strategy for PDAC treatment.

Conclusions: Our work unravels a central role of extracellular lipid supply in ensuring fatty acid provision in cancer cells, unmasking a previously unappreciated metabolic vulnerability of PDAC cells.

See original publication No 1

Original publications

1. Saliakoura M, Rossi Sebastiano M, Nikdima I, Pozzato C, **Konstantinidou G**: Restriction of extracellular lipids renders pancreatic cancer dependent on autophagy. *J Exp Clin Cancer Res.* 41 (2022), 1-12.

Group Prof. Hans-Uwe Simon / Prof. Shida Yousefi

Photo: Group Simon/Yousefi

Group members:

- Kevin Oberson, Lab Technician
- Evelyne Kozlowski, Lab Technician
- Dr. Joanna Boros-Majewska, Lab Technician
- Dr. Darko Stojkov, Postdoctoral fellow
- Peng Shuang, PhD student (until May 2022)
- Dr. Nikita Markov, Postdoctoral fellow
- Lea Gigon, PhD student
- Yihe Chen, PhD student
- Aref Hosseini, PhD student
- Timothée Fettrelet, PhD student
- Birkenfeld Lena, PhD guest student (Sep - Nov 2022)
- Sharapova Gulnaz, PhD guest student (Nov - Dec 2022)
- Kurbangaleeva Sirina, PhD guest student (Nov - Dec 2022)
- Apinya Chanwangpong, M.Sc. pharm. student (since Jan 2022)
- Glodjajic Ella, M.Sc. student (since Nov 2022)
- Dutoit Danielle, M.Sc. pharm. student (Jan - June 2022)
- Miholic Marta, M.Sc. student (Feb - July 2022)

We are interested in mechanisms regulating granulocyte functions, such as the release of inflammatory mediators and anti-microbial defense mechanisms. Extracellular DNA trap formation by granulocytes is a newly defined anti-microbial mechanism. Previous reports from our group revealed that extracellular DNA trap formation by neutrophils, eosinophils, and ba-

sophils does not require their death, and that DNA traps are composed of mitochondrial DNA and granule proteins.

Moreover, we are interested in the role of apoptosis and autophagy in inflammatory diseases and cancer. Several diseases serve as models to study such processes. In particular, we investigate pathogenic mechanisms of the following diseases: Atopic dermatitis, hypereosinophilic syndromes, and eosinophilic esophagitis. Our research goal is the identification of new drug targets for future therapeutic approaches in these diseases. Besides research into pathogenesis, we have developed several *in vitro* and *in vivo* test systems to determine potential effects of a given drug on the immune system.

Our research requires a network of physician-scientists from many different clinics. Most of the participating groups are located at the Faculty of Medicine of the University of Bern. Results of these collaborative interactions can be seen in the following abstracts, which briefly describe our research activities in 2022.

Nascent RHOH acts as a molecular brake on actomyosin-mediated effector functions of inflammatory neutrophils.

Peng S, Stojkov D, Gao J, Oberson K, Latzin P, Casaulta C, Yousefi S, Simon HU

In contrast to molecular changes associated with increased inflammatory responses, little is known about intracellular counter-regulatory mechanisms that control signaling cascades associated with functional responses of neutrophils. Active RHO GTPases are typically considered as effector proteins that elicit cellular responses. Strikingly, we show here that RHOH, although being constitutively GTP-bound, limits neutrophil degranulation and the formation of neutrophil extracellular traps (NETs). Mechanistically, RHOH is induced under inflammatory conditions and binds to non-muscle myosin heavy chain IIA (NMHC IIA) in activated neutrophils in order to inhibit the transport of mitochondria and granules along actin filaments, which is partially reverted upon disruption of the interaction with NMHC IIA by introducing a mutation in RhoH at lysine 34 (RhoHK34A). In parallel, RHOH inhibits actin polymerization presumably by modulating RAC1 activity. *In vivo* studies using RhoH-/- mice, demonstrate an increased antibacterial defense capability against *Escherichia coli* (*E. coli*). Collectively, our data reveal a previously undefined role of RHOH as a molecular brake for actomyosin-mediated neutrophil effector functions, which represents an intracellular regulatory axis involved in controlling the strength of an antibacterial inflammatory response.

See original publication No 1

Characterization of eosinophilic esophagitis variants by clinical, histological, and molecular analyses

Greuter T, Straumann A, Fernandez-Marrero Y, Germic N, Hosseini A, Yousefi S, Simon D, Collins MH, Bussmann C, Chehade M, Dellon ES, Furuta GT, Gonsalves N, Hirano I, Moawad FJ, Biedermann L, Safroneeva E, Schoepfer AM, Simon HU

Objective: Physicians are increasingly confronted with patients presenting with symptoms of esophageal dysfunction resembling eosinophilic esophagitis (EoE), but absence of significant esophageal eosinophilia. The purpose of this study was to characterize and classify this group of EoE variants.

Design: Patients from six EoE-centers with symptoms of esophageal dysfunction, but peak eosinophil counts of <60/mm² (<15/hpf) in esophageal biopsies and absence of gastro-esophageal reflux disease (GERD) were included. Clinical, endoscopic, (immuno)-histological, and molecular features were determined and compared with EoE, GERD, and healthy controls.

Results: We included 69 patients with EoE variants. Endoscopic abnormalities were found in 53.6%. We identified three histological subtypes: EoE-like esophagitis (36/69, 52.2%), lymphocytic esophagitis (14/69, 20.3%), and non-specific esophagitis (19/69, 27.5%). Immunohistochemistry revealed-in contrast to EoE-no significant increase in inflammatory cell infiltrates compared with GERD and healthy controls, except for lymphocytes in lymphocytic esophagitis. EoE-typical Th2-response was absent in all EoE variants. However, considerable structural changes were detected based on histology and protein expression. Using next generation mRNA sequencing, we found the three EoE variants to have distinct molecular fingerprints partially sharing pronounced traits of EoE. Hierarchical sample clustering of RNA sequencing data confirmed the presence of an EoE-like (characterized by eotaxin-3 expression), non-specific, and lymphocytic variant cluster (characterized by CD3 cells and TSLP expression).

