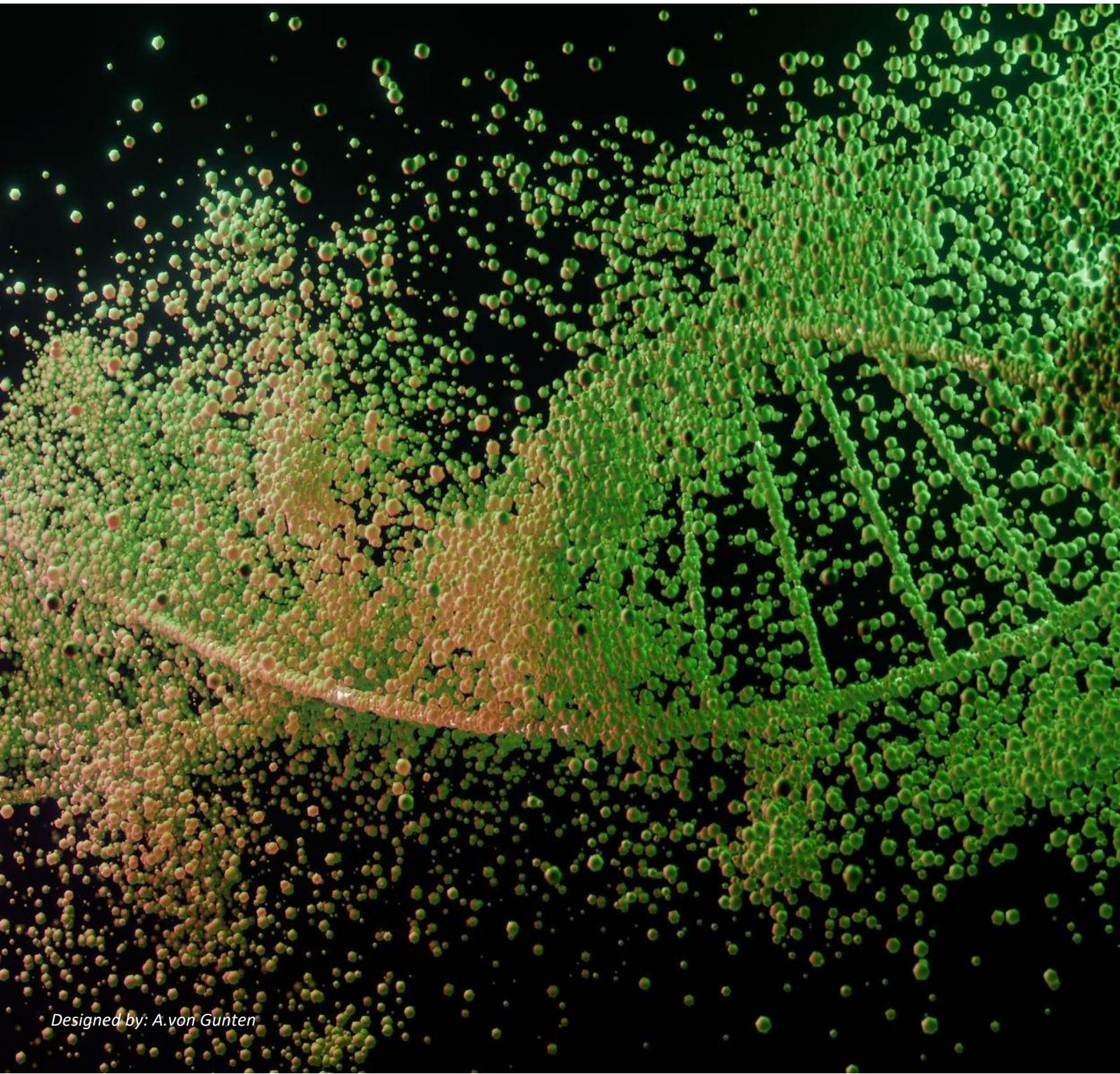


Institut für Pharmakologie PKI
www.pki.unibe.ch

Jahresbericht 2023



Annual Report 2023

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

**Institute of Pharmacology
University of Bern**

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1. Introduction

1.1. Vorwort

Diesen Jahresbericht müssen wir mit einer aussergewöhnlichen Mitteilung beginnen:

Im Dezember 2023 starb Frau Prof. Andrea Huwiler, die seit Oktober 2021 die interimistische Führung des PKI übernommen hatte, völlig unerwartet. Wir sind sehr traurig über diesen Verlust und würdigen die Leistungen von Frau Huwiler, die sie für die Unterstützung und Dienste in der Führung und Entwicklung des PKI erbracht hat. Ihre Forschungsprojekte können von den Mitarbeiter*innen im Institut fortgesetzt werden. Herr Prof. von Gunten hat die Betreuung der Gruppe übernommen. Ich selbst bin als geschäftsführender Direktor seit Dezember 2023 eingesprungen, da meine Nachfolge zur Zeit noch nicht geregelt ist. Wir rechnen damit, dass mein(e) Nachfolger*in im Herbst 2024 die Führung des PKI übernehmen wird. Weiterhin führe ich meine, nun verkleinerte, Forschungsgruppe in Bern, dies neben meiner Tätigkeit als Präsident der Medizinischen Hochschule Brandenburg (MHB) in Deutschland.

Dies ist der dreiundzwanzigste umfassende Jahresbericht des Instituts für Pharmakologie (PKI) der Medizinischen Fakultät der Universität Bern. Das PKI hat auch im Jahr 2023 seine Aufgaben in Lehre und Forschung innerhalb der Medizinischen Fakultät vorbildlich erfüllt. 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. Mit der Rekrutierung von Prof. Haschke haben sich neue Möglichkeiten der Zusammenarbeit mit der Klinischen Pharmakologie eröffnet, sowohl in der *biologischen Grundlagen-* als auch in der *klinischen Forschung*, beides Kernaufgaben der Pharmakologie.

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. Auch im Jahr 2023 trugen wir dazu bei, die Kommunikation zwischen WissenschaftlerInnen und Öffentlichkeit zu fördern.

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 Therapeutics; 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.

Im Jahr 2023 arbeiteten 18 Doktorand*innen (PhD), davon konnten vier ihre Promotion erfolgreich abschliessen. Die Mitarbeiter*innen des PKI (ohne Klinische Pharmakologie) publizierten im Jahr 2023 insgesamt 24 Originalarbeiten sowie 20 Übersichtsartikel in internationalen Fachzeitschriften. Mehrere Mitarbeiter*innen des PKI wurden mit Forschungspreisen ausgezeichnet. Alle Forschungsgruppen des PKI wurden mit namhaften Beiträgen des Schweizerischen Nationalfonds unterstützt. Diese Aufzählung belegt den hohen Stellenwert, den die Forschung an unserem Institut besitzt.

Wir danken allen Mitarbeiter*innen für ihren Einsatz, welcher auch im Jahr 2023 zu einer Bilanz beitrug, die internationalen Massstäben gerecht wird. Ebenso danken wir allen Sponsor*innen, Kollaborationspartner*innen und Freund*innen des Instituts.



Prof. Dr. med. Dr. Dr. h.c. mult. Hans-Uwe Simon

Bern, März 2024

1.2. Foreword

This year's Annual Report, we have to start with extraordinary information:

In December 2023, Prof. Andrea Huwiler unexpectedly passed away. She served as director of the PKI since October 2021. Our staff mourns for this loss. We thank Prof. Huwiler for her support and service. The lab members of her group continue to work at the PKI under the supervision of Prof. von Gunten. I am the President of Brandenburg Medical School (MHB) in Germany and continue to lead my small research group at the PKI. The Rector of the University of Bern and the Dean of the Faculty of Medicine asked me to lead the institute until my successor will start at the PKI. We expect that the PKI will have a new director sometimes in fall in 2024.

This is the twenty-third comprehensive annual report of the Institute of Pharmacology (PKI) of the Medical Faculty of the University of Bern. We have worked hard to fulfil optimally our tasks in teaching and research within the Medical Faculty in the past year. After moving to the INO-building of the University Hospital (Inselspital) in 2015, we have enjoyed excellent conditions for successful research. We share floor F of the building with the Center for Laboratory Medicine and have jointly developed the available infrastructure. We organize multiple joint teaching and research projects with this Center to further accentuate the field of "Precision Medicine". In April 2017, Prof. Manuel Haschke with his research group joined our institute and now facilitates our research in the field of Clinical Pharmacology. The presence of his group opens up new opportunities for collaboration in both *clinical research* and *basic biological science*.

The PKI wants to succeed in both areas and, therefore, maintains close contacts with several clinics at the Inselspital as well as with other research institutes of the University. In doing so, we hope to strengthen both translational research and teaching in the Medical Faculty. In addition, we are very much interested in collaborating with industry on new developments. Finally, we have also made an effort to promote communication between scientists and the public in 2023. All our current activities are summarized here below.

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.

In 2023, the PKI employed 18 in PhD students; four of them successfully completed their doctorates. In 2023, PKI scientists published a total of 24 original and 20 review articles in international journals. Several PKI staff members were awarded research prizes. All research groups are supported with considerable contributions from the Swiss National Science Foundation. In summary, we carry out research of a high standard which plays a very important role at the PKI.

