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UNIVERSITÄT
BERN

Institut für Pharmakologie

PKI

Jahresbericht

2017

Annual Report 2017

Institut für Pharmakologie (PKI) der Universität Bern

Institute of Pharmacology University of Bern

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Inhaltsverzeichnis

1. Introduction

1.1. Vorwort

Dies ist der siebzehnte umfassende Jahresbericht des Instituts für Pharmakologie (PKI) der Universität Bern. Das PKI hat auch im Jahr 2017 seine Aufgaben in Lehre und Forschung innerhalb der Medizinischen Fakultät vorbildlich erfüllt. Nach unserem Umzug im Jahr 2015 bietet uns das INO-Gebäude des Inselspitals hervorragende Bedingungen für eine erfolgreiche Forschungstätigkeit. Mit dem Zentrum für Labormedizin teilen wir uns den Stock F und nutzen gemeinsam die vorhandene Infrastruktur. In Lehre und Forschung wurden inzwischen zahlreiche neue Projekte gestartet, mit dem Ziel die personalisierte Medizin weiter zu entwickeln. Im April 2017 startete Prof. Dr. Manuel Haschke mit seiner Forschungsgruppe für Klinische Pharmakologie in unser Institut und inzwischen sind auch seine zwei aus Basel mitgebrachten Massenspektrometer installiert. Wir sind überzeugt, dass sich mit der Rekrutierung von Prof. Haschke neue Möglichkeiten der Zusammenarbeit eröffnen werden, sowohl in der *biologischen Grundlagen-* als auch in der *klinischen Forschung*, beides Kernaufgaben der Pharmakologie, bzw. klinischen Pharmakologie.

Das PKI arbeitet eng mit verschiedenen Kliniken des Inselspitals und mit anderen Forschungseinrichtungen der Universität Bern zusammen. Damit wollen wir helfen, die translationale Forschung sowie die Aus-, Weiter- und Fortbildung an der Medizinischen Fakultät zu stärken. Zum anderen sind wir an der Zusammenarbeit mit Firmen interessiert, wie die weiter hinten aufgeführten gegenwärtigen Kontakte der einzelnen Forschungsgruppen zeigen. Auch im Jahr 2017 trugen wir dazu bei, die Kommunikation zwischen WissenschaftlerInnen und Öffentlichkeit zu fördern.

Neben unserer regulären Lehrtätigkeit im 3. und 6. Studienjahr Medizin sowie der Ausbildung der ZahnmedizinerInnen sind einige DozentInnen des Instituts zusätzlich in die Immunologie-Ausbildung von StudentInnen der Biologie (Naturwissenschaftliche Fakultät der Universität Bern) einbezogen. Weiterhin sind wir auch für die Pharmakologie-Ausbildung in B.Sc.- und M.Sc.-Kursen für Biomedizin der Universität Bern verantwortlich. Ebenso führen wir gegenwärtig die Pharmakologie-Ausbildung im 3. Studienjahr Medizin an der Universität Fribourg durch. Die DozentInnen 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 (Prof. Simon). Diese Bildungsangebote werden weitgehend aus eigenen finanziellen Mitteln und Sponsorengeldern bestritten. Im Institut arbeiten gegenwärtig 19 DoktorandInnen, und 3 DoktorandInnen (PhD) haben im Berichtsjahr ihre Arbeit erfolgreich abgeschlossen.

Die Mitarbeiter und Mitarbeiterinnen des PKI (ohne Klinische Pharmakologie) publizierten im Jahr 2017 insgesamt 27 Originalarbeiten sowie 19 Übersichtsartikel in internationalen Fachzeitschriften (Summe der „impact factors“ >250). MitarbeiterInnen des Instituts wurden zu insgesamt 29 Vorträgen bzw. Seminaren eingeladen. Mehrere MitarbeiterInnen des PKI wurden mit Forschungspreisen ausgezeichnet. Gegenwärtig werden 8 MitarbeiterInnen mit namhaften Beiträgen des Schweizerischen Nationalfonds unterstützt. Zahlreiche Persönlichkeiten besuchten das Institut und hielten Forschungsseminare. Prof. von Gunten war Mitorganisator des Jahreskongresses der Schweizerischen Gesellschaft für Pharmakologie und Toxikologie (SGPT). Prof. Kaufmann organisiert gemeinsam mit Prof. Tschan (Institut für Pathologie, Universität Bern) und Prof. Brunner (Lehrstuhl Biochemische Pharmakologie, Universität Konstanz, Deutschland) das „10th Swiss Apoptosis Meeting (SAM)“ (12.-14.9.2018), zu dem wir ca. 200 TeilnehmerInnen aus dem In- und Ausland erwarten. Seit 2014 ist das Institut für Pharmakologie Bestandteil eines Europäischen Netzwerks für Doktoranden innerhalb des EU-Programms für Forschung und Innovation „HORIZON 2020“. Diese Aufzählung belegt den hohen Stellenwert, den die Forschung in unserem Institut besitzt.

Der Direktor des PKI Prof. Simon ist gegenwärtig als Dekan der Medizinischen Fakultät der Universität Bern tätig. Zusätzlich nimmt das PKI auch ausserhalb der Universität wissenschaftspolitische Verantwortung für die Medizin und die Biowissenschaften wahr. Prof. Simon amtet als Past-Präsident der International Eosinophil Society (IES) und ist Vice-Chair der Immunopharmacology Section der International Union of Basic and Clinical Pharmacology (IUPHAR). Prof. von Gunten ist Präsident der Schweizerischen Gesellschaft für Experimentelle Pharmakologie (SGEP).

Ich danke allen Mitarbeiterinnen und Mitarbeitern für ihren Einsatz, welcher auch im Jahr 2017 zu einer Bilanz beitrug, die internationalen Massstäben gerecht wird. Ebenso danke ich allen Sponsoren und Freunden des Instituts.

Prof. Dr. med. Hans-Uwe Simon, PhD, Dr. h.c. Bern, Januar 2018
Direktor

1.2. Foreword

This is the seventeenth comprehensive annual report for our Institute of Pharmacology (PKI) of the University of Bern. We have worked hard to fulfil optimally our tasks in teaching and research within the Medical Faculty in the past year. After moving to the INO-building of the University Hospital (Inselspital) in 2015, we have found excellent conditions for successful research. We share floor F of the building with the Center for Laboratory Medicine and have jointly developed the available infrastructure. We organize multiple joint teaching and research projects with this Center to further accentuate the field of “Precision Medicine”. In April 2017, Prof. Manuel Haschke with his research group joined our institute and now facilitates our research in the field of Clinical Pharmacology. Meanwhile, the two mass spectrometers of the Haschke group have been moved from Basel and are operating in our institute. We are convinced that his group will strengthen us and open up new opportunities for collaboration in both *clinical research* and *basic biological science*.

The PKI wants to succeed in both areas and, therefore, maintains close contacts with several clinics at the Inselspital as well as with other research institutes of the University. In doing so, we hope to strengthen both translational research and teaching in the Medical Faculty. In addition, we are very much interested in collaborating with industry on new developments. Finally, we have also made an effort to promote communication between scientists and the public in 2017. 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. At present, we are also responsible for the teaching Pharmacology to students of Medicine and Biomedicine of the University of Fribourg. 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, 19 PhD students work at the PKI, and in 2017, three PhD students 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 Prof. Simon). Significantly, these additional events were financed exclusively by external sponsors.

Research is our other main activity. In 2017, staff members of the PKI (without Clinical Pharmacology) published 27 original and 19 review articles in international peer-reviewed journals (the sum of the “impact factors” is more than 250). Co-workers of the institute were invited to present 29 lectures or seminars. Several PKI members received research prizes. The research projects of 8 co-workers are currently supported by grants from the Swiss National Science Foundation. Several internationally prominent researchers visited our institute to present seminars. Prof. von Gunten was a member of the organizing committee for the annual meeting of the Swiss Society of Pharmacology and Toxicology (SSPT). Prof. Kaufmann, together with Prof. Tschan (Institute of Pathology, University of Bern) and Prof. Brunner (Department of Biochemical Pharmacology, Univ. of Konstanz, Germany), currently organize an international congress (10th Swiss Apoptosis Meeting; September 12-14, 2018), which will attract up to 200 scientists interested in the fields of “Cell Death and Autophagy”. Moreover, since 2014, the Institute of Pharmacology has been part of a Training Network for PhD students within the EU Framework Program for Research and Innovation „HORIZON 2020“. In summary, research of a high standard is being carried out and plays a very important role at the PKI.

Prof. Simon is the Dean of the Medical Faculty of the University of Bern. He also serves as the Past-President of the International Eosinophil Society (IES) and is currently the Vice-Chair of the Immunopharmacology Section of the International Union of Basic and Clinical Pharmacology (IUPHAR). Prof. von Gunten serves as president of the Swiss Society of Experimental Pharmacology (SSEP).

I thank all co-workers in the institute for their hard work. These efforts have contributed in an important way to the success of the PKI in 2017. 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 2018

2. Staff 2017

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
Prof. Dr.	Friis, Robert	PhD*
PD Dr.	Späth, Peter	PhD*

Scientific Staff

Dr.	Adams, Olivia	Postdoctoral fellow* (since Aug 2017)
	Aeschlimann, Salome	Lab Technician (since Aug 2017)
Dr.	Amini, Poorya	Postdoctoral fellow (until April 2017)
	April, Simon	M.Sc. student* (until Jan 2017)
	Bachmann, Daniel	Research Assistant
	Blanchard, Olivier	PhD student*
	Brandl, Fabian	PhD student*
	Büchler, Flavia	Lab Technician (until July 2017)
	Burkhard, Fabian	M.Sc. biomed. student* (until Jan 2017)
	Erhardt, Martin	PhD student (since May 2017)
	Fallegger, Angela	M.Sc. biomed. student* (until Jan 2017)
Dr.	Fernandez Marrero, Yuniel	Postdoctoral fellow* (since July 2017)
	Frangez, Ziva	PhD student*
Dr.	Frias Boligan, Kayluz	Postdoctoral fellow*
	Fuchs, Katharina	MMed student* (until May 2017)
	Germic, Nina	PhD student
	Glück, Angéline	M.Sc. biomed. student* (since July 2017)
	Graeter, Stefanie	PhD student*
	Haas, Quentin	PhD student*
	Haxholli, Deis	PhD student*
Dr.	He, Zhaoyue	Postdoctoral fellow
	Jenni, Aurelio Leandro	PhD student (until Jan 2017)
	Karlen, Hélène	M.Sc. biomed. student* (since July 2017)
	Klapan, Kim	PhD student*
	Kozlowski, Evelyne	Lab Technician
	Kremenovic, Mirela	M. Sc. student (since Jan 2017)
	Künzli, Yves	M.Sc. Immun. student* (since Jan 2017)
Dr.	Liu, He	Postdoctoral fellow*
	Lutz, Sarah	M.Sc. biomed. student* (until Jan 2017)
	Maillard-van Laer, Marianne	Lab Technician
	Maneva Timcheva, Tankica	Lab Technician* (until May 2017)

	Markov, Nikita	PhD student (since Oct 2017)
	Moolan, Robin	M.Sc. student* (since Aug 2017)
	Muli, Kevin	M.Sc. biomed. student* (since Dec 2017)
	Naim, Samara	PhD student* (since Sep 2017)
	Naser, Riim	Lab Technician*
	Oberson, Kevin	Lab Technician
	Peng, Shuang	PhD student* (since Oct 2017)
	Reali, Luca	PhD student (until March 2017)
	Reinhart, Ramona	PhD student*
	Rossi Sebastiano, Matteo	PhD student
	Saliakoura, Maria	PhD student* (since Sep 2017)
	Schnüriger, Noah	M.Sc. biomed. student* (since Sep 2017)
	Stark, Manuel	PhD student (since April 2017)
	Stepanovska, Bisera	PhD student
Dr.	Stojkov, Darko	Postdoctoral fellow
Dr.	Wang, Xiaoliang	Postdoctoral fellow
	Zürcher, Marc	M.Sc. student* (since Feb 2017)

Principal Investigator – Clinical Pharmacology

Prof. Dr.	Haschke, Manuel	MD

Scientific Staff – Clinical Pharmacology

PD Dr.	Bohlender, Jürgen	MD
Dr.	Liakoni, Evangelia	MD
Dr.	Sandbaumhüter, Friederike	PhD, postdoctoral fellow (since July 2017)
Dr.	Geiling, Katharina	MD
	Scholz, Irene	med.pract

External University Teachers

Dr.	Bürgi, Sibylle	PhD*
PD Dr.	Cachelin, Armand	MD, PhD*
Prof. Dr.	Mlinaric, Irena	PhD* (Visiting Prof., Univ. of Ljubljana, Slovenia)

Guest Scientists

Prof. Dr.	Simon, Dagmar	MD*, Dept. Dermatology, Inselspital, Univ. Bern
Dr.	Sokollik, Christiane	MD*, Dept. Pediatrics, Inselspital, Univ. Bern
Dr.	Schwalm, Stephanie	PhD*, Dept. of Pharmacology, Univ. Frankfurt
PD Dr.	Spirk, David	MD*, Sanofi-Aventis AG
	Dorvignit Pedroso, Denise	PhD student*, University of Havanna (Cuba)
	Perez, Claudia	PhD student*, Universidad de Chile

Office

	Berger, Jana	Secretary, 50%
	Scherrer, Debora	Secretary, 70%
	Wyss, Anne*	External computer support

Workshop / House Keeping

	Andres Hans	(until March 2017)
	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,
Treatment of Skin Diseases,
Bern, January 26, 2017

Summer School 2017

Members of the Institute of Pharmacology of the University of Bern together with participants of our International Summer School in Zäziwil; July 23 - 25, 2017.
Our guest speakers from Germany, Prof. Peter Ruth, Abken Hinrich and Harald Renz, are seen.