Conclusion: All EoE variants are clinically and histologically active conditions despite the absence of esophageal eosinophilia. EoE variants appear to be part of a disease spectrum, where classical EoE represents the most common and apparent phenotype.

See original publication No 2

Original publications

1. Peng S, Stojkov D, Gao J, Oberson K, Latzin P, Casaulta C, **Yousefi S, Simon HU**: Nascent RHOH acts as a molecular brake on actomyosin-mediated effector functions of inflammatory neutrophils. PLoS Biol. 20 (2022), e3001794.
2. Greuter T, Straumann A, Fernandez-Marrero Y, Germic N, Hosseini A, **Yousefi S, Simon D, Collins MH, Bussmann C, Chehade M, Dellon ES, Furuta GT, Gonsalves N, Hirano I, Moawad FJ, Biedermann L, Safroneeva E, Schoepfer AM, Simon HU**: Characterization of eosinophilic esophagitis variants by clinical, histological, and molecular analyses: A cross-sectional multi-center study. Allergy 77 (2022), 2520-2533.
3. Stojkov D, Claus MJ, Kozlowski E, Oberson K, Schären OP, Benarafa C, **Yousefi S, Simon HU**: NET formation is independent of gasdermin D and pyroptotic cell death. Sci Signal. 16 (2023), eabm0517
4. Radonjic-Hoesli S, Martignoni Z, Cazzaniga S, Furrer DI, **Simon HU, Bürgler C, Simon D**: Characteristics of Dermatological Patients With Blood Eosinophilia: A Retrospective Analysis of 453 Patients. J Allergy Clin Immunol Pract. 10 (2022), 1229-1237.
5. Bon L, Safroneeva E, Bussmann C, Biedermann L, Schreiner P, Vavricka SR, Schoepfer AM, McCright-Gill T, **Simon HU, Straumann A, Chehade M, Greuter T**: Close follow-up is associated with fewer stricture formation and results in earlier detection of histological relapse in the long-term management of eosinophilic esophagitis. United European Gastroenterol J. 10 (2022), 308-318.

6. Fallegger A, Priola M, Artola-Borán M, Núñez NG, Wild S, Gurtner A, Becher B, **Yousefi S, Simon HU**, Arnold IC, Müller A: TGF-β production by eosinophils drives the expansion of peripherally induced neuropilin- ROR γ t+ regulatory T-cells during bacterial and allergen challenge. *Mucosal Immunol.* 15 (2022), 504-514.
7. Artola-Borán M, Fallegger A, Priola M, Jeske R, Waterboer T, Dohlman AB, Shen X, Wild S, He J, Levesque MP, **Yousefi S, Simon HU**, Cheng PF, Müller A: Mycobacterial infection aggravates Helicobacter pylori-induced gastric preneoplastic pathology by redirection of de novo induced Treg cells. *Cell Rep.* 38 (2022), 3-21.
8. Haas Q, Markov N, Muerner L, Rubino V, Benjak A, Haubitz M, Baerlocher GM, Ng CKY, Münz C, Riether C, Ochsenbein AF, **Simon HU**, von Gunten S: Siglec-7 represents a glyco-immune checkpoint for non-exhausted effector memory CD8+ T cells with high functional and metabolic capacities. *Front Immunol.* 13 (2022), 996746.

Review articles

1. Idrisova KF, **Simon HU**, Gomzikova MO: Role of Patient-Derived Models of Cancer in Translational Oncology. *Cancers* 15 (2023), 139.
2. Peng S, Gao J, Stojkov D, **Yousefi S, Simon HU**: Established and emerging roles for mitochondria in neutrophils. *Immunol Rev.*, doi: 10.1111/imr.13158. Online ahead of print.
3. Valent P, Klion AD, Roufosse F, Simon D, Metzgeroth G, Leiferman KM, Schwaab J, Butterfield JH, Sperr WR, Sotlar K, Vandenberghe P, Hoermann G, Haferlach T, Moriggl R, George TI, Akin C, Bochner BS, Gotlib J, Reiter A, Horny HP, Arock M, **Simon HU**, Gleich GJ: Proposed refined diagnostic criteria and classification of eosinophil disorders and related syndromes. *Allergy* 78 (2022), 47-59.
4. Kaufmann T, **Simon HU**: Pharmacological Induction of Granulocyte Cell Death As Therapeutic Strategy. *Annu Rev Pharmacol Toxicol.*, doi: 10.1146/annurev-pharmtox-051921-115130. Online ahead of print.
5. Radonjic-Hoesli S, Pavlov N, **Simon HU**, Simon D: Are blood cytokines reliable biomarkers of allergic disease diagnosis and treatment responses? *J Allergy Clin Immunol.* 150 (2022), 251-258.
6. Klapan K, Simon D, Karaulov A, Gomzikova M, Rizvanov A, **Yousefi S, Simon HU**: Autophagy and Skin Diseases. *Front Pharmacol.* 13 (2022), 844756.
7. Stojkov D, Gigon L, Peng S, Lukowski R, Ruth P, Karaulov A, Rizvanov A, Barlev NA, **Yousefi S, Simon HU**: Physiological and Pathophysiological Roles of Metabolic Pathways for NET Formation and Other Neutrophil Functions. *Front Immunol.* 13 (2022), 826515.
8. Cristinziano L, Modestino L, Antonelli A, Marone G, **Simon HU**, Varricchi G, Galdiero MR: Neutrophil extracellular traps in cancer. *Semin Cancer Biol.* 79 (2022), 91-104.