We would like to thank all our staff for their commitment, which also contributed to a balance sheet in 2023 that meets international standards. We would also like to thank all sponsors, collaborators and friends of the Institute.



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

Bern, March 2024

2. Staff 2023

Director

Prof. Dr.	Huwiler, Andrea	PhD (ad interim)
Prof. Dr.	Simon, Hans Uwe	MD, PhD, Dr. h.c. mult. (since Dec. 2023)

Deputy Director

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

Prof. Dr.	Huwiler, Andrea	PhD
Prof. Dr.	Kaufmann, Thomas	PhD
PD Dr.	Konstantinidou, Georgia	PhD
Prof. Dr.	Simon, Hans Uwe	MD, PhD, Dr. h.c. mult.
Prof. Dr.	von Gunten, Stephan	MD, PhD, MBA, MME
Prof. Dr.	Yousefi, Shida	PhD
PD Dr.	Späth, Peter	PhD

Scientific Staff

	Ananthanarayan, Aparna	M.Sc. student (since Nov 2023)
	Bachmann, Daniel	Lab Technician
	Bessire, Marcine	B.Sc. student (Feb - Apr 2023)
Dr.	Boros-Majewska, Joanna	Lab Technician
	Chen, Yihe	PhD student* (until Apr 2023)
Dr.	Christen, Mira	Scientific support
	D'Agostino, Jessica	PhD student
	Falco, Simone	PhD student*
	Felder, Corinne	M.Sc. student (Jan - Jun 2023)
	Fettelet, Timothée	PhD student
	Fitzpatrick Georgia	Guest student (since Nov 2023)
	Garczyk, Maciej	PhD student
	Gigon, Lea	PhD student
	Glodjajic, Ella	M.Sc. student
	Gosheva, Gordana	M.Sc. student (Feb - Jul 2023)
Dr.	Gyimesi, Gergely	Senior Research Assistant (since Sep 2023)
Dr.	He, Zhaoyue	Postdoctoral fellow
	Hevia Hernandez, Giselle	PhD student
	Holm, Katrine	M.Sc. student (since Sep 2023)
	Hosseini, Aref	PhD student
	Hugonnet Marjolaine, Claire	PhD student (until May 2023)
	Jazaeri, Ali	PhD student
	JeanRichard, Philippe	PhD student
	Katsaros, Dimitrios Alexander	PhD student (since Dec 2023)
	Khidr, Shaimaa	PhD student (until Sep 2023)
	Kurbangaleeva, Sirina	Guest student (Nov – Dec 2023)
	Manaila, Roxana	PhD student
Dr.	Markov, Nikita	Postdoctoral fellow
	Mürner, Lukas	PhD student
	Nasser, Riim	Lab Technician
	Oberson, Kevin	Lab Technician
	Outeiro de Pinho, Gonçalo	PhD student (since Mar 2023)

	Pelliello, Giulia	Guest student* (since Nov 2023)
	Pitaktrairat, Muthita	M.Sc. student (since Sep 2023)
	Rebai, Sabina	M.Sc. student (Feb - Mar 2023)
	Roth, Jana	M.Sc. student (Jan - Jul 2023)
	Sanchez Fernández, Celtia	B.Sc. student (Feb - Apr 2023)
	Schenk, Marion	M.Sc. student (Jul – Aug 2023)
	Sharapova, Gulnaz	Guest student (Nov – Dec 2023)
Dr.	Stepanovska Tanturovska, Bisera	Postdoctoral fellow
Dr.	Stojkov, Darko	Postdoctoral fellow
	Toledo, Darien	PhD student
	von Gunten, Aldona	Technical Specialist
	Wu, Lyang	PhD student*
	Zwahlen, Vanessa	B.Sc. student (Feb - Apr 2023)

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

Principal Investigators – Clinical Pharmacology

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

Scientific Staff – Clinical Pharmacology

Dr.	Van der Velpen, Vera	PhD, Scientist and Lead LC-MS lab
	Žajdlíková, Kristina	Lab technician
	Hirt, Mats	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	MD, Study physician by CPT specialty trainee
	Kern, Charlotte	PhD student
	Christen, Samuel	PhD student
	Kotoula, Christina	PhD student

Guest Scientists

Prof. Dr.	Simon, Dagmar	MD, Dept. Dermatology, Inselspital, Univ. Bern
Dr.	Nageswara Rao Tata	Dr. PhD Leitung Laborforschung Stammzellbiologie, Kantonsspital St. Gallen
Dr.	Marchev Andrey	Guest Scientist (Jul – Sep 2023)

External University Teachers

Dr.	Bürgi, Sibylle	PhD
Prof. Dr.	Spirk, David	MD, MMD, Sanofi-Aventis AG

Office

Joray, Celine	Secretary
Opitz, Krystyna	Secretary
Sutovska, Vanda	Secretary
Conforti, Isa	Workshop / House Keeping

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



Advances in Pharmacology-
Pharmacotherapy in
Rheumatology.
Bern, January 25th, 2023

Summer School



Members of the Institute of Pharmacology of the University of Bern together with participants of our International Summer School in Bönigen; August 20 - 22th 2023

3. Teaching Activities

3.1. Lectures

Lectures for Medical Students: Pharmacology

Date	Lecturer	Titel of the lecture
Feb 28, 2023	Prof. Stephan von Gunten	Hormone aus pharmakol. Sicht 1 (1h)
Feb 28, 2023	Prof. Stephan von Gunten	Hormone aus pharmakol. Sicht 2 (1h)
Mar 13, 2023	Prof. Stephan von Gunten	Antidiabetika (1h)
Mar 13, 2023	Prof. Stephan von Gunten	Lipide, Urikostatika (1h)
Mar 21, 2023	Prof. Andrea Huwiler	Allgemeinanästheika (1h)
Mar 22, 2023	Prof. Andrea Huwiler	Anti-Parkinson + Antidementiva (1h)
Apr 03, 2023	Prof. Andrea Huwiler	Antiepileptika (1h)
Apr 17, 2023	Prof. Andrea Huwiler	Psychopharmakologie (1h)
Apr 19, 2023	Prof. Andrea Huwiler	Antidepr. + Anxiolytika (1h)
Apr 19, 2023	Prof. Andrea Huwiler	Anxiolytika und Hypnotika (1h)
Apr 24, 2023	Prof. Andrea Huwiler	Antipsychotika (1h)
Apr 25, 2023	Prof. Andrea Huwiler	Lokalanästhetika (1h)
May 08, 2023	Prof. Thomas Kaufmann	Immunmodulation (1h)
Sep 21, 2023	Prof. Andrea Huwiler	Einführung und Pharmakokinetik I
Sep 27, 2023	Prof. Hans-Uwe Simon	Pharmakodynamik 1 (1h)
Sep 27, 2023	Prof. Hans-Uwe Simon	Pharmakodynamik 2 (1h)
Oct 03, 2023	Prof. Hans-Uwe Simon	Entzündungshemmung TB1 (1h)
Oct 03, 2023	Prof. Hans-Uwe Simon	Toxikologie TB1 (1h)
Oct 10, 2023	Prof. Hans-Uwe Simon	Pharmakotherapie bei Lungenerkrankungen (1h)
Oct 24, 2023	Prof. David Spirk	Pharmakologie der Hämostase (1h)
Nov 06, 2023	Prof. Thomas Kaufmann	Pharmakologie des vegetativen Nervensystems (1h)
Nov 06, 2023	Dr. Bisera Stepanovska Tanturovska	Behandlung der Angina pectoris und Herzinsuffizienz (1h)
Nov 08, 2023	Prof. Thomas Kaufmann	Wochensynthese (1h)
Nov 14, 2023	Prof. Stephan von Gunten	Antihypertensiva (1h)
Nov 14, 2023	Prof. Stephan von Gunten	Antiarrhythmika (1h)
Dez 11, 2023	Prof. Stephan von Gunten	Diuretika 1 (1h)
Dez 11, 2023	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 28, 2023	Prof. Thomas Kaufmann	Entwicklung des Lebens (2h)
Oct 16, 2023	Prof. Thomas Kaufmann	Zellstoffwechsel (1h)
Oct 19, 2023	Prof. Thomas Kaufmann	Fachsprechstunde (1h)
Nov 02, 2023	Prof. Thomas Kaufmann	Zelltod 2 (1h)

Special seminars for Medical Students: Basic principles of living systems / cells and organisms

Date	Lecturer	Titel of the lecture
Mar 12, 2023	Prof. Stephan von Gunten	Immunpharmakologie PHA1 (2h)
Mar 13, 2023	Prof. Thomas Kaufmann	Modulation des Zelltodes - aktueller Stand und neue Entwicklungen (2h)
Mar 20, 2023	PD Dr.Georgia Konstantinidou	Tumorpharmakologie (2h)