3. Teaching Activities

3.1. Lectures

Lectures for Medical Students: Pharmacology

Date	Lecturer	Titel of the lecture
Mar 20, 2017	Prof. Stephan von Gunten	Hormone aus pharmakol. Sicht (Teil 1)
Mar 20, 2017	Prof. Stephan von Gunten	Hormone aus pharmakol. Sicht (Teil 2)
Mar 22, 2017	Prof. Stephan von Gunten	Lipidsenker + Behandlung der Gicht
Mar 27, 2017	Prof. Stephan von Gunten	Antidiabetika
Mar 29, 2017	Prof. Andrea Huwiler	Pharmakologie von Narkosemitteln und Muskelrelaxantien I
Mar 29, 2017	Prof. Andrea Huwiler	Pharmakologie von Narkosemitteln und Muskelrelaxantien II
Apr 12, 2017	Prof. Andrea Huwiler	Antiepileptika
Apr 26, 2017	Prof. Andrea Huwiler	Therapie von M. Parkinson und Demenz
Apr 26, 2017	Prof. Andrea Huwiler	Lokalanästhetika
Apr 26, 2017	Prof. Andrea Huwiler	Neurologie-Blocksynthese
May 01, 2017	Prof. Andrea Huwiler	Psychopharmakologie
May 08, 2017	Prof. Andrea Huwiler	Antidepressiva, Anxiolytika und Stimmungsstabilisatoren
May 08, 2017	Prof. Andrea Huwiler	Antipsychotika
May 10, 2017	Prof. Andrea Huwiler	Schmerz und Analgesiologie (Teil 1)
May 10, 2017	Prof. Andrea Huwiler	Schmerz und Analgesiologie (Teil 2)
May 18, 2017	Prof. Hans-Uwe Simon	Immunmodulation
Sep 18, 2017	Prof. Hans-Uwe Simon	Pharmakodynamik (Teil 1)
Sep 18, 2017	Prof. Hans-Uwe Simon	Pharmakodynamik (Teil 2)
Sep 26, 2017	Prof. Hans-Uwe Simon	Entzündungshemmung
Sep 26, 2017	Prof. Hans-Uwe Simon	Einführung in die Toxikologie
Oct 18, 2017	Prof. Hans-Uwe Simon	Pharmakotherapie bei Lungenkrankheiten
Nov 01, 2017	PD Dr. David Spirk	Pharmakologie der Hämostase
Oct 31, 2017	Prof. U. Zangemeister-Wittke	Pharmakologie des vegetativen Nervensystems
Oct 31, 2017	Prof. U. Zangemeister-Wittke	Antihypertensiva
Nov 07, 2017	PD Dr. David Spirk	Behandlung der Herzinsuffizienz und Angina pectoris
Nov 15, 2017	Prof. U. Zangemeister-Wittke	Antiarrhythmika
Dec 11, 2017	Prof. U. Zangemeister-Wittke	Diuretika (Teil 1)
Dec 11, 2017	Prof. U. Zangemeister-Wittke	Diuretika (Teil 2)

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

Lectures for Medical Students: Cell Biology

Date	Lecturer	Titel of the lecture
Sep 28, 2017	Prof. Thomas Kaufmann	Entwicklung des Lebens
Oct 12, 2017	Prof. Thomas Kaufmann	Zellstoffwechsel
Oct 26, 2017	Prof. Thomas Kaufmann	Zelltod 2

Seminars for Medical Students: Pharmacology

Date	Lecturer	Titel of the lecture
Apr 06, 2017	Prof. Stephan von Gunten	Functional Glycomics - Neue Optionen für die Tumor- und Entzündungspharmakologie
Apr 06, 2017	Prof. Thomas Kaufmann	Modulation des Zelltodes - aktueller Stand und neue Entwicklungen
Apr 24, 2017	Prof. Hans-Uwe Simon	Personalisierte Arzneimitteltherapie
Apr 24, 2017	Prof. U. Zangemeister-Wittke	Gezielte Tumortherapie mit Antikörpern und Immunkonjugaten

Lectures for Medical Students: Pathology

Date	Lecturer	Title of the lecture
Sep 20, 2017	Dr. Christina Merz-Stöckle	Adaptation und Zellschäden

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

Date	Lecturer	Title of the lecture
Feb 05, 2017	Prof. Hans-Uwe Simon	Rezeptoren, Dosis-Wirkungskurven,
Feb 05, 2017	Prof. Hans-Uwe Simon	Antagonisten, Applikationsarten
Feb 19, 2017	Prof. U. Zangemeister-Wittke	Einführung in die Pharmakokinetik
Feb 21, 2017	Prof. Andrea Huwiler	Narkose, Beruhigungsmittel
Feb 28, 2017	Prof. U. Zangemeister-Wittke	Pharmakologie des vegetativen Nervensystems
Mar 07, 2017	Prof. Andrea Huwiler	Pharmakologie der Atemwege
Mar 12, 2017	PD Dr. Armand Cachelin	Analgetika
Mar 28, 2017	Prof. Thomas Kaufmann	Pharmakogenetik, Interaktionen
Apr 03, 2017	PD Dr. David Spirk	Pharmakologie der Herzerkrankungen

Apr 03, 2017	PD Dr. David Spirk	Pharmakologie der Herzerkrankungen
Apr 11, 2017	Prof. Stephan von Gunten	Psychopharmaka
Apr 18, 2017	Dr. Sibylle Bürgi	Antidiabetika, Lokalanästhetika
Apr 30, 2017	Dr. Sibylle Bürgi	Antibiotika
May 02, 2017	Dr. Sibylle Bürgi	Antidiabetika
May 09, 2017	Prof. Stephan von Gunten	Magensäurehemmung

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

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

Date	Lecturer	Title of the lecture
Feb 23, 2017	Prof. Stephan von Gunten	Introduction
Feb 23, 2017	Prof. Stephan von Gunten	Immunopharmacology

Written examination and oral tests: Prof. von Gunten

Lecture for Natural Sciences Faculty: Cellular and Molecular Immunology (Coordinator: Dr. Leslie Saurer)

Date	Lecturer	Title of the lecture
Nov 02, 2017	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 06, 2017	Prof. Andrea Huwiler	Lipid mediators in inflammation
May 11, 2017	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
Dec 07, 2017	Prof. Shida Yousefi Prof. Stephan von Gunten Prof. Thomas Kaufmann	Immunological Methods (1 day)
Dec 08, 2017	Prof. Shida Yousefi Prof. Stephan von Gunten Prof. Thomas Kaufmann	Immunological Methods (1 day)
Dec 14, 2017	Prof. Shida Yousefi Prof. Stephan von Gunten Prof. Thomas Kaufmann	Immunological Methods (1 day)
Dec 15, 2017	Prof. Shida Yousefi Prof. Stephan von Gunten Prof. Thomas Kaufmann	Immunological Methods (1 day)
Dec 21, 2017	Prof. Shida Yousefi Prof. Stephan von Gunten Prof. Thomas Kaufmann	Immunological Methods (1 day)
Dec 22, 2017	Prof. Shida Yousefi Prof. Stephan von Gunten Prof. Thomas Kaufmann	Evaluation (4 h)

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

Date	Lecturer	Title of the lecture
Sep 22, 2017	Prof. Stephan von Gunten	Gastrointestinal tract
Oct 13, 2017	Prof. Stephan von Gunten	Endocrine and reproductive system
Sep 29, 2017	PD Dr. David Spirk	Haemopoietic system and haemostasis
Oct 06, 2017	Prof. Shida Yousefi	Antiinfectious therapy
Oct 20, 2017	Prof. Georgia Konstantinidou	Immune system
Nov 03, 2017	Prof. Andrea Huwiler	Nervous system
Nov 17, 2017	Prof. U. Zangemeister-Wittke	Heart and vascular system
Oct 27, 2017	Prof. Shida Yousefi	Lungs and kidneys

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: Dr. Philippe Krebs)

Date	Lecturer	Title of the lecture
Sep 18, 2017	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 20, 2017	Prof. Shida Yousefi	Laser scanning microscopy and specific applications (FRET, FRAP, spectral unmixing) and digital image restoration (Huygen and Imaris software)

External teaching activities: University of Fribourg (Medical and Biomedical Sciences students)

Date	Lecturer	Title of the lecture
Sep 20, 2017	Prof. Hans-Uwe Simon	Pharmakodynamik 1
Sep 20, 2017	Prof. Hans-Uwe Simon	Pharmakodynamik 2
Sep 20, 2017	Prof. Hans-Uwe Simon	Entzündungspharmakologie
Sep 20, 2017	Prof. Hans-Uwe Simon	Toxikologie
Sep 27, 2017	Prof. Carlo Largiadèr	Pharmakogenetik
Sep 27, 2017	Prof. U. Zangemeister-Wittke	Pharmakokinetik 1
Sep 27, 2017	Prof. U. Zangemeister-Wittke	Pharmakokinetik 2
Sep 27, 2017	Prof. U. Zangemeister-Wittke	Tumorpharmakologie

External teaching activities: University of Zurich (Molecular Medicine)

Date	Lecturer	Title of the lecture
May 2017 (total 6h)	Prof. U. Zangemeister- Wittke	Molecular Cell Biology for students of human and dental medicine

Lectures for Medical Students: Clinical Pharmacology

Date	Lecturer	Titel of the lecture
Feb 14, 2017	Dr. Evangelia Liakoni	Herzinsuffizienz
Feb 15, 2017	PD Dr. Jürgen Bohlender	Arterielle Hypertonie
Apr 06, 2017	Prof. Manuel Haschke	Schmerztherapie
May 24, 2017	Dr. Evangelia Liakoni	Legale und illegale Süchte
May 30, 2017	Prof. Manuel Haschke	Notfallmedikamente
May 30, 2017	Dr. Evangelia Liakoni	Psychopharmakologie
May 31, 2017	Prof. Manuel Haschke	Intoxikationen
May 31, 2017	PD Dr. Jürgen Bohlender	Antikoagulation 1
May 31, 2017	PD Dr. Jürgen Bohlender	Antikoagulation 2
June 1, 2017	PD Dr. Jürgen Bohlender	Diabetes

June 1, 2017	PD Dr. Jürgen Bohlender	Dyslipidämie
Sept 27, 2017	Prof. Manuel Haschke	Pharmacokinetics
Nov 15, 2017	Prof. Manuel Haschke	Interaktionen
Nov 15, 2017	Prof. Manuel Haschke	Unerwünschte Arzneimittelwirkungen

Lectures for Dental Medicine Students: Clinical Pharmacology

Date	Lecturer	Titel of the lecture
Nov 08, 2017	PD Dr. Jürgen Bohlender	Pat. mit chron. med. Problemen
Nov 15, 2017	Irene Scholz	Antikoagulation
Nov 22, 2017	Prof. Manuel Haschke	Antibiotika
Nov 29, 2017	PD Jürgen Bohlender	Pat. mit akuten med. Problemen
Dec 06, 2017	Dr. Evangelia Liakoni	Analgetika
Dec 13, 2017	Dr. Katharina Geiling	UAW Mundhöhle

Clinical Pharmacology Lectures: University Hospital/Inselspital Bern

Date	Lecturer	Titel of the lecture
May 02, 2017	Prof. Manuel Haschke	Grundlagen Klin Pharmakologie (TS)
May 23, 2017	Prof. Manuel Haschke	Therapeutic Drug Monitoring (TS)
Jun 06, 2017	Prof. Manuel Haschke	TDM Antiepileptika (TS)
Aug 15, 2017	Prof. Manuel Haschke	Opioide (TS)
Sept 7, 2017	Prof. Manuel Haschke	Arzneimittelinteraktionen (DTS)
Sept 7, 2017	Dr. Evangelia Liakoni	Dosisanpassungen (DTS)
Sept 7, 2017	PD Dr. Jürgen Bohlender	Interaktionen Krankheit Medi (DTS)
Sept 15, 2017	Prof. Manuel Haschke	Pharmakokinetik I (TS)
Oct 12, 2017	Dr. Evangelia Liakoni	Vor-/Nachteile Drogentests (BENOMED)
Oct 24, 2017	Prof. Manuel Haschke	Pharmakokinetik II (TS)
Nov 07, 2017	Prof. Manuel Haschke	Pharmakokinetik III (TS)
Nov 09, 2017	Prof. Manuel Haschke	Direct oral anticoagulants (BETAKLI)
Nov 28, 2017	Prof. Manuel Haschke	Arzneimittelinteraktionen (KAIM WB)
Dec 05, 2017	Prof. Manuel Haschke	Drug related problems (TS)