9. Mucke J, **Simon HU**, Burmester GR: The Safety of Antirheumatic Drugs. Dtsch Arztebl Int. 119 (2022), 81-87.
10. Idrisova KF, **Simon HU**, Gomzikova MO: Role of patient-derived modelsof cancer in translational oncology. Cancers (Basel) 15 (2022), 139.
11. **Simon HU**: Legends of allergology and immunology: Alex Straumann. Allergy 78 (2023), 596-595.

Comments

1. Mucke J, **Simon HU**, Burmester GR: In Reply. Dtsch Arztebl Int. 119 (2022), 33-34.

Group Prof. Stephan von Gunten



Photo: Group Von Gunten

Group members:

- Daniëlle Verschoor, PhD student (until July 2022)
- Marjolaine Claire Hugonet, PhD student
- Darien Toledo, PhD student
- Giselle Hevia Hernandez, PhD student
- Lukas Mürner, PhD student
- Aldona von Gunten, Technical Specialist
- Mira Christen, Lab Technician
- Jankovic Jovana, M.Sc. student (until Aug 2022)
- Gräub Isabel, M.Sc. student (Feb - Apr 2022)
- Graber Michelle, B.Sc. student (Feb - May 2022)
- Roos Nadine, B.Sc. student (Feb - May 2022)

Our laboratory is interested in molecular mechanisms that control inflammation and cancer. In particular, we focus on protein-carbohydrate interactions in the immune system and on anti-inflammatory effects mediated by Siglec receptors. Sigecls are carbohydrate-binding receptors (lectins) that have recently received particular attention in light of the capacity to mediate cell death, anti-proliferative effects, and inhibition of cellular activities. We recently identified natural autoantibodies within human intravenous immunoglobulin (IVIG) as endogenous Siglec receptor ligands. The group leader Prof. Dr. S. von Gunten is a participating investigator at the Consortium of Functional Glycomics (www.functionalglycomics.org) that aims at

defining paradigms by which protein-carbohydrate interactions mediate cell communication. Our group has collaborations with scientists and clinicians from many international and local academic institutions, companies and hospitals.

Siglec-7 represents a glyco-immune checkpoint for non-exhausted effector memory CD8⁺ T cells with high functional and metabolic capacities

Haas Q, Markov N, Muerner L, Rubino V, Benjak A, Haubitz M, Baerlocher GM, Ng CKY, Münz C, Riether C, Ochsenbein AF, Simon HU, von Gunten S

While inhibitory Siglec receptors are known to regulate myeloid cells, less is known about their expression and function in lymphocytes subsets. Here we identified Siglec-7 as a glyco-immune checkpoint expressed on non-exhausted effector memory CD8⁺ T cells that exhibit high functional and metabolic capacities. Seahorse analysis revealed higher basal respiration and glycolysis levels of Siglec-7⁺ CD8⁺ T cells in steady state, and particularly upon activation. Siglec-7 polarization into the T cell immune synapse was dependent on sialoglycan interactions *in trans* and prevented actin polarization and effective T cell responses. Siglec-7 ligands were found to be expressed on both leukemic stem cells and acute myeloid leukemia (AML) cells suggesting the occurrence of glyco-immune checkpoints for Siglec-7⁺ CD8⁺ T cells, which were found in patients' peripheral blood and bone marrow. Our findings project Siglec-7 as a glyco-immune checkpoint and therapeutic target for T cell-driven disorders and cancer.

See original publication No 1

Original publications

1. Haas Q, Markov N, Muerner L, Rubino V, Benjak A, Haubitz M, Baerlocher GM, Ng CKY, Münz C, Riether C, Ochsenbein AF, Simon HU, **von Gunten S**: Siglec-7 represents a glyco-immune checkpoint for non-exhausted effector memory CD8⁺ T cells with high functional and metabolic capacities. *Front Immunol.* 13 (2022), 1-14.
2. Wolf B, Piksa M, Beley I, Patoux A, Besson T, Cordier V, Voedisch B, Schindler P, Stöllner D, Perrot L, **von Gunten S**, Brees D, Kammüller M: Therapeutic antibody glycosylation impacts antigen recognition and immunogenicity. *Immunology* 166 (2022), 380-407.

Review articles and Editorials

1. Von Achenbach C, Hevia Hernandez G, **von Gunten S**: The Choice between Intravenous and Subcutaneous Immunoglobulins: Aspects for Consideration. *Pharmacology*. (2022), 1-8.
2. Gorochov G, **von Gunten S**: Diversification of IgA Antibody Specificities by Mild Chemical Modification? *Pharmacology*. 107 (2022), 339-340.

Book chapter

1. Angata T, **von Gunten S**, Schnaar RL, Varki A: I-Type Lectins. *Essentials of Glycobiology*. 4 (2022), Chapter 35.

Group Prof. Manuel Haschke (Clinical Pharmacology)

Photo: Group Haschke

Group members:

- Evangelia Liakoni, MD
- Felix Hammann, MD, PhD
- Vera van der Velpen, PhD, Scientist and Lead LC-MS lab
- Mats Hirt, Lab technician
- Verena Schöning, PhD, Postdoctoral fellow
- Stefan Weiler, MD
- Elias Bekka, MD, Study physician by CPT specialty trainee
- Laura Hermann, MD, Study physician by CPT specialty trainee
- Charlotte Kern, PhD student
- Samuel Christen, PhD student
- Aurélie Pahud de Mortanges, PhD student

Our research activities deal with questions related to drug metabolism, clinical toxicology, nicotine dependence, pain treatment as well as the use of machine learning and modeling tools for the support of clinical trials. We run clinical studies investigating the pharmacokinetics and pharmacodynamics of different nicotine salt and free-base nicotine e-liquids applied by an open vape pod system. In patients willing to stop cigarette smoking we investigate the impact of the nicotine concentration on the efficacy of a nicotine salt vape pod system as smoking cessation tool. Another SNF project investigates the effect of paracetamol in patients treated with strong opioids using a double-blind drug withdrawal design. In a further set of projects,

ivermectin is investigated in the framework of an endectocide-based malaria intervention field-trial in Africa. The clinical data gathered in these studies are linked with quantitative data on drug and metabolite concentrations, which are produced by our in-house mass spectrometry lab (2 LC-MS/MS instruments) positioned within the PKI laboratory infrastructure. In addition, our LCMS-lab also develops methods and produces data for collaborative research projects with the other PKI research groups.

