Annual Report 2020

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 zwanzigste umfassende Jahresbericht des Instituts für Pharmakologie (PKI) der Universität Bern. Infolge der Corona-Pandemie hatten wir im Jahr 2020 neue Herausforderungen anzunehmen. Nach einem Lockdown im Frühjahr folgte das Arbeiten mit einem Schutzkonzept, welches wir erfolgreich umsetzen. So konnte die Verzögerung in den Forschungsprojekten in den meisten Fällen maximal reduziert werden. Lehre und ein Grossteil unserer Kommunikation erfolgte mit digitalen Mitteln. Wissenschaftliche Meetings waren nur teilweise möglich. Trotz dieser Umstände können wir mitteilen, dass das PKI auch im Jahr 2020 seine Aufgaben in Lehre und Forschung innerhalb der Medizinischen Fakultät vorbildlich erfüllt hat.

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 weiter zu entwickeln. 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 im 3. und 6. Studienjahr Medizin sowie der Ausbildung der Zahnmediziner*innen sind einige Dozent*innen des Instituts zusätzlich in die Immunologieausbildung von Student*innen der Biologie (Naturwissenschaftliche Fakultät der Universität Bern) einbezogen. Weiterhin sind wir auch für die Pharmakologieausbildung in B.Sc.- und M.Sc.-Kursen für Biomedizin der Universität Bern verantwortlich. Ebenso führen wir seit September 2019 die Pharmakologieausbildung im 3. Studienjahr Pharmazie an unserer Universität, die seit 2 Jahren ein Vollstudium für Pharmazie anbietet, durch. 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 Prof. Konstantinidou sind Mitglieder einer Betreuungskommission innerhalb dieses Ausbildungsprogramms für Doktorandinnen und Doktoranden. 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 mich organisiert wird. Diese Bildungsangebote werden weitgehend aus eigenen finanziellen Mitteln und Sponsorengeldern bestritten. Im Institut arbeiten gegenwärtig 21 Doktorand*innen, und 4 Doktorand*innen (PhD) haben im Berichtsjahr ihre Arbeiten erfolgreich abgeschlossen.

Die Mitarbeiter*innen des PKI (ohne Klinische Pharmakologie) publizierten im Jahr 2020 insgesamt 41 Originalarbeiten sowie 19 Übersichtsartikel in internationalen Fachzeitschriften (Summe der „impact factors“ >300). Mitarbeiter*innen des Instituts wurden trotz vieler Kongressabsagen zu insgesamt 16 Vorträgen bzw. Seminaren eingeladen. Mehrere Mitarbeiter*innen des PKI wurden mit Forschungspreisen ausgezeichnet. Gegenwärtig werden 8 Mitarbeiter*innen (ohne Klinische Pharmakologie) mit namhaften Beiträgen des Schweizerischen Nationalfonds unterstützt. Prof. Simon erhielt im Dezember 2020 einen sogenannten Mega-Grant der Russischen Regierung. Weiterhin ist unser Institut mit einem Projekt von Herrn Prof. von Gunten im interfakultären Berner Zentrum für Präzisionsmedizin vertreten. Prof. Kaufmann organisiert gegenwärtig gemeinsam mit Prof. Tschan (Institut für Pathologie, Universität Bern) und Prof. Brunner (Lehrstuhl Biochemische Pharmakologie, Universität Konstanz, Deutschland) das „11th Swiss Apoptosis and Autophagy Meeting (SA^{2}M)“ (8.-10.9.2021), welches wir, abhängig von der aktuellen Corona-Lage, vor Ort, als Online- oder als Hybridveranstaltung mit bis zu 200 Teilnehmer*innen aus dem In- und Ausland durchführen werden. Diese Aufzählung belegt den hohen Stellenwert, den die Forschung in unserem Institut besitzt.

Ich danke allen Mitarbeiterinnen und Mitarbeitern für ihren Einsatz, welcher auch im Jahr 2020 zu einer Bilanz beitrug, die internationalen Massstäben gerecht wird. Ebenso danke ich allen Sponsoren und Freunden des Instituts.

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

Bern, Januar 2021

1.2. Foreword

This is the twentieth comprehensive annual report of the Institute of Pharmacology (PKI) of the University of Bern. Owing to the Corona pandemic, we had to manage several new challenges. After a lockdown in spring, we had to work according to a safety concept, which we successfully implemented in our institute. This way, the delay of progress in our research project could be very much limited. Teaching and a large part of our communication was done by digital tools. Scientific meetings were often impossible to organize and cancelled. In spite of these circumstances, we fulfilled our tasks in teaching and research within the Faculty of Medicine 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”. The PKI 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. We offer a broad spectrum of laboratory methods and have experiences in both *clinical research* and *basic biological science*. All our current activities are summarized here below.

Besides the regular teaching in the third and sixth year medical student curriculum and in the teaching of dental students, we are responsible for teaching Pharmacology in both B.Sc. and M.Sc. courses in Biomedicine. Some of the PKI staff are additionally involved in the Immunology M.Sc. programmes within the Natural Science Faculty of our university. In September 2019, we also started teaching Pharmacology to students of Pharmacy of our University, which newly offers a full study in Pharmacy. Of course, we also actively participate in the graduate program for MD/PhD students of the University of Bern (Graduate School for Cellular and Biomedical Sciences). Prof. Kaufmann, Prof. von Gunten and Prof. Konstantinidou are members of the tutoring committee “Cell Biology” within that school. Currently, 21 PhD students work at the PKI, and in 2020, four PhD student successfully completed their doctoral studies. Also important for the institute are additional teaching activities outside the medical curriculum, such as seminars (Current Topics in Pharmacology and Theranostics; jointly organized with the Center of Laboratory Medicine) and the

Summer School (organized by myself). Significantly, these additional events were financed exclusively by external sponsors.

Research is our other main activity. In 2020, staff members of the PKI (without Clinical Pharmacology) published 41 original and 19 review articles in international peer-reviewed journals (the sum of the “impact factors” is above 300). Despite of the cancellation of many congresses, co-workers of the institute were invited to present 16 lectures or seminars. Several PKI members received research prizes. The research projects of 8 co-workers (without Clinical Pharmacology) are currently supported by grants from the Swiss National Science Foundation. In December 2020, Prof. Simon received a so-called “mega-grant” from the Russian government. With a project of Prof. von Gunten, we are also integrated in the Interfaculty Center for Precision Medicine of the University of Bern. Prof. Kaufmann, together with Prof. Tschan (Institute of Pathology, University of Bern) and Prof. Brunner (Department of Biochemical Pharmacology, Univ. of Constance, Germany), are in the process of organizing an international congress (11th Swiss Apoptosis and Autophagy Meeting; September 8-10, 2021), which, depending on the Corona situation will be held as physical, online or hybrid event with up to 200 national and international scientists interested in the fields of “Cell Death and Autophagy”. In summary, we carry out research of a high standard which plays a very important role at the PKI.

I thank all co-workers of the institute for their hard work. These efforts have contributed in an important way to the success of the PKI in 2020. I am grateful to all the sponsors and friends of the institute for their support.

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

Bern, January 2021

2. Staff 2020

Director

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

Deputy Director

Prof. Dr.	Huwiler, Andrea	PhD

Principal Investigators

Prof. Dr.	Huwiler, Andrea	PhD
Prof. Dr.	Kaufmann, Thomas	PhD
SNF Prof.	Konstantinidou, Georgia	PhD*
Prof. Dr.	Simon, Hans Uwe	MD, PhD
Prof. Dr.	von Gunten, Stephan	MD, PhD, MME
Prof. Dr.	Yousefi, Shida	PhD
Prof. Dr.	Zangemeister-Wittke, Uwe	PhD
PD Dr.	Späth, Peter	PhD*

Scientific Staff

	Arnold, Janine	Bachelor student*
	Bachmann, Daniel	Lab Technican
	Chen, Yihe	PhD student*
	Christen, Mira	Lab Technican*
	Claus, Mike	Lab Technican
	Erhardt, Martin	PhD student
	Falco, Simone	PhD student* (since Oct 2020)
	Fartelj, David	M.Sc. student* (until Aug 2020)
	Fettrelet, Timothée	M.Sc. student*
Dr.	Frangez, Ziva	Postdoctoral fellow*
	Furer, Alexander	Technical Specialist*
Dr.	Germic, Nina	Postdoctoral fellow
	Gigon, Lea	PhD student
Dr.	Haas, Quentin	PhD student (until April 2020); Postdoctoral fellow (May-August 2020)
	Hafizi, Redona	PhD student
	Hämmerli, Corinne	Bachelor student*
Dr.	He, Zhaoyue	Postdoctoral fellow*
	Hemmann, Mike	M.Sc. student*
	Hevia Hernandez, Giselle	PhD student*
	Hosseini, Aref	PhD student (since Jan 2020)
	Hugonnet Marjolaine, Claire	PhD student
Dr.	Imeri, Faik	Postdoctoral fellow*
	JeanRichard, Philippe	M.Sc. pharm. student* (until Sep 2020)
	Klapan, Kim	PhD student*
	Kozlowski, Evelyne	Lab Technician
	Leroux, Cédric	PhD student (since April 2020)
	Maillard-van Laer, Marianne	Lab Technician (until March 2020)
	Markov, Nikita	PhD student
	Motta, Fabrizio	M.Sc. student*
	Mulaki, Jehona	M.Sc. student*
	Mürner, Lukas	PhD student*

	Naim, Samara	PhD student*
	Nasser, Riim	Lab Technician
	Oberson, Kevin	Lab Technician
	Paschoud, Thierry	M.Sc. student*
	Peng, Shuang	PhD student*
	Pozzato, Chiara	PhD student*
Dr.	Rossi Sebastiano, Matteo	Postdoctoral fellow (until Aug 2020)
	Saliakoura, Maria	PhD student* (until Dec 2020)
	Singh, Pushpita	PhD student* (since Oct 2020)
	Steiner, Katharina	M.Sc. student*
	Stepanovska Tanturovska, Bisera	Postdoctoral fellow
Dr.	Stojkov, Darko	Postdoctoral fellow (until April 2020)
Dr.	Thapa, Asmita	Postdoctoral fellow (since Oct 2020)
	Toledo Darien	PhD student
	Verschoor, Daniëlle	PhD student
	von Gunten, Aldona	Technical Specialist*
	Weiss, Fabian	PhD student*
	Wyss, Jacqueline	M.Sc. student*
	Zahiroddini, Peymaneh	M.Sc. student*

Principal Investigator – Clinical Pharmacology

Prof. Dr.	Haschke, Manuel	MD

Scientific Staff – Clinical Pharmacology

Dr.	Liakoni, Evangelia	MD
	van der Velpen, Vera	PhD
	Scholz, Irene	med. pract.
	Hammann, Felix	MD, PhD

External University Teachers

Dr.	Bürgi, Sibylle	PhD*
PD Dr.	Cachelin, Armand	MD, PhD*
Prof. Dr.	Mlinarič-Raščan, Irena	PhD* (Adjunct Prof., Univ. of Ljubljana, Slovenia)
Prof. Dr.	Levi-Schaffer, Francesca	PhD* (Adjunct Prof., Hebrew Univ. Jerusalem, Israel)
Prof. Dr.	Shi, Yufang	PhD* (Adjunct Prof., Shanghai Jiaotong, PR China)

Guest Scientists

Prof. Dr.	Simon, Dagmar	MD*, Dept. Dermatology, Inselspital, Univ. Bern
Dr.	Schwalm, Stephanie	PhD*, Dept. of Pharmacology, Univ. Frankfurt
Prof. Dr.	Spirk, David	MD*, Sanofi-Aventis AG

Office

	Scherrer, Debora	Secretary, 80%
	Cookman, Sabrina	Secretary, 60% (until June 2020)
	Joray, Celine	Secretary, 60%
	Wettstein, Valentina	Secretary, 60% (since June 2020)

Workshop / House Keeping

Conforti, Isa

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

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

Progress in Pharmacology in Cardiovascular Disease: From Prevention to Intervention. Bern, January 22, 2020

Summer School

Members of the Institute of Pharmacology of the University of Bern together with participants of our International Summer School in Bönigen; July 26 - 28, 2020.