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

Date	Lecturer	Title of the lecture
Feb 06, 2023	Prof. Hans-Uwe Simon	Rezeptoren, Dosis-Wirkungskurven Antagonisten, Applikationsarten
Feb 15, 2023	Prof. Thomas Kaufmann	Pharmakologie des VNS
Feb 22, 2023	Prof. Thomas Kaufmann	Interaktionen & Pharmakogenetik
Mar 06, 2023	Prof. David Spirk	Herz-Kreislauf Medikamente Antithrombotika
Mar 08, 2023	Prof. Thomas Kaufmann	Pharmakologie der Atemwege
Mar 20, 2023	Prof. Stephan von Gunten	Pharmakologie des Knochens
Mar 22, 2023	Prof. Stephan von Gunten	Magensäurehemmung
Mar 29, 2023	Prof. Andrea Huwiler	Narkose, Beruhigungsmittel
Apr 03, 2023	Prof. Andrea Huwiler	Analgetika
Apr 19, 2023	Dr. Sibylle Bürgi	Antidiabetika
Apr 26, 2023	Dr. Sibylle Bürgi	Lokalanästhetika
May 01, 2023	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 03, 2023	Prof. Andrea Huwiler	Depressionen, Schlafstörungen (2h)
Mar 09, 2023	Prof. Andrea Huwiler	Depressionen, Schlafstörungen (2h)
Mar 10, 2023	Prof. Andrea Huwiler	Schizophrenie, Psychosen, Demenz (2h)
Mar 16, 2023	Prof. Andrea Huwiler	Schizophrenie, Psychosen, Demenz (2h)
Mar 17, 2023	Prof. Andrea Huwiler	Nozizeption, Anästhesie (2h)
Mar 31, 2023	Prof. Stephan von Gunten	Knochenkrankheiten, Osteoporose, Gicht (2h)
Apr 04, 2023	Prof. Stephan von Gunten	Knochenkrankheiten, Osteoporose, Gicht (2h)
Apr 06, 2023	Prof. Stephan von Gunten	Gelenkkrankheiten, Arthrose, Arthritis (2h)
May 11, 2023	Prof. Andrea Huwiler	Epilepsie (2h)
May 12, 2023	Prof. Andrea Huwiler	Parkinson (2h)
May 24, 2023	PD Dr. Georgia Konstantinidou	Prostataerkrankungen (2h)
Sep 19, 2023	Prof. Hans-Uwe Simon	Grundlagen/ Pharmakodynamik (2h)
Sep 21, 2023	Prof. Hans-Uwe Simon	Grundlagen/ Pharmakodynamik (1h)
Sep 21, 2023	Prof. Hans-Uwe Simon	Arzneimittelallergien (1h)
Sep 26, 2023	Prof. Hans-Uwe Simon	Experimentelle Toxikologie (2h)
Nov 16, 2023	Prof. Stephan von Gunten	Säureassoziierte KH (1h)
Nov 16, 2023	Prof. Stephan von Gunten	Erbrechen (1h)
Nov 21, 2023	Prof. Stephan von Gunten	Motilitätsstörungen (1h)
Nov 21, 2023	Prof. Stephan von Gunten	Entzündliche Darmerkrankungen (1h)
Nov 28, 2023	PD Dr. Georgia Konstantinidou	Tumor Innerer Organe, part 1 (2h)
Nov 30, 2023	PD Dr. Georgia Konstantinidou	Tumor Innerer Organe, part 2 (2h)
Dec 05, 2023	PD Dr. Georgia Konstantinidou	Tumorimmunologie (2h)
Dec 07, 2023	Prof. Thomas Kaufmann	Krankheiten des Immunsystems, Transplantation (2h)
Dec 12, 2023	Prof. Thomas Kaufmann	Krankheiten des Immunsystems, Transplantation (2h)
Dec 14, 2023	Prof. Thomas Kaufmann	Anämien (2h)
Dec 19, 2023	Prof. Thomas Kaufmann	Leukämien (2h)
Dec 21, 2023	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 23, 2023	Prof. Stephan von Gunten	Introduction to Clinical Immunology (1h)
Feb 23, 2023	Prof. Stephan von Gunten	Glycoimmunology (1h)
Mar 02, 2023	PD Dr. Georgia Konstantinidou	Immunopharmacology (1h)

Written examination: Prof. Stephan von Gunten

Lecture for Natural Sciences Faculty: Cellular and Molecular Immunology (Coordinator: Prof. Martin Bachmann)

Date	Lecturer	Title of the lecture
Sep 21, 2023	Prof. Thomas Kaufmann	Cell death in the immune system (2h)

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 06, 2023	PD Dr. Georgia Konstantinidou	Lipid mediators in inflammation (2h)
May 11, 2023	Dr. Darko Stojkov	Inflammation - good or bad? Resolution of inflammation – apoptosis (2h)

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

Date	Lecturer	Title of the lecture
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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 22, 2023	Lukas Mürner	Gastrointestinal tract (2h)
Sep 29, 2023	Prof. David Spirk	Thrombosis and haemostasis (2h)
Oct 06, 2023	Dr. Nageswara Rao Tata	Haematological malignancies (2h)
Oct 13, 2023	Dr. Darko Stojkov	Antiinfectious therapy (2h)
Oct 20, 2023	PD Dr. Georgia Konstantinidou	Immune system (2h)
Oct 27, 2023	Prof. Stephan von Gunten	Endocrine and reproductive system (2h)
Nov 03, 2023	Dr. Darko Stojkov	Lungs and kidneys (2h)
Nov 10, 2023	Dr. Bisera Stepanovska Tanturovska	Nervous system (2h)
Dec 01, 2023	Dr. Bisera Stepanovska Tanturovska	Heart and vascular system (2h)

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

Date	Lecturer	Title of the lecture
Nov 02, 2023	Prof. Stephan von Gunten	Ethics and its governance in the 21st 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
Jan 25, 2023	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
Sep 19, 2023	Prof. Thomas Kaufmann	Cell damage (1h)

Cell Biology tutorial "Happy Cell" 2023 (5.0 ECTS), CTS/KSL 7606

Date	Lecturer	Title of the lecture
Oct 18, 2023	Prof. Thomas Kaufmann	Chapter 15 Cell signaling (2h)
Nov 08, 2023	Dr. Darko Stojkov	Chapter 17 The Cell Cycle Chapter 18 Cell Death (2h)

Lectures for Medical Students: Clinical Pharmacology

Date	Lecturer	Titel of the lecture
Jan 31, 2023	Prof. Manuel Haschke	Pharmakologie GIT
Jan 31, 2023	Prof. Manuel Haschke	Säuresekretion
Feb 06, 2023	PD Felix Hammann	Pharmakokinetik 3&4 (2h)
Mar 02, 2023	PD Evangelia Liakoni	Analgetika
Mar 02, 2023	PD Evangelia Liakoni	Antikoagulantien & Thrombozytenhemmer
Mar 06, 2023	PD Stefan Weiler	Notfall-Medikamente
Mar 20, 2023	Prof. Manuel Haschke	Vertiefungsseminar Pharmakologie
Mar 20, 2023	PD Stefan Weiler	Arterielle Hypertonie u. Herzinsuffizienz
Mar 20, 2023	PD Stefan Weiler	Diabetes u. Dyslipidämie
Mar 20, 2023	Prof. Manuel Haschke	Antibiotika
Apr 26, 2023	Prof. Manuel Haschke	Schmerzmittel 1&2 (2h)
Sep 21, 2023	PD Felix Hammann	Pharmakokinetik 1&2 (2h)
Sep 25, 2023	PD Felix Hammann	Wochensynthese
Oct 11, 2023	Prof. Evangelia Liakoni	Interaktionen
Oct 11, 2023	Prof. Evangelia Liakoni	Unerwünschte Wirkungen

Lectures for Dental Medicine Students: Clinical Pharmacology

Date	Lecturer	Titel of the lecture
Feb 20, 2023	PD Stefan Weiler	Einführung in die Pharmakokinetik (2h)
Oct 25, 2023	Dr. Elias Bekka	Antikoagulation
Nov 01, 2023	PD Felix Hammann	Pat. mit akuten med. Problemen
Nov 08, 2023	PD Felix Hammann	Pat. mit chronischen med. Problem
Nov 15, 2023	Prof. Manuel Haschke	Antibiotika 1
Nov 22, 2023	Prof. Manuel Haschke	Antibiotika 2
Nov 29, 2023	Sarah Banholzer	UAW im Mund
Dec 06, 2023	Prof. Evangelia Liakoni	Analgetika 1
Dec 13, 2023	Prof. Evangelia Liakon	Analgetika 2