External Lectures: Clinical Pharmacology

Date	Lecturer	Titel of the lecture
May 03, 2017	Dr. Evangelia Liakoni	New drugs of abuse (SGAIM)
Sept 14, 2017	Prof. Manuel Haschke	Update opioids (Pharmathemen)
Nov 23, 2017	Prof. Manuel Haschke	Antikoagulantien (Pharmathemen)
Nov 23, 2017	Dr. Evangelia Liakoni	Interaktionen Antiepileptika (Pharmathemen)

3.2. Coordination PBL Medical Students, 3rd year (2017/2018)

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 III and IV)
Prof. Stephan von Gunten (block V)
Prof. Andrea Huwiler (blocks VI, VII and VIII)

3.3. Tutorials (study year 2017/2018)

For Medical students 3rd year:
Prof. Thomas Kaufmann
Dr. Zhaoyue He
Dr. He Liu
Prof. Georgia Konstantinidou
Stefanie Graeter, M.Sc.
Dr. Christina Merz-Stöckle

For PhD students,
Graduate School for Cellular and Biomedical Sciences, course "Happy Cell":
Prof. Shida Yousefi
Prof. Thomas Kaufmann

3.4. Elective Module Supervision

For Biomedical Sciences students:
Alexandra Wallimann (Prof. Shida Yousefi)
Laura Jerly (Prof. Thomas Kaufmann)
Lisa Ständer (Prof. Thomas Kaufmann)

3.5. Seminars of Invited Speakers

Date	Teacher	Title of the seminar	Host
Mar 01, 2017	Prof. Thanos Halazonetis, Dept. of Molecular Biology, University of Geneva	Mechanisms of oncogene-induced DNA replication stress	G. Konstantinidou
Mar 22, 2017	Prof. Holger Stark, Dept. Pharmazeutische Chemie, Universität Düsseldorf	Histamine H3 receptor antagonists – from bench to bedside: A new medical entity to treat narcolepsy	A. Huwiler
Mar 29, 2017	Prof. Thierry Soldati, Dept. of Biochemistry, University of Geneva	Of amoebae and men: dissecting conserved cell-intrinsic defense mechanisms against infection	H.-U. Simon
April 12, 2017	Prof. Mirjam Schenk, Institute of Pathologie, University of Bern	Induction of effective anti-tumour immunity by targeting dendritic cells	S. von Gunten
April 19, 2017	Prof. Donald Branch, University of Toronto and Canadian Blood Services (CAN)	Repurposing approved drugs for use in Ebola and HIV/AIDS	S. von Gunten
April 26, 2017	Prof. Giulia Caron, Dept. of Pharmacy and Molecular Biotechnology and Health Sciences, University of Turin (I)	Ask not what you can do for discovering a new drug, ask what is still missing to do that	G. Konstantinidou
April 28, 2017	Nikita Markov, visiting PhD student of Prof. Gerry Melino, Medical Council Research, Leicester, UK	REPS2 as a putative target of p73 transcription factor	H.-U. Simon
May 03, 2017	Prof. Christoph Schlapbach, Klinik für Dermatologie, Inselspital	Th9“ and Th2 cells: same same but different?	H.-U. Simon
May 10, 2017	Dr. Yury Belyaev, Microscopy Imaging Center and Institute of Anatomy, University of Bern	Huygens Remote Manager – web-based batch deconvolution for microscopy images	S. Yousefi
July 05, 2017	Dr. Ueli Nachbur, The Walter and Eliza Hall Instititue of Medical Research, Melbourne, Australia	How to target NOD signaling in inflammatory diseases	T. Kaufmann

Aug 29, 2017	Prof. Jan Klohs, Institute for Biomedical Engineering, University of Zurich and ETH Zurich	Non-invasive imaging of the diseased brain: from microstructure to cellular events	H.-U. Simon
Sep 06, 2017	Dr. Carine Blanchard, Nestlé Research Center, Lausanne	Food allergy and eosinophilic esophagitis: genetics, epigenetics and nutrition	H.-U. Simon
Sep 27, 2017	Prof. Luca Scorrano, Scientific Director, Venetian Institute of Molecular medicine, Padua (BIC Seminar)	Keeping mitochondria in shape: a matter of life and death	H.-U. Simon
Oct 10, 2017	Dr. Doriano Fabbro, PIQUR Therapeutics AG, Basel	Targeted therapies for cancer: potentials and limitations	A. Huwiler
Oct 18, 2017	Prof. Renato Zenobi, Department of Chemistry and Applied Biosciences, ETH Zurich	Exhalomics by ambient mass spectrometry	C. Bovet
Nov 01, 2017	Prof. Bernd Bodenmiller, Institute of Molecular Life Sciences, University of Zurich	Highly multiplexed analysis of the tumor ecosystem by mass cytometry	C. Bovet
Nov 08, 2017	Prof. Etienne Meylan, ISREC, EPFL, Lausanne	Neutrophils and tumor cell SNAIL establish a vicious dialogue in lung adenocarcinoma	G. Konstantinidou
Nov 28, 2017	Prof. Dorothea Fiedler Leibniz-Institut für Molekulare Pharmakologie (FMP), Berlin, Germany	Elucidating inositol pyrophosphate function with chemical tools	G. Konstantinidou
Nov 29, 2017	Prof. Philipp Latzin, Klinik für Kinderheilkunde, Universität Bern	BILD-cohort: a longitudinal birth cohort focusing on the development of airways and allergies	H.-U. Simon
Dec 14, 2017	Dr. Xavier Casadevall, Institute for Chemical and Bioengineering, Department of Chemistry and Applied Biosciences, ETH Zurich	Single cell assays and biomimetics for pharmaceutical research	H.-U. Simon

3.6. Academic Degrees

Radonjic Susanne, PhD, University of Bern
Thesis: Adhesion-included eosinophil cytolysis requires the RIPK3-MLKL signaling Pathway which is counter-regulated by autophagy (March 2017)
Supervisor: Prof. Hans-Uwe Simon

Fernandez Yuniel, PhD, University of Bern
Thesis: Insight into the biophysical and functional characterization of the BCL2 family member BOK (Juni 2017)
Supervisor: Prof. Thomas Kaufmann

Reinhart Ramona, PhD, University of Bern
Thesis: The importance of BCL-2 family members in cell survival and cell death regulation of basophil (October 2017)
Supervisor: Prof. Thomas Kaufmann

April Simon, M.Sc., University of Bern
Thesis: The role of glycolytic and mitochondrial bioenergetics in adult stem cell differentiation (Jan 2017)
Supervisors: Prof. Hans-Uwe Simon, Dr. He Liu

Burkhard Fabian, M.Sc., University of Bern
Thesis: Involvement of phospholipase A2 subtypes in breast cancer metastasis formation (Jan 2017)
Supervisor: Prof. Andrea Huwiler, Prof. Uwe Zangemeister-Wittke

Fallegger Angela, M.Sc., University of Bern
Thesis: Generation and analysis of mouse mast cell protease 8-deficient basophils (Jan 2017)
Supervisor: Prof. Thomas Kaufmann

Lutz Sarah, M.Sc., University of Bern
Thesis: Role of Siglec-9 inhibitory receptor in the modulation of natural killer cell responses against cancer (Jan 2017)
Supervisor: Prof. Stephan von Gunten

Fuchs Katharina, MMed, University of Bern
Thesis: Siglec expression on immunocompetent cells (Jan 2017)
Supervisor: Prof. Stephan von Gunten

Grosek Martin, M.Sc. pharm., University of Ljubljana
Thesis: Establishing ATG5 knockout cells using genome editing (March 2017)
Supervisors: Prof. Irena Mlinarič Raščan, Prof. Hans-Uwe Simon

Srajner Luka, M.Sc. pharm., University of Ljubljana
Thesis: Investigation of neutrophil extracellular DNA traps (Oct 2017)
Supervisors: Prof. Irena Mlinarič Raščan, Prof. Hans-Uwe Simon

4. Research Activities

4.1. Research Projects and Publications

Group Prof. Andrea Huwiler

Group members: Olivier Blanchard, PhD student[1]
Fabian Burkhard, M.Sc. student[1]
Aurelio Leandro Jenni, PhD student[1]
Kevin Muli, M.Sc. student[1]
Manuel Stark, PhD student[1]
Marianne Maillard-van Laer, Lab Technician[1]
Isolde Römer, Technician[2]
Stephanie Schwalm, Dr., Postdoc[1,2]
Bisera Stepanovska, PhD student[1]

[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 pathophysiological 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 growrh.

Sphingosine kinase-2 deficiency ameliorates kidney fibrosis by up-regulating Smad7 ina mouse model of unilateral ureteral obstruction
Schwalm S, Beyer S, Frey H, Haceni R, Grammatikos G, Thomas D, geisslinger G, Schaefer L, Huwiler A*, Pfeilschifter J* (shared last authorship)
Kidney fibrosis is a hallmark of chronic kidney disease and leads to extracellular matrix accumulation, organ scarring, and loss of kidney function. In this study, we investigated the role of sphingosine kinase-2 (SPHK2) on the progression of tubular fibrosis by using a mouse unilateral ureteral obstruction (UUO) model. We found that SPHK2 protein and activity are up-regulated in fibrotic renal tissue. Functionally, Sphk2-deficient ($Sphk2^{-/-}$) mice showed an attenuated fibrotic response to UUO compared with wild-type mice, as demonstrated by reduced collagen abundance and decreased expression of fibronectin-1, collagen I, α-smooth muscle actin, connective tissue growth factor (CTGF), and plasminogen activator inhibitor (PAI-1). More important, these changes were associated with increased expression of the antifibrotic protein Smad7 and higher levels of sphingosine in $Sphk2^{-/-}$ UUO kidneys.

Mechanistically, sphingosine ameliorates transforming growth factor-β-induced collagen accumulation, CTGF, and PAI-1 expression, but enhances Smad7 protein expression in primary kidney fibroblasts. In a complementary approach, in human Sphk2-overexpressing mice, UUO resulted in exacerbated signs of fibrosis with increased collagen accumulation, higher expression levels of fibronectin-1, collagen I, α-smooth muscle actin, CTGF, and PAI-1, but decreased Smad7 expression. SPHK2 plays an important role in kidney fibrogenesis by modulating transforming growth factor-β signaling. Thus, SPHK2 might be an attractive new target for the treatment of fibrosis in chronic kidney disease.
See publication No 2

Original publications

1. Hsieh LT, Nastase MV, Roedig H, Zeng-Brouwers J, Poluzzi C, Schwalm S, Fork C, Tredup C, Brandes RP, Wygrecka M, **Huwiler A**, Pfeilschifter J, Schaefer L: Biglycan- and Sphingosine Kinase-1 Signaling Crosstalk Regulates the Synthesis of Macrophage Chemoattractants. Int. J. Mol. Sci. 18 (2017), E595.

2. Schwalm S, Beyer S, Frey H, Haceni R, Grammatikos G, Thomas D, Geisslinger G, Schaefer L, **Huwiler A***, Pfeilschifter J* (*shared last authorship): Sphingosine Kinase-2 Deficiency Ameliorates Kidney Fibrosis by Up-Regulating Smad7 in a Mouse Model of Unilateral Ureteral Obstruction. Am J Pathol. 187 (2017), 2413-2429.

3. Vasilakaki S, Pastukhov O, Mavromoustakos TM, **Huwiler A**, Kokotos G: Small peptides able to suppress prostaglandin E_2 generation in renal mesangial cells. Molecules, in press.

Review articles

1. **Huwiler A**, Zangemeister-Wittke U: The sphingosine 1-phosphate receptor modulator fingolimod as a therapeutic agent: recent findings and new perspectives. Pharmacol Ther.17 (2017), 30285-1.

2. **Huwiler A**, Pfeilschifter J: Sphingolipid signaling in renal fibrosis. Matrix Biol., in press.