3. Teaching Activities

3.1. Lectures

Lectures for Medical Students: Pharmacology

Date	Lecturer	Titel of the lecture
Mar 03, 2020	Prof. Stephan von Gunten	Hormone aus pharmakol. Sicht (Teil 1)
Mar 03, 2020	Prof. Stephan von Gunten	Hormone aus pharmakol. Sicht (Teil 2)
Mar 09, 2020	Prof. Stephan von Gunten	Lipidsenker + Behandlung der Gicht
Mar 09, 2020	Prof. Stephan von Gunten	Antidiabetika
Mar 17, 2020	Prof. Andrea Huwiler	Therapie von M. Parkinson und Demenz
Mar 23, 2020	Prof. Andrea Huwiler	Lokalanästhetika
Mar 30, 2020	Prof. Andrea Huwiler	Antiepileptika
Mar 31, 2020	Prof. Andrea Huwiler	Pharmakologie von Narkosemitteln und Muskelrelaxantien I
Mar 31, 2020	Prof. Andrea Huwiler	Pharmakologie von Narkosemitteln und Muskelrelaxantien II
Apr 06, 2020	Prof. Andrea Huwiler	Psychopharmakologie
Apr 20, 2020	Prof. Andrea Huwiler	Antidepressiva, Anxiolytika
Apr 20, 2020	Prof. Andrea Huwiler	Antipsychotika und Stimmungsstabilisatoren
Apr 21, 2020	Prof. Manuel Haschke	Schmerz und Analgesiologie (Teil 1)
Apr 21, 2020	Prof. Manuel Haschke	Schmerz und Analgesiologie (Teil 2)
May 05, 2020	Prof. Hans-Uwe Simon	Immunmodulation
Sep 16, 2020	Prof. Hans-Uwe Simon	Pharmakodynamik (Teil 1)
Sep 16, 2020	Prof. Hans-Uwe Simon	Pharmakodynamik (Teil 2)
Sep 28, 2020	Prof. Hans-Uwe Simon	Entzündungshemmung
Sep 28, 2020	Prof. Hans-Uwe Simon	Einführung in die Toxikologie
Oct 06, 2020	Prof. Hans-Uwe Simon	Pharmakotherapie bei Lungenkrankheiten
Oct 20, 2020	Prof. David Spirk	Pharmakologie der Hämostase
Oct 27, 2020	Prof. U. Zangemeister-Wittke	Pharmakologie des vegetativen Nervensystems
Nov 03, 2020	Prof. David Spirk	Behandlung der Herzinsuffizienz und Angina pectoris
Nov 04, 2020	Prof. U. Zangemeister-Wittke	Antihypertensiva, Antiarrhythmika
Nov 24, 2020	Prof. U. Zangemeister-Wittke	Diuretika (Teil 1), Diuretika (Teil 2)

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 24, 2020	Prof. Thomas Kaufmann	Entwicklung des Lebens
Oct 08, 2020	Prof. Thomas Kaufmann	Zellstoffwechsel
Oct 29, 2020	Prof. Thomas Kaufmann	Zelltod 2

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

Date	Lecturer	Titel of the lecture
Mar 10, 2020	Prof. U. Zangemeister-Wittke	Gezielte Tumortherapie mit Antikörpern und Immunkonjugaten
Mar 19, 2020	Prof. Thomas Kaufmann	Modulation des Zelltodes - aktueller Stand und neue Entwicklungen
Mar 26, 2020	Prof. Stephan von Gunten	Functional Glycomics - Neue Optionen für die Tumor- und Entzündungspharmakologie
Mar 26, 2020	Prof. Hans-Uwe Simon	Personalisierte Arzneimitteltherapie

Power Point or Camptasia presentations with voice recording were provided.

Lectures for Dental Medicine Students: Pharmacology (Coordinator: Prof. Uwe Zangemeister-Wittke)

Date	Lecturer	Title of the lecture
Feb 03, 2020	Prof. U. Zangemeister-Wittke	Einführung in die Pharmakokinetik
Feb 17, 2020	Prof. Hans-Uwe Simon	Rezeptoren, Dosis-Wirkungskurven,
Feb 17, 2020	Prof. Hans-Uwe Simon	Antagonisten, Applikationsarten
Feb 19, 2020	Prof. Thomas Kaufmann	Pharmakogenetik, Interaktionen
Feb 26, 2020	Prof. U. Zangemeister-Wittke	Pharmakologie des vegetativen Nervensystems
Mar 11, 2020	Prof. Andrea Huwiler	Narkose, Beruhigungsmittel
Mar 18, 2020	Prof. Andrea Huwiler	Pharmakologie der Atemwege
Mar 23, 2020	PD Dr. Armand Cachelin	Analgetika
Mar 25, 2020	Prof. Stephan von Gunten	Pharmakologie des Knochens
Apr 01, 2020	Prof. Stephan von Gunten	Magensäurehemmung
Apr 6, 2020	Prof. David Spirk	Herz-Kreislauf Medikamente, Antithrombotika
Apr 8, 2020	Dr. Sibylle Bürgi	Antidiabetika
Apr 22, 2020	Dr. Sibylle Bürgi	Lokalanästhetika

Apr 27, 2020	Dr. Sibylle Bürgi	Antibiotika

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

From March 18 online presentations with Camptasia.

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

Date	Lecturer	Title of the lecture
Feb 21, 2020	Prof. Andrea Huwiler	Depressionen
Feb 27, 2020	Prof. Andrea Huwiler	Schlafstörungen
Feb 28, 2020	Prof. Andrea Huwiler	Schizophrenie, Psychosen, Demenz
Mar 5, 2020	Prof. Andrea Huwiler	Nacieption
Mar 6, 2020	Prof. Andrea Huwiler	Anästhesie
Mar 19, 2020	Prof. Stephan von Gunten	Knochenkrankheiten, Osteoporose, Gicht
Mar 20, 2020	Prof. Stephan von Gunten	Gelenkkranheiten, Arthrose
Mar 26, 2020	Prof. Stephan von Gunten	Arthritis
Apr 9, 2020	Prof. Andrea Huwiler	Epilepsie, Parkinson
Apr 23, 2020	Prof. Hans-Uwe Simon	Krankheiten des Immunsystems
Apr 24, 2020	Prof. Uwe Zangemeister	Tumorimmunologie
Apr 30, 2020	Prof. Uwe Zangemeister	Prostataerkrankungen
Sep 15, 2020	Prof. Hans-Uwe Simon	Pharmakodynamik 1
Sep 15, 2020	Prof. Hans-Uwe Simon	Pharmakodynamik 2
Sep 17, 2020	Prof. Hans-Uwe Simon	Pharmakodynamik 3
Sep 17, 2020	Prof. Hans-Uwe Simon	Arzneimittelallergien
Sep 22, 2020	Prof. Hans-Uwe Simon	Experimentelle Toxikologie 1
Sep 22, 2020	Prof. Hans-Uwe Simon	Experimentelle Toxikologie 2
Oct 22, 2020	Prof. Stephan von Gunten	Säureassoziierte KH / Erbrechen
Oct 27, 2020	Prof. Stephan von Gunten	Motilitätsstörungen / Entzündliche Darmerkrankungen
Nov 19, 2020	Prof. Georgia Konstantinidou	Zytostatika, Teil 1
Nov 24, 2020	Prof. Georgia Konstantinidou	Zytostatika, Teil 2
Nov 26, 2020	Prof. Thomas Kaufmann	Anämien
Dec 1, 2020	Prof. Thomas Kaufmann	Leukämien
Dec 3, 2020	Prof. Thomas Kaufmann	Lymphome

The lectures from March 16 to May 31 and from October 27 to December 31, 2020, were recorded and made available online.

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

Date	Lecturer	Title of the lecture
Feb 20, 2020	Prof. Stephan von Gunten	Introduction
Feb 20, 2020	Prof. Stephan von Gunten	Glycoimmunology
May 14, 2020	Prof. Georgia Konstantinidou	Immunopharmacology

Written examination and oral tests: Prof. Stefan von Gunten

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

Date	Lecturer	Title of the lecture
Sep 17, 2020	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
April 02, 2020	Prof. Georgia Konstantinidou	Lipid mediators in inflammation
May 07, 2020	Prof. Shida Yousefi	Inflammation - good or bad? Resolution of inflammation - apoptosis

Practical work for Natural Science Faculty: Immunology II (Coordinator: Prof. Thomas Kaufmann)

Date	Lecturer	Title of the lecture

This practical course organized by the Faculty of Natural Sciences was carried out online. Prof. Simon and Prof. von Gunten contributed with lectures on current research topics in Immunology.

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 18, 2020	Prof. Stephan von Gunten	Gastrointestinal tract

Sep 25, 2020	Prof. David Spirk	Haemopoietic system and haemostasis
Oct 02, 2020	Prof. Shida Yousefi	Lungs and kidneys
Oct 09, 2020	Prof. Stephan von Gunten	Endocrine and reproductive system
Oct 16, 2020	Prof. Georgia Konstantinidou	Immune system
Oct 23, 2020	Prof. Thomas Kaufmann	Antiinfectious therapy
Oct 30, 2020	Prof. U. Zangemeister-Wittke	Heart and vascular system
Nov 06, 2020	Prof. Andrea Huwiler	Nervous system

The lectures from October 23 to December 31, 2020, were presented online via Zoom.

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 05, 2020	Prof. Georgia Konstantinidou	Oncogenes – how to target them

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: PD Dr. Philippe Krebs)

Date	Lecturer	Title of the lecture
Sep 21, 2020	Prof. Thomas Kaufmann	Cell damage

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 23, 2020	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" 2019 (5.0 ECTS), CTS/KSL 7606"

Date	Lecturer	Title of the lecture
Oct 14, 2020 2 hours	Prof. Thomas Kaufmann	Chapter 15 (Cell signaling)

Lectures for Medical Students: Clinical Pharmacology (*switched to online lectures on March 16)

Date	Lecturer	Titel of the lecture
Feb 03, 2020	Prof. Manuel Haschke	Pharmakologie: Laxativa, Antidiarrhoika, Antiemetika
Feb 03, 2020	Prof. Manuel Haschke	Hemmung der Säuresekretion
Feb 10, 2020	PD Felix Hammann	Pharmakokinetik 3&4 (2 Lekt.)
Feb 25, 2020	PD Evangelia Liakoni	Analgetika
Feb 27, 2020	PD Evangelia Liakoni	Antikoagulantien & Thrombozytenhemmer
Feb 27, 2020	Irene Scholz	Notfallmedikamente
*March 16, 2020	PD Felix Hammann	Arterielle Hypertonie u. Herzinsuffizienz
March 16, 2020	PD Felix Hammann	Diabetes u. Dyslipidämie
March 16, 2020	Prof. Manuel Haschke	Antiinfektiva
April 21, 2020	Prof. Manuel Haschke	Schmerzmittel 1&2 (2 Lekt.)
Sep 22, 2020	PD Felix Hammann	Pharmakokinetik 1&2 (2 Lekt.)
Oct 02, 2020	PD Evangelia Liakoni	Interaktionen
Oct 02, 2020	PD Evangelia Liakoni	Nebenwirkungen

Online Lectures for Dental Medicine Students: Clinical Pharmacology

Date	Lecturer	Titel of the lecture
Oct 21, 2020	PD Felix Hammann	Pat. mit akuten med. Problemen
Oct 28, 2020	PD Felix Hammann	Pat. mit chronischen med. Problem
Nov 04, 2020	Irene Scholz	Antikoagulation
Nov 11, 2020	Irene Scholz	UAW im Mund
Nov 25, 2020	Irene Scholz	Antibiotika 1
Dec 02, 2020	Irene Scholz	Antibiotika 2
Dec 09, 2020	Prof. Manuel Haschke	Analgetika 1
Dec 16, 2020	Prof. Manuel Haschke	Analgetika 2

Lectures for Pharmacy Students (Bachelor): Clinical Pharmacology (*switched to online lectures on March 16)

Date	Lecturer	Titel of the lecture
Feb 18, 2020	PD Felix Hammann	Biopharmazie
Feb 20, 2020	PD Felix Hammann	Asthma, COPD, Pneumonien
Feb 21, 2020	PD Felix Hammann	Asthma, COPD, Pneumonien
Feb 25, 2020	Irene Scholz	Biopharmazie
March 06, 2020	PD Evangelia Liakoni	Schmerz, neuropathisch
March 10, 2020	PD Felix Hammann	Biopharmazie