Lectures for Pharmacy Students (Bachelor): Clinical Pharmacology

Date	Lecturer	Titel of the lecture
Feb 23, 2023	PD Evangelia Liakoni	Asthma, COPD, Pneumonien
Feb 24, 2023	PD Evangelia Liakoni	Asthma, COPD, Pneumonien
Feb 28, 2023	PD Felix Hammann	Biopharmazie
Mar 07, 2023	Dr. Verena Schöning	Biopharmazie
Mar 10, 2023	PD Felix Hammann	Einführung Pharmazeutische Wissenschaft
Mar 14, 2023	PD Felix Hammann	Biopharmazie
Mar 21, 2023	PD Felix Hammann	Biopharmazie
Mar 23, 2023	Prof. Manuel Haschke	Opioidanalgetika
Mar 24, 2023	Dr. Laura Hermann	Nicht-Opioid Analgetika
Mar 28, 2023	PD Felix Hammann	Biopharmazie
Mar 30, 2023	PD Evangelia Liakoni	Schmerz, neuropathisch
Mar 30, 2023	Prof. Manuel Haschke	Kopfschmerzen, Migräne
Apr 04, 2023	Dr. Vera van der Velpen	Biopharmazie
Apr 18, 2023	PD Felix Hammann	Biopharmazie
Apr 21, 2023	Prof. Stephan Krähenbühl	Schilddrüsenkrankheiten
Apr 25, 2023	PD Felix Hammann	Biopharmazie
Apr 27, 2023	Prof. Manuel Haschke	Hypophysäre Störungen
Apr 28, 2023	PD Evangelia Liakoni	Dyslipidämie
May 02, 2023	Samuel Christen	Biopharmazie
May 04, 2023	PD Stefan Weiler	Diabetes
May 05, 2023	Prof. Stephan Krähenbühl	Geschlechtshormone, Kontrazeptiva
May 09, 2023	Prof. Manuel Haschke	Biopharmazie
May 16, 2023	Prof. Carlo Largiadèr	Biopharmazie
May 23, 2023	Prof. Carlo Largiadèr	Biopharmazie
May 25, 2023	PD Felix Hammann	Nierenkrankheiten, Dialyse, Dosisanpassung
May 26, 2023	PD Felix Hammann	HWI, Inkontinenz
May 30, 2023	Prof. Manuel Haschke	Biopharmazie
Jun 01, 2023	PD Stefan Weiler	Polypharmazie
Jun 02, 2023	PD Evangelia Liakoni	Klinische Toxikologie
Sep 28, 2023	PD Stefan Weiler	Pharmakokinetik I & II
Oct 03, 2023	PD Stefan Weiler	Pharmakokinetik III
Oct 12, 2023	Sarah Banholzer	Arzneimittelsicherheit/unerwünschte Ereignisse/ Pharmakovigilanz
Oct 17, 2023	PD Stefan Weiler	Virale und retrovirale KH
Oct 19, 2023	PD Stefan Weiler	Pilzkrankungen Mycobacterielle KH
Oct 24, 2023	Prof. Manuel Haschke	Bakterielle Infektionen I & II
Oct 26, 2023	Prof. Manuel Haschke	Bakterielle Infektionen III & IV
Oct 31, 2023	PD Stefan Weiler	Parasiten / Malaria
Nov 02, 2023	PD Felix Hammann	Hypertonie
Nov 07, 2023	PD Felix Hammann	Herzinsuffizienz, Rhythmusstörungen
Nov 09, 2023	Prof. Stephan Krähenbühl	Venöse KH
Nov 14, 2023	Prof. Stephan Krähenbühl	Arterielle KH

Lectures for Pharmacy Students (Master): Clinical Pharmacology

Date	Lecturer	Titel of the lecture
Mar 30, 2023	PD Stefan Weiler	Antikoagulantien – Bridging
Apr 06, 2023	PD Stefan Weiler	Geriatric / Niereninsuffizienz (3h)
Apr 20, 2023	PD Evangelia Liakoni	Beurteilung von Labor-Parametern (TDM) (2h)
Sep 19, 2023	Sarah Banholzer	Vertiefung Pharmakovigilanz

3.2. Coordination PBL Medical Students 3rd year (2023/2024)

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, IX)

3.3. Tutorials (study year 2023/2024)

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. Thomas Kaufmann

Dr. Darko Stojkov

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 18, 2023	Prof. Dr. Patrycja Nowak-Sliwinska, Institute of Pharmaceutical Sciences, University of Geneva	Why one drug is not enough?	G. Konstantinidou
Feb 01, 2023	PD Dr. Stephan Kellenberger, Department of Biomedical Sciences, University of Lausanne	Cellular roles and molecular mechanisms of acid-sensing ion channels	A. Huwiler
Feb 28, 2023	Prof. Rami Aqeilan, Lautenberg Center for Immunology and Cancer Research, Hebrew University – Hadassah Medical School, Jerusalem, Israel	Non-canonical roles for long and fragile genes in cancer and neuropathologies	H.-U. Simon
Mar 14, 2023	Prof. Dr. Andreas Strasser, The Walter and Eliza Hall Institute of Medical Research (WEHI), Melbourne, Australia	How does the tumour suppressor p53 prevent the development of cancer?	T. Kaufmann
Mar 15, 2023	Prof. Dr. Manuele Rebsamen, Department of Immunobiology, University of Lausanne	Solute carriers in metabolism and (auto)immunity: molecular mechanisms and therapeutic potential	G. Konstantinidou
Jun 22, 2023	Dr. Gergely Gyimesi, Department of Biomedical Research/ Nephrology, University of Bern	SLC Atlas: towards a unified view	A. Huwiler
Oct 11, 2023	PD Dr. med. Tatiana Breanova-Ertl, Universitätsklinik für Neurologie, Inselspital, Bern	N-Acetyl-L-Leucine: A symptomatic drug with neuroprotective potential?	A. Huwiler

Oct 18, 2023	Prof. Dr. med. Pier Paolo Scaglioni, Division of Hematology Oncology, University of Cincinnati, USA	Lipid metabolism regulates ferroptosis in lung cancer	G. Konstantinidou
Nov 15, 2023	Prof. Dr. med. Dagmar Meyer zu Heringdorf, Pharmazentrum Frankfurt, Frankfurt am Main	News in cellular Ca ²⁺ signalling by sphingosine 1-phosphate	A. Huwiler

3.5. Academic Degrees

Verschoor Danielle, PhD, University of Bern

Thesis: “Granulocytes; fragile, but resilient Unraveling the treatment resistance of granulocytes” (Feb 2023)
Supervisor: Prof. Stephan von Gunten

Hugonnet Marjolane, PhD, University of Bern

Thesis: “Sweet control: Sialoglycans in lymphocyte-mediated immunity” (Oct 2023)
Supervisor: Prof. Stephan von Gunten

Gigon Lea, PhD, University of Bern

Thesis: “Synergistic antimicrobial function of eosinophil major basic protein and mitochondrial DNA, two components of eosinophil extracellular traps” (Nov 2023)
Supervisor: Prof. Hans-Uwe Simon

Hosseini Aref, PhD, University of Bern

Thesis: “The role of eosinophils in the homeostasis of adipose tissue” (Dec 2023)
Supervisor: Prof. Hans-Uwe Simon

Corinne Felder, M.Sc. pharm., University of Basel

Thesis: “Development of a novel functional mast cell assay to diagnose allergies” (Jun 2023)
Supervisor: PD Dr. Urs Duthaler, Prof. Hans-Uwe Simon

Roth Jana, M.Sc., University of Bern

Thesis: “Characterization and development of a cellular assay to detect allergies” (Jun 2023)
Supervisor: Prof. Thomas Kaufmann

Gosheva Gordana, M.Sc. pharm., University of Ljubljana

Thesis: “Characterization of pore formation by major basic protein in cell membranes” (Oct 2023)
Supervisor: Prof. Hans-Uwe Simon

Bessire Marcine, B.Sc., University of Bern

Thesis: “Characterization of Recombinant Siglec-Fc: From Production to Functional Analysis” (May 2023)
Supervisor: Prof. Stephan von Gunten

Sánchez Fernández Celia, B.Sc. pharm, University of Bern

Thesis: “Identification of Siglec-7 ligands and Siglec-9 ligands on cancer-derived exosomes” (May 2023)
Supervisor: Prof. Stephan von Gunten

Zwahlen Vanessa, B.Sc., University of Bern

Thesis: “The effects of dexamethasone on primed and unprimed eosinophils” (Jun 2023)
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
 Roxana Manaila, PhD student
 Jessica D'Agostino, PhD student
 Shaimaa Khidr, PhD student
 Dr. Andrey Marchev, Guest Scientist
 Dr. Gergely Gyimesi, Senior Research Assistant
 Helen Broughton, MD student

In memoriam Prof. Dr Andrea Huwiler 1966-2023

It is with great sadness that we remember Prof. Andrea Huwiler, a passionate pharmacologist, committed university lecturer and respected scientist.

Born in Norway in 1966, she joined the Institute of Pharmacology in 2006 and left a lasting impression. She has served as Director since 2021, making a significant contribution to our growth and success.

Prof. Andrea Huwiler was a dedicated researcher and an inspiring teacher. Her passion for pharmacology and her tireless efforts to advance the field were admirable. She paid particular attention to young scientists and students, whom she taught and supported with her expertise.

Mrs. Andrea Huwiler will be remembered as a warm-hearted, helpful, caring and highly inspiring person. We will miss her deeply.

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.