Original publications

1. Duthaler U, Bachmann F, Suenderhauf C, Grandinetti T, Pfefferkorn F, **Haschke M**, Hruz P, Bouitbir J, Krähenbühl S. Liver Cirrhosis Affects the Pharmacokinetics of the Six Substrates of the Basel Phenotyping Cocktail Differently. *Clin Pharmacokinet*. 2022 Jul;61(7):1039-1055. doi: 10.1007/s40262-022-01119-0. Epub 2022 May 16. PMID: 35570253; PMCID: PMC9287224.
2. Varum F, Thorne H, Bravo R, Gilgen D, Hartig C, Nicolas GP, Wild D, Liakoni E, **Haschke M**. Targeted colonic release formulations of mesalazine - A clinical pharmacoscintigraphic proof-of-concept study in healthy subjects and patients with mildly active ulcerative colitis. *Int J Pharm*. 2022 Sep 25;625:122055. doi: 10.1016/j.ijpharm.2022.122055. Epub 2022 Aug 1. PMID: 35926752.
3. **Schöning V, Liakoni E**, Baumgartner C, Exadaktylos AK, Hautz WE, Atkinson A, **Hammann F**. Revalidating the prognostic COVID-19 severity assessment (COSA) score for variants of concern. *J Transl Med*. 2022 Sep 23;20(1):427. doi: 10.1186/s12967-022-03634-x. PMID: 36138462; PMCID: PMC9503266.
4. Heier EC, Eyer F, Rabe C, Geith S, Dargan PI, Wood DM, Heyerdahl F, Dines AM, Giraudon I, Erik Hovda K, Yates C, Vallersnes OM, Miró Ò, Liechti ME, Zellner T; **Euro-DEN Research Group**. Clinical effect of ethanol co-use in patients with acute drug toxicity involving the use of central nervous system depressant recreational drugs. *Eur J Emerg Med*. 2022 Aug 1;29(4):291-300. doi: 10.1097/MEJ.0000000000000932. Epub 2022 Apr 8. PMID: 35404314.
5. Crulli B, Dines AM, Blanco G, Giraudon I, Eyer F, Liechti ME, Miró Ò, Hovda KE, Heyerdahl F, Yates C, Vallersnes OM, Wood DM, Dargan PI; **Euro-DEN Plus Research Group**. Novel psychoactive substances-related presentations to the emergency departments of the European drug emergencies network plus (Euro-DEN plus) over the six-year period 2014-2019. *Clin Toxicol (Phila)*. 2022 Nov 2;1-10. doi: 10.1080/15563650.2022.2137524. Epub ahead of print. PMID: 36322684.
6. Buetler VA, Braunshausen AM, Weiler S, Klukowska-Rötzler J, Exadaktylos AE, **Liakoni E**. Characteristics of emergency department presentations following ingestion of *Taxus baccata* (yew). *Clin Toxicol (Phila)*. 2022
7. **Schöning V, Hammann F**. Drug-Disease Severity and Target-Disease Severity Interaction Networks in COVID-19 Patients. *Pharmaceutics*. 2022 Aug 30;14(9):1828. doi: 10.3390/pharmaceutics14091828. PMID: 36145576; PMCID: PMC9504398.

8. Schöning V, Kern C, Chaccour C, Hammann F. Effectiveness of Antiviral Therapy in Highly-Transmissible Variants of SARS-CoV-2: A Modeling and Simulation Study. *Front Pharmacol.* 2022 Feb 9;13:816429. doi: 10.3389/fphar.2022.816429. PMID: 35222030; PMCID: PMC8864116.
9. Gnägi R, Zúñiga F, Brunkert T, Meyer-Massetti C. Development of a medication literacy assessment instrument (MELIA) for older people receiving home care. *J Adv Nurs.* 2022 Dec;78(12):4210-4220. doi: 10.1111/jan.15429. Epub 2022 Sep 2. PMID: 36052608.
10. Schmid Y, Galicia M, Vogt SB, Liechti ME, Burillo-Putze G, Dargan PI, Dines AM, Giraudon I, Heyerdahl F, Hovda KE, Wood DM, Yates C, Miró O; (on behalf of the Euro-DEN Plus Research Group). Differences in clinical features associated with cannabis intoxication in presentations to European emergency departments according to patient age and sex. *Clin Toxicol (Phila).* 2022 Aug;60(8):912-919. doi: 10.1080/15563650.2022.2060116. Epub 2022 Apr 11. PMID: 35404194.

Review articles

1. Benowitz NL, Liakoni E. Tobacco use disorder and cardiovascular health. *Addiction.* 2022 Apr;117(4):1128-1138. doi: 10.1111/add.15703. Epub 2021 Oct 20. PMID: 34590373.