March 11, 2020	PD Felix Hammann	Biopharmazie
March 12, 2020	PD Evangelia Liakoni	Nicht-opioid Analgetika
March 12, 2020	Prof. Manuel Haschke	Kopfschmerzen, Migräne
March 13, 2020	Irene Scholz	Opioidanalgetika
March 17, 2020	PD Felix Hammann	Biopharmazie
March 24, 2020	PD Evangelia Liakoni	Biopharmazie
March 26, 2020	Prof. Manuel Haschke	Schilddrüsenkrankheiten
March 27, 2020	Irene Scholz	Hypophysäre Störungen
March 31, 2020	Prof. Manuel Haschke	Biopharmazie
April 02, 2020	Prof. Manuel Haschke	Diabetes
April 02, 2020	PD Evangelia Liakoni	Dyslipidämie
April 03, 2020	PD Evangelia Liakoni	Dyslipidämie
April 03, 2020	PD Evangelia Liakoni	Geschlechtshormone, Kontrazeptiva
April 09, 2020	PD Evangelia Liakoni	Geschlechtshormone, Kontrazeptiva
Sept 24, 2020	Sarah Banholzer	drug safety/adverse events/pharamcovigilance
Sept 29, 2020	PD Evangelia Liakoni	Pharmakokinetik I & II
Oct 01, 2020	PD Evangelia Liakoni	Pharmakokinetik III
Oct 13, 2020	PD Felix Hammann	Hypertonie
Oct 14, 2020	PD Felix Hammann	Herzinsuffizienz, Rhythmusstörungen
Oct 15, 2020	Prof. Stephan Krähenbühl	Arterielle KH
Oct 20, 2020	Prof. Stephan Krähenbühl	Venöse KH
Oct 29, 2020	Prof. Manuel Haschke	Virale und retrovirale KH
Nov 03, 2020	Prof. Manuel Haschke	Pilzerkrankungen Mycobacterielle KH
Nov 05, 2020	Prof. Manuel Haschke	Bakterielle Infektionen I & II
Nov 10, 2020	Prof. Manuel Haschke	Bakterielle Infektionen III & IV
Nov 12, 2020	Prof. Manuel Haschke	Parasiten / Malaria
Dec 08, 2020	PD Felix Hammann	Nierenkrankheiten, Dialyse, Dosisanpassung Nieren-/Lebererkrankungen
Dec 10, 2020	Irene Scholz	HWI, Inkontinenz
Dec 15, 2020	PD Evangelia Liakoni	Klinische Toxikologie

Online Lectures for Pharmacy Students (Master): Clinical Pharmacology

Date	**Lecturer**	**Titel of the lecture**
Sep 15, 2020	Sarah Banholzer	Arzneimittelsicherheit: Pharmakovigilanz – Vertiefung

3.2. Coordination PBL Medical Students, 3rd year (2020/2021)

Core group member:
Prof. Andrea Huwiler

Representatives of Pharmacology for teaching blocks:
Prof. Hans-Uwe Simon (blocks I, II, and IX)
Prof. Uwe Zangemeister-Wittke (blocks IV and V)
Prof. Stephan von Gunten (block V)
Prof. Andrea Huwiler (blocks VI, VII and VIII)

3.3. Tutorials (study year 2020/2021)

For Medical students 3rd year:

Prof. Georgia Konstantinidou	Prof. Thomas Kaufmann
Dr. Zhaoyue He	Lukas Mürner
Kim Klapan	Samara Naim

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. Elective Module Supervision

For Biomedical Sciences students:
Laura Patricia Leuenberger (Georgia Konstantinidou)
Jehona Mulaki (Georgia Konstantinidou)
Jean-Philippe Ioannou (Daniel Bachmann & Thomas Kaufmann)
Nicole Pietrogiovanna (Daniel Bachmann & Thomas Kaufmann)

*3.5. Seminars of Invited Speakers**

*Owing to the Corona crisis, most planned seminar were cancelled.

Date	Teacher	Title of the seminar	Host
Jan 29, 2020	Prof. Dr. Cezmi A. Akdis, Director Swiss Institute of Allergy and Asthma Research (SIAF), University of Zurich	Epithelial barrier hypothesis for allergic and inflammatory diseases	H.-U. Simon
Mar 10, 2020	Joseena Mariam Iype, Zentrum für Labormedizin, Inselspital Bern	CyTOF – A new technology for the characterization of cells	S. Yousefi
Oct 21, 2020	Dr. Rao Tata Nageswara, Department for Biomedical Research (DBMR)and University Clinic of Hematology, Inselspital	Biology and vulnerabilities of leukemic stem cells	A. Huwiler

3.6. Academic Degrees

Konstantinidou Georgia, Privatdozentin (Habilitation), Faculty of Medicine, University of Bern
October 2020

Germic Nina, PhD, University of Bern
Thesis: ATG5 promotes eosinophil hematopoiesis but inhibits eosinophil effector functions – implications for cancer and bacterial infections (March 2020)
Supervisor: Prof. Hans-Uwe Simon

Rossi Sebastiano Matteo, PhD, University of Bern
Thesis: Targeting lipid metabolism in pancreatic ductal adenocarcinoma (March 2020)
Supervisor: Prof. Georgia Konstantinidou

Haas Quentin, PhD, University of Bern
Thesis: The role of Siglec-7 and Siglec-9 on cytotoxic T cells (March 2020)
Supervisor: Prof. Stephan von Gunten

Stephanovska Bisera, PhD, University of Bern
Thesis: Sphingosine 1-phosphate signaling in *in vitro* and *in vivo* models of inflammation (April 2020)
Supervisor: Prof. Andrea Huwiler

Saliakoura Maria, PhD, University of Bern
Thesis: Regulation of lipid metabolism in lung adenocarcinomas (December 2020)
Supervisor: Prof. Georgia Konstantinidou

Wenger Nicolas, M.Med., University of Bern
Thesis: Pulmonary embolism and deep vein thrombosis: Similar but different (October 2020)
Supervisor: Prof. David Spirk

Mürner Lukas, M.Sc., University of Bern
Thesis: Cell-type-specific expression of SIGLEC7and SIGLEC9 is associated with differential promoter methylation and investigation of the isoform-specific interactomes of Siglec-7 and -9 (May 2020)
Supervisor: Prof. Stephan von Gunten

Zahiroddini Peymaneh, M.Sc., University of Bern
Thesis: The role of XIAP in the regulation of TNF-induced inflammation and cell death of neutrophils (November 2020)
Supervisor: Prof. Thomas Kaufmann

Steiner Katharina, M.Sc., University of Bern
Thesis: In vitroanalysis of arecombinant human IgG1 Fc hexamer on neutrophils (December 2020)
Supervisor: Prof. Stephan von Gunten

JeanRichard Philippe, M.Sc.pharm., University of Basel
Thesis: The role of BK and TRPV2 channels for neutrophil metabolism and NET-formation (June 2020)
Supervisor: Prof. Hans-Uwe Simon

Fartelj David, M.Sc.pharm., University of Ljubljana
Thesis: The role of selected mitochondrial proteins in neutrophil extracellular DNA trap formation (September 2020)
Supervisor: Prof. Hans-Uwe Simon

4. Research Activities

4.1. Research Projects and Publications

Group Prof. Andrea Huwiler

Group members: Marianne Maillard-van Laer, Lab Technician[1]
Riim Nasser, Lab Technician[1]
Dr. Faik Imeri, postdoctoral fellow[1]
Dr. Bisera Stepanovska Tanturovska, PhD student/postdoctoral fellow [1]
Redona Hafizi, PhD student[1]
Jehona Mulaki, M.sc. student[1]
Helen Broughton. M.med. student[1]
Isolde Römer, Technician[2]
Stephanie Schwalm, Dr., postdoctoral fellow[2]

[1]Institute of Pharmacology, University of Bern
[2]Institut für Allgemeine Pharmakologie und Toxikologie, Universität Frankfurt/Main

Our research is focused on sphingolipids and their contribution to physiological and patho-physiological processes that 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.

Morpholino analogues of fingolimod as novel and selective $S1P_1$ ligands with in vivo efficacy in a mouse model of experimental antigen-induced encephalomyelitis
Stepanovska B, Zivkovic A, Enzmann G, Tietz S, Homann T, Kleuser B, Engelhardt B, Stark H, Huwiler A
Multiple sclerosis (MS) is a chronic, inflammatory, autoimmune disease of the central nervous system (CNS) which is associated with lower life expectancy and disability. The experimental antigen-induced encephalomyelitis (EAE) in mice is a useful animal model of MS, which allows exploring the etiopathogenetic mechanisms and testing novel potential therapeutic drugs. A new therapeutic paradigm for the treatment of MS was introduced in 2010 through the sphingosine 1-phosphate (S1P) analogue fingolimod (FTY720, Gilenya®), which acts as a functional $S1P_1$ antagonist on T lymphocytes to deplete these cells from the blood. In this study, we synthesized two novel structures, ST-1893 and ST-1894, which are derived from fingolimod and chemically feature a morpholine ring in the polar head group. These compounds showed a selective $S1P_1$ activation profile and a sustained $S1P_1$ internalization in

cultures of $S1P_1$-overexpressing Chinese hamster ovary (CHO)-K1 cells, consistent with a functional antagonism. In vivo, both compounds induced a profound lymphopenia in mice. Finally, these substances showed efficacy in the EAE model, where they reduced clinical symptoms of the disease, and, on the molecular level, they reduced the T-cell infiltration and several inflammatory mediators in the brain and spinal cord. In summary, these data suggest that $S1P_1$-selective compounds may have an advantage over fingolimod and siponimod, not only in MS but also in other autoimmune diseases.
See original publication No 1

Ceramide kinase is upregulated in metastatic breast cancer cells and contributes to migration and invasion by activation of PI 3-kinase and Akt
Schwalm S, Erhardt M, Römer I, Pfeilschifter J, Zangemeister-Wittke U, Huwiler A
Ceramide kinase (CerK) is a lipid kinase that converts the proapoptotic ceramide to ceramide 1-phosphate, which has been proposed to have pro-malignant properties and regulate cell responses such as proliferation, migration, and inflammation. We used the parental human breast cancer cell line MDA-MB-231 and two single cell progenies derived from lung and bone metastasis upon injection of the parental cells into immuno-deficient mice. The lung and the bone metastatic cell lines showed a marked upregulation of CerK mRNA and activity when compared to the parental cell line. The metastatic cells also had increased migratory and invasive activity, which was dose-dependently reduced by the selective CerK inhibitor NVP-231. A similar reduction of migration was seen when CerK was stably downregulated with small hairpin RNA (shRNA). Conversely, overexpression of CerK in parental MDA-MB-231 cells enhanced migration, and this effect was also observed in the non-metastatic cell line MCF7 upon CerK overexpression. On the molecular level, CerK overexpression increased the activation of protein kinase Akt. The increased migration of CerK overexpressing cells was mitigated by the CerK inhibitor NVP-231, by inhibition of the phosphoinositide 3-kinase (PI3K)/Akt pathway and the Rho kinase, but not by inhibition of the classical extracellular signal-regulated kinase (ERK) pathway. Altogether, our data demonstrate for the first time that CerK promotes migration and invasion of metastatic breast cancer cells and that targeting of CerK has potential to counteract metastasis in breast cancer.
See original publication No 2

Downregulation of S1P lyase improves barrier function in human cerebral microvascular endothelial cells following an inflammatory challenge
Stepanovska B, Lange A, Schwalm S, Pfeilschifter J, Coldewey SM, Huwiler A
Sphingosine 1-phosphate (S1P) is a key bioactive lipid that regulates a myriad of physiological and pathophysiological processes including endothelial barrier function, vascular tone, vascular inflammation and angiogenesis. Various S1P receptor subtypes have been suggested to be involved in the regulation of these processes whereas the contribution of intracellular S1P (iS1P) through intracellular targets is little explored. In this study, we used the human cerebral microvascular endothelial cell line HCMEC/D3 to stably downregulate the S1P lyase (SPL-kd) and evaluate the consequences on endothelial barrier function and on molecular factors that regulate barrier tightness under normal and inflammatory conditions. Results showed that in SPL-kd cells, transendothelial electrical resistance, as a measure of barrier integrity, was regulated in a dual manner. SPL-kd cells had a delayed barrier build up, a shorter interval of a stable barrier and thereafter a continuous breakdown. Contrariwise, a protection was seen from the rapid proinflammatory cytokine-mediated barrier breakdown. On the molecular level, SPL-kd caused an increased basal protein expression of the adherens junction molecules PECAM-1, VE-cadherin and β-catenin, increased activity of the signaling kinases protein kinase C, AMP-dependent kinase and p38-MAPK, , but reduced protein expression of the transcription factor c-Jun. However, the only factors that were significantly altered in TNFα/SPL-kd compared to TNFα/control cells, which could explain the

observed protection, were VCAM-1, IL-6, MCP-1, and c-Jun. Furthermore, lipid profiling revealed that dihydro-S1P and S1P were strongly enhanced in TNFα-treated SPL-kd cells.
In summary, our data suggest that SPL inhibition is a valid alternative to achieve increased junctional molecules expression, dampened inflammatory response and augmented barrier integrity during inflammatory challenge.
See original publication No 3