Loss of S1P Lyase Expression in Human Podocytes Causes a Reduction in Nephrin Expression That Involves PKC δ Activation

Imeri F, Stepanovska Tanturovska B, Manaila R, Pavenstädt H, Pfeilschifter J, Huwiler A
Sphingosine 1-phosphate (S1P) lyase (SPL, Sgpl1) is an ER-associated enzyme that irreversibly degrades the bioactive lipid, S1P, and thereby regulates multiple cellular functions attributed to S1P. Biallelic mutations in the human Sgpl1 gene lead to a severe form of a particular steroid-resistant nephrotic syndrome, suggesting that the SPL is critically involved in maintaining the glomerular ultrafiltration barrier, which is mainly built by glomerular podocytes. In this study, we have investigated the molecular effects of SPL knockdown (kd) in human podocytes to better understand the mechanism underlying nephrotic syndrome in patients. A stable SPL-kd cell line of human podocytes was generated by the lentiviral shRNA transduction method and was characterized for reduced SPL mRNA and protein levels and increased S1P levels. This cell line was further studied for changes in those podocyte-specific proteins that are known to regulate the ultrafiltration barrier. We show here that SPL-kd leads to the downregulation of the nephrin protein and mRNA expression, as well as the Wilms tumor suppressor gene 1 (WT1), which is a key transcription factor regulating nephrin expression. Mechanistically, SPL-kd resulted in increased total cellular protein kinase C (PKC) activity, while the stable downregulation of PKC δ revealed increased nephrin expression. Furthermore, the pro-inflammatory cytokine, interleukin 6 (IL-6), also reduced WT1 and nephrin expression. In addition, IL-6 caused increased PKC δ Thr505 phosphorylation, suggesting enzyme activation. Altogether, these data demonstrate that nephrin is a critical factor downregulated by the loss of SPL, which may directly cause podocyte foot process effacement as observed in mice and humans, leading to albuminuria, a hallmark of nephrotic syndrome. Furthermore, our in vitro data suggest that PKC δ could represent a new possible pharmacological target for the treatment of a nephrotic syndrome induced by SPL mutations.

Keywords: Wilms tumor suppressor gene 1; glomerular disease; nephrin; nephrotic syndrome; podocytes; protein kinase Cdelta; sphingosine 1-phosphate; sphingosine 1-phosphate lyase.

See original publication No 1

Original publications

1. Imeri F, Stepanovska Tanturovska B, Manaila R, Pavenstädt H, Pfeilschifter J, **Huwiler A**: Loss of S1P Lyase Expression in Human Podocytes Causes a Reduction in Nephrin Expression That Involves PKC δ Activation. *Int J Mol Sci.* 24 (2023), 1-15.
2. Beyođlu D, Schwalm S, Semmo N, **Huwiler A**, Idle JR: Hepatitis C Virus Infection Upregulates Plasma Phosphosphingolipids and Endocannabinoids and Downregulates Lyso-phosphoinositols. *Int J Mol Sci.* 24 (2023), 1-17.

Review article & Editorials

1. Manaila R, **Huwiler A**: Polypharmacy in acute and chronic kidney diseases. *Inn Med (Heidelb)* 65. (2023), 22-28.
2. **Huwiler A**: Topical Collection: New Insights on Sphingolipids in Health and Disease. *Int J Mol Sci.* 24 (2023), 1-5.
3. **Huwiler A**, Beck KF, Pfeilschifter J: Cross-Regulation of the Cellular Redox System, Oxygen, and Sphingolipid Signalling. *Metabolites* 13 (2023), 1-21.
4. Stepanovska Tanturovska B, Manaila R, Fabbro D, **Huwiler A**: Lipids as Targets for Renal Cell Carcinoma Therapy. *Int J Mol Sci.* 24 (2023), 1-25.

Group Prof. Thomas Kaufmann



Photo: Group Kaufmann

Group members: Philippe JeanRichard, PhD student
 Ali Jazaeri, PhD student
 Lyang Wu, PhD student
 Daniel Bachmann, Lab Technician
 Jana Roth, M.Sc. student
 Fitzpatrick Georgia, M.Sc. guest student
 Ananthanarayan, Aparna, M.Sc. student

Our group is interested in the molecular mechanisms of programmed cell death (PCD), in particular apoptosis and necroptosis, their physiological and pathophysiological roles and the link between cell death and inflammation. Apoptosis is recognized as the most relevant (patho-) physiological form of PCD, with deregulated apoptosis being a major characteristic of many cancer cells, while 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.

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 “non-apoptotic” roles 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 and cellular proliferation.

Novel classes of small molecule inhibitors targeting central cell death pathways, in particular BH3 mimetics and Smac mimetics, respectively, are of great interest in our lab. We explore ways to directly kill highly resistant cancer cells with the right combination of these highly specific drugs, or to sensitize cells towards classical chemotherapeutics. Furthermore, we hypothesize that BH3 mimetics have a potential to selectively kill subsets of activated immune cells.

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 neutrophil, macrophage, basophil or mast cell lineages. Those cells can be differentiated in vitro into mature effector cells in nearly unlimited numbers. An advantage of “Hoxb8” cells over primary cells 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 mast cells, we have established a functional mast cell activation test (MAT) using Hox8 mast cells, in which the type I allergic reaction (mediated by IgE > IgE receptor) can be mimicked in a safe and efficient manner in a test tube. This test allows to study molecular mechanisms of many allergies, with a special focus on food allergies.

Original publication

1. Lambrecht R, Rudolf F, Ückert AK, Sladky VC, Phan TS, Jansen J, Naim S, **Kaufmann T**, Keogh A, Kirschnek S, Mangerich A, Stengel F, Leist M, Villunger A, Brunner T: Non-canonical BIM-regulated energy metabolism determines drug-induced liver necrosis. *Cell Death Differ.* 31 (2024), 119-131.

Review articles

1. Bachmeier-Zbären N, Kinet JP, **Kaufmann T**, Eggel A: Mast cell activation test. *Science Direct* (2023), 1-11
2. Vitale I, Pietrocola F, Guilbaud E, Aaronson SA, Abrams JM, Adam D, Agostini M, Agostinis P, Alnemri ES, Altucci L, Amelio I, Andrews DW, Aqeilan RI, Arama E, Baehrecke EH, Balachandran S, Bano D, Barlev NA, Bartek J, Bazan NG, Becker C, Bernassola F, Bertrand MJM, Bianchi ME, Blagosklonny MV, Blander JM, Blandino G, Blomgren K, Borner C, Bortner CD, Bove P, Boya P, Brenner C, Broz P, Brunner T, Damgaard RB, Calin GA, Campanella M, Candi E, Carbone M, Carmona-Gutierrez D, Cecconi F, Chan FK, Chen GQ, Chen Q, Chen YH, Cheng EH, Chipuk JE, Cidlowski JA, Ciechanover A, Ciliberto G, Conrad M, Cubillos-Ruiz JR, Czabotar PE, D'Angiolella V, Daugaard M, Dawson TM, Dawson VL, De Maria R, De Strooper B, Debatin KM, Deberardinis RJ, Degtarev A, Del Sal G, Deshmukh M, Di Virgilio F, Diederich M, Dixon SJ, Dynlacht BD, El-Deiry WS, Elrod JW, Engeland K, Fimia GM, Galassi C, Ganini C, Garcia-Saez AJ, Garg AD, Garrido C, Gavathiotis E, Gerlic M, Ghosh S, Green DR, Greene LA, Grone-meyer H, Häcker G, Hajnóczky G, Hardwick JM, Haupt Y, He S, Heery DM, Hengartner MO, Hetz C, Hildeman DA, Ichijo H, Inoue S, Jäättelä M, Janic A, Joseph B, Jost PJ, Kanneganti TD, Karin M, Kashkar H, **Kaufmann T**,...: Apoptotic cell death in disease-Current understanding of the NCCD 2023. *Cell Death Differ.* 30 (2023),1038-1154.
3. **Kaufmann T**, Simon HU: Pharmacological Induction of Granulocyte Cell Death As Therapeutic Strategy. *Annu Rev Pharmacol Toxicol.* 67 (2023), 231-247.

Group PD Dr. Georgia Konstantinidou



Photo: Group Konstantinidou

Group members:

Simone Falco, PhD student
 Maciej Garczyk, PhD student
 Gonçalo Outeiro de Pinho, PhD student
 Giulia Pelliello, PhD guest student
 Muthita Pitaktrairat, M.Sc. student
 Katrine Holm, M.Sc. student
 Zhaoyue He, Postdoctoral fellow

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.

Original publication

1. Deng H, Ge H, Dubey C, Losmanova T, Medová M, **Konstantinidou G**, Mutlu SM, Birrer FE, Brodie TM, Stroka D, Wang W, Peng RW, Dorn P, Marti TM: An optimized protocol for the generation and monitoring of conditional orthotopic lung cancer in the KP mouse model using an adeno-associated virus vector compatible with biosafety level 1. *Cancer Immunol Immunother.* 71 (2023), 4457-4470.

Review

1. Saliakoura M, **Konstantinidou G**: Lipid Metabolic Alterations in KRAS Mutant Tumors: Unmasking New Vulnerabilities for Cancer Therapy. *Int J Mol Sci.* 24 (2023), 1-16.