Case reports

1. Stutz U S, Braun A, Zubler F, Vock C, Liakoni E. Rezidivierender Priapismus – unerwünschte Wirkung einer Therapie mit Neuroleptika. DOI: <https://doi.org/10.4414/smf.2022.08769>. Veröffentlichung: 20.03.2022. Swiss Med Forum. 2022;22(00)
2. Buetler VA, Agbariah N, Schild DP, Liechti FD, Wieland A, Andina N, Hammann F, Kremer Hovinga JA. Immune-Mediated Thrombotic Thrombocytopenic Purpura Following mRNA-Based COVID-19 Vaccine BNT162b2: Case Report and Mini-Review of the Literature. *Front Med (Lausanne).* 2022 May 17;9:890661. doi: 10.3389/fmed.2022.890661. PMID: 35655852; PMCID: PMC9152022.
3. Banholzer S, Helbling A, Haschke M. "Erfolgreiche Re-Exposition mit COVID-19-mRNA-Impfung in reduzierter Dosierung bei Patienten mit klinischem Verdacht auf Peri-/Myokarditis nach erster COVID-19-Impfung." Vigilance-News, Swissmedic, 2022. 28.

Additional Publications by PKI Members

Original publications

Dopheide JF, Gillmann P, **Spirk D**, Khorrami Borozadi M, Adam L, Drexel H: False versus True Statin Intolerance in Patients with Peripheral Artery Disease. *J Clin Med.* 11 (2022), 1-12.

Voci D, Götschi A, Held U, Bingisser R, Colucci G, Duerschmied D, Fumagalli RM, Gerber B, Hasse B, Keller DL, Konstantinides SV, Mach F, Rampini SK, Righini M, Robert-Ebadi H, Rosemann T, Roth-Zetsche S, Sebastian T, Simon NR, **Spirk D**, Stortecky S, Vaisnora L, Kucher N, Barco S; OVID investigators: Enoxaparin for outpatients with COVID-19: 90-day results from the randomised, open-label, parallel-group, multinational, phase III OVID trial. *Thromb Res* 22 (2022), 2-8.

Wolf S, **Spirk D**, Forgo G, Sebastian T, Voci D, Kucher N, Barco S: Prevalent use of high-intensity statin therapy and LDL-C target attainment among PAD patients undergoing angioplasty. *Vasa.* 51 (2022), 357-364.

Müller S, Titti L, Speed V, Roberts L, Patel J, Patel R, Arya R, Kucher N, **Spirk D**, Sahin K, Beyer-Westendorf J: Pooled Analysis of Rivaroxaban therapy for acute venous thromboembolism in FIRST registry, SWIVTER and DRESDEN NOAC registry. *Res Pract Thromb Haemost.* 6 (2022), 1-6.

Wenger N, Sebastian T, Beer JH, Mazzolai L, Aujesky D, Hayoz D, Engelberger RP, Korte W, Voci D, Kucher N, Barco S, **Spirk D**: Differences in duration of anticoagulation after pulmonary embolism and deep vein thrombosis: Findings from the SWISS Venous ThromboEmbolism Registry (SWIVTER). *Thromb Res.* 220 (2022), 65-71.

Frey V, Sebastian T, Barco S, **Spirk D**, Hayoz D, Périard D, Kucher N, Betticher D, Engelberger RP: Impact of concomitant popliteal vein thrombosis in patients with acute iliofemoral deep vein thrombosis treated with endovascular early thrombus removal. *Vasa.* 51 (2022), 282-290.

Barco S, Voci D, Held U, Sebastian T, Bingisser R, Colucci G, Duerschmied D, Frenk A, Gerber B, Götschi A, Konstantinides SV, Mach F, Robert-Ebadi H, Rosemann T, Simon NR, Speichbach H, **Spirk D**, Stortecky S, Vaisnora L, Righini M, Kucher N; OVID investigators: Enoxaparin for primary thromboprophylaxis in symptomatic outpatients with COVID-19 (OVID): a randomised, open-label, parallel-group, multicentre, phase 3 trial. *Lancet Haematol.* 9 (2022), 585-593.

Sudano I, Mach F, Moccetti T, Burkard T, Fahe C, Delabays A, Rickli H, Keller PF, Dopheide J, Bodenmann S, Fiolka T, Ehret G, **Spirk D**: Optimized Treatment of Refractory Hypercholesterolemia in Patients With Atherosclerotic Cardiovascular Disease or Heterozygous Familial Hypercholesterolemia With Alirocumab (OPTIMIZE). *Front Cardiovasc Med.* 9 (2022), 1-9.

Räber L, Ueki Y, Otsuka T, Losdat S, Häner JD, Lonborg J, Fahrni G, Iglesias JF, van Geuns RJ, Ondracek AS, Radu Juul Jensen MD, Zanchin C, Stortecky S, **Spirk D**, Siontis GCM, Saleh L, Matter CM, Daemen J, Mach F, Heg D, Windecker S, Engström T, Lang IM, Koskinas KC; PACMAN-AMI collaborators: Effect of Alirocumab Added to High-Intensity Statin Therapy on Coronary Atherosclerosis in Patients With Acute Myocardial Infarction: The PACMAN-AMI Randomized Clinical Trial. *JAMA*. 327 (2022), 1771-1781.

Neuenschwander J, Sebastian T, Barco S, **Spirk D**, Kucher N: A novel management strategy for treatment of pelvic venous disorders utilizing a clinical screening score and non-invasive imaging. *Vasa*. 51 (2022), 182-189.

Spirk D, Sebastian T, Beer JH, Mazzolai L, Aujesky D, Hayoz D, Engelberger RP, Korte W, Kucher N, Barco S: Role of age, sex, and specific provoking factors on the distal versus proximal presentation of first symptomatic deep vein thrombosis: analysis of the SWISS Venous ThromboEmbolism Registry (SWIVTER). *Intern Emerg Med*. 17 (2022), 799-803.