Group Prof. Thomas Kaufmann

Group members: Ramona Reinhart, PhD student
Yuniel Fernandez Marrero, PhD student
Daniel Bachmann, research assistant
Samara Naim, PhD student
Angela Fallegger, M.Sc. student (BMSc)
Noah Schnüriger, M.Sc. student

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 crosslinking 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. So far, we have demonstrated that BOK is much more widely expressed than previously reported and, intriguingly, we found that although it has the potential to induce apoptosis when highly expressed, BOK localizes preferentially to the membranes of the ER and Golgi apparatus rather than to mitochondria. The subcellular localization of BOK correlates with its association with IP3 receptors (Ca^{2+} channels on the ER) and a deregulated ER stress response of *Bok*-deficient cells. Interestingly, BOK is prominently also found in nuclear fractions and we observed that BOK modulates cellular proliferation. We are currently testing the biophysical properties of recombinant BOK on artificial lipid vesicles and isolated organelles, the role of BOK at the ER/Golgi and the role of BOK in the nucleus, for which we hypothesize a role in the regulation of cellular proliferation.

BOK promotes chemical-induced hepatocarcinogenesis in mice
Rabachini T, Fernandez-Marrero Y, Montani M, Loforese G, Sladky V, He Z, Bachmann D, Wicki S, Villunger A, Stroka D, Kaufmann T
BCL-2-related ovarian killer (BOK) is a conserved and widely expressed BCL-2 family member with sequence homology to pro-apoptotic BAX and BAK, but with poorly understood pathophysiological function. Since several members of the BCL-2 family are critically involved in the regulation of hepatocellular apoptosis and carcinogenesis we aimed to establish whether loss of BOK affects diethylnitrosamine (DEN)-induced hepatocarcinogenesis in mice. Short-term exposure to DEN lead to upregulation of BOK mRNA and protein in the liver. Of note, induction of CHOP and the pro-apoptotic BH3-only proteins PUMA and BIM by DEN was strongly reduced in the absence of BOK. Accordingly, Bok -/- mice were significantly protected from DEN-induced acute hepatocellular apoptosis and associated inflammation. As a consequence, Bok -/- animals were partially protected against chemical-induced hepatocarcinogenesis showing fewer and, surprisingly, also smaller tumors than WT controls. Gene expression profiling revealed that downregulation of BOK results in upregulation of genes involved in cell cycle arrest. Bok -/- hepatocellular carcinoma (HCC) displayed higher expression levels of the cyclin kinase inhibitors p19INK4d and p21cip1. Accordingly, hepatocellular carcinoma in Bok -/- animals, BOK-deficient human HCC cell lines, as well as non-transformed cells, showed significantly less proliferation than BOK-proficient controls. We conclude that BOK is induced by DEN, contributes to DEN-induced hepatocellular apoptosis and resulting hepatocarcinogenesis. In line with its previously reported predominant localization at the endoplasmic reticulum, our findings support a role of BOK that links the cell cycle and cell death machineries upstream of mitochondrial damage.
See publication No 1

BH3 mimetics efficiently induce apoptosis in mouse basophils and mast cells
Reinhart R, Rohner L, Wicki S, Fux M, Kaufmann T
Basophil granulocytes and mast cells are recognized for their roles in immunity and are central effectors of diverse immunological disorders. Despite their similarities, there is emerging evidence for non-redundant roles of the circulating yet scarce basophils and tissue-resident mast cells, respectively. Because of their importance in allergic pathogenesis, specific induction of apoptosis in basophils and mast cells may represent an interesting novel

treatment strategy. The pro-inflammatory cytokine interleukin-3 serves as a key factor for basophil and mouse mast cell survival. Interleukin-3 increases the expression of anti-apoptotic BCL-2 family members, such as BCL-2, BCL-XL or MCL-1; however, little is known how strongly these individual proteins contribute to basophil survival. Here, we were applying small molecule inhibitors called BH3 mimetics, some of which show remarkable success in cancer treatments, to neutralize the function of anti-apoptotic BCL-2 family members. We observed that expression levels of anti-apoptotic BCL-2 proteins do not necessarily correlate with their respective importance for basophil survival. Whereas naive in vitro-differentiated mouse basophils efficiently died upon BCL-2 or BCL-XL inhibition, interleukin-3 priming rendered the cells highly resistant toward apoptosis, and this could only be overcome upon combined targeting of BCL-2 and BCL-XL. Of note, human basophils differed from mouse basophils as they depended on BCL-2 and MCL-1, but not on BCL-XL, for their survival at steady state. On the other hand, and in contrast to mouse basophils, MCL-1 proved critical in mediating survival of interleukin-3 stimulated mouse mast cells, whereas BCL-XL seemed dispensable. Taken together, our results indicate that by choosing the right combination of BH3 mimetic compounds, basophils and mast cells can be efficiently killed, even after stimulation with potent pro-survival cytokines such as interleukin-3. Because of the tolerable side effects of BH3 mimetics, targeting basophils or mast cells for apoptosis opens interesting possibilities for novel treatment approaches.
See original publication No 2

BOK displays cell death-independent tumor suppressor activity in non-small cell lung carcinoma
Moravcikova E, Krepela E, Donnenberg VS, Donnenberg AD, Benkova K, Rabachini T, Fernandez-Marrero Y, Bachmann D, Kaufmann T
Since the genomic region containing the Bcl-2-related ovarian killer (BOK) locus is frequently deleted in certain human cancers, BOK is hypothesized to have a tumor suppressor function. In the present study, we analyzed primary non-small cell lung carcinoma (NSCLC) tumors and matched lung tissues from 102 surgically treated patients. We show that BOK protein levels are significantly downregulated in NSCLC tumors as compared to lung tissues ($P<0.001$). In particular, we found BOK downregulation in NSCLC tumors of grades two ($P=0.004$, $n=35$) and three ($P=0.031$, $n=39$) as well as in tumors with metastases to hilar (pN1) ($P=0.047$, $n=31$) and mediastinal/subcarinal lymph nodes (pN2) ($P=0.021$, $n=18$) as opposed to grade one tumors ($P=0.688$, $n=7$) and tumors without lymph node metastases ($P=0.112$, $n=51$). Importantly, in lymph node positive patients, BOK expression greater than the median value was associated with longer survival ($P=0.002$, Mantel test). Using in vitro approaches, we provide evidence that BOK overexpression is inefficient in inducing apoptosis but that it inhibits TGFβ-induced migration and epithelial-to-mesenchymal transition (EMT) in lung adenocarcinoma-derived A549 cells. We have identified epigenetic mechanisms, in particular BOK promoter methylation, as an important means to silence BOK expression in NSCLC cells. Taken together, our data point toward a novel mechanism by which BOK acts as a tumor suppressor in NSCLC by inhibiting EMT. Consequently, the restoration of BOK levels in low-BOK-expressing tumors might favor the overall survival of NSCLC patients.
See original publication No 3

The membrane activity of BOK involves formation of large, stable toroidal pores and is promoted by cBID
Fernández-Marrero Y, Bleicken S, Das KK, Bachmann D, **Kaufmann T***, Garcia-Saez AJ* (shared senior authorship)
The BCL-2 family members are key regulators of the intrinsic apoptotic pathway, which is defined by permeabilization of the mitochondrial outer membrane by members of the BAX-

like subfamily. BOK is classified as a BAX-like protein; however, its (patho-)physiological role remains largely unclear. We therefore assessed the membrane permeabilization potential of C-terminally truncated recombinant BOK, BOKΔC. We show that BOKΔC can permeabilize liposomes mimicking the composition of mitochondrial outer membrane, but not of endoplasmic reticulum, forming large and stable pores over time. Importantly, pore formation was enhanced by the presence of cBID and refractory to the addition of antiapoptotic BCL-XL. However, isolated mitochondria from Bax/Bak/ cells were resistant to BOK-induced cytochrome c release, even in the presence of cBID. Taken together, we show that BOKΔC can permeabilize liposomes, and cooperate with cBID, but its role in directly mediating mitochondrial permeabilisation is unclear and may underlie a yet to be determined negative regulation.
See original publication No 4

Original publications

1. Rabachini T, Fernandez-Marrero Y, Montani M, Loforese G, Sladky V, He Z, Bachmann D, Wicki S, Villunger A, Stroka D, **Kaufmann T**: BOK promotes chemical-induced hepatocarcinogenesis in mice. Cell Death Differ. (2017), doi: 10.1038/s41418-017-0008-0 (Epub ahead of print)

2. Reinhart R, Rohner L, Wicki S, Fux M, **Kaufmann T**: BH3 mimetics efficiently induce apoptosis in mouse basophils and mast cells. Cell Death Differ. 25 (2018), 204-216.

3. Moravcikova E, Krepela E, Donnenberg VS, Donnenberg AD, Benkova K, Rabachini T, Fernandez-Marrero Y, Bachmann D, **Kaufmann T**: BOK displays cell death-independent tumor suppressor activity in non-small cell lung carcinoma. Int J Cancer 141 (2017), 2050–2061.

4. Fernández-Marrero Y, Bleicken S, Das KK, Bachmann D, **Kaufmann T***, Garcia-Saez AJ* (shared senior authorship): The membrane activity of BOK involves formation of large, stable toroidal pores and is promoted by cBID.
FEBS Journal 284 (2017), 711-724.

5. Schneider C, Wicki S, Graeter S, Tankica MT, Keller CW, Quast I, Leontyev D, Iglika KD, Käsermann F, Jakob SM, Dimitrova PA, Branch DR, Cummings RD, Lünemann JD, **Kaufmann T**, Simon HU, von Gunten S: IVIG regulates the survival of human but not mouse neutrophils. Sci. Rep. 7 (2017), 1296.

6. Haimovici A, Humbert M, Federzoni EA, Shan-Krauer D, Brunner T, Frese S, **Kaufmann T**, Torbett BE, Tschan MP: PU.1 supports TRAIL-induced cell death by inhibiting NF-κB-mediated cell survival and inducing DR5 expression.
Cell Death Differ 24 (2017), 866-877.

7. Hagmann B, Odermatt A, **Kaufmann T**, Dahinden C, and Fux M.: Balance between IL-3 and type-I-interferons and their interrelationship with FasL dictates lifespan and effector functions of human basophils. Clin Exp Allergy 47 (2017), 71-84.

Review article

1. Sharma S, **Kaufmann, T**, and Biswas S. Impact of inhibitor of apoptosis proteins on immune modulation and inflammation. Immunol Cell Biol. 95 (2017), 236-243.

Group Prof. Georgia Konstantinidou

Group members: Deis Haxholli, PhD student
Matteo Rossi Sebastiano, PhD student
Maria Saiakoura, 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.

Original publication

Ioris RM, Galié M, Ramadori G, Anderson JG, Charollais A, **Konstantinidou G**, Brenachot X, Aras E, Goga A, Ceglia N, Sebastián C, Martinvalet D, Mostoslavsky R, Baldi P, Coppari R: SIRT6 suppresses cancer stem-like capacity in tumors with PI3K activation independently of its deacetylase activity.
Cell Rep. 18 (2017), 1858-1868.

Group Prof. Hans-Uwe Simon

Group members:
Salome Aeschlimann, Technician*
Kevin Oberson, Technician
Flavia Büchler, Technician*,***
Evelyne Kozlowski, Technician*
Riim Naser, Technician*,**
Dr. Zhaoyue He, Postdoc
Dr. He Liu, Postdoc
Dr. Darko Stojkov, Postdoc*
Dr. Xiaoliang Wang, Postdoc
Ziva Frangez, PhD student
Nina Germic, PhD student
Kim Klapan, PhD student**
Peng Shuang, PhD student*
Nikita Markov, PhD student*
Dr. Poorya Amini, PhD student*
Simon April, M.Sc. student
Yves Künzli, M.Sc. student
Robin Moolan, M.Sc. student*
Angéline Glück, M.Sc. student***
Hélène Karlen, M.Sc. student*

*Joint supervision together with Prof. S. Yousefi.
**Joint supervision together with Prof. D. Simon.
***Joint supervision together with Dr. C. Sokollik.

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 Medical Faculty of the University of Bern. Results of these collaborative interactions can be seen in the following abstracts, which briefly describe our research activities in 2017.