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



Photo: Group Simon/Yousefi

Group members: Kevin Oberson, Lab Technician
 Dr. Joanna Boros-Majewska, Lab Technician
 Dr. Darko Stojkov, Postdoctoral fellow
 Dr. Nikita Markov, Postdoctoral fellow
 Lea Gigon, PhD student
 Yihe Chen, PhD student
 Aref Hosseini, PhD student
 Timothée Fettelet, PhD student
 Gulnaz Sharapova, PhD guest student
 Sirina Kurbangaleeva, PhD guest student
 Ella Glodjajic, M.Sc. student
 Corinne Felder, M.Sc. student
 Gordana Gosheva, M.Sc. student

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 basophils 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, hy-

pereosinophilic 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 2023.

The regulatory role of eosinophils in adipose tissue depends on autophagy

Hosseini A, Germic N, Markov N, Stojkov D, Oberson K, Yousefi S, Simon HU

Obesity is a metabolic condition that elevates the risk of all-cause mortality. Brown and beige adipose tissues, known for their thermogenic properties, offer potential therapeutic targets for combating obesity. Recent reports highlight the role of immune cells, including eosinophils, in adipose tissue homeostasis, while the underlying mechanisms are poorly understood. To study the role of autophagy in eosinophils in this process, we used a genetic mouse model lacking autophagy-associated protein 5 (Atg5), specifically within the eosinophil lineage. The absence of Atg5 in eosinophils led to increased body weight, impaired glucose metabolism, and alterations in the cellular architecture of adipose tissue. Our findings indicate that Atg5 modulates the functional activity of eosinophils within adipose tissue rather than their abundance. Moreover, RNA-seq analysis revealed upregulation of arginase 2 (Arg2) in Atg5-knockout eosinophils. Increased Arg2 activity was shown to suppress adipocyte beiging. Furthermore, we observed enrichment of the purine pathway in the absence of Atg5 in eosinophils, leading to a proinflammatory shift in macrophages and a further reduction in beiging. The data shed light on the importance of autophagy in eosinophils and its impact on adipose tissue homeostasis by suppressing Arg2 expression and limiting inflammation in adipose tissue.

Keywords: adipose tissue, arginase 2, Atg5, autophagy, beiging, eosinophils, macrophages.

See original publication No 1

Syntaxin-4 and SNAP23 are involved in neutrophil degranulation, but not in the release of mitochondrial DNA during NET formation

Gigon L, Fettlelet T, Miholic M, McLeish KR, Yousefi S, Stojkov D, Simon HU

Neutrophils are a specialized subset of white blood cells, which have the ability to store pre-formed mediators in their cytoplasmic granules. Neutrophils are well-known effector cells involved in host protection against pathogens through diverse mechanisms such as phagocytosis, degranulation, extracellular traps, and oxidative burst. In this study, we provide evidence highlighting the significance of the SNARE proteins syntaxin-4 and synaptosomal-associated protein (SNAP) 23 in the release of azurophilic granules, specific granules, and the production of reactive oxygen species in human neutrophils. In contrast, the specific blockade of either syntaxin-4 or SNAP23 did not prevent the release of mitochondrial dsDNA in the process of neutrophil extracellular trap (NET) formation. These findings imply that degranulation and the release of mitochondrial dsDNA involve at least partially distinct molecular pathways in neutrophils.

Keywords: EET; NET; SNAP23; degranulation; eosinophils; mitochondrial DNA; neutrophils; syntaxin-4.

See original publication No 2

NET formation is independent of gasdermin D and pyroptotic cell death

Stojkov D, Claus MJ, Kozlowski E, Oberson K, Schären OP, Benarafa C, Yousefi S, Simon HU

Neutrophil extracellular traps (NETs) are DNA scaffolds coated with granule proteins that are released by neutrophils to ensnare and kill bacteria. NET formation occurs in response to many stimuli through independent molecular pathways. Although NET release has been equated to a form of lytic cell death, live neutrophils can rapidly release antimicrobial NETs. Gasdermin D (GSDMD), which causes pyroptotic death in macrophages, is thought to be required for NET formation by neutrophils. Through experiments with known physiological activators of NET formation and ligands that activate canonical and noncanonical inflammasome signaling pathways, we demonstrated that *Gsdmd*-deficient mouse neutrophils were as competent as wild-type mouse neutrophils in producing NETs. Furthermore, GSDMD was not cleaved in wild-type neutrophils during NET release in response to inflammatory mediators. We found that activation of both canonical and noncanonical inflammasome signaling pathways resulted in GSDMD cleavage in wild-type neutrophils but was not associated with cell death. Moreover, NET formation as a result of either pathway of inflammasome activation did not require GSDMD. Together, these data suggest that NETs can be formed by viable neutrophils after inflammasome activation and that this function does not require GSDMD.

Keywords: GSDMD; mitochondrial DNA; neutrophils; NET.

See original publication No 3

The BK channel limits the pro-inflammatory activity of macrophages

Chen Y, Markov N, Gigon L, Hosseini A, Yousefi S, Stojkov D, Simon HU

Macrophages play a crucial role in the innate immune response, serving as key effector cells in the defense against pathogens. We employed BK-knockout macrophages and noted that the absence of BK channel promotes the polarization of macrophages towards a pro-inflammatory phenotype, known as M1 macrophages. Specifically, the absence of the BK channel resulted in a significant increase in the secretion of the pro-inflammatory cytokine IL-6 and enhanced the activity of extracellular signal-regulated kinases 1 and 2 (Erk1/2 kinases), Ca²⁺/calmodulin-dependent protein kinase II (CaMKII), and the transcription factor ATF-1 within M1 macrophages. Additionally, the lack of the BK channel promoted the activation of the AIM2 inflammasome without affecting the activation of the NLRC4 and NLRP3 inflammasomes. To further investigate the role of the BK channel in regulating AIM2 inflammasome activation, we utilized BK channel inhibitors, such as paxilline and iberiotoxin, along with the BK channel activator NS-11021. Pharmacological inactivation of the BK channel increased, and its stimulation inhibited IL-1 β production following AIM2 inflammasome activation in wild-type macrophages. Moreover, wild-type macrophages displayed increased calcium influx when activated with the AIM2 inflammasome, whereas BK-knockout macrophages did not due to the impaired extracellular calcium influx upon activation. Furthermore, under conditions of calcium-free medium, IL-1 β production following AIM2 inflammasome activation was increased in both wild-type and BK-knockout macrophages. This suggests that the BK channel is required for the influx of extracellular calcium in macrophages, thus limiting AIM2 inflammasome activation.

See original publication No 4

Original publications

1. Hosseini A, Germic N, Markov N, Stojkov D, Oberson K, **Yousefi S, Simon HU**: The regulatory role of eosinophils in adipose tissue depends on autophagy. *Front. Immunol.* (2024), 3:14:1331151. doi: 10.3389/fimmu.2023.1331151. eCollection 2023.
2. Gigon L, Fettlelet T, Miholic M, McLeish KR, **Yousefi S, Stojkov D, Simon HU**: Syntaxin-4 and SNAP23 are involved in neutrophil degranulation, but not in the release of mitochondrial DNA during NET formation. *Front Immunol.* 14 (2023), doi: 10.3389/fimmu.2023.1272699. eCollection 2023.
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. Chen Y, Markov N, Gigon L, Hosseini A, **Yousefi S, Stojkov D, Simon HU**: The BK channel limits the pro-inflammatory activity of macrophages. *Cells* 13 (2023) 322.
5. Hosseini A, Stojkov D, Fettlelet T, Bilyy R, **Yousefi S, Simon HU**: Transcriptional Insights of Oxidative Stress and Extracellular Traps in Lung Tissues of Fatal COVID-19 Cases. *Int J Mol Sci.* 24 (2023), doi: 10.3390/ijms24032646.
6. Heil A, Kuehlewindt T, Godat A, **Simon HU**, Simon D, Schreiner P, Saner C, Vavricka SR, Biedermann L, Safroneeva E, Rossel JB, Limacher A, Straumann A, Schoepfer AM, Greuter T: Histological Phenotyping in Eosinophilic Esophagitis: Localized Proximal Disease Is Infrequent but Associated with Less Severe Disease and Better Disease Outcome. *Int Arch Allergy Immunol.* (2023),1-10. doi: 10.3389/fimmu.2023.1272699. eCollection 2023.
7. Greuter T, Straumann A, Fernandez-Marrero Y, Germic N, Hosseini A, Chanwangpong 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**: A multicenter long-term cohort study of eosinophilic esophagitis variants and their progression to EoE over time. *Clin Transl Gastroenterol.* (2024), doi: 10.14309/ctg.0000000000000664. Online ahead of print.
8. Thormann K, Lüthi AS, Deniau F, Heider A, Cazzaniga S, Radonjic-Hoesli S, Lehmann M, Schlapbach C, Herzog EL, Kreuzer M, Zinkernagel MS, Akdis CA, Zysset-Burri DC, **Simon HU**, Simon D: Dupilumab-associated ocular surface disease is characterized by a shift from Th2/Th17 toward Th1/Th17 inflammation. *Allergy.* (2024), doi: 10.1111/all.16045. Online ahead of print.