Validation of highly selective sphingosine kinase 2 inhibitors SLM6031434 and HWG-35D as effective anti-fibrotic treatment options in a mouse model of tubulointerstitial fibrosis
Schwalm S, Beyer S, Hafizi R, Trautmann S, Geisslinger G, Adams DR, Pyne S, Pyne N, Schaefer L, Huwiler A[#] Pfeilschifter J[#] ([#]shared senior authorship)

Renal fibrosis is characterized by chronic inflammation and excessive accumulation of extracellular matrix and progressively leads to functional insufficiency and even total loss of kidney function. In this study we investigated the anti-fibrotic potential of two highly selective and potent SK2 inhibitors, SLM6031434 and HWG-35D, in unilateral ureter obstruction, a model for progressive renal fibrosis, in mice. In both cases, treatment with SLM6031434 or HWG-35D resulted in an attenuated fibrotic response to UUO in comparison to vehicle-treated mice as demonstrated by reduced collagen accumulation and a decreased expression of collagen-1 (Col1), fibronectin-1 (FN-1), connective tissue growth factor (CTGF), and α-smooth muscle actin (α-SMA). Similar to our previous study in Sphk2$^{-/-}$ mice, we found an increased protein expression of Smad7, a negative regulator of the pro-fibrotic TGFβ/Smad signaling cascade, accompanied by a strong accumulation of sphingosine in SK2 inhibitor-treated kidneys. Treatment of primary renal fibroblasts with SLM6031434 and HWG-35D dose-dependently increased Smad7 expression and ameliorated the expression of Col1, FN-1 and CTGF.
In summary, these data prove the anti-fibrotic potential of SK2 inhibition in a mouse model of renal fibrosis, thereby validating SK2 as pharmacological target for the treatment of fibrosis in chronic kidney disease.
See original publication No 4

Original publications

1. Stepanovska B, Zivkovic A, Enzmann G, Tietz S, Homann T, Kleuser B, Engelhardt B, Stark H, **Huwiler A**: Morpholino analogues of fingolimod as novel and selective $S1P_1$ ligands with in vivo efficacy in a mouse model of experimental antigen-induced encephalomyelitis.
   Int J Mol Sci. 21 (2020), 6463.

2. Schwalm S, Erhardt M, Römer I, Pfeilschifter J, Zangemeister-Wittke U, **Huwiler A:** Ceramide kinase Is upregulated in metastatic breast cancer cells and contributes to migration and invasion by activation of PI 3-kinase and Akt.
   Int J Mol Sci. 21 (2020), 1396.

3. Stepanovska B, Lange AI, Schwalm S, Pfeilschifter J, Coldewey SM, **Huwiler A**: Downregulation of S1P lyase improves barrier function in human cerebral microvascular endothelial cells following an inflammatory challenge.
   Int J Mol Sci. 21 (2020), 1240.

4. Schwalm S, Beyer S, Hafizi R, Trautmann S, Geisslinger G, Adams DR, Pyne S, Pyne N, Schaefer L, **Huwiler A***, Pfeilschifter J*: Validation of highly selective sphingosine ki-

nase 2 inhibitors SLM6031434 and HWG-35D as effective anti-fibrotic treatment options in a mouse model of tubulointerstitial fibrosis. Cell Signal. (2020). In press. * shared senior authorship.

Review article

1. Stepanovska Tanturovska B, **Huwiler A**: Cenerimod. Sphingosine 1-phosphate receptor 1 (S1P1) agonist, Treatment of systemic lupus erythematosus.
Drugs of the Future 45 (2020), 785.

Group Prof. Thomas Kaufmann

Group members: Samara Naim, PhD student
Peymaneh Zahiroddini, M.Sc. student
Fabrizio Motta, M.Sc. student
Daniel Bachmann, Lab Technician

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. Rohner L, Reinhart R, Iype J, Bachmann S, **Kaufmann T**, Fux M: Impact of BH3-mimetics on human and mouse blood leukocytes: A comparative study.
Sci Rep. 10 (2020), 222.

2. Wehrli M, Schneider C, Cortinas-Elizondo F, Verschoor D, Frias Boligan K, Adams OJ, Hlushchuk R, Engelmann C, Daudel F, Villiger PM, Seibold F, Yawalkar N, Vonarburg C, Miescher S, Lötscher M, **Kaufmann T**, Münz C, Mueller C, Djonov V, Simon HU, von Gunten S: IgA triggers cell death of neutrophils when primed by inflammatory mediators.
J Immunol. 10 (2020), 2640-2648.

Review article

1. Naim S, **Kaufmann T:** The multifaceted roles of the BCL-2 family member BOK.
Front Cell Dev Biol. 8 (2020), 574338.

Group Prof. Georgia Konstantinidou

Group members:
Chiara Pozzato, PhD student
Dr. Matteo Rossi Sebastiano, postdoctoral fellow
Maria Saliakoura, PhD student
Cédric Leroux, PhD student
Dr. Asmita Thapa, postdoctoral fellow
Simone Falco, PhD student

Cancer cells undergo oncogene-directed reprogramming in order 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. In particular, 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.

PLCγ1 suppression promotes the adaptation of KRAS-mutant lung adenocarcinomas to hypoxia
Saliakoura M, Rossi Sebastiano M, Pozzato C, Heidel FH, Schnöder TM, Savic Prince S, Bubendorf L, Pinton P, A Schmid R, Baumgartner J, Freigang S, Berezowska SA, Rimessi A, Konstantinidou G
Mutant KRAS modulates the metabolic plasticity of cancer cells to confer a growth advantage during hypoxia, but the molecular underpinnings are largely unknown. Using a lipidomic screen, we found that PLCγ1 is suppressed during hypoxia in KRAS-mutant human lung adenocarcinoma cancer cell lines. Suppression of PLCγ1 in hypoxia promotes a less oxidative cancer cell metabolism state, reduces the formation of mitochondrial reactive oxygen species and switches tumour bioenergetics towards glycolysis by impairing Ca^{2+} entry into the mitochondria. This event prevents lipid peroxidation, antagonizes apoptosis and increases cancer cell proliferation. Accordingly, loss of function of Plcg1 in a mouse model of $Kras^{G12D}$-driven lung adenocarcinoma increased the expression of glycolytic genes, boosted tumour growth and reduced survival. In patients with KRAS-mutant lung adenocarcinomas, low PLCγ1 expression correlates with increased expression of hypoxia markers and predicts poor patient survival. Thus, our work reveals a mechanism of cancer cell adaptation to hypoxia with potential therapeutic value.
See original publication No 1

ACSL3-PAI-1 signaling axis mediates tumor-stroma crosstalk promoting pancreatic cancer progression
Rossi Sebastiano M, Pozzato C, Saliakoura M, Yang Z, Peng RW, Galiè M, Oberson K, Simon HU, Karamitopoulou E, Konstantinidou G
Pancreatic ductal adenocarcinoma (PDAC) is characterized by marked fibrosis and low immunogenicity, features that are linked to treatment resistance and poor clinical outcomes. Therefore, understanding how PDAC regulates the desmoplastic and immune stromal components is of great clinical importance. We found that acyl-CoA synthetase long-chain 3 (ACSL3) is up-regulated in PDAC and correlates with increased fibrosis. Our in vivo results show that *Acsl3* knockout hinders PDAC progression, markedly reduces tumor fibrosis and

tumor-infiltrating immunosuppressive cells and increases cytotoxic T cell infiltration. This effect is, at least in part, due to decreased plasminogen activator inhibitor-1 (PAI-1) secretion from tumor cells. Accordingly, *PAI-1* expression in PDAC positively correlates with markers of fibrosis and immunosuppression and predicts poor patient survival. We found that PAI-1 pharmacological inhibition strongly enhances chemo- and immunotherapeutic response against PDAC, increasing survival of mice. Thus, our results unveil ACSL3-PAI-1 signaling as a requirement for PDAC progression with druggable attributes.
See original publication No 2

The ACSL3-LPIAT1 signaling drives prostaglandin synthesis in non-small cell lung cancer
Saliakoura M, Reynoso-Moreno I, Pozzato C, Rossi Sebastiano M, Galié M, Gertsch J, Konstantinidou G
Enhanced prostaglandin production promotes the development and progression of cancer. Prostaglandins are generated from arachidonic acid (AA) by the action of cyclooxygenase (COX) isoenzymes. However, how cancer cells are able to maintain an elevated supply of AA for prostaglandin production remains unclear. Here, by using lung cancer cell lines and clinically relevant $Kras^{G12D}$-driven mouse models, we show that the long-chain acyl-CoA synthetase (ACSL3) channels AA into phosphatidylinositols to provide the lysophosphatidylinositol-acyltransferase 1 (LPIAT1) with a pool of AA to sustain high prostaglandin synthesis. LPIAT1 knockdown suppresses proliferation and anchorage-independent growth of lung cancer cell lines and hinders in vivo tumorigenesis. In primary human lung tumors, the expression of LPIAT1 is elevated compared with healthy tissue and predicts poor patient survival. This study uncovers the ACSL3-LPIAT1 axis as a requirement for the sustained prostaglandin synthesis in lung cancer with potential therapeutic value.
See original publication No 3

Original publications

1. Saliakoura M, Rossi Sebastiano M, Pozzato C, Heidel FH, Schnöder TM, Savic Prince S, Bubendorf L, Pinton P, A Schmid R, Baumgartner J, Freigang S, Berezowska SA, Rimessi A, **Konstantinidou G**: PLCγ1 suppression promotes the adaptation of KRAS-mutant lung adenocarcinomas to hypoxia.
Nat Cell Biol. 11 (2020), 1382-1395.

2. Rossi Sebastiano M, Pozzato C, Saliakoura M, Yang Z, Peng RW, Galiè M, Oberson K, Simon HU, Karamitopoulou E, **Konstantinidou G:** ACSL3-PAI-1 signaling axis mediates tumor-stroma crosstalk promoting pancreatic cancer progression.
Sci Adv. 6 (2020), eabb9200.

3. Saliakoura M, Reynoso-Moreno I, Pozzato C, Rossi Sebastiano M, Galié M, Gertsch J, **Konstantinidou G**: The ACSL3-LPIAT1 signaling drives prostagladin synthesis in non-small cell lung cancer. Oncogene 14 (2020), 2948-2960.

4. Ramadori G, Ioris RM, Villanyi Z, Firnkes R, Panasenko OO, Allen G, **Konstantinidou G**, Aras E, Brenachot X, Biscotti T, Charollais A, Luchetti M, Bezrukov F, Santinelli A, Samad M, Baldi P, Collart MA, Coppari R: FKBP10 regulates protein translation to sustain lung cancer growth.
Cell Rep.11 (2020), 3851-3863.

Editorial

1. **Konstantinidou G**, Rimessi A: Editorial: Oncogenic RAS-dependent reprogramming of cellular plasticity. Front Oncol. 10 (2020), 588.

Group Prof. Hans-Uwe Simon

Group members: Kevin Oberson, Lab Technician*
Meike Claus, Lab Technician*
Evelyne Kozlowski, Lab Technician*
Dr. Zhaoyue He, Postdoctoral fellow
Dr. Darko Stojkov, Postdoctoral fellow
Dr. Ziva Frangez, Postodoctoral fellow
Dr. Nina Germic, Postdoctoral fellow*
Kim Klapan, PhD student**
Peng Shuang, PhD student*
Nikita Markov, PhD student
Lea Gigon, PhD student*
Yihe Chen, PhD student*
Aref Hosseini, PhD student*
Philippe JeanRichard, M.Sc. pharm. student
David Fartelj, M.Sc. student*
Jacqueline Wyss, M.Sc. student
Timothée Fettrelet, M.Sc. student*

*Joint supervision together with Prof. S. Yousefi.
**Joint supervision together with Prof. D. Simon.

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, eosinophilic esophagitis, bullous pemphigoid and malignant melanoma. 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. Moreover, we are involved in several clinical drug studies. 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 2020.