Adhesion-induced eosinophil cytolysis requires the receptor-interacting protein kinase 3 (RIPK3)-mixed lineage kinase-like (MLKL) signaling pathway, which is counterregulated by autophagy

Radonjic-Hoesli S, Wang X, de Graauw E, Stoeckle C, Styp-Rekowska B, Hlushchuk R, Simon D, Spaeth PJ, Yousefi S, Simon HU

BACKGROUND: Eosinophils are a subset of granulocytes that can be involved in the pathogenesis of different diseases, including allergy. Their effector functions are closely linked to their cytotoxic granule proteins. Release takes place through several different mechanisms, one of which is cytolysis, which is associated with release of intact granules, so-called clusters of free eosinophil granules. The mechanism underlying this activation-induced form of cell death in eosinophils has remained unclear. OBJECTIVE: We aimed to elucidate the molecular mechanism of eosinophil cytolysis. METHODS: Isolated blood eosinophils were incubated on glass cover slips coated with intravenous immunoglobulin (IVIG) and inactive complement component 3b (iC3b). A morphological characterization of the distinct stages of the proposed cascade was addressed by means of time-lapse automated fluorescence microscopy, electron microscopy, and immunohistochemistry. Experiments with pharmacological inhibitors were performed to elucidate the sequence of events within the cascade. Tissue samples of patients suffering from eosinophilic skin diseases or eosinophilic esophagitis were used for *in vivo* analyses. RESULTS: Following eosinophil adhesion, we observed reactive oxygen species (ROS) production, early degranulation, and granule fusion processes leading to a distinct morphology exhibiting cytoplasmic vacuolization and, finally, to cytolysis. Using a pharmacological approach, we demonstrate the presence of a receptor-interacting protein kinase 3 (RIPK3) – mixed lineage kinase-like (MLKL) signaling pathway in eosinophils, which, following its activation, leads to the production of high levels of reactive oxygen species (ROS) in a p38 mitogen-activated protein kinase (MAPK) and phosphatidylinositol 3'-kinase (PI3K) - dependent manner. All these steps are required for cytoplasmic vacuolization and subsequent cytolysis to occur. Interestingly, triggering cytolysis is associated with an induction of autophagy in eosinophils and additional stimulation of autophagy by pharmacological inhibition of the mechanistic target of rapamycin (mTOR) counter-regulates cell death. Moreover, MLKL phosphorylation, cytoplasmic vacuolization, and cytolysis were observed in eosinophils under *in vivo* inflammatory conditions. CONCLUSION: We report that adhesion-induced eosinophil cytolysis takes place by a RIPK3-MLKL-dependent necroptosis which can be counter-regulated by autophagy.

See original publication No 1

Neither eosinophils nor neutrophils require ATG5-dependent autophagy for extracellular DNA trap formation

Germic N, Stojkov D, Oberson K, Yousefi S, Simon HU

The importance of extracellular traps (ETs) in innate immunity is well established, but the molecular mechanisms responsible for their formation remain unclear and in scientific dispute. ETs have been defined as extracellular DNA scaffolds associated with the granule proteins of eosinophils or neutrophils. They are capable of killing bacteria extracellularly. Based mainly on results with phosphoinositide 3-kinase (PI3K) inhibitors such as 3-methyladenine (3-MA) and wortmannin which are commonly used to inhibit autophagy, several groups have reported that autophagy is required for neutrophil extracellular trap (NET) formation. We decided to investigate this apparent dependence on autophagy for ET release and generated genetically modified mice that lack, specifically in eosinophils or neutrophils, autophagy-related (Atg) 5, a gene encoding a protein essential for autophagosome formation. Interestingly, neither eosinophils nor neutrophils from Atg5-deficient mice exhibited abnormalities in ET formation upon physiological activation or exposure to low concentrations of PMA, although we could confirm that human and mouse eosinophils and neutrophils, after pre-treatment with inhibitors of class III PI3K, show a block both in reactive oxygen species (ROS) production and in ET formation. The so-called late autophagy inhibitors bafilomycin A1 and chloroquine, on the other hand, were without effect.

These data indicate that ET formation occurs independently of autophagy and that the inhibition of ROS production and ET formation in the presence of 3-MA and wortmannin is likely owing to their additional ability to block the class I PI3Ks which are involved in signaling cascades initiated by triggers of ET formation.
See original publication No 2

Evidence of an abnormal epithelial barrier in active, untreated and corticosteroid-treated eosinophilic esophagitis
Simon D, Page B, Vogel M, Bussmann C, Blanchard C, Straumann A, Simon HU
BACKGROUND: Eosinophilic esophagitis (EoE) is a chronic, immune/antigen-mediated disease characterized by symptoms related to esophageal dysfunction and an eosinophil-predominant inflammation. This study has aimed to investigate whether the recently observed sensitization to Candida albicans in EoE patients is owing to pre-existing disease and its underlying abnormal epithelial barrier or, alternatively, is linked to corticosteroid (CS) therapy. METHODS: Medical histories, as well as serum and tissue samples of 60 EoE patients (15 CS-naive, 45 with current or previous CS therapy) and 20 controls, stored in the Swiss Eosinophilic Esophagitis Database (SEED) and Biobank, were analyzed. We applied ImmunoCAP to measure IgE levels and immunofluorescence techniques to examine epithelial barrier components. RESULTS: EoE patients had higher total IgE levels and were more frequently sensitized to Candida albicans than controls. In EoE tissue specimens, increased numbers of eosinophils and mast cells, a higher expression levels of thymic stromal lymphopoietin (TSLP), cathelicidin, proteases, i.e. the kallikreins (KLK)-5 and KLK-7, were observed as compared with controls, while reduced expression of lympho-epithelial Kazal-type-related inhibitor (LEKTI), filaggrin, E-cadherin, claudin, occludin, demoglein-1 was found, independent of CS therapy. In CS-treated EoE, significantly lower numbers of CD1a+ cells and cathelicidin expression were noted as compared to CS-naive EoE. CONCLUSION: This study provides further evidence that EoE is associated with an abnormal epithelial barrier and postulates that CS therapy, by reducing innate immune mechanisms, may promote Candida albicans colonization and likely subsequent sensitization.
See original publication No 3

Original publications

1. Radonjic-Hoesli S, Wang X, de Graauw E, Stoeckle C, Styp-Rekowska B, Hlushchuk R, Simon D, Spaeth PJ, Yousefi S, **Simon HU**: Adhesion-induced eosinophil cytolysis requires the receptor-interacting protein kinase 3 (RIPK3)-mixed lineage kinase-like (MLKL) signaling pathway, which is counterregulated by autophagy. J Allergy Clin Immunol. 140 (2017), 1632-1642.

2. Germic N, Stojkov D, Oberson K, Yousefi S, **Simon HU**: Neither eosinophils nor neutrophils require ATG5-dependent autophagy for extracellular DNA trap formation. Immunology 152 (2017), 517-525.

3. Simon D, Page B, Vogel M, Bussmann C, Blanchard C, Straumann A, **Simon HU**: Evidence of an abnormal epithelial barrier in active, untreated and corticosteroid-treated eosinophilic esophagitis. Allergy 73 (2018), 239-247.

4. de Graauw E, Sitaru C, Horn M, Borradori L, Yousefi S, **Simon HU***, Simon D* (shared senior authorship): Evidence for a role of eosinophils in blister formation in bullous pemphigoid. Allergy 72 (2017), 1105-1113.

5. de Graauw E, Sitaru C, Horn MP, Borradori L, Yousefi S, Simon D, **Simon HU**: Monocytes enhance neutrophil-induced blister formation in an ex vivo model of bullous pemphigoid. Allergy 73 (2018), in press.

6. Vicari AP, Schoepfer AM, Meresse B, Goffin L, Léger O, Josserand S, Guégan N, Yousefi S, Straumann A, Cerf-Bensussan N, **Simon HU**, Chvatchko Y: Discovery and characterization of a novel humanized anti-IL-15 antibody and its relevance for the treatment of refractory celiac disease and eosinophilic esophagitis. MAbs. 9 (2017), 927-944.

7. Stojkov D, Amini P, Oberson K, Sokollik C, Duppenthaler A, **Simon HU**, Yousefi S: ROS and glutathionylation balance cytoskeletal dynamics in neutrophil extracellular trap formation. J Cell Biol. 216 (2017), 4073-4090.

8. Gevaert E, Zhang N, Krysko O, Lan F, Holtappels G, De Ruyck N, Nauwynck H, Yousefi S, **Simon HU**, Bachert C: Extracellular eosinophilic traps in association with Staphylococcus aureus at the site of epithelial barrier defects in severe airway inflammation. J Allergy Clin Immunol. 139 (2017), 1849-1860.

9. Weber B, Schlapbach C, Stuck M, **Simon HU**, Borradori L, Beltraminelli H, Simon D: Distinct interferon-gamma and interleukin-9 expression in cutaneous and oral lichen planus. J Eur Acad Dermatol Venereol. 31 (2017), 880-886.

10. Schneider C, Wicki S, Graeter S, Tankica MT, Keller CW, Quast I, Leontyev D, Iglika KD, Käsermann F, Jakob SM, Dimitrova PA, Branch DR, Cummings RD, Lünemann JD, Kaufmann T, **Simon HU**, von Gunten S: IVIG regulates the survival of human but not mouse neutrophils. Sci Rep. 7 (2017), 1296.

11. Mortezavi A, Salemi S, Rupp NJ, Rüschoff JH, Hermanns T, Poyet C, Randazzo M, **Simon HU**, Moch H, Sulser T, Wild P, Eberli D: Negative LC3b immunoreactivity in cancer cells is an independent prognostic predictor of prostate cancer specific death. Oncotarget 8 (2017), 31765-31774.

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1. Simon D, Straumann A, Schoepfer AM, **Simon HU**: Current concepts in eosinophilic esophagitis. Allergo J Int. 26 (2017), 258-266.

2. **Simon HU**, Friis R, Tait SW, Ryan KM: Retrograde signaling from autophagy modulates stress responses. Sci Signal. 10 (2017), eaag2791.

3. Benarafa C, **Simon HU**: Role of granule proteases in the life and death of neutrophils. Biochem Biophys Res Commun. 482 (2017), 473-481.

4. Gevaert E, Yousefi S, Bachert C, **Simon HU**: Extracellular eosinophil traps - Reply. J. Allergy Clin Immunol. (2018), in press.

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6. Sokollik C, **Simon HU**: Physiologie der eosinophilen Granulozyten. Ther. Umschau 74 (2017), 291-296.

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12. Bieber T, **Simon HU**: Allergy – committed to progress in allergy and immunology. Allergy 73 (2018), in press.

13. **Simon HU**: International Archives of Allergy and Immunology: A commitment to serving the community worldwide. Int. Arch. Allergy Immunol. 175 (2018), 1-2.

Book chapters

1. **Simon HU**, Friis R, Colombo MI: Autophagy. In: eLS (Encyclopedia of Life Sciences). John Wiley & Sons, Ltd: Chichester, UK, (2017). DOI 10.1002/9780470015902.a0021581.pub2

2. Yousefi S, **Simon HU**: NETosis – Does it really represent nature's "suicide bomber"? In: NETosis 2: The excitement continues (Eds. M.J. Kaplan, M. Radic and M. Herrmann): eBook, Frontiers in Immunology, 2017, p. 194-197. DOI 10.3389/978-2-88945-379-5

Group Prof. Stephan von Gunten

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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.

IVIG regulates the survival of human but not mouse neutrophils
Schneider C, Wicki S, Graeter S, Tankica MT, Keller CW, Quast I, Leontyev D, Iglika KD, Käsermann F, Jakob SM, Dimitrova PA, Branch DR, Cummings RD, Lünemann JD, Kaufmann T, Simon HU, von Gunten S
Intravenous immunoglobulin (IVIG) are purified IgG preparations made from the pooled plasma from thousands of healthy donors and are being tested in preclinical mouse models. Inherent challenges, however, are the pluripotency of IVIG and its xenogeneicity in animals. IVIG can alter the viability of human neutrophils via agonistic antibodies to Fas and Siglec-9. In this study, we compared the effects of IVIG on human and mouse neutrophils using different death assays. Different commercial IVIG preparations similarly induced cytokine-dependent death in human neutrophils, whereas they had no effects on the survival of either peripheral blood or bone marrow neutrophils from C57BL/6 or BALB/c mice. $F(ab')_2$ but not Fc fragments of IVIG induced death of human neutrophils, whereas neither of these IVIG fragments, nor agonistic monoclonal antibodies to human Fas or Siglec-9 affected the viability of mouse neutrophils. Pooled mouse IgG, which exhibited a different immunoprofile compared to IVIG, also had no effect on mouse cells. Together, these observations demonstrate that effects of IVIG on neutrophil survival are not adequately reflected in current

mouse models, despite the key role of these cells in human inflammatory and autoimmune diseases.
See original publication

Original publication

Schneider C, Wicki S, Graeter S, Tankica MT, Keller CW, Quast I, Leontyev D, Iglika KD, Käsermann F, Jakob SM, Dimitrova PA, Branch DR, Cummings RD, Lünemann JD, Kaufmann T, Simon HU, **von Gunten S**: IVIG regulates the survival of human but not mouse neutrophils. Sci Rep. 7 (2017), 1296.

Review articles/Editorials

1. Kouskoura T, Katsaros C, **von Gunten S**: The potential use of pharmacological agents to modulate orthodontic tooth movement (OTM).
   Front Physiol. 8 (2017), 67.

2. Schneider C, Illi M2, Lötscher M, Wehrli M, **von Gunten S**: Isolation of antibodies from human plasma, saliva, breast milk, and gastrointestinal fluid. Methods Mol Biol. 1643 (2017), 23-31.

3. Boligan KF, **von Gunten S**: Innate lymphoid cells in asthma: cannabinoids on the balance.
   Allergy 72 (2017), 839-841.