Maurer M, Magerl M, Betschel S, Aberer W, Ansotegui IJ, Aygören-Pürsün E, Banerji A, Bara NA, Boccon-Gibod I, Bork K, Bouillet L, Boysen HB, Brodzski N, Busse PJ, Bygum A, Caballero T, Cancian M, Castaldo AJ, Cohn DM, Csuka D, Farkas H, Gompels M, Gower R, Grumach AS, Guidos-Fogelbach G, Hide M, Kang HR, Kaplan AP, Katelaris CH, Kiani-Alikhan S, Lei WT, Lockey RF, Longhurst H, Lumry W, MacGinnitie A, Malbran A, Martinez Saguer I, Matta Campos JJ, Nast A, Nguyen D, Nieto-Martinez SA, Pawankar R, Peter J, Porebski G, Prior N, Reshef A, Riedl M, Ritchie B, Sheikh FR, Smith WB, **Spaeth PJ**, Stobiecki M, Toubi E, Varga LA, Weller K, Zanichelli A, Zhi Y, Zuraw B, Craig T: The international WAO/EAACI guideline for the management of hereditary angioedema - The 2021 revision and update. *Allergy*. 77 (2022), 1961-1990.

Maurer M, Magerl M, Betschel S, Aberer W, Ansotegui IJ, Aygören-Pürsün E, Banerji A, Bara NA, Boccon-Gibod I, Bork K, Bouillet L, Boysen HB, Brodzski N, Busse PJ, Bygum A, Caballero T, Cancian M, Castaldo AJ, Cohn DM, Csuka D, Farkas H, Gompels M, Gower R, Grumach AS, Guidos-Fogelbach G, Hide M, Kang HR, Kaplan AP, Katelaris CH, Kiani-Alikhan S, Lei WT, Lockey RF, Longhurst H, Lumry W, MacGinnitie A, Malbran A, Martinez Saguer I, Matta Campos JJ, Nast A, Nguyen D, Nieto-Martinez SA, Pawankar R, Peter J, Porebski G, Prior N, Reshef A, Riedl M, Ritchie B, Sheikh FR, Smith WB, **Spaeth PJ**, Stobiecki M, Toubi E, Varga LA, Weller K, Zanichelli A, Zhi Y, Zuraw B, Craig T: The international WAO/EAACI guideline for the management of hereditary angioedema - The 2021 revision and update. *World Allergy Organ J*. 15 (2022), 1-15

4.2. Organization of Meetings and Courses

Prof. Hans-Uwe Simon

Symposium of the Swiss Society of Pharmacology and Toxicology (SSPT):
Progress in Pharmacology - Pharmacotherapies of pain and pharmacology of cannabinoids
Bern (CH), Jan 19, 2022

Workshop on "Cell Death and Disease" (together with C. Brancolini, K.-M. Debatin and P.H. Krammer), Villa Vigoni, Laveno di Menaggio, Como (I), June 22-25, 2022

Prof. Stephan von Gunten

Swiss Society of Pharmacology and Toxicology Spring Meeting 2022,
Outbreak COVID-19
Bern (CH), Apr 28, 2022.

21th III-Bern International Summer School, Translational Medicine, Drug Discovery and Inspiration, Bönigen (CH), Aug 21-23, 2022

Prof. Thomas Kaufmann

21th III-Bern International Summer School, Translational Medicine, Drug Discovery and Inspiration, Bönigen (CH), Aug 21-23, 2022

PD Dr. Georgia Konstantinidou

LS2 Annual Meeting 2022, organizer of symposium "Advances in Translational Pharmacology",~500 participants, Zürich (CH)

Swiss Society of Pharmacology and Toxicology Spring Meeting 2022,
Outbreak COVID-19

Bern (CH), Apr 28, 2022

4.3. Referee Work for Grant Bodies

Prof. Andrea Huwiler

Deutsche Forschungsgemeinschaft (DFG)
Swiss National Science Foundation (SNF)

Prof. Thomas Kaufmann

Agence Nationale de la Recherche (ANR)
Austrian Science Fund (FWF)
German Research Foundation (DFG)
L'Oréal Österreich

National Science Centre Poland
Swiss Cancer League
Swiss National Science Foundation (SNF)

Prof. Hans-Uwe Simon

Swiss National Science Foundation (SNF)
Novartis Foundation

Swiss Cancer League
European Research Council (ERC)

PD Dr. Georgia Konstantinidou

European Research Council (ERC)
 Swiss National Science Foundation (SNF)

Bernese Cancer league
 Austrian Science Fund (FWF)

Prof. Stephan von Gunten

Swiss National Science Foundation (SNF)
 Canadian Glycomics Network
 Best Cancer Now

Dutch Cancer Society (DCS)

4.4. Awards**Dr. Bisera Stepanovska-Tanturovska****Sphingolipid Club poster presentation award**

14th Meeting of the Sphingolipid Club, Pozzilli (IT), Sep 2022

Roxana Manaila**Sphingolipid Club oral presentation award**

14th Meeting of the Sphingolipid Club, Pozzilli (IT), Sep 2022

Timothée Louis Fettrelet**Faculty Prize for the master project****"Single-Cell Characterization of Eosinophils"**

University of Lausanne, Lausanne (CH), June 2022

Chiara Pozzato**Prize for best presentation**

Swiss Society of Experimental Pharmacology (SSEP), LS2 Annual Meeting 2022,
 Zurich (CH), Apr 2022

Dr. Darko Stojkov**Prize for excellent poster presentation**

Swiss Society of Pharmacology and Toxicology (SSPT), SSPT Spring Meeting 2022,
 Bern (CH), Apr 2022

4.5. Travel support**Dr. Bisera Stepanovska Tanturovska**

SSPT Travel grant to participate at the 14th Meeting of the Sphingolipid Club, Pozzilli (IT),
 Sep 2022

4.6. Mobility fellowship**Mürner Lukas**

Universität Bern (CH), Harvard Medical School, Boston (USA)
 Harvard University, National Center for Functional Glycomics, Prof. Richard Cummings
 (Nov 2021 – Dec 2022)

5. Administrative, Advisory, and Honorary Posts

Dr. Zhaoyue He

Coordinator for PC work at the PKI

Webmaster at the PKI

Prof. Andrea Huwiler

Member of the Ernennungs- und Habilitationskommission (EHK), Medical Faculty, University of Bern

Member of the Evaluation Committee, Postdoc mobility grants, Swiss National Science Foundation

President of the Commission Pharmacology/Physiology of the German Society of Nephrology (DGfN)

Member of the Advisory Editorial Board of Naunyn Schmiedeberg's Archives of Pharmacology

Member of the Editorial Board of the International Journal of Molecular Sciences

Collection Editor of the Topical Collection of "Sphingolipids in health and disease" in Int. J. Mol. Sci.; Section: Mol. Pharmacol.