Biochemical re-programming of human dermal stem cells to neurons by increasing mitochondrial membrane potential
Liu H, He Z, Leonhard April S, Trefny MP, Rougier JS, Salemi S, Olariu R, Widmer HR, Simon HU
Stem cells are generally believed to contain a small number of mitochondria, thus accounting for their glycolytic phenotype. We demonstrate here, however, that despite an indispensable glucose dependency, human dermal stem cells (hDSCs) contain very numerous mitochondria. Interestingly, these stem cells segregate into two distinct subpopulations. One exhibits high, the other low-mitochondrial membrane potentials (Δψm). We have made the same observations with mouse neural stem cells (mNSCs) which serve here as a complementary model to hDSCs. Strikingly, pharmacologic inhibition of phosphoinositide 3-kinase (PI3K) in-

creased the overall Δψm, decreased the dependency on glycolysis and led to formation of TUJ1 positive, electrophysiologically functional neuron-like cells in both mNSCs and hDSCs, even in the absence of any neuronal growth factors. Furthermore, of the two, it was the Δψm-high subpopulation which produced more mitochondrial reactive oxygen species (ROS) and showed an enhanced neuronal differentiation capacity as compared to the Δψm-low subpopulation. These data suggest that the Δψm-low stem cells may function as the dormant stem cell population to sustain future neuronal differentiation by avoiding excessive ROS production. Thus, chemical modulation of PI3K activity, switching the metabotype of hDSCs to neurons, may have potential as an autologous transplantation strategy for neurodegenerative diseases.

See original publication No 1

Mepolizumab failed to affect bullous pemphigoid: a randomized, placebo-controlled, double-blind phase 2 pilot study

Simon D, Yousefi S, Cazzaniga S, Bürgler C, Radonjic S, Houriet C, Heidemeyer K, Klötgen HW, Kozlowski E, Borradori L, Simon HU

Background: Bullous pemphigoid (BP) is associated with eosinophil infiltration in the skin. Eosinophils are assumed to contribute directly to blister formation upon activation with IL-5 and in the presence of bullous pemphigoid IgG autoantibodies.

Objective: To investigate the efficacy and safety of an anti-IL-5 monoclonal antibody therapy.

Methods: In this randomized, placebo-controlled, double-blind, phase 2 study, 30 patients received as an add-on therapy to corticosteroids, four intravenous injections of either mepolizumab 750 mg (n=20) or placebo (n=10), spaced 4 weeks apart over 12 weeks. The primary endpoint was the cumulative rate of relapse-free patients assessed 4 weeks after treatment and during follow-up to week 36. Cutaneous inflammation was monitored using immunofluorescence techniques.

Results: The proportion of relapse-free patients was the same between mepolizumab and placebo groups. Mepolizumab was well tolerated and safe. Mepolizumab had no impact on eosinophil numbers in the skin, but significantly lowered blood eosinophil numbers compared with placebo (p=0.007).

Conclusion: In this pilot study, mepolizumab did not show any significant effect on disease course in bullous pemphigoid patients. Factors responsible for this failure might be related either to the study design such as limited sample size and short treatment period, to the lack of a significant reduction in tissue eosinophils, or to a subordinate role of eosinophils in the pathogenesis of bullous pemphigoid.

See original publication No 2

RIPK3-MLKL-mediated neutrophil death requires concurrent activation of fibroblast activation protein-α

Wang X, Gessier F, Perozzo R, Stojkov D, Hosseini A, Amirshahrokhi K, Kuchen S, Yousefi S, Lötscher P, Simon HU

Cytokine-primed neutrophils can undergo a nonapoptotic type of cell death using components of the necroptotic pathway, including receptor-interacting protein kinase-3 (RIPK3), mixed lineage kinase-like (MLKL) and NADPH oxidase. In this report, we provide evidence for a potential role of serine proteases in CD44-mediated necroptotic death of GM-CSF-primed human neutrophils. Specifically, we observed that several inhibitors known to block the enzymatic function of fibroblast activation protein-α (FAP-α) were able to block CD44-mediated reactive oxygen species production and cell death, but not FAS receptor-mediated apoptosis. To understand how FAP-α is involved in this nonapoptotic death pathway, we performed immunoblotting experiments in the presence and absence of inhibitors of RIPK3, MLKL, p38 MAPK, PI3K, and FAP-α. The results of these experiments suggested that FAP-α is active in parallel with RIPK3, MLKL, and p38 MAPK activation but proximal to PI3K and

NADPH oxidase activation. Interestingly, neutrophils isolated from the joints of patients suffering from rheumatoid arthritis underwent a GM-CSF-independent necroptosis following CD44 ligation; this effect was also blocked by both FAP-α and MLKL inhibitors. Taken together, our evidence shows that the RIPK3-MLKL pathway activates NADPH oxidase but requires, in addition to p38 MAPK and PI3K, a serine protease activity, whereby FAP-α is the most likely candidate. Thus, FAP-α could be a potential drug target in neutrophilic inflammatory responses to avoid exaggerated nonapoptotic neutrophil death, leading to tissue damage.
See original publication No 3

BIF-1 inhibits both mitochondrial and glycolytic ATP production: its downregulation promotes melanoma growth.
Frangež Ž, Fernández-Marrero Y, Stojkov D, Seyed Jafari SM, Hunger RE, Djonov V, Riether C, Simon HU
Endophilin B1, also known as BAX-interacting protein 1 (BIF-1), is part of the endophilin B protein family, and is a multifunctional protein involved in the regulation of apoptosis, autophagy, and mitochondrial morphology. The role of BIF-1 in cancer is controversial since previous reports indicated to both tumor-promoting and tumor-suppressive roles, perhaps depending on the cancer cell type. In the present study, we report that BIF-1 is significantly downregulated in both primary and metastatic melanomas, and that patients with high levels of BIF-1 expression exhibited a better overall survival. Depleting BIF-1 using CRISPR/Cas9 technology in melanoma cells resulted in higher proliferation rates both in vitro and in vivo, a finding that was associated with increased ATP production, metabolic acidification, and mitochondrial respiration. We also observed mitochondrial hyperpolarization, but no increase in the mitochondrial content of BIF-1-knockout melanoma cells. In contrast, such knockout melanoma cells were equally sensitive to anticancer drug- or UV irradiation-induced cell death, and exhibited similar autophagic activities as compared with control cells. Taken together, it appears that downregulation of BIF-1 contributes to tumorigenesis in cutaneous melanoma by upregulating mitochondrial respiration and metabolism, independent of its effect on apoptosis and autophagy.
See original publication No 4

Original publications

1. Liu H, He Z, Germič N, Ademi H, Frangež Ž, Felser A, Peng S, Riether C, Djonov V, Nuoffer JM, Bovet C, Mlinarič-Raščan I, Zlobec I, Fiedler M, Perren A, **Simon HU**: ATG12 deficiency leads to tumor cell oncosis owing to diminished mitochondrial biogenesis and reduced cellular bioenergetics.
Cell Death Differ. 27 (2020), 1965–1980.

2. Simon D, Yousefi S, Cazzaniga S, Bürgler C, Radonjic S, Houriet C, Heidemeyer K, Klötgen HW, Kozlowski E, Borradori L, **Simon HU**: Mepolizumab failed to affect bullous pemphigoid: a randomized, placebo-controlled, double-blind phase 2 pilot study.
Allergy 75 (2020), 669–672.

3. Wang X, Gessier F, Perozzo R, Stojkov D, Hosseini A, Amirshahrokhi K, Kuchen S, Yousefi S, Lötscher P, **Simon HU**: RIPK3-MLKL-mediated neutrophil death requires concurrent activation of fibroblast activation protein-α.
J Immunol. 205 (2020), 1653-1663.

4. Frangež Ž, Fernández-Marrero Y, Stojkov D, Seyed Jafari SM, Hunger RE, Djonov V, Riether C, **Simon HU**: BIF-1 inhibits both mitochondrial and glycolytic ATP production: its downregulation promotes melanoma growth.
Oncogene. 39 (2020), 4944-4955.

5. He Z, Liu H, Moch H, **Simon HU**: Machine learning with autophagy-related proteins for discriminating renal cell carcinoma subtypes.
Sci Rep. 10 (2020), 720.

6. Frangež Ž, Seyed Jafari SM, Hunger RE, **Simon HU**: Loss of concurrent regulation of the expression of BIF-1, BAX and Beclin-1 in primary and metastatic melanoma.
Biochemistry (Moscow) 85 (2020), 1442-1451.

7. Müller I, Strozyk E, Schindler S, Beissert S, Oo HZ, Sauter T, Lucarelli P, Raeth S, Hausser A, Al Nakouzi N, Fazli L, Gleave ME, Liu H, **Simon HU**, Walczak H, Green DR, Bartek J, Daugaard M, Kulms D: Cancer cells employ nuclear caspase-8 to overcome the p53-dependent G2/M checkpoint through cleavage of USP28.
Mol Cell. 77 (2020), 970-984.

8. Arnold IC, Artola-Boran M, Gurtner A, Bertram K, Bauer M, Frangez Z, Becher B, Kopf M, Yousefi S, **Simon HU**, Tzankov A, Müller A: The GM-CSF-IRF5 signaling axis in eosinophils promotes antitumor immunity through activation of type 1 T cell responses.
J Exp Med. 217 (2020), e20190706.

9. Rossi Sebastiano M, Pozzato C, Saliakoura M, Yang Z, Peng RW, Galiè M, Oberson K, **Simon HU**, Karamitopoulou E, Konstantinidou G: ACSL3-PAI-1 signaling axis mediates tumor-stroma crosstalk promoting pancreatic cancer progression.
Sci Adv. 6 (2020), eabb9200.

10. Wehrli M, Schneider C, Cortinas-Elizondo F, Verschoor D, Frias Boligan K, Adams OJ, Hlushchuk R, Engelmann C, Daudel F, Villiger PM, Seibold F, Yawalkar N, Vonarburg C, Miescher S, Lötscher M, Kaufmann T, Münz C, Mueller C, Djonov V, **Simon HU**, von Gunten S: IgA triggers cell death of neutrophils when primed by inflammatory mediators.
J Immunol. 10 (2020), 2640-2648.

11. Schreiner P, Meissgeier S, Safroneeva E, Greuter T, Rogler G, Schoepfer A, Simon D, **Simon HU**, Biedermann L, Straumann A: Disease progression and outcomes of pregnancies in women with eosinophilic esophagitis.
Clin Gastroenterol Hepatol. 11 (2020), 2456-2462.

12. Wandrer F, Frangež Ž, Liebig S, John K, Vondran F, Wedemeyer H, Veltmann C, Pfeffer TJ, Shibolet O, Schulze-Osthoff K, **Simon HU**, Bantel H: Autophagy alleviates amiodarone-induced hepatotoxicity.
Arch Toxicol. 94 (2020), 3527-3539.

13. Karlen H, Yousefi S, **Simon HU**, Simon D: IL-15 expression pattern in atopic dermatitis.
Int Arch Allergy Immunol. 6 (2020), 417-421.

14. Graeter S, Schneider C, Verschoor D, von Däniken S, Seibold F, Yawalkar N, Villiger P, Dimitrov JD, Smith DF, Cummings RD, **Simon HU**, Vassilev T, von Gunten S: Enhanced pro-apoptotic effects of Fe(II)-modified IVIG on human neutrophils.
Front Immunol. 11 (2020), 973.

15. Cazzaniga S, Wiedmer C, Frangež Ž, Shafighi M, Beltraminelli H, Weber B, Simon D, Naldi L, **Simon HU**, Hunger RE, Seyed Jafari SM: Association of vascular endothelial growth factor subtypes with melanoma patients' characteristics and survival: A semantic connectivity map analysis.
Acta Derm Venereol. 100 (2020), 100.

16. Surmiak M, Gielicz A, Stojkov D, Szatanek R, Wawrzycka-Adamczyk K, Yousefi S, **Simon HU**, Sanak M: LTB4 and 5-oxo-ETE from extracellular vesicles stimulate neutrophils in granulomatosis with polyangiitis. J Lipid Res. 61 (2020), 1-9.

17. Biedermann L, Holbreich M, Atkins D, Chehade M, Dellon ES, Furuta GT, Hirano I, Gonsalves N, Greuter T, Gupta S, Katzka DA, De Rooij W, Safroneeva E, Schoepfer A, Schreiner P, Simon D, **Simon HU**, Warners M, Bredenoord AJ, Straumann A: Food-induced immediate response of the esophagus - A newly identified syndrome in patients with eosinophilic esophagitis.
Allergy 76 (2021), 339-347.

18. Rohner MH, Thormann K, Cazzangia S, Yousefi S, **Simon HU**, Schlapbach C, Simon D: Dupliumab reduces inflammation and restores the skin barrier in patients with atopic dermatitis.
Allergy, in press. doi: 10.1111/all.14664. Online ahead of print.