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6. Adams OJ, Stanczak MA, **von Gunten S**, Läubli H: Targeting sialic acid-Siglec interactions to reverse immune suppression in cancer. Glycobiology, in press.

Group Prof. Shida Yousefi

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**Joint supervision together with Dr. C. Sokollik.

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.

ROS and glutathionylation balance cytoskeletal dynamics in neutrophil extracellular trap formation
Stojkov D, Amini P, Oberson K, Sokollik C, Duppenthaler A, Simon HU, Yousefi S
The antimicrobial defense activity of neutrophils partly depends on their ability to form neutrophil extracellular traps (NETs), but the underlying mechanism controlling NET formation remains unclear. We demonstrate that inhibiting cytoskeletal dynamics with pharmacological agents or by genetic manipulation prevents the degranulation of neutrophils and mitochondrial DNA release required for NET formation. Wiskott-Aldrich syndrome protein-deficient neutrophils are unable to polymerize actin and exhibit a block in both degranulation and DNA release. Similarly, neutrophils with a genetic defect in NADPH oxidase fail to induce either actin and tubulin polymerization or NET formation on activation. Moreover, neutrophils deficient in glutaredoxin 1 (Grx1), an enzyme required for deglutathionylation of actin and tubulin, are unable to polymerize either cytoskeletal network and fail to degranulate or release DNA. Collectively, cytoskeletal dynamics are achieved as a balance between reactive oxygen species-regulated effects on polymerization and glutathionylation on the one hand and the Grx1-mediated deglutathionylation that is required for NET formation on the other.
See original publication No 1

Original publications

1. Stojkov D, Amini P, Oberson K, Sokollik C, Duppenthaler A, Simon HU, **Yousefi S**: ROS and glutathionylation balance cytoskeletal dynamics in neutrophil extracellular trap formation. J Cell Biol. 216 (2017), 4073-4090.

2. Radonjic-Hoesli S, Wang X, de Graauw E, Stoeckle C, Styp-Rekowska B, Hlushchuk R, Simon D, Spaeth PJ, **Yousefi S**, Simon HU: Adhesion-induced eosinophil cytolysis requires the receptor-interacting protein kinase 3 (RIPK3)-mixed lineage kinase-like (MLKL) signaling pathway, which is counterregulated by autophagy. J Allergy Clin Immunol. 140 (2017), 1632-1642.

3. Germic N, Stojkov D, Oberson K, **Yousefi S**, Simon HU: Neither eosinophils nor neutrophils require ATG5-dependent autophagy for extracellular DNA trap formation. Immunology 152 (2017), 517-525.

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5. Vicari AP, Schoepfer AM, Meresse B, Goffin L, Léger O, Josserand S, Guégan N, **Yousefi S**, Straumann A, Cerf-Bensussan N, Simon HU, Chvatchko Y: Discovery and characterization of a novel humanized anti-IL-15 antibody and its relevance for the treatment of refractory celiac disease and eosinophilic esophagitis. MAbs. 9 (2017), 927-944.

6. Gevaert E, Zhang N, Krysko O, Lan F, Holtappels G, De Ruyck N, Nauwynck H, **Yousefi S**, Simon HU, Bachert C: Extracellular eosinophilic traps in association with Staphylococcus aureus at the site of epithelial barrier defects in severe airway inflammation. J Allergy Clin Immunol. 139 (2017), 1849-1860.

7. de Graauw E, Sitaru C, Horn MP, Borradori L, **Yousefi S**, Simon D, Simon HU: Monocytes enhance neutrophil-induced blister formation in an ex vivo model of bullous pemphigoid. Allergy 73 (2018), in press.

Correspondence

Gevaert E, **Yousefi S**, Bachert C, Simon HU: Extracellular eosinophil traps - Reply. J Allergy Clin Immunol. (2018), in press.

Book chapter

Yousefi S, Simon HU: NETosis – Does it really represent nature's "suicide bomber"? In: NETosis 2: The excitement continues (Eds. M.J. Kaplan, M. Radic and M. Herrmann): eBook, Frontiers in Immunology, 2017, p. 194-197.
DOI 10.3389/978-2-88945-379-5

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We are interested in translational aspects of molecular oncology, biomarker validation and tumor targeting with rationally engineered and pharmacologically improved protein-drug conjugates. For tumor targeting we use Designed Ankyrin Repeat Proteins (DARPins), as highly stable non-IgG scaffold proteins, for site-specific and orthogonal conjugation, to yield 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 protein carrying both a thiol and an azide group for thiol-maleimide conjugation and strain-promoted azide-alkyne cycloaddition (SPAAC). Based on this technology, we have generated nanomedicines payloaded with cytotoxins of various origins including domain I-truncated Pseudomonas Aeruginosa Exotoxin A and 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, we use well-defined cell lines from solid human tumors to investigate the role of various components of the sphingolipid signaling pathway in malignant progression and metastasis.

Original publication

Graumann R, Di Capua GA, Oyarzún JE, Vásquez MA, Liao C, Brañes JA, Roa I, Casanello P, Corvalán AH, Owen GI, Delgado I, **Zangemeister-Wittke U**, Ziegler A: Expression of teneurins is associated with tumor differentiation and patient survival in ovarian cancer. PLoS One. 12 (2017), e0177244.

Review article

Huwiler A**, Zangemeister-Wittke U**: The sphingosine 1-phosphate receptor modulator fingolimod as a therapeutic agent: recent findings and new perspectives.
Pharmacol Ther., in press.

Group Prof. Manuel Haschke (Clinical Pharmacology)

Group members: Friederike Sandbaumhüter, PhD
Jürgen Bohlender, MD
Evangelia Liakoni, MD
Katharina Geiling, MD
Irene Scholz, med pract

We are interested in mechanisms of drug toxicity and factors responsible for variations of drug metabolism. A key technology for the identification and quantitative analysis of exogenous and endogenous compounds used as biomarkers for toxicity or metabolism is liquid chromatography tandem mass spectrometry (LC-MS/MS). We therefore invested substantial efforts to install two highly sensitive LC-MS/MS systems, which will be fully operational at the start of 2018. The systems will be used to establish quantitative analytics for the phenotyping of phase I drug metabolizing enzymes, renin-angiotensin system peptides, and to determine drug concentrations in samples from clinical phase I studies or from patients referred to our outpatient clinics (e.g. antihypertensive drugs).
In addition to our research activities our group invests a considerable amount of time and effort for clinical duties provided for the University Hospital Bern to improve efficacy and safety in the clinical use of drugs. Our activities include a consiliary service (>250 expert reports), evaluation of patients with drug-related problems (adverse drug effects, pharmacogenetics, phenotyping) or difficult to treat arterial hypertension in the outpatient clinics and regular drug safety screenings of inpatients on medical wards. In addition, we manage the regional pharmacovigilance center where we work up and evaluate reports on adverse drug events (>280/year), which then are fed into the national (Swiss Regulatory Authority) and international (WHO) adverse drug event databases. In December 2017 our center successfully passed an official inspection by the Swiss Regulatory Authority (SwissMedic).

Mechanisms and Genetics of Metamizole-induced Agranulocytosis (MH)
For this SNF-funded project, a cohort of patients after metamizole-induced agranulocytosis (MIA) will be compared with a cohort of metamizole tolerant patients and a cohort of never-exposed subjects in a genome-wide association study (collaboration with U. Amstutz, Clinical Chemistry, Inselspital Bern). In addition, direct toxocitiy mechanisms (collaboration with S. Krähenbühl, Clin.Pharm Basel) as well as immune mediated mechanisms (collaboration D. Yerli, Immunology, Inselspital Bern) be investigated.

Phenotyping of phase I drug metabolism (MH)
To determine activity of major drug metabolizing cytochrome P450 enzymes we recently developed a new phenotyping cocktail based on widely available low dose probe drugs. For easier clinical application we developed a new combination capsule (CombiCap) containing mini-tab formulations of all six probe drugs. After initial testing in healthy volunteers, this

CombiCap will now be used to characterize phase I drug metabolism in patients with different diseases (e.g. liver cirrhosis).

Renin-Angiotensin-System (RAS) peptide profiles (MH)
Angiotensin I and II are degraded by ACE and other peptidases to smaller peptide fragments, which can be quantified using LC-MS/MS. Cardiovascular drugs such as ACE-inhibitors or angiotensin receptor blockers lead to characteristic changes in RAS peptide profiles. These profiles have been characterized in clinical trials with healthy subjects as well as in patients with newly diagnosed or difficult to control arterial hypertension. In conjunction with cardiovascular drug concentrations (also quantified by LC-MS/MS) we will test, whether these profiles allow a better discrimination between adherence-related problems and true drug-related problems.

New Biomarkers and Difficult-to-Treat Hypertension (JB)
This project investigates the profile of plasmatic angiotensin peptides and of tubular epithelial channel proteins in urinary exosomes to refine the classification of hypertension and to predict the therapeutic efficacy of blocking angiotensin vs. aldosterone dependent mechanisms. It is funded by the Swiss Kidney Foundation.

Immunocytological characteristics of tumoral renin expression (JB)
This project investigates the immunocytological characetristics of rare and ectopic tumoral renin expression in using confocal fluorescence.

Angiotensinergic innervation of cardiovascular organs (JB)
Angiotensin II is increasingly recognized as a neuropeptide co-transmitter also in the peripheral autonomic nervous system where it may represent a new therapeutic target. This project investigates the phenotypic characteristics of angiotensin-expressing fibers that innervate cardio-vascular organs using immunocytological techniques.

Blood pressure targets in elderly patients with risk factors (JB)
Optimal blood pressure targets in elderly hypertensive patients are currently debated. In this project, elderly hypertensives are characterized in various clinical situations to identify factors that may be useful to guide antihypertensive treatment decisions.

Effect of P-gp and CYP3A4-induction on PK and PD of Rivaroxaban (EL)
Open-label, sequential treatment study to investigate the influence of the combined P-gp and CYP3A4 inducer hypericum perforatum (St. John's wort) on the pharmacokinetics and pharmacodynamics of rivaroxaban in 12 healthy volunteers. CYP activity will be phenotyped at start of each session using fexofenadine po, midazolam iv and a stable midazolam isotope (MidazolamD3) po. By using simultaneous doses of deuterated formulations (stable isotope) of midazolam via different routes of administration (iv/po), the relative contribution of intestinal and hepatic CYP3A4 activity can be evaluated. Primary outcomes include the Cmax, tmax, ke, t1/2, and AUC of rivaroxaban (PK evaluation) and factor Xa activity (PD evaluation), displayed as maximal effect (Emax) and parametrized by calculating the area under the time-effect curves (AUEC). Ethics approval Dec 2017, clinical trial 2018.

Epidemiological study statin intolerance and risk of myopathy (EL)
Propensity score (PS) matched sequential cohort research using the Clinical Practice Research Datalink (CPRD) to assess the risk of myopathy and the risk of unspecified statin intolerance associated with hydrophilic statin use, when compared with lipophilic statin use.

Participation to the European Drug Emergency Network (EuroDEN) (EL)
Our department is part of the European Drug Emergencies Network (Euro-DEN), a project established in 2013 and currently collecting data on acute recreational drug toxicity from 31 centres in 21 countries across Europe. Data on acute toxicity of recreational substances contribute to the current knowledge of acute drug toxicity, and most importantly on the potential harms of novel psychoactive substances, thus helping to optimize patient treatment and preventive measures. The findings of the project are published regularly in form of descriptive studies, case reports and also subanalyses of special interest (e.g. recreational use of prescription and over the counter drugs, focus on specific age groups (e.g. young adults), presentations associated with particular medical problems (e.g. psychosis) or substances (e.g. GHB)).

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3. Blaser L, Hassna H, Hofmann S, Holbro A, **Haschke M**, Rätz Bravo A, Zeller A, Krähenbühl S, Taegtmeyer A: Leucopenia associated with metamizole: a case-control study. Swiss Med Wkly. 147 (2017), w14438.

4. Erb S, Letang E, Glass TR, Natamatungiro A, Mnzava D, Mapesi H, **Haschke M**, Duthaler U, Berger B, Muri L, Bader J, Marzolini C, Elzi L, Klimkait T, Langewitz W, Battegay M; Kilombero Ulanga Antiretroviral Cohort (KIULARCO) study group. Health care provider communication training in rural Tanzania empowers HIV-infected patients on antiretroviral therapy to discuss adherence problems. HIV Med. 18 (2017), 623-634.

5. Krisai P, **Haschke M**, Buser PT, Mueller C: Ticagrelor induced systemic inflammatory response syndrome. BMC Cardiovasc Disord. 17 (2017), 14.

6. Bohlender JM, Nussberger J, Birkhäuser F, Grouzmann E, Thalmann GN, Imboden H: Resetting of renal tissular renin-angiotensin and bradykinin-kallikrein systems after unilateral kidney denervation in rats. Histochem Cell Biol. 147 (2017), 585-593.