Member of the Editorial Board of Experimental Pharmacology and Drug Discovery, Frontiers in Pharmacology

Prof. Thomas Kaufmann

Member of the Supervision commission "Cell Biology" within the Graduate School for Cellular and Biomedical Sciences of the University of Bern, since 2009

Member of the Editorial Board, Cell Death and Disease

Member of Ethical Board, Cell Death and Differentiation, Cell Death and Disease, Cell Death and Discovery

Member of the Editorial Board, Frontiers in Molecular and Cellular Oncology

Member of the Editorial Board, Frontiers in Cell and Developmental Biology - Cell Death and Survival

Member of the Editorial Board, International Archives of Allergy and Immunology

Member of the Editorial Board, Pharmacology

Coordinator for FACS, Fluorescence Microscope

Coordinator FPLC (Äkta)

Safety Officer PKI (GeSiBe)

PD Dr. Georgia Konstantinidou

Member of the Supervision commission "Cell Biology" within the Graduate School for Cellular and Biomedical Sciences of the University of Bern.

Member of the doctorate course of Molecular Medicine (role: lecturer from foreign University) at the University of Ferrara, Italy.

Secretary of the Swiss Society of Experimental Pharmacology (SSEP)

Associate Editor, *Frontiers in Molecular and Cellular Oncology*

Associate Editor, *Biomedicines*

Member of the Bern Center for Precision Medicine (BCPM).

Prof. Hans-Uwe Simon

President, Brandenburg Medical School, Germany

Member of the German National Academy of Sciences (Deutsche Akademie der Naturforscher Leopoldina)

Member of the Swiss Academy of Medical Sciences (SAMW)

President of the Novartis Foundation for Biomedical Research

Member of the board, EoE Foundation Switzerland

Swiss-EU mobility program, Coordinator Pharmacology/Pharmacy, University of Bern

Editor-in-Chief, *Cell Death & Disease*

Editor-in-Chief, *International Archives of Allergy and Immunology*

PD Dr. Peter Späth

Member of the Kreuth Immunoglobulin Working Group 'European Consensus Proposal for Immunoglobulin Therapies'; member of the expert group drafting an update of the core Summary of Product Characteristics' for human immunoglobulin preparations

Core team member for preparing a "Measles Intravenous Immunoglobulin G Guideline" The team work resulted in the following publications becoming effective 1 January 2022:

Guideline on core SmPC for human normal immunoglobulin for intravenous administration (IVIg) - EMA/CHMP/BPWP/94038/2007 Rev.5

Guideline on the clinical investigation of human normal immunoglobulin for intravenous administration (IVIg) - EMA/CHMP/BPWP/94033/2007 rev. 4

Member of the expert group drafting an update of the 'core Summary of Product Characteristics' for subcutaneous normal human immunoglobulin preparations

Prof. Stephan von Gunten

Executive Committee Member of The Federation of European Pharmacological Societies (EPHAR; since June 2022)

Editor-in-Chief, PHARMACOLOGY, International Journal of Experimental and Clinical Pharmacology, Karger Publishers, Basel, Switzerland

Past-president and Board Member of the Swiss Society of Experimental Pharmacology (SSEP)

Board Member of the Swiss Society of Pharmacology and Toxicology (SSPT)

Participating Investigator of the US National Institutes of Health (NIH)-funded “Consortium for Functional Glycomics” (CFG; www.functionalglycomics.org)

Editor of “Literature Highlights”, Immunopharmacology Section, International Union of Basic and Clinical Pharmacology (IUPHAR)

Editorial Board Member of “Allergy”, European Journal of Allergy and Clinical Immunology

Editorial Board Member, International Archives of Allergy and Immunology

Coordinator library at the PKI

Prof. Shida Yousefi

Coordinator for Radioactive Work,

Coordinator of confocal Microscopy

Coordinator of imaging analysis

Prof. David Spirk

Global Fellow in Medicines Development of the International Federation of Associations of Pharmaceutical Physicians and Pharmaceutical Medicine (IFAPP)

Fellow of the European Society of Cardiology (ESC)

Member of the Scientific Award Committee, Swiss Society of Pharmaceutical Medicine (SSPM)

Member of the Editorial Board, Frontiers in Cardiovascular Medicine

Prof. Manuel Haschke

Head, Drug and Therapeutics Committee, Inselgruppe Bern

PD Evangelia Liakoni

Executive Committee member of the Swiss Society of Clinical Pharmacology and Toxicology (SSCPT)

Scientific and Meetings Committee member European Association of Poisons Centres and Clinical Toxicologists (EAPCCT)

Swiss Society of Clinical Pharmacology and Toxicology (SSCPT) Delegierte FMH-Gutachterstelle

Member Critical Incident Reporting System (CIRS) Commission General Internal Medicine, Inselspital, University Hospital

Member of the Graduate School for Health Sciences (GHS) expert committee III (clinical sciences).