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1. Stojkov D, **Yousefi S, Simon HU**: NETs: Important players in asthma? *J Allergy Clin Immunol.* 153 (2024), 100-102. doi: 10.1016/j.jaci.2023.09.031
2. Jesenak M, Diamant Z, Simon D, Tufvesson E, Seys SF, Mukherjee M, Lacy P, Vijverberg S, Slisz T, Sediva A, **Simon HU**, Striz I, Plevkova J, Schwarze J, Kosturiak R, Alexis NE, Untersmayr E, Vasakova MK, Knol E, Koenderman L: Eosinophils-from cra-

- dle to grave: An EAACI task force paper on new molecular insights and clinical functions of eosinophils and the clinical effects of targeted eosinophil depletion. *Allergy*. (2023), doi: 10.1111/all.15884. Online ahead of print.
3. Brichkina A, **Simon HU**: A novel role for mitochondrial fission in macrophages: trained innate immunity induced by beta-glucan. *Cell Mol Immunol*. 20 (2023), 864-866.
 4. **Simon HU**: Legends of allergology and immunology: Alex Straumann. *Allergy*. 78 (2023), 596-598.
 5. Shuvalov O, Kirdeeva Y, Daks A, Fedorova O, Parfenyev S, **Simon HU**, Barlev NA: Phytochemicals Target Multiple Metabolic Pathways in Cancer. *Antioxidants (Basel)*. 12 (2023), doi: 10.3390/antiox12112012.
 6. Gigon L, Fettlelet T, **Yousefi S**, Simon D, **Simon HU**: Eosinophils from A to Z. *Allergy*. 78 (2023), 1810-1846.
 7. Vitale I, Pietrocola F, Guilbaud E, Aaronson SA, Abrams JM, Adam D, Agostini M, Agostinis P, Alnemri ES, Altucci L, Amelio I, Andrews DW, Aqeilan RI, Arama E, Baehrecke EH, Balachandran S, Bano D, Barlev NA, Bartek J, Bazan NG, Becker C, Bernassola F, Bertrand MJM, Bianchi ME, Blagosklonny MV, Blander JM, Blandino G, Blomgren K, Borner C, Bortner CD, Bove P, Boya P, Brenner C, Broz P, Brunner T, Damgaard RB, Calin GA, Campanella M, Candi E, Carbone M, Carmona-Gutierrez D, Cecconi F, Chan FK, Chen GQ, Chen Q, Chen YH, Cheng EH, Chipuk JE, Cidlowski JA, Ciechanover A, Ciliberto G, Conrad M, Cubillos-Ruiz JR, Czabotar PE, D'Angiolella V, Daugaard M, Dawson TM, Dawson VL, De Maria R, De Strooper B, Debatin KM, Deberardinis RJ, Degtarev A, Del Sal G, Deshmukh M, Di Virgilio F, Diederich M, Dixon SJ, Dynlacht BD, El-Deiry WS, Elrod JW, Engeland K, Fimia GM, Galassi C, Ganini C, Garcia-Saez AJ, Garg AD, Garrido C, Gavathiotis E, Gerlic M, Ghosh S, Green DR, Greene LA, Gronemeyer H, Häcker G, Hajnóczky G, Hardwick JM, Haupt Y, He S, Heery DM, Hengartner MO, Hetz C, Hildeman DA, Ichijo H, Inoue S, Jäättelä M, Janic A, Joseph B, Jost PJ, Kanneganti TD, Karin M, Kashkar H, Kaufmann T, **Simon HU** ...: Apoptotic cell death in disease-Current understanding of the NCCD 2023. *Cell Death Differ*. 30 (2023), 1097-1154.
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 10. Kaufmann T, **Simon HU**: Pharmacological Induction of Granulocyte Cell Death as Therapeutic Strategy. *Annu Rev Pharmacol Toxicol*. 63 (2023), 231-247.
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Group Prof. Stephan von Gunten



Photo: Group von Gunten

Group members: Marjolaine Claire Hugonnet, PhD student
 Darien Toledo, PhD student
 Giselle Hevia Hernandez, PhD student
 Lukas Mürner, PhD student
 Katsaros Dimitrios Alexander, PhD student
 Aldona von Gunten, Technical Specialist
 Mira Christen, PhD, Scientific support
 Marcine Bessire, B.Sc. student
 Celtia Sanchez Fernández, B.Sc. student
 Vanessa Zwahlen, B.Sc. student

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. Siglecs 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.

Original publications

1. Plattner K, Augusto G, Muerner L, **von Gunten S**, Jörg L, Engeroff P, Bachmann MF, Vogel M: IgE glycosylation is essential for the function of omalizumab. *Allergy*. 78 (2023), 2546-2549.
2. Zhu C, Potenza DM, Yang Y, Ajalbert G, Mertz KD, **von Gunten S**, Ming XF, Yang Z: Role of pulmonary epithelial arginase-II in activation of fibroblasts and lung inflammation. *Aging Cell*. 22 (2023, doi: 10.1111/ace1.13790).
3. Démouilins T, Schulze K, Ebensen T, Techakriengkrai N, Nedumpun T, Englezou PC, Gerber M, Hlushchuk R, Toledo D, Djonov V, **von Gunten S**, McCullough KC, Liniger M, Guzmán CA, Suradhat S, Ruggli N: Coatsome-replicon vehicles: Self-replicating RNA vaccines against infectious diseases. *Nanomedicine*. 49 (2023), doi: 10.1016/j.nano.2023.102655
4. Almizraq RJ, Frias Boligan K, Lewis BJB, Cen S, Whetstone H, Spirig R, Käsermann F, Campbell IK, **von Gunten S**, Branch DR: Modulation of Neutrophil Function by Recombinant Human IgG1 Fc Hexamer in the Endogenous K/BxN Mouse Model of Rheumatoid Arthritis. *Pharmacology*. 108 (2023), 176-187.
5. Mehta AY, Tilton CA, Muerner L, **von Gunten S**, Heimburg-Molinaro J, Cummings RD: Reusable glycan microarrays using a microwave assisted wet-erase (MAWE) process. *Glycobiology*. 2023 Nov 14: cwad091. doi: 10.1093/glycob/cwad091. Online ahead of print.

Review article

1. **von Gunten S**, Schneider C, Imamovic L, Gorochov G: Antibody diversity in IVIG: Therapeutic opportunities for novel immunotherapeutic drugs. *Front Immunol*. 14 (2023), doi: 10.3389/fimmu.2023.1166821.

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
- 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
- Christina Kotoula, PhD student
- Kristina Žajdlíková, Lab technician
- Mats Hirt, Lab technician
- Ji-Ae Park Student assistant

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. In a clinical study supported by SNF we investigate the impact of the nicotine concentration on the efficacy of a nicotine salt vape pod system as smoking cessation tool in patients willing to stop smoking. Another SNF project investigates whether paracetamol provides any additional analgesic effect in patients treated with strong opioids using a double-blind drug withdrawal design. In a third SNF project in collaboration with Prof. M. Wertli, we compare the effect of ibuprofen vs metamizole with or without short intervention in a randomized, double-blind clinical trial in patients with acute or subacute low

back pain. In a further set of projects funded by a large UNITAID grant, ivermectin is investigated in the framework of an endectocide-based malaria intervention field trial in Africa.

Original publications

1. Buetler VA, Braunshausen AM, Weiler S, Klukowska-Rötzler J, Exadaktylos AK, **Liakoni E.**: Characteristics of emergency department presentations following ingestion of *Taxus baccata* (yew). Clin Toxicol (Phila). 2023 Jan 3:1-6. doi: 10.1080/15563650.2022.2158097. Epub ahead of print. PMID: 36594830.
2. **Kern C**, Müller P, Chaccour C, Liechti ME, **Hammann F**, Duthaler U.: Pharmacokinetics of ivermectin metabolites and their activity against Anopheles stephensi mosquitoes. Malar J. 2023 Jun 24;22(1):194. doi: 10.1186/s12936-023-04624-0. PMID: 37355605; PMCID: PMC10290335.
3. Vallersnes OM, Dines AM, Wood DM, Heyerdahl F, Hovda KE, Yates C, Giraudon I, Caganova B, Ceschi A, Galicia M, **Liakoni E**, Liechti ME, Miró Ò, Nosedá R, Persett PS, Pöld K, Schmid Y, Scholz I, Vigorita F, Dargan PI.: Self-discharge during treatment for acute recreational drug toxicity: an observational study from emergency departments in seven European countries. Int J Emerg Med. 2023 Nov 29;16(1):86. doi: 10.1186/s12245-023-00566-1. PMID: 38030969; PMCID: PMC10685690.