7. Bohlender J, Nussberger J, Ménard J, Bohlender B: Prevalence of carotid artery stenosis in nonagenarians: Survey in a primary care hospital. Ann Cardiol Angiol (Paris). 66 (2017), 130-134.

8. Bohlender J, Nussberger J, Tevaearai H, Imboden H: Angiotensinergic innervation of the human right atrium: implications for cardiac reflexes. Am J Hypertens. (2017), doi: 10.1093/ajh/hpx163. [Epub ahead of print]

9. Dolder PC, Holze F, Liakoni E, Harder S, Schimd Y, Liechti ME: Alcohol acutely enhances decoding of positive emotions and emotional concern for positive stimuli and facilitates the viewing of sexual images. Psychopharmacology (Berl) 234 (2017), 41-51.

10. Stoller A, Dolder PC, Bodmer M, Hammann F, Rentsch KM, Exadaktylos AK, Liechti ME, Liakoni E; Mistaking 2C-P for 2C-B: What a difference a letter makes. J Anal Toxicol. 41 (2017), 77-79.

11. Liakoni E, Müller S, Stoller A, Ricklin M, Liechti ME, Exadaktylos AK: Presentations to an urban emergency department in Bern, Switzerland associated with acute recreational drug toxicity. Scand J Trauma Resusc Emerg Med. 25 (2017), 26.

12. Miró O, Galicia M, Dargan P, Dines AM, Giraudon I, Heyerdahl F, Hovda KE, Yates C, Wood DM, Euro-DEN Research Group: Liakoni E, Liechti ME, Jürgens G, Pedersen CB, O'Connor N, Markey G, Moughty A, Lee C, Anand JS, Puiguriguer J, Homar C, Eyer F, Vallersnes OM, Persett PS, Chevillard L, Mégarbane B, Paasma R, Waring WS, Pöld K, Rabe C, Kabata P: Intoxications by gamma hydroxybutyrate and related analogies: clinical characteristics and comparison between pure intoxication and that combined with other substances of abuse. Toxicology Letters 277 (2017), 84-91.

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15. Meier S, **Haschke M**, Zahner C, Kruttschnitt E, Drewe J, Liakoni E, Hammann F, Gaab J: Effects of a fixed herbal drug combination (Ze 185) to an experimental acute stress setting in healthy men – an explorative randomized placebo-controlled double blind study. Phytomedicine, in press.

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17. Sandbaumhüter FA, Theurillat R, Bettschart-Wolfensberger R, Thormann W: Effect oft he α2-receptor agonists medetomidine, detomidine, xylazine, and romifidine on the ketamine metabolism in equines assessed with enantioselective capillary electrophoresis. Electrophoresis 38 (2017), 1895-1904.

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Haschke M, Liechti M: Metamizol: Nutzen und Risiken im Vergleich zu Paracetamol und NSAR. Swiss Medical Forum 17 (2017), 1067–1073.

Rexhaj E, Messerli FH, Cerny D, Bohlender J: Salt and Blood Pressure: Cutting Through the Scientific Fog. Curr Hypertens Rep. 19 (2017), 47.

Book chapter

Wertli M, Perrig M, Brachlow J, John H, Bohlender J: Endokrine Urologie. In: Urologische Fragen in der Praxis, 2. Auflage, Uni-Med Verlag: Bremen (2017).

Additional Publications by PKI Members

Original publications

Lejeune A, Martin L, Santibanez S, Thee S, Gratopp A, **Späth P**, Mankertz A, Kallinich T, von Bernuth H: Postexposure prophylaxis with intravenous immunoglobulin G prevents infants from getting measles. Acta Paediatr. 106 (2017), 174-177.

Spirk D, Stuck AK, Hager A, Engelberger RP, Aujesky D, Kucher N. Electronic alert system for improving appropriate thromboprophylaxis in hospitalized medical patients: a randomized controlled trial. J Thromb Haemost 15 (2017), 2138-46.

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Engelberger RP, Stuck A, **Spirk D**, Willenberg T, Haine A, Periard D, Baumgartner I, Kucher N. Ultrasound-assisted versus conventional catheter-directed thrombolysis for acute iliofemoral deep vein thrombosis: 1-year follow-up data of a randomized-controlled trial. J Thromb Haemost 15 (2017), 1351-60.

Review articles/Editorials

Pilch KS, **Spaeth PJ**, Yuki N, Wakerley BR. Therapeutic complement inhibition: a promising approach for treatment of neuroimmunological diseases. Expert Rev Neurother 17 (2017), 579-591.

Petrova-Slater I, Denegri A, Pasotti E, Rossi MG, **Spirk D**, Riesen WF, Moccetti T, Moccetti M. Inhibitors of PCSK9. Rev Med Suisse 13 (2017), 821-825.

Stuck AK, **Spirk D**, Schaudt J, Kucher N. Risk assessment models for venous thromboembolism in acutely ill medical patients. A systematic review. Thromb Haemost 117 (2017), 801-808.

4.2. Congress Invitations

Prof. Hans-Uwe Simon
World Immune Regulation Meeting XI, Davos (CH); March 15-18, 2017;
Adhesion-induced eosinophil cytolysis requires the RIPK3-MLKL signaling pathway which is counter-regulated by autophagy.

Workshop on “Cell Death and Disease”, Villa Vigoni, Loveno di Menaggio, Como (I); June 14-17, 2017;
Mechanism of eosinophil cytolysis.

Annual Meeting of the European Allergy and Clinical Immunology (EAACI), Helsinki (Finland), June 17-21, 2017;
Eosinophilic syndrome: Anything new?

CDD*Retreat* on Cancer Biology, Capri (I), June 27-30, 2017;
Eosinophils in cancer.

10th Biennial Symposium of the International Eosinophil Society (IES), Gothenburg (S), July 19-23, 2017;
State-of-the Art: Molecular mechanisms regulating eosinophil granule protein release and toxicity.

26th European Academy of Dermatology and Venerology (EADV) Congress, Geneva (CH), Sept. 13-17, 2017;
Eosinophil function in health and disease: Consequences for treatment.

25th Euroconference on Apoptosis, Leuven (B), Sept. 27-29, 2017;
Cell death and phagocytosis: Brief historical introduction.

Falk Symposium 208: Eosinophilic Esophagitis – Medical and Dietary Treatment, Berlin (D), Oct. 4-5, 2017;
The role of the eosinophil in EoE: A key player or an innocent bystander?

9th Dermatological Meeting in Ticino: From the bench to the clinic, Bellinzona (CH); Oct. 26, 2017;
Novel pathways regulating the formation of neutrophil extracellular DNA traps.

The 8th *Cell Death & Disease* Symposium on Precision Medicine and Cell Therapy, Changzhou (China); Nov. 4-6, 2017;
Eosinophil cytolysis requires the RIPK3-MLKL signaling pathway which is counter-regulated by autophagy.

Neutrophil Extracellular Traps, Berlin (D); Nov. 16-17, 2017;
Understanding the molecular pathway of NET formation: The mitochondrial-cytoskeletal interaction.

Celebrating Science, Faculty of Pharmacy, University of Ljubljana, Ljubljana (Slovenia); Dec. 6, 2017;
The function of eosinophils: Different views over time.

Prof. Thomas Kaufmann
2nd Workshop on Cell Death and Inflammation: The Chicken and Egg Paradox, Zurich, Nov 7 – 8 2017; Peculiarities of death-receptor and mitochondrial mediated cell death in granulocytes.

11th PhD workshop on Molecular Mechanisms and Therapeutic Approaches in Cancer, Institute of Cell Biology and Immunology, University of Stuttgart, Sep 20-22 2017, Freudenstadt (DE); *keynote speaker:* What the BOK! Two and a half stories about a poorly understood BCL-2 family member.

Prof. Georgia Konstantinidou
The 10th Annual World Cancer Congress 2017 (WCC-2017), Barcellona, Spain; 19-21 May 2017; Lipid Metabolic Regulation of KRAS-mutant tumors.

Prof. Stephan von Gunten
93th Congress of the European Orthodontic Society (EOS), Montreux (CH), June 5-10, 2017; Drugs in orthodontics: a pharmacologist's perspective.

Prof. Shida Yousefi
25th Cytomeet, Bern (CH); Jan. 24, 2017;
Cytoskeletal regulation of mitochondrial DNA release and NET formation.

MIC Mini Symposium: Image analysis in microscopy, Bern (CH); April 5, 2017;
Cytoskeletal regulation of mitochondrial DNA release and NET formation.

4.3. Seminar Invitations

Prof. Hans-Uwe Simon
Faculty of Pharmacy, University of Ljubljana, Slovenia; March 31, 2017;
guest of Prof. Dr. Irena Mlinaric-Rascan:
The molecular mechanism of eosinophil cytolysis.

Molecular, Cellular, and Clinical Allergology (MCCA) lecture,
Medical University of Vienna (A); May 8, 2017; guest of Prof. Dr. Winfried Pickl:
Hypereosinophilic syndromes.

Prof. Thomas Kaufmann
Institute of Molecular Medicine and Cell Research, University of Freiburg i. Brsg. (DE), January 20, 2017; guest of Prof C. Borner (SFB850 series); The Bcl-2 family member BOK and its role in chemical induced hepatocarcinogenesis.

Prof. Georgia Konstantinidou
Theodor Kocher Institute, Bern (CH); July 10, 2017; Lipid Metabolic Regulation of KRAS-mutant tumors.

Prof. Stephan von Gunten
Centre d'Immunologie et des Maladies Infectieuse(CIMI), Faculté de Mèdicines Pierre et Marie Curie, Paris (F), December 20, 2017; guest of Prof. Guy Gorochow: Therapeutic immunoglobulins: insights on repertoires and mechanisms.

Center for Chronic Immunodeficiency (CCI), University of Freiburg, Freiburg (G), November 24, 2017; guest of Prof. Bodo Grimbacher: The human repertoire of glycan-specific antibodies in health and disease.

Novartis Institutes for Biomedical Research, Translational Medicine – Preclinical Safety, Basel (CH), May 8th, 2017; guest of Dr. Michael Kammueller: Basic and novel aspects of humoral and cellular glycoimmunology.

Department of Hematology, University Hospital of Bern, Bern (CH), Feb 13, 2017; guest of Prof. Gabriela Baerlocher: The tumor glycan shield – implications for immunotherapy.

Dep. of Medicine, Fribourg (CH), January 25, 2017; Tumor immunology – impact of the tumor glycan shield.

Dr. He Liu
Neurozentrum, University Hospital Bern, Bern (CH); Feb 22, 2017;
guest of Prof. Dr. Andrew Chan:
The metabolic feature of human dermal stem cells and its implication in neuronal differentiation.

Institute of Infectious Diseases (IFIK), University of Bern, Bern (CH); Feb 24, 2017;
guest of Prof. Dr. Stephen Leib:
The metabolic feature of human dermal stem cells and its implication in neuronal differentiation.