PD Felix Hammann

Executive Board member Swiss Society for Clinical Pharmacology and Toxicology (Treasurer)

PD Stefan Weiler

Executive Committee member of the Swiss Society of Clinical Pharmacology and Toxicology (SSCPT)

Member of the Human Medicines Expert Committee of Swissmedic, nominated by the Agency Council of Swissmedic

Academic Editor of Swiss Medical Weekly

Full member of the American Academy of Clinical Toxicology

Editorial Board member of Pharma-Kritik (Ed. Etzel Gysling)

Advisory Board member of Swiss Medical Forum

Kevin Oberson

Biological Safety officer PKI (BSO)

Daniel Bachmann

Chemical Safety officer PKI (CSO)

All PKI principal investigators served as tutors in graduation committees of the Graduate School for Cellular and Biomedical Sciences of the University of Bern.

6. Services

6.1. Confocal Microscopy

The facility hosts three laser scanning microscopes (LSM 5 Exciter, LSM 510 and LSM 800, Carl Zeiss Microimaging GmbH, Jena), which may be used by members of the Medical Faculty at a small charge (CHF 50 per h). The facility for confocal microscopy and image analysis in our institute is part of the Microscopy Imaging Center (MIC) of the University of Bern and operated by Prof. S. Yousefi.

6.2. Flow Cytometry

The Institute of Pharmacology is equipped with Becton-Dickinson FACSCalibur (4 color), and FACSVerse 8 color Flow Cytometer instruments and FACSLyric able to detect up to 12 colors. A service is provided for analyzing potential pathogenic mechanisms of eosinophilic disorders and other inflammatory diseases. Monitoring of patients under immunomodulatory therapy is also included. The costs are currently covered by research grants of the coordinator (Prof. H.-U. Simon, FAMH Clinical Immunology), who can also be consulted for scientific support. Usage of the flow cytometer by non-members of the institute within collaborative projects is also possible.

6.3. Imaging Mass Cytometry and Mass Cytometry Platform

With Helios and Hyperion, we enable clinicians and scientists to enhance their clinical studies and research with high-parameter spatial single cell solutions. Usage of the Imaging Mass Cytometry and Mass Cytometry Platform by non-members of the institute is also possible.

7. Public work

7.1. Bürgi prize

Our institute donates the Bürgi Prize, which rewards the best original publication addressing a problem in the fields of Experimental or Clinical Pharmacology every other year. The applicant should be first author of the publication and not older than 35 years

8. Sponsors

8.1. Research Grants

Prof. Andrea Huwiler

Swiss National Science Foundation (grant No. 310030-153346/1)

Prof. Thomas Kaufmann

Swiss National Science Foundation (grant No 310030_201199)

Innosuisse-Swiss Innovation Agency; co-applicant, # 52202.1 IP-LS

PD Dr. Georgia Konstantinidou

Swiss National Science Foundation, SNF-Professorship until July 2022 (grant No. PP00P3_194810)

Novartis Foundation for Biological-Medical Research, Novartis, Basel (CH)

Innosuisse-Swiss Innovation Agency #40922.1 IP-LS

Swiss Cancer League (KFS-5115-08-2020)

Swiss National Science Foundation project grant from October 2022 (grant No 310030_212418)

Prof. Hans-Uwe Simon

Swiss National Science Foundation (grant No. 310030_184816)

Russian Government Program “Recruitment of the Leading Scientists into the Russian Institutions of Higher Education”

Prof. Stephan von Gunten

Swiss National Science Foundation (grant No. 310030_184757/1)

Swiss National Science Foundation (grant No. 310030E_205559); co-applicant

Swiss Cancer League (KFS-4958-02-2020)

Prof. Shida Yousefi

Swiss National Science Foundation (grant No. 31003A_173215)

Prof. Manuel Haschke

Swiss National Science Foundation “Impact of the nicotine concentration on the efficacy of a nicotine salt vape pod system as smoking cessation tool” (32003B_189132)

Swiss National Science Foundation “Efficacy of Metamizole or Ibuprofen With or Without a Short Educational Intervention Compared to Standard Care in Acute and Subacute Low Back Pain (EMISI): A Multicenter Randomized Factorial Trial” (32003B_179346)

PD Evangelia Liakoni

Swiss National Science Foundation “Impact of the nicotine concentration on the efficacy of a nicotine salt vape pod system as smoking cessation tool”, grant No. 32003B_189132 (main applicant, 425'360 CHF)

Swiss National Science Foundation “Effect of paracetamol in addition to WHO Step III opioids in chronic cancer pain control - a randomized, placebo-controlled parallel group study”, Swiss National Science Foundation, grant No. 32003B_201072/1 (main applicant, 400'863 CHF)

CTU-Forschungsgrant 2019-06 „Randomized crossover study comparing the pharmacokinetics and pharmacodynamics of two different nicotine salt concentration vape system pods and an electronic cigarette using free-base nicotine“(main applicant, 76'300 CHF)

PD Felix Hammann

Broad One Health Endectocide-based Malaria Intervention in Africa (BOHEMIA, unitaid.org)
2019 – 2024

Potentiated aminoglycosides: a novel antimicrobial strategy to prevent urinary tract infections (UROPOT TRIAL), Fondation Leenaards (leenards.ch)
2023 – 2025

8.2. Meetings

Swiss Society of Pharmacology and Toxicology (SSPT): Progress in Pharmacology – Progress in Pharmacology, Focus on Cardiovascular Disease: Prevention to Intervention; Bern (CH), Jan 19th, 2022

Almirall AG

Cannapharm AG

Pure holding AG

Schibano (Swiss Pharma)

Sintetica

21th International Summer School

Seehotel La Terrasse, CH 3806 - Bönigen, Aug 21 – 23, 2022

Carl Zeiss AG, Feldbach

GSK, Münchenbuchsee

Mycosynth AG, Balgach

Pfizer AG, Zürich

Medizinische Fakultät, Universität Bern

Zentrum für Labormedizin, Inselspital Bern

Graduate School for Cellular and Biomedical Sciences, Universität Bern

SCNAT

SSPT

8.3. Other Support

Bürgi Fonds Seminar series of the institute