Review articles and Editorials

1. **Simon HU**, Yousefi S, Germic N, Arnold IC, Haczku A, Karaulov AV, Simon D, Rosenberg HF: The cellular functions of eosinophils: Collegium Internationale Allergologicum (CIA) Update 2020.
Int Arch Allergy Immunol. 181 (2020), 11-23.

2. Yousefi S, Simon D, Stojkov D, Karsonova A, Karaulov A, **Simon HU:** In vivo evidence for extracellular DNA trap formation.
Cell Death Dis. 11 (2020), 300.

3. **Simon HU**, Karaulov AV, Bachmann MF: Strategies to prevent SARS-CoV-2-mediated eosinophilic disease in association with COVID-19 vaccination and infection.
Int Arch Allergy Immunol. 181 (2020), 624-628.

4. Simon D, **Simon HU**: Relationship of skin barrier breakdown and eosinophilic esophagitis.
J Allergy Clin Immunol. 145 (2020), 90-92.

5. Markov N, **Simon HU**: IL-37: A new player in the chronic rhinosinusitis arena.
J Allergy Clin Immunol. 145 (2020), 105-107.

6. Piacentini M, Shi Y, **Simon HU**: 10 years of Cell Death & Disease.
Cell Death Dis. 11 (2020), 1064.

7. von Gunten S, **Simon HU**: Linking glucocorticoid-induced osteoporosis to osteoimmunology.
Cell Death Dis. 11 (2020), 1026.

8. Maurer M, Eyerich K, Eyerich S, Ferrer M, Gutermuth J, Hartmann K, Jakob T, Kapp A, Kolkhir P, Larenas-Linnemann D, Park HS, Pejler G, Sánchez-Borges M, Schäkel K, Simon D, **Simon HU**, Weller K, Zuberbier T, Metz M: Urticaria: Collegium Internationale Allergologicum (CIA) Update 2020**.**
Int Arch Allergy Immunol. 181 (2020), 321-333.

9. Graeter S, **Simon HU**, von Gunten S: Granulocyte death mediated by specific antibodies in intravenous immunoglobulin (IVIG).
Pharmacol Res. 154 (2020), 104168.

10. Gigon L, Yousefi S, Karaulov A, **Simon HU**: Mechanisms of toxicity mediated by neutrophil and eosinophil granule proteins.
Allergol Int. 70 (2021), 30-38.

Group Prof. Stephan von Gunten

Group members: Dr. Quentin Haas, postdoctoral fellow
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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 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.

IgA triggers cell death of neutrophils when primed by inflammatory mediators
Wehrli M, Schneider C, Cortinas-Elizondo F, Verschoor D, Frias Boligan K, Adams OJ, Hlushchuk R, Engelmann C, Daudel F, Villiger PM, Seibold F, Yawalkar N, Vonarburg C, Miescher S, Lötscher M, Kaufmann T, Münz C, Mueller C, Djonov V, Simon HU, von Gunten S
IVIG preparations consisting of pooled IgG are increasingly used for the treatment of autoimmune diseases. IVIG is known to regulate the viability of immune cells, including neutrophils. We report that plasma-derived IgA efficiently triggers death of neutrophils primed by cytokines or TLR agonists. IgA-mediated programmed neutrophil death was PI3K-, p38 MAPK-, and JNK-dependent and evoked anti-inflammatory cytokines in macrophage cocultures. Neutrophils from patients with acute Crohn's disease, rheumatoid arthritis, or sepsis were susceptible to both IgA- and IVIG-mediated death. In contrast to IVIG, IgA did not promote cell death of quiescent neutrophils. Our findings suggest that plasma-derived IgA might provide a therapeutic option for the treatment of neutrophil-associated inflammatory disorders.
See original publication No 1

Enhanced pro-apoptotic effects of Fe(II)-modified IVIG on human neutrophils
Graeter S, Schneider C, Verschoor D, von Däniken S, Seibold F, Yawalkar N, Villiger P, Dimitrov JD, Smith DF, Cummings RD, Simon HU, Vassilev T, von Gunten S
Mild modification of intravenous immunoglobulin (IVIG) has been reported to result in enhanced polyspecificity and leveraged therapeutic effects in animal models of inflammation. Here, we observed that IVIG modification by ferrous ions, heme or low pH exposure, shifted the repertoires of specificities in different directions. Ferrous ions exposed Fe(II)-IVIG, but not heme or low pH exposed IVIG, showed increased pro-apoptotic effects on neutrophil granulocytes that relied on a FAS-dependent mechanism. These effects were also observed in human neutrophils primed by inflammatory mediators or rheumatoid arthritis joint fluid *in vitro*, or patient neutrophils *ex vivo* from acute Crohn's disease. These observations indicate that IVIG-mediated effects on cells can be enhanced by IVIG modification, yet specific modification conditions may be required to target specific molecular pathways and eventually to enhance the therapeutic potential.
See original publication No 2

Xenogeneic Neu5Gc and self-glycan Neu5Ac epitopes are immune targets in multiple sclerosis
Boligan KF, Oechtering J, Keller CW, Peschke B, Rieben R, Bovin N, Kappos L, Cummings RD, Kuhle J, von Gunten S*, Lünemann JD* (*shared last authorship)
To explore the repertoire of glycan-specific immunoglobulin G (IgG) antibodies in treatment-naive patients with relapsing-remitting multiple sclerosis (RRMS). A systems-level approach combined with glycan array technologies was used to determine specificities and binding reactivities of glycan-specific IgGs in treatment-naive patients with RRMS compared with patients with noninflammatory and other inflammatory neurologic diseases. We identified a unique signature of glycan-binding IgG in MS with high reactivities to the dietary xenoglycan N-glycolylneuraminic acid (Neu5Gc) and the self-glycan N-acetylneuraminic acid (Neu5Ac). Increased reactivities of serum IgG toward Neu5Gc and Neu5Ac were additionally observed in an independent, treatment-naive cohort of patients with RRMS. Patients with MS show increased IgG reactivities to structurally related xenogeneic and human neuraminic acids. The discovery of these glycan-specific epitopes as immune targets and potential biomarkers in MS merits further investigation.
See original publication No 3

Original publications

1. Wehrli M, Schneider C, Cortinas-Elizondo F, Verschoor D, Frias Boligan K, Adams OJ, Hlushchuk R, Engelmann C, Daudel F, Villiger PM, Seibold F, Yawalkar N, Vonarburg C, Miescher S, Lötscher M, Kaufmann T, Münz C, Mueller C, Djonov V, Simon HU, **von Gunten S**: IgA triggers cell death of neutrophils when primed by inflammatory mediators. J Immunol. 205 (2020), 2640-2648.

2. Graeter S, Schneider C, Verschoor D, von Däniken S, Seibold F, Yawalkar N, Villiger P, Dimitrov JD, Smith DF, Cummings RD, Simon HU, Vassilev T, **von Gunten S**: Enhanced pro-apoptotic effects of Fe (II)-modified IVIG on human neutrophils.
Front Immunol. 11 (2020), 973.

3. Boligan KF, Oechtering J, Keller CW, Peschke B, Rieben R, Bovin N, Kappos L, Cummings RD, Kuhle J, **von Gunten S***, Lünemann JD*: Xenogeneic Neu5Gc and self-glycan Neu5Ac epitopes are potential immune targets in MS.
Neurol Neuroimmunol Neuroinflamm. 7 (2020), e676.
*shared last authorship

4. Luetscher RND, McKitrick TR, Gao C, Mehta AY, McQuillan AM, Kardish R, Boligan KF, Song X, Lu L, Heimburg-Molinaro J, **von Gunten S**, Alter G, Cummings RD: Unique repertoire of anti-carbohydrate antibodies in individual human serum.
Sci Rep. 10 (2020), 15436.

5. Yu Y, Ladeiras D, Xiong Y, Boligan KF, Liang X, **von Gunten S**, Hunger RE, Ming XF, Yang Z: Arginase-II promotes melanoma migration and adhesion through enhancing hydrogen peroxide production and STAT3 signaling.
J Cell Physiol. 235 (2020), 9997-10011.

6. Sterlin D, Fadlallah J, Adams O, Fieschi C, Parizot C, Dorgham K, Rajkumar A, Autaa G, El-Kafsi H, Charuel JL, Juste C, Jönsson F, Candela T, Wardemann H, Aubry A, Capito C, Brisson H, Tresallet C, Cummings RD, Larsen M, Yssel H, **von Gunten S**, Gorochov G: Human IgA binds a diverse array of commensal bacteria.
J Exp Med. 217 (2020), e20181635.

*7. Sterlin D, Fadlallah J, Adams O, Fieschi C, Parizot C, Dorgham K, Rajkumar A, Autaa G, El-Kafsi H, Charuel JL, Juste C, Jönsson F, Candela T, Wardemann H, Aubry A, Capito C, Brisson H, Tresallet C, Cummings RD, Larsen M, Yssel H, **von Gunten S**, Gorochov G: **Correction:** Human IgA binds a diverse array of commensal bacteria.
J Exp Med. 217 (2020), e2018163501152020c.*

8. Engeroff P, Plattner K, Storni F, Thoms F, Frias Boligan K, Muerner L, **von Gunten S**, Eggel A, Bachmann MF, Vogel M: Glycan-specific IgG anti-IgE autoantibodies are protective against allergic anaphylaxis.
J Allergy Clin Immunol., in press. doi: 10.1016/j.jaci.2020.11.031. Online ahead of print.

9. Wang J, **von Gunten S**, Beldi G, Grandgirard D, Leib SL, Gottstein B: Digest the sugar, kill the parasite: A new experimental concept in treating alveolar Echinococcosis.
Pharmacol., in press. doi: 10.1159/000509355. Online ahead of print.

Review articles and Editorials

1. Graeter S, Simon HU, **von Gunten S:** Granulocyte death mediated by specific antibodies in intravenous immunoglobulin (IVIG).
Pharmacol Res. 154 (2020), 104168.

2. Spinetti T, Meisel C, **von Gunten S**, Schefold JC: Immune biomarker-based enrichment in sepsis trials. Crit Care. 24 (2020), 58.

3. **von Gunten S:** The future of Pharmacology: Towards more personalized pharmacotherapy and reverse translational research.
Pharmacol. 105 (2020), 1-2.

4. **von Gunten S:** Secondary-type carbohydrate modification as a driver of epithelial-mesenchymal transition and features of cancer stem sells.
Pharmacol. 105 (2020), 244-245.

5. **von Gunten S**, Simon HU: Linking glucocorticoid-induced osteoporosis to osteoimmunology.
Cell Death Dis. 11 (2020), 1026.

6. **von Gunten S**: Inflamm-Aging: Arginase-II as stage setter in age-related adipose tissue inflammation.
Pharmacol. 105 (2020), 489-490.

7. Cummings RD, **von Gunten S:** Targeting the laminated layer of Echinococcus multilocularis as a potential therapeutic strategy.
Pharmacol., in press. doi:10.1159/000512769. Online ahead of print.

Group Prof. Shida Yousefi

Group members: Meike Claus, Technician*
Evelyne Kozlowski, Technician*
Kevin Oberson, Technician*
Dr. Nina Germic, Postdoctoral fellow*
Shuang Peng, PhD student*
Yihe Chen, PhD student*
Lea Gigon, PhD student *
Aref Hosseini, PhD student*
David Fartelj, M.Sc. student*
Timothée Fettrelet, M.Sc. student*

*Joint supervision together with Prof. H.-U. Simon.

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. Our aim is to investigate mouse and human neutrophils with respect to their extracellular DNA trap formation and the molecular events required.

Original publications

1. Arnold IC, Artola-Boran M, Gurtner A, Bertram K, Bauer M, Frangez Z, Becher B, Kopf M, **Yousefi S**, Simon HU, Tzankov A, Müller A: The GM-CSF-IRF5 signaling axis in eosinophils promotes antitumor immunity through activation of type 1 T cell responses. J Exp Med. 217 (2020), e20190706.

2. Wang X, Gessier F, Perozzo R, Stojkov D, Hosseini A, Amirshahrokhi K, Kuchen S, **Yousefi S**, Lötscher P, Simon HU: RIPK3-MLKL-Mediated Neutrophil Death Requires Concurrent Activation of Fibroblast Activation Protein-α. J Immunol. 205 (2020), 1653-1663.

3. Karlen H, **Yousefi S**, Simon HU, Simon D: IL-15 Expression Pattern in Atopic Dermatitis. Int Arch Allergy Immunol. 6 (2020), 417-421.