4.4. Organization of Meetings and Courses

Prof. Hans-Uwe Simon
Symposium of the Swiss Society of Pharmacology and Toxicology (together with task force SSPT): Progress in Pharmacology – Treatment of Skin Diseases;
Bern (CH), January 26, 2017

Workshop on “Cell Death and Disease” (together with C. Brancolini, K.-M. Debatin and P.H. Krammer), Villa Vigoni, Loveno di Menaggio, Como (I), June 14-17, 2017

16th III-Bern International Summer School,
Zäziwil (CH), July 23 – 25, 2017

Falk Symposium 208: Eosinophilic Esophagitis – Medical and Dietary Treatment (together with A. Straumann, G.T. Furuta, I. Hirano, A. Schoepfer),
Berlin (D), Oct. 4-5, 2017

Prof. Stephan von Gunten
Annual Meeting 2017 of the Swiss Society for Pharmacology and Toxicology (together with task force SSPT), Bern (CH), April 20, 2017

4.5. Invited Chairperson at Congresses

Prof. Hans-Uwe Simon

Symposium of the Swiss Society of Pharmacology and Toxicology:
Progress in Pharmacology – Treatment of Skin Diseases, Morning session;
Bern (CH), January 26, 2017

World Immune Regulation Meeting XI; Plenary Session 7: Exposome,
genes & immune regulation;
Davos (CH); March 15-18, 2017

Annual Meeting of the European Allergy and Clinical Immunology (EAACI);
Symposium 25: Treatment and monitoring of eosinophilic esophagitis;
Helsinki (Finland), June 17-21, 2017

10th Biennial Symposium of the International Eosinophil Society (IES);
Workshop on Needs in Eosinophil Research (TREAD);
Gothenburg (S), July 19-23, 2017

10th Biennial Symposium of the International Eosinophil Society (IES);
Session 4: Eosinophilic differentiation and effector functions;
Gothenburg (S), July 19-23, 2017

25th Euroconference on Apoptosis; Session: Cell death & phagocytosis;
Leuven (B), Sept. 27-29, 2017

Falk Symposium 208: Eosinophilic Esophagitis – Medical and Dietary Treatment;
Session VII: Outlook; Berlin (D), Oct. 4-5, 2017

2nd Type-2 Immunity Meeting; Afternoon session;
Bern (CH), Dec. 15, 2017

Prof. Thomas Kaufmann

16th TNF Superfamily Meeting, Apr 17-21 2017, Singapore (SG); Session 4, TNF & Cancer

Prof. Georgia Konstantinidou
Annual Meeting 2017 of the Swiss Society for Pharmacology and Toxicology; Session "Young Investigator Research", Bern (CH), April 20, 2017

Prof. Stephan von Gunten
Annual Meeting 2017 of the Swiss Society for Pharmacology and Toxicology; Session "Young Investigator Research", Bern (CH), April 20, 2017

4.6. Referee Work for Peer-Reviewed Journals

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

Prof. Andrea Huwiler
Biochem. Pharmacol.
Biochim. Biophys. Acta
Blood
Br. J. Pharmacol.
Cellular signaling
Circ. Res.
Clin. Chem. Lab. Med.
Diabetologica
Eur. J. Pharmacol.
Exp. Cell Res.
FEBS letters
Frontiers in Pharmacology
Hormone Metabol. Res.
J. Am. Soc. Nephrol.
J. Biol. Chem.
J. Cell. Biochem.
J. Cell. Physiol.
J. Exp. Pharmacol. Ther.
Kidney and Blood Pressure Research
Kidney Int.
Naunyn Schmiedeb. Arch. Pharmacol.
Planta Medica

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
Hepatology
Immunology and Cell Biology
International Archives of Allergy and Immunologie
International Review of Cell and Molecular Biology
J. Hepatology
J. Molecular Cell Biology
J. Neuroscience
Methods
Molecular Cancer Therapeutics
Mol. Cell. Oncology
Oncogene
PLoS One
Scientific Reports
Trends in Cell Biology

Prof. Georgia Konstantinidou
Cell Death Dis.

Dr. He Liu
Allergy
Cell Death Dis.
Cell Death Differ.
Frontiers in Oncology

Prof. Hans-Uwe Simon
Allergy
Apoptosis
Autophagy
Blood
J. Cell Cycle
J. Clin. Invest.
EMBO Journal
EMBO Reports
Gut
J. Allergy Clin. Immunol.
J. Exp. Med.
J. Immunol.
J. Leukoc. Biol.
J. Cell Sci.
Oncogene
Frontiers Oncology

Science Signaling
Eur. J. Immunol.
FASEB J.
Cell Death Differ.
Cell Death Dis.
FEBS letters
Mol. Cell. Oncology
Nat. Med.
N. Engl. J. Med.
Cell Reports

PD Dr. Peter Späth
J. Immunol. Res.

Prof. Stephan von Gunten
Allergy
Am. J. Respir. Cell Mol. Biol.
Ann. Sports Med. Res.
Arthritis Res. Ther.
Blood
BMC Biotech.
Cell Death Differ.
Cell Death Dis.
Curr. Med. Chem.
Frontiers Oncology
Gene Therapy
Glycobiol.
Immunol. Cell Biol.
Immunol. Lett.
Int. Immunopharm.
J. Allergy Clin. Immunol.
J. Clin. Invest.
J. Immunol.
J. Immunotox.
Med. Inflamm.
Respiration
Oncotarget
Pathobiology
PLoS One
Respi. Res.
Tuberculosis

Prof. Shida Yousefi
Cell Biol. Int.
Cell Biochem. Biophys.
Cell Death Differ.
Cell Death Dis.
Frontiers of Immunology
Eur. J. Immunol.
Exp. Lung Res.
Int. J. Mol. Sci.
Immunology
J. Vasc. Intervent. Radiol.
Respir. Res.
Scientific Reports
Int. J. Biochem. Cell Biol.
Thorax

Prof. Uwe Zangemeister-Wittke
Bioconjug. Chem.
Cell Death Dis.
Expert Opin. Drug Delivery
Frontiers in Oncology
Mol. Cell. Biol.
Oncotarget
Toxins

Prof. Manuel Haschke
Analytical Chemistry
Clinical Pharmacokinetics
Eur J Clin Pharmacol
Rapid Comm Mass Spec
Swiss Medical Weekly

PD Dr. Jürgen Bohlender
J Am Soc Hypertens
Swiss Med Forum
J Hypertens

Dr. Evangelia Liakoni
Clin Tox
Current Drug Abuse Reviews
Open Access Emergency Medicine
Case Reports in Emergency Medicine
Drug Healthcare and Patient Safety
Swiss Medical Weekly

4.7. Referee Work for Grant Bodies

Dr. Zhaoyue He
Swiss Cancer League

Prof. Andrea Huwiler
Deutsche Forschungsgemeinschaft (DFG)
Swiss National Science Foundadtion (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)

Dr. He Liu
Swiss Cancer League

Prof. Hans-Uwe Simon
Swiss National Science Foundation (SNF)
Italian Association for Cancer Res.
Swiss Cancer League
Novartis Foundation

Prof. Stephan von Gunten
Canadian Glycomics Network
Dutch Cancer Society (DCS)
Netherlands Organisation for Scientific Research (NWO)

Prof. Uwe Zangemeister-Wittke
Swiess National Science Fundation
Swiss Cancer League
Qatar National Research Fund (QNRF)

4.8. Awards

Prof. Hans-Uwe Simon
Honorary doctorate (Dr. h.c.)
University of Ljubljana, Slovenia, December 5, 2017

Bisera Stepanovska
Novartis Institute of Biomedical Research Prize 2017 for excellent poster Presentation
Spring Meeting of the Swiss Society of Pharmacology and Toxicology (SSPT), Bern (CH), April 20, 2017

PD Dr. Jürgen Bohlender
Poster Award, 49th Annual Meeting of the Swiss Society of Nephrology, Forum Fribourg, Granges-Paccot, December 7-8, 2017

5. Administrative, Advisory, and Honorary Posts

Dr. Zhaoyue He
Coordinator for PC work at the PKI
Webmaster at the PKI

Prof. Andrea Huwiler
President of the Ernennungs- und Habilitationskommission (EHK), Medical Faculty, University of Bern

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

Member of the Editorial Board of Cellular and Molecular Neurobiology

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, Allergy

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, Oncotarget

Member of the World Allergy Organization (WAO) Special Committee on Eosinophils, Mast Cells & Basophils

Coordinator for FACS, Fluorescence Microscope, and Chemicals at the PKI

Coordinator FPLC (Äkta)

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.

Prof. Hans-Uwe Simon
Dean, Medical Faculty, University of Bern

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

Vice-Chair, Immunopharmacology Section, International Union of Basic and Clinical Pharmacology (IUPHAR), since 2013

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

Member of the Scientific Committee, Swiss Cancer League

Workshop Representative of the Mechanisms of Allergy/Asthma/ Immunology (MAAI) section of the American Academy of Allergy, Asthma and Immunology (AAAAI)

Chair, Cells and Mediators of Allergic Inflammation Committee, American Academy of Allergy, Asthma and Immunology (AAAAI)

Editor-in-Chief, Allergy

Editor-in-Chief, Cell Death & Disease

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

Section Editor, Apoptosis

Member of the Scientific Board, Allergologie

Member of the Advisory Board, Allergo-Journal

Member of the Editorial Board, Cell Death and Differentiation

Associate Editor, Frontiers in Oncology

Associate Editor, Molecular & Cellular Oncology

PD Dr. Peter Späth
Member of the Scientific Board, 10th C1 Inhibitor Deficiency Workshop, Budapest (H), May 18 -21, 2017

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

Prof. Stephan von Gunten
President of the Swiss Society of Experimental Pharmacology (SSEP)

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

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

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

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

Topic Editor, Frontiers Oncology

Coordinator library at the PKI

Prof. Shida Yousefi
Editorial Assistant, Editorial Office, Allergy

Coordinator for Radioactive Work at the PKI

Coordinator for 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

Review Editor, Frontiers in Molecular and Cellular Oncology

Prof. Manuel Haschke
Head, Drug and Therapeutics Committee, Inselgruppe Bern

PD Dr. Jürgen Bohlender
Member of the Advisory Board, Edoxaban (Lixiana®), Daiichi Sankyo (Schweiz) AG

Dr. Evangelia Liakoni
Board member of the Swiss Society of Clinical Pharmacology and Toxicology (SSCPT)

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

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 700, 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. 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

Jolanda Schwendimann

Vernissage: June 15, 2017

Welcome: Prof. H.-U. Simon / Prof. M. Fiedler

Duration of the exhibition: June 15 – July 15, 2017

More information:

http://www.pki.unibe.ch/ueber_uns/aktivitaeten/vernissages/index_ger.html

8. Sponsors

8.1. Research Grants

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

Prof. Thomas Kaufmann
Swiss National Science Foundation, project grant No 31003A_173006
Swiss National Science Foundation, project grant 31003A_149387

Swiss National Science Foundation, project grant 310030E_150805 (part of FOR2036)
Novartis Foundation for Biological-Medical Research, Novartis, Basel (CH)

Prof. Georgia Konstantinidou
Swiss National Science Foundation, SNF-Professorship (grant No. PP00P3_163929)
Novartis Foundation for Biological-Medical Research, Novartis, Basel (CH)

Prof. Hans-Uwe Simon
Swiss National Science Foundation (grant No. 310030-166473)
Swiss Cancer League (KFS-3703-08-2015)
Allergie-Stiftung Ulrich Müller-Gierok, Bern
HORIZON 2020, Marie Sklodowska-Curie Actions, MEL-PLEX
CALYPSO BIOTECH SA, Plan-les-Ouates

Prof. Stephan von Gunten
Swiss National Science Foundation (SNSF) Grant Nr. 310030_162552
Swiss Cancer League / Swiss Cancer Research foundation (SCL/SCR) Grant Nr. KFS-3941-08-2016
Palleon Pharmaceuticals Inc., Waltham MA (USA)

Prof. Shida Yousefi
Swiss National Science Foundation (grant No. 310030-173215)

Prof. Uwe Zangemeister-Wittke
Swiss National Science Foundation (grant No. 310030E-132762)
Swiss National Science Foundation (grant No. 310030A-138201)
Sassella-Stiftung of the Zürcher Kantonalbank

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

PD Dr. Jürgen Bohlender
Swiss Kidney Foundation (grant SNS-AEBS)

Dr. Evangelia Liakoni
Bayer (Schweiz) AG, Zürich (IIR-C-2016-3362)
sanofi-aventis (schweiz) AG, VERNIER
Bangerter Rhyner Stiftung, Bern
Burgergemeinde Bern

8.2. Meetings

Swiss Society of Pharmacology and Toxicology (SSPT): Progress in Pharmacology – Treatment of Skin Diseases, Bern, Jan 26, 2017
Sanofi-Aventis AG, Vernier
Roche Pharma (Schweiz) AG, Reinach
Novartis Pharma Schweiz AG / Sandoz, Rotkreuz
Janssen-Cilag AG, Zug
GlaxoSmithKline AG, Münchenbuchsee
AstraZeneca AG, Zug

Member companies of the Kontaktgruppe für Forschungsfragen (KGF), Basel:
Novartis and RocheBiotest (Schweiz) AG
Eli Lilly, Vernier
Biotest, Rupperswil
Almirall AG, Wallisellen
Galderma Schweiz AG, Egerkingen
MEDA Pharma GmbH, Wangen ZH
Celgene GmbH, Zürich
Pierre Fabre Dermo-Cosmétique, Allschwil
Leo Pharma, Regensdorf

16th Ill-Bern International Summer School
APPENBERG, CH 3532 – Zäziwil, July 23 – 25, 2017
Carl Zeiss AG, Feldbach
Sanofi-Aventis (Schweiz) AG, Vernier
Lucerna Chem AG, Luzern
BD Biosciences, Allschwil
Pfizer AG, Zürich
Zentrum für Labormedizin, Inselspital Bern
Schweiz. Kommission für Molekularbiologie
Swiss Committee for Molecular Biology (SKMB), Geneva
Graduate School for Cellular and Biomedical Sciences, Universität Bern

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

AstraZeneca, Zug
Novartis AG, Rotkreuz

8.4. Travel Support

Ramona Reinhart
Swiss Society of Pharmacology and Toxicology (SSPT) (25th Conference of the ECDO, Leuven (Belgium), September 27-29, 2017)

Nina Germic
The Graduate School for Cellular and Biomedical Sciences (GCB) of the University of Bern (10th Biennial Symposium of the International Eosinophil Society (IES), Gothenburg (Sweden), July 19-23, 2017)

8.5. Other Support

Bürgi Fonds Seminar series of the institute