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Case report

1. Fuest L, **Banholzer S**, **Haschke M**, Vögelin E, **Weiler S**. Lokale Gewebeschädigung nach Wundspülung unter Druck mit Antiseptikum Swiss Medical Forum 2023;23(37):1292–1294

Other publications

1. **Banholzer S**, Scholz I, **Haschke M**, Stammschulte T. COVID-19-Impfstoffe: Wird die Einstufung «medizinisch wichtig» in den UAW-Meldungen korrekt angewendet, und gibt es Unterschiede zwischen den Meldungen von medizinischen Fachpersonen und von Patienten? Swissmedic Vigilance-News | Edition 31 – November 2023.
2. **Bekka E**, **Weiler S**. Interaktionen von Phytopharmaka. pharma-kritik 2023; 45(3)
3. Nosedá R, Franchi M, Pagnamenta A, Müller L, Dines AM, Giraudon I, Heyerdahl F, Eyer F, Hovda KE, Liechti ME, Miró Ò, Vallersnes OM, Yates C, Dargan PI, Wood DM, Ceschi A, On Behalf Of The **Euro-DEN Plus Research Group**. Determinants of Admission to Critical Care Following Acute Recreational Drug Toxicity: A Euro-DEN Plus Study. J Clin Med. 2023 Sep 14;12(18):5970. doi: 10.3390/jcm12185970. PMID: 37762912; PMCID: PMC10532086.

Additional Publications by PKI Members

Original publications

Wortmann JK, Barco S, Fumagalli RM, Voci D, Hügel U, Cola R, **Spirk D**, Kucher N, Sebastian T. Coagulation-monitored, dose-adjusted catheter-directed thrombolysis or pharmacomechanical thrombus removal in deep vein thrombosis. *Vasa*. 52 (2023), 416-422.

Ueki Y, Häner JD, Losdat S, Gargiulo G, Shibutani H, Bär S, Otsuka T, Kavaliauskaite R, Mitter VR, Temperli F, **Spirk D**, Stortecky S, Siontis GCM, Valgimigli M, Windecker S, Gutmann C, Koskinas KC, Mayr M, Räber L: Effect of Alirocumab Added to High-Intensity Statin on Platelet Reactivity and Noncoding RNAs in Patients with AMI: A Substudy of the PACMAN-AMI Trial. *Thromb Haemost*. 2023 Sep 11. doi: 10.1055/a-2156-7872.

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Barco S, Virdone S, Götschi A, Ageno W, Arcelus JI, Bingisser R, Colucci G, Cools F, Duerschmied D, Gibbs H, Fumagalli RM, Gerber B, Haas S, Himmelreich JCL, Hobbs R, Hohbohm L, Jacobson B, Kayani G, Lopes RD, MacCallum P, Micieli E, Righini M, Robert-Ebadi H, Rocha AT, Rosemann T, Sawhney J, Schellong S, Sebastian T, **Spirk D**, Stortecky S, Turpie AGG, Voci D, Kucher N, Pieper K, Held U, Kakkar AK; OVID and ETHIC Investigators: Enoxaparin for symptomatic COVID-19 managed in the ambulatory setting: An individual patient level analysis of the OVID and ETHIC trials. *Thromb Res*. 230 (2023), 27- 32.

Bär S, Kavaliauskaite R, Otsuka T, Ueki Y, Häner JD, Siontis GCM, Stortecky S, Shibutani H, Temperli F, Kaiser C, Iglesias JF, Jan van Geuns R, Daemen J, **Spirk D**, Engstrøm T, Lang I, Windecker S, Koskinas KC, Losdat S, Räber L: Impact of alirocumab on plaque regression and haemodynamics of non-culprit arteries in patients with acute myocardial infarction: a pre-specified substudy of the PACMAN-AMI trial. *EuroIntervention*. 19 (2023), 286- 296.

Voci D, Fedeli U, Valerio L, Schievano E, Righini M, Kucher N, **Spirk D**, Barco S: Mortality rate related to peripheral arterial disease: A retrospective analysis of epidemiological data (years 2008-2019). *Nutr Metab Cardiovasc Dis*. 33 (2023), 516- 522.

Voci D, Götschi A, Held U, Bingisser R, Colucci G, Duerschmied D, Fumagalli RM, Gerber B, Hasse B, Keller DI, Konstantinides SV, Mach F, Rampini SK, Righini M, Robert-Ebadi H, Rosemann T, Roth-Zetsche S, Sebastian T, Simon NR, **Spirk D**, Stortecky S, Vainora 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*. 221 (2023), 157- 163.

4.2. Organization of Meetings and Courses

Prof Andrea Huwiler

LS2 Annual Meeting 2023, organizer of symposium “Advances in Translational Pharmacology”, ~500 participants, Zürich (CH)

Prof. Hans-Uwe Simon

Workshop on “Cell Death and Disease” (together with C. Brancolini, K.-M. Debatin and P.H. Krammer), Villa Vigoni, Lovenno di Menaggio, Como (I), Sep 06-09, 2023

Prof. Stephan von Gunten

Symposium of the Swiss Society of Pharmacology and Toxicology (SSPT):
Progress in Pharmacology – Pharmacotherapy in Rheumatology
Bern (CH), Jan 25, 2023

Swiss Society of Pharmacology and Toxicology Spring Meeting 2023,
The Curious case of...Ageing
Bern (CH), Apr 18, 2023.

21th III-Bern International Summer School, Translational Medicine, Drug Discovery and Inspiration, Bönigen (CH), Aug 20-22, 2023

Prof. Thomas Kaufmann

21th III-Bern International Summer School, Translational Medicine, Drug Discovery and Inspiration, Bönigen (CH), Aug 20-22, 2023

12th Swiss Apoptosis and Autophagy Meeting (SA²M), Co-organizer, Bern (CH), Sep 7-8, 2023

PD Dr. Georgia Konstantinidou

Swiss Society of Pharmacology and Toxicology Spring Meeting 2023,
The Curious case of...Ageing
Bern (CH), Apr 18, 2023

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)	National Science Centre Poland
Austrian Science Fund (FWF)	Swiss Cancer League
German Research Foundation (DFG)	Swiss National Science Foundation (SNF)
L'Oréal Österreich	

Prof. Hans-Uwe Simon

Swiss National Science Foundation (SNF)	Swiss Cancer League
Novartis Foundation	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)
Dutch Cancer Society (DCS)

Canadian Glycomics Network
Best Cancer Now

4.4. Awards

Lukas Mürner**Prize poster presentation award**

Society for Glycobiology (SfG) at the 2023
Hawaii, HI, USA, Nov 2023.

Marjolaine Hugonnet**Prize for the best poster (category Pharmacology)**

Swiss Society of Experimental Pharmacology (SSEP), LS2 Annual Meeting 2023,
Zurich (CH), Feb 2023

4.5. Travel support

Jazaerijouneghani Ali

GCB Travel grant to participate at the European Workshop on Cell Death,
Fiuggi (IT) Jun 4-9, 2023

JeanRichard-dit-Bressel, Philippe

GCB Travel grant to participate at the European Workshop on Cell Death,
Fiuggi (IT) Jun 4-9, 2023

Darien Toledo Santamaria

SSPT Travel grant to participate at the 22th Meeting Barrier-and Transporter-Days,
Bad Herrenalb (GE), May 2023

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 of the Brandenburg Medical School (MHB), 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 2023:

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](http://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 and 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, University Hospital Bern

Prof. 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) (until May 2023)

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)

Associate Editor Frontiers in Pharmacology

Member of the American Society of Tropical Medicine and Hygiene

Member of the Bern Center for Precision Medicine

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

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.

The prize winner in 2023 was Dr. Redona Hafizi, University of Bern, for the best original publication addressing a problem in the fields of Experimental or Clinical Pharmacology: Sphingosine kinases 1 and 2 differentially regulate erythropoietin synthesis in mouse renal interstitial fibroblast-like cells.

Dr. Hafizi presented a public lecture on April 20, 2023, at the SSPT Spring Meeting.

8. Sponsors

8.1. Research Grants

Prof. Andrea Huwiler

Swiss National Science Foundation (grant No. 310030_219605/1)

Prof. Thomas Kaufmann

Swiss National Science Foundation (grant No 310030_201199)

PD Dr. Georgia Konstantinidou

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 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. 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)

Prof. 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)

PD Dr. 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 (UROBOT TRIAL), Fondation Leenards (leenards.ch) 2023 – 2025.

8.2. Meetings

Swiss Society of Pharmacology and Toxicology (SSPT): Progress in Pharmacology – Progress in Pharmacology, Pharmakotherapie in der Rheumatologie; Bern (CH), Jan 25th, 2023

Pfizer AG
Eli Lilly (Suisse) SA
CSL Vifor AG
GSK

**22th International Summer School
Seehotel La Terrasse, CH 3806 - Bönigen, Aug 20 – 22, 2023**

Bristol Myers Squibb (BMS)
Cannapharm AG, Burgdorf
Meintrup DWS Laborgeräte
Mepha-Teva
Mycrosynth AG, Balgach
Medizinische Fakultät, Universität Bern
Zentrum für Labormedizin, Inselspital Bern
Graduate School for Cellular and Biomedical Sciences, Universität Bern

8.3. Other Support

Bürgi Fonds Seminar series of the institute