4. Simon D, **Yousefi S**, Cazzaniga S, Bürgler C, Radonjic S, Houriet C, Heidemeyer K, Klötgen HW, Kozlowski E, Borradori L, Simon HU: Mepolizumab failed to affect bullous pemphigoid: a randomized, placebo-controlled, double-blind phase 2 pilot study. Allergy 75 (2020), 669–723.

5. Surmiak M, Gielicz A, Stojkov D, Szatanek R, Wawrzycka-Adamczyk K, **Yousefi S**, Simon HU, Sanak M: LTB4 and 5-oxo-ETE from extracellular vesicles stimulate neutrophils in granulomatosis with polyangiitis.
J Lipid Res. 2020 61(1):1-9.

6. Rohner MH, Thormann K, Cazzangia S, **Yousefi S**, Simon HU, Schlapbach C, Simon D: Dupliumab reduces inflammation and restores the skin barrier in patients with atopic dermatitis.
Allergy, in press. doi: 10.1111/all.14664. Online ahead of print.

Review articles

1. **Yousefi S**, Simon D, Stojkov D, Karsonova A, Karaulov A, Simon HU: In vivo evidence for extracellular DNA trap formation.
Cell Death Dis. 11 (2020), 300.

2. Simon HU, **Yousefi S**, Germic N, Arnold IC, Haczku A, Karaulov AV, Simon D, Rosenberg HF: The cellular functions of eosinophils: Collegium Internationale Allergologicum (CIA) Update 2020.
Int Arch Allergy Immunol. 181 (2020), 11-23.

3. Gigon L, **Yousefi S**, Karaulov A, Simon HU: Mechanisms of toxicity mediated by neutrophil and eosinophil granule proteins.
Allergol Int. 70 (2021), 30-38.

Group Prof. Uwe Zangemeister-Wittke

Group members: Martin Erhardt, PhD student
Fabian Weiss, PhD student[1]
Fabian Brandl, PhD student[1] (until October 2020)
Hannes Merten, PhD student[1] (until August 2020)

[1]Institute of Biochemistry, University of Zürich

Our research is dedicated to translational aspects of molecular oncology and tumor targeting using rationally engineered and pharmacologically improved fusion proteins and protein-drug conjugates. For tumor targeting we employ Designed Ankyrin Repeat Proteins (DARPins) as highly stable non-IgG scaffold proteins for site-specific and orthogonal conjugation, to generate drug conjugates of defined stoichiometry and optimized pharmacokinetics. The affinity-maturated DARPins were genetically modified and expressed in in a special E. coli strain to obtain proteins carrying both a thiol and an azide group for thiol-maleimide conjugation and strain-promoted azide-alkyne cycloaddition (click chemistry). Based on this technology, we have generated nanomedicines payloaded with cytotoxins of various origins, including domain I-truncated Pseudomonas Aeruginosa Exotoxin A engineered to a prodrug activated by specific enzymes in tumor-tissues, and the antimitotic agent Monomethyl Auristatin F (MMAF). To quantitatively improve tumor localization, the serum half-life of the bioconjugates was extended by site-specific conjugation with serum albumin or the synthetic unstructured polypeptides PAS or XTEN with variable length. In addition, in collaboration with A. Huwiler (see project description above) we use established human tumor cell lines from primary tumors and from metastases of different sites to investigate the role of various components of the sphingolipid signaling pathway in malignant progression and metastasis.

Original publications

1. Brandl F, Busslinger S, **Zangemeister-Wittke U**, Plückthun A: Optimizing the anti-tumor efficacy of protein-drug conjugates by engineering the molecular size and half-life. J Control Release 327 (2020), 186-197.

2. Schwalm S, Erhardt M, Römer I, Pfeilschifter J, **Zangemeister-Wittke U**, Huwiler A: Ceramide kinase is upregulated in metastatic breast cancer cells and contributes to migration and invasion by activation of PI 3-kinase and Akt. Int J Mol Sci. 21 (2020), 1396-1408.

Group Prof. Manuel Haschke (Clinical Pharmacology)

Group members: Evangelia Liakoni, MD
Felix Hammann, MD, PhD
Irene Scholz, med pract
Vera van der Velpen, PhD

We are interested in mechanisms of drug toxicity and factors responsible for variations in the metabolism of xenobiotics. We use a cocktail of low-dose probe drugs to investigate alterations in phase I metabolism in outpatients with suspected intolerance to normal drug doses. In a clinical study, we quantified the effect of the CYP- and P-gp-inducer hypericum perforatum (a component of St. John's wort preparations used as antidepressant) on the pharmacokinetics and pharmacodynamics of the direct oral factor Xa inhibitor rivaroxaban. We conducted a genome-wide association study to search for potential genetic risk factors for metamizole-induced agranulocytosis, comparing patients with this adverse drug reaction with metamizole-tolerant and never-exposed subjects. As part of the European Drug Emergency Network (EuroDEN) data on toxicity of recreational drugs and novel psychoactive substances is collected and analyzed at regular intervals. In the nicotine field, two studies are in preparation. In a first smaller clinical study in healthy volunteers, pharmacokinetics and pharmacodynamics of two different nicotine salt concentrations will be compared with free base nicotine using an open vape pod system. In a subsequent larger study, the efficacy of a nicotine salt vape pod system as a smoking cessation tool will be tested in adult smokers willing to quit smoking. In another project, arthropods are investigated as new pharmacokinetic model organisms in the framework of an endectocide-based malaria intervention trial in Africa.

Original publications

1. Cismaru AL, Grimm L, Rudin D, Ibañez L, Liakoni E, Bonadies N, Kreutz R, Hallberg P, Wadelius M, EuDAC Collaborators, **Haschke M**, Largiadèr CR, Amstutz U (2020): High-throughput sequencing to investigate associations between HLA genes and metamizole-induced agranulocytosis.
   Front Genet. 11 (2020), 951.

2. Scholz I, Liakoni E, Hammann F, Grafinger KE, Duthaler U, Nagler M, Krähenbühl S, **Haschke M**: Effects of Hypericum perforatum (St John's wort) on the pharmacokinetics and pharmacodynamics of rivaroxaban in humans.
   Br J Clin Pharmacol., in press. doi: 10.1111/bcp.14553. Online ahead of print.

3. Cismaru AL, Rudin D, Ibañez L, Liakoni E, Bonadies N, Kreutz R, Carvajal A, Lucena MI, Martin J, Sancho Ponce E, Molokhia M, Eriksson N, EuDAC collaborators, Krähenbühl S,. Largiadèr CR, **Haschke M**, Hallberg P, Wadelius M, Amstutz U: Genome-wide association study of metamizole-induced agranulocytosis in European populations.
   Genes 11 (2020), 1275.

4. Bachmann F, Blaser L, **Haschke M**, Krähenbühl S, Duthaler U: Development and validation of an LC-MS/MS method for the bioanalysis of the major metamizole metabolites in human plasma.
   Bioanalysis 12 (2020), 175-189.

5. Stojkov K, Silzle T, Stussi G, Schwappach D, Bernhard J, Bowen D, Čermák J, Dinmohamed AG, Eeltink C, Eggmann S, Fenaux P, Germing U, **Haschke M**, Hellstrom-Lindberg E, Heger M, van de Loosdrecht AA, Passweg J, Pfeilstöcker M, Platzbecker U, Malcovati L, de Almeida AM, Mittelman M, Morgenthaler C, Steensma DP, Santini V, Stauder R, Symeonidis A, Schär S, Maddox C, de Witte T, Bohlius J, Bonadies N: Guideline-based indicators for adult patients with myelodysplastic syndromes. Blood Adv.16 (2020), 4029-4044.

6. Suenderhauf C, Berger B, Puchkov M, Schmid Y, Müller S, Huwyler J, **Haschke M**, Krähenbühl S, Duthaler U: Pharmacokinetics and phenotyping properties of the Basel phenotyping cocktail combination capsule in healthy male adults. Br J Clin Pharmacol. 86 (2020), 352-361.

Review articles

1. Grafinger KE, Liechti ME, Liakoni E: Clinical value of analytical testing in patients presenting with new psychoactive substances intoxication. Br J Clin Pharmacol. 86 (2020), 429–436.

2. Banholzer S, **Haschke M**: Fallbericht: Valproat während der Schwangerschaft – kongenitale Missbildungen und Beeinträchtigung der Entwickung. Swissmedic Vigilance-News Ed. 24 (2020), 7-10.

3. Liakoni E, Hammann F, **Haschke M**: Hydroxychloroquin und Corona virus disease 2019. Swiss Med Forum 3134 (2020), 441-445.

Additional Publications by PKI Members

Original publications

Wahn V, Aberer W, Aygören-Pürsün E, Bork K, Eberl W, Faßhauer M, Krüger R, Magerl M, Martinez-Saguer I, **Späth P**, Staubach-Renz P, Weber-Chrysochoou C: Hereditary angioedema in children and adolescents - A consensus update on therapeutic strategies for German-speaking countries.
Pediatr Allergy Immunol. 31 (2020), 974-989.

Spirk D, Sebastian T, Barco S, Banyai M, Beer JH, Mazzolai L, Baldi T, Aujesky D, Hayoz D, Engelberger RP, Kaeslin T, Korte W, Escher R, Husmann M, Blondon M, Kucher N: Clinical outcomes of incidental venous thromboembolism in cancer and noncancer patients: The SWIss Venous ThromboEmbolism Registry (SWIVTER).
Thromb Haemost., in press. doi: 10.1055/s-0040-1720977. Online ahead of print.

Sebastian T, Barco S, Engelberger RP, **Spirk D**, Schindewolf M, Baumann F, Baumgartner I, Kucher N: Duplex ultrasound investigation for the detection of obstructed iliocaval venous stents.
Eur J Vasc Endovasc Surg. 3 (2020), 443-450.

Spirk D, Noll S, Burnier M, Rimoldi S, Noll G, Sudano I: First Line combinAtion therapy in the treatment of Stage II and III Hypertension (FLASH).
Front Cardiovasc Med. 7 (2020), 46.

Zanchin C, Ueki Y, Losdat S, Fahrni G, Daemen J, Ondracek AS, Häner JD, Stortecky S, Otsuka T, Siontis GCM, Rigamonti F, Radu M, **Spirk D**, Kaiser C, Engstrom T, Lang I, Koskinas KC, Räber L: In vivo relationship between near-infrared spectroscopy-detected lipid-rich plaques and morphological plaque characteristics by optical coherence tomography and intravascular ultrasound: a multimodality intravascular imaging study.
Eur Heart J Cardiovasc Imaging, in press. doi: 10.1093/ehjci/jez318. Online ahead of print.

Review article

Dalakas MC, Alexopoulos H, **Spaeth P**: Complement in neurological disorders and emerging complement-targeted therapeutics.
Nat Rev Neurol. 16 (2020), 601-617.

4.2. Congress Invitations

Prof. Hans-Uwe Simon
2020 National Cheng Kung University (NCKU) International Virtual Forum on COVID-19, Tainan (Taiwan); April 21, 2020:
COVID-19 testing and vaccination: Research activities of the University of Bern, Switzerland.

Austrian Eos Summit, Vienna (Austria); Oct. 23, 2020 (virtual meeting, sponsored by GSK):
The biology of eosinophils and their role in disease.

Virtual scientific meeting: 30 years Department of Clinical Immunology and Allergology (1990-2020), Sechenov University Moscow (Russia); Nov. 16, 2020:
Molecular and immunological characteristics of the inflammatory response in esophagitis.

12th EADV Dermatological Meeting in Ticino, Bellinzona (CH); Nov. 21, 2020 (virtual):
Expression and function of the BK channel in neutrophils.

Molecular Allergology Congress (MAC-2020), Moscow (Russia); Dec. 1-2, 2020 (virtual):
Eosinophil effector functions are regulated by autophagy.

Prof. Thomas Kaufmann
Second LS2 Autophagy Workshop, Fribourg (CH); Sept. 7, 2020:
Cell death.

Prof. Georgia Konstantinidou
Second LS^2 Autophagy Workshop, Fribourg (CH); Sept. 7, 2020:
In vivo cancer models.

Prof. Stephan von Gunten
Bern Center for Precision Medicine (BCPM) Members' Retreat 2020, Gurten-Park im Grünen, Wabern (CH); Jan. 31, 2020:
Integrating data from multiple platforms: Functional glycomics - patient immunoprofiles in cancer.

4.3. Seminar Invitations

Prof. Hans-Uwe Simon
Molecular, Cellular, and Clinical Allergology (MCCA) online lecture,
Medical University of Vienna, Vienna (A); Dec. 16, 2020; Guest of Prof. Winfried Pickl and Prof. Rudolf Valenta:
Mast cells and basophils: Biological properties and role in health and disease.

Molecular, Cellular, and Clinical Allergology (MCCA) online lecture,
Medical University of Vienna, Vienna (A); Dec. 17, 2020; Guest of Prof. Winfried Pickl and Prof. Rudolf Valenta:
Eosinophils: Biological properties and role in allergic diseases.

Prof. Georgia Konstantinidou
Department of Biomedical Sciences, University of Lausanne, Lausanne (CH), Sept. 8, 2020;
guest of Prof. Christian Widmann:
Understanding KRAS-driven tumor biology.

Prof. Stephan von Gunten
CIMI research centre, Sorbonne University, Paris (F), January 27, 2020;
guest of Prof. Guy Gorochow:
Glycoimmunology – novel insights.

Department of Molecular Mechanisms of Disease, University of Zurich, Zurich (CH),
Febr. 12, 2020; guest of Prof. Michael Hottiger and Dr. Tobias Suter:
Tumor glycans as targets for cancer immunotherapy.

Department for BioMedical Research (DBMR), University of Bern, Bern (CH),
Febr. 25, 2020; guest of Prof. Andrew Macpherson:
Glycans as antigens and immune check-points.

Institute of Physiology & Institute of Veterinary Physiology, University of Zurich, Zurich (CH),
May 10, 2020; guest of Prof. Thierry Hennet:
Glycoimmunology – Antibodies and immune checkpoints.

Bern Center for Precision Medicine (BCPM) Webinar Series, Online, September 10, 2020;
Functional glycomics - patient immunoprofiles in cancer.

4.4. Organization of Meetings and Courses

Prof. Hans-Uwe Simon
Symposium of the Swiss Society of Pharmacology and Toxicology (SSPT):
Progress in Pharmacology - Focus on Cardiovascular Disease,
Bern (CH), Jan. 22, 2020

19th III-Bern International Summer School,
Bönigen (CH), July 26-28, 2020

Prof. Georgia Konstantinidou
2nd Bern Cancer Research Cluster (BCRC) retreat.
Online meeting (CH), Oct. 15, 2020

4.5. Invited Chairperson at Congresses

Prof. Hans-Uwe Simon
Symposium of the Swiss Society of Pharmacology and Toxicology (SSPT): Progress in Pharmacology – Focus on Cardiovascular Disease, Morning session; Bern (CH), Jan. 22, 2020.

Virtual scientific meeting: 30 years Department of Clinical Immunology and Allergology (1990-2020), Sechenov University (Moscow, Russia); Plenary Session: Biologicals in the practice of an allergologist-immunologist: today and tomorrow; Moscow (Russia), Nov. 16, 2020.

4.6. Referee Work for Peer-Reviewed Journals

Dr. Zhaoyue He
Cell Death Differ.
Cell Death Dis.

Dr. Ziva Frangez
Cell Death Dis.
Int. Arch. Allergy Immunol.

Prof. Andrea Huwiler
Biochem. Pharmacol.
Biochim. Biophys. Acta
Br. J. Pharmacol.
Cellular Signaling
Cell. Physiol. Biochem
Clin. Chem. Lab. Med.
Eur. J. Pharmacol.
Frontiers in Pharmacology
Int. J. Mol. Sci.
J. Cell. Biochem.
J. Exp. Pharmacol. Ther.
Naunyn Schmiedeb. Arch. Pharmacol.

Prof. Thomas Kaufmann
Acta Tropica
Advances in Medicine
Apoptosis
Allergy
BioEssays
Cell Communication and Signaling
Cell Death Differ.
Cell Death Dis.
Cellular & Molecular Immunology
Eur. J. Immunol.
FEBS Letter
FEBS Journal
Frontiers in Molecular and Cellular Oncology
Future Oncology
Immunology and Cell Biology
Int. Arch. Allergy Immunology
Trends Cell Bioology
Int. Rev. Cell Mol. Biol.
Sci. Rep.
J. Hepatology
J. Molecular Cell Biology
J. Neuroscience
Methods
Molecular Cancer Therapeutics
Mol. Cell. Oncology
Oncogene
PLoS One
Hepatology

Prof. Georgia Konstantinidou
Cell Death Dis.
Oncotarget
Frontiers in Oncology
J Exp Clin Res
eLIFE
Cancer research
Cancers

Prof. Hans-Uwe Simon

Allergy
Apoptosis
Autophagy
Blood
FEBS J.
Eur. J. Acad. Dermatol. Venerol.
Eur. J. Immunol.
Cell Death Differ.
Cell Death Dis.
Gut
J. Allergy Clin. Immunol.
J. Exp. Med.
J. Immunol.
Oncogene
Nat. Commun.
N. Engl. J. Med.
Sci. Adv,
Cell Rep.

PD Dr. Peter Späth

BMJ Open
Neurology
Therap. Adv. in Neurol. Disord.
Rev. on Rec. Clin. Trials

Dr. Bisera Stepanovska Tanturovska

Biochem. Pharmacol.

Prof. Stephan von Gunten

ACS Chemical Biology
ACS Omega
Allergy
Am. J. Respir. Cell Mol. Biol.
Ann. Sports Med. Res.
Arch Immunol Ther Exp
Arch Toxicol
Arthritis Res. Ther.
Blood
BMC Biotech.
Cell Death Differ.
Cell Death Dis.
Cell Mol Immunol
Comput Biol Chem
Curr. Med. Chem.
Cytotherapy
FASEB
Frontiers Oncology
Frontiers Pediatrics
Gene Therapy
Glycoconj J
Glycobiol.
Immunol. Cell Biol.
Immunol. Lett.
Int Arch Allergy Immunol
Int. Immunopharm.
JACI pract
J. Allergy Clin. Immunol.
J. Clin. Invest.
J Invest. Dermatol
J. Immunol.
J. Immunotox.
Med. Inflamm.
Nat Chem Biol
Respiration
Oncotarget
Pathobiology
Pediatrics
PLoS Pathogens
PLoS One
PNAS
Respir. Res
Scientific Reports
Tuberculosis
Tumor biology

Prof. Shida Yousefi

Cell Biol. Int.
Cell Biochem. Biophys.
Cell Death Differ.
Cell Death Dis.
Eur. J. Immunol.
Exp. Lung Res.
Int. J. Mol. Sci.
Immunology
J. Vasc. Intervent. Radiol.
J. Cell. Biochem.
Respir. Res.
Sci. Rep.
Int. J. Biochem. Cell Biol.
Thorax
Virulance

Prof. Uwe Zangemeister-Wittke

Bioconjug. Chem.
J. Control. Release
Cell Death Dis.
Cancers
Int. J. Mol. Sciences
Proteins

Prof. Manuel Haschke

British J Clin Pharmacol
Pediatric Drugs

PD Evangelia Liakoni

Annals of Internal Medicine
Academic Psychiatry
Bioanalysis
Case reports in Emergency Medicine
Journal of Occup. Med. and Tox.
Pharmacology
Plos One
Swiss Medical Forum

PD Felix Hammann

J. Med. Chem.
Sci. Rep.

4.7. 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)

Prof. Georgia Konstantinidou

European Research Council (ERC)
Bernese Cancer league

Prof. Stephan von Gunten

Canadian Glycomics Network
Best Cancer Now
Dutch Cancer Society (DCS)

Prof. Uwe Zangemeister-Wittke

La Caixa Foundation, Barcelona
Netherlands Organisation for Scientific Research
Qatar National Research Fund (QNRF)

4.8. Awards

Prof. Hans-Uwe Simon
Phoenix Wissenschaftspreis Bern
Bern (CH), Nov 2020

Prof. Shida Yousefi
Phoenix Wissenschaftspreis Bern
Bern (CH), Nov 2020

Dr. Darko Stojkov
Phoenix Wissenschaftspreis Bern
Bern (CH), Nov 2020

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

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 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)

Prof. 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

Prof. Hans-Uwe Simon
Dean, Faculty of Medicine, University of Bern (until July 2020)

President, Collegium of the Deans of the Swiss Faculties of Medicine (until July 2020)

Vorstandsmitglied, Universitäre Medizin Schweiz (until July 2020)

Mitglied der Direktion, Insel Gruppe AG (until July 2020)

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

Head, EoE biobank, Swiss EoE Cohort Study (SEECS)

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

Visiting-Professor, Medical University of Moscow – Department of Clinical Immunology and Allergology, Sechenov University, Moscow (Russia)

Visiting-Professor, Institute of Fundamental Medicine and Biology, Kazan Federal University, Kazan (Russia)

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" for public consultation in fall 2020

Member of taskforce for the 2021 revision and update of the WAO/EAACI HAE guideline – delegated for the recommendations on „Nomenclature and diagnosis of HAE" (HAE=hereditary angioedema)

Prof. Stephan von Gunten
Editor-in-Chief, PHARMACOLOGY

President of the Swiss Society of Experimental Pharmacology (SSEP) (until April 2020)

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

Coordinator library at the PKI

Prof. Shida Yousefi
Coordinator for Radioactive Work, Confocal Microscopy and Imaging Analysis at the PKI

Prof. Uwe Zangemeister-Wittke
Consultant of the Human SwissMedic Expert Committee

Consultant of the Scientific Committee of the Facultad de Medicina, Clinica Alemana-Universidad del Desarrollo, Santiago de Chile

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)

Board member of the Working Group Medication and Patient Safety, Inselspital, University Hospital

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

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

All PKI principal investigators served as tutors in graduation committes 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.

7. Public work

Art Exhibition

No exhibition in 2020 owing to Corona pandemic.

8. Sponsors

8.1. Research Grants

Dr. Faik Imeri
Swiss National Science Foundation (grant No. 310030_175561)

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

Prof. Thomas Kaufmann
Swiss National Science Foundation (grant No 31003A_173006)

Prof. Georgia Konstantinidou
Swiss National Science Foundation, SNF-Professorship until July 2020 (grant No. PP00P3_163929) and 2-year prolongation from August 2020 (grant No. PP00P3_194810)
Novartis Foundation for Biological-Medical Research, Novartis, Basel (CH)
Innosuisse-Swiss Innovation Agency #40922.1 IP-LS
Helmut Horten Stiftung

Prof. Hans-Uwe Simon
Swiss National Science Foundation (grant No. 310030_184816)
HORIZON 2020, Marie Sklodowska-Curie Actions, MEL-PLEX
GSK Switzerland Pharma, Münchenbuchsee, Switzerland
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 Cancer League (KFS-4958-02-2020)
Palleon Pharmaceuticals Inc., Waltham MA (USA)
Bern Center for Precision Medicine (BCPM) Grant

Prof. Shida Yousefi
Swiss National Science Foundation (grant No. 31003A_173215)

Prof. Uwe Zangemeister-Wittke
Swiss National Science Foundation (grant No. 31003A_170134)
Sassella-Stiftung of the Zürcher Kantonalbank

Prof. Manuel Haschke
Swiss National Science Foundation (grant No. 31003A_160206 / 32003B_179346)

PD Evangelia Liakoni
Swiss National Science Foundation (grant No. 32003B_189132)
CTU- Forschungsgrant 2019-06

PD Felix Hammann
Broad One Health Endectocide-based Malaria Intervention in Africa (BOHEMIA, unitaid.org)

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. 22, 2020
Sanofi-Aventis AG, Vernier
Amgen Switzerland AG, Rotkreuz
Bayer (Schweiz) AG, Zürich
Bristol-Myers Squibb SA, Cham
Novartis Pharma Schweiz AG, Rotkreuz
Pfizer AG, Zürich

19th III-Bern International Summer School
Seehotel La Terrasse, CH 3806 - Bönigen, July 26 – 28, 2020
Bucher Biotec, Basel
Carl Zeiss AG, Feldbach
GSK, Münchenbuchsee
Mycrosynth AG, Balgach
Pfizer AG, Zürich
Zentrum für Labormedizin, Inselspital Bern
Graduate School for Cellular and Biomedical Sciences, Universität Bern

8.3. Seminar Series

„Current topics in Pharmacology and Theranostics“ (organized together with the Center of Laboratory Medicine and Division of Clinical Pharmacology, University Hospital Bern, Inselspital)
GSK, Münchenbuchsee

8.4. Travel Support

No travel support in 2020.

8.5. Other Support

Bürgi Fonds Seminar series of the institute