Annual Report 2016

Institut für Pharmakologie (PKI)
der Universität Bern

Institute of Pharmacology
University of Bern

Address: Inselspital, INO-F
CH-3010 Bern
Switzerland

Tel.: +41 31 632 3281
E-mail: debora.scherrer@pki.unibe.ch

An online copy of this report can be obtained at http://www.pki.unibe.ch/

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1. Introduction

1.1. Vorwort

Dies ist der sechzehnte umfassende Jahresbericht des Instituts für Pharmakologie (PKI) der Universität Bern. Das PKI hat auch im Jahr 2016 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 August 2016 rekrutierten wir Frau Prof. Dr. Georgia Konstantinidou, die eine Professur des Schweizerischen Nationalfonds erhielt. Im April 2017 wird Prof. Dr. Manuel Haschke mit seiner Forschungsgruppe für Klinische Pharmakologie in unser Institut eintreten. Wir sind überzeugt, dass die beiden Gruppen neue Möglichkeiten der Zusammenarbeit eröffnen werden, sowohl in der biologischen Grundlagen- als auch in der klinischen Forschung, beides Kernaufgaben der Pharmakologie.

Das PKI arbeitet eng mit verschiedenen Kliniken des Inselspitals und mit anderen Forschungseinrichtungen der Universität Bern zusammen. Damit wollen wir helfen, die translationale Forschung sowie die Aus-, Weiter- und Fortbildung an der Medizinischen Fakultät zu stärken. Zum anderen sind wir an der Zusammenarbeit mit Firmen interessiert, wie die weiter hinten aufgeführten gegenwärtigen Kontakte der einzelnen Forschungsgruppen zeigen. Auch im Jahr 2016 trugen wir dazu bei, die Kommunikation zwischen WissenschaftlerInnen und Öffentlichkeit zu fördern.

Neben unserer regulären Lehrtätigkeit im 3. 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 ist Mitglied 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 21 DoktorandInnen, und 7 DoktorandInnen (PhD) haben im Berichtsjahr ihre Arbeit erfolgreich abgeschlossen.

Die Mitarbeiter und Mitarbeiterinnen des Instituts für Pharmakologie publizierten im Jahr 2016 insgesamt 30 Originalarbeiten sowie 16 Übersichtsartikel in internationalen Fachzeitschriften (Summe der „impact factors“ >200). MitarbeiterInnen des Instituts wurden zu insgesamt 25 Vorträgen bzw. Seminaren eingeladen. Mehrere MitarbeiterInnen des PKI wurden mit Forschungspreisen ausgezeichnet. Gegenwärtig werden 7 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 organisierte gemeinsam mit Prof. Tschan (Institut für Pathologie, Universität Bern) und Prof. Brunner (Lehrstuhl Biochemische Pharmakologie, Universität Konstanz, Deutschland) das „9th Swiss Apoptosis Meeting (SAM)“ (8.-9.9.2016), zu dem wir ca. 200 TeilnehmerInnen aus dem In- und Ausland begrüssen durften. 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 seit 01.08.2016 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 2016 zu einer Bilanz beitrug, die internationalen Massstäben gerecht wird. Ebenso danke ich allen Sponsoren und Freunden des Instituts.

Prof. Dr. med. Hans-Uwe Simon
Direktor

Bern, Januar 2017

1.2. Foreword

This is the sixteenth 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 this floor F of the building with the Center of Laboratory Medicine and have jointly developed the available infrastructure. We have organized multiple joint teaching and research projects with the goal to further accentuate the field of “Stratified Medicine”. In August 2016, we recruited Prof. Georgia Konstantinidou who has received a professorship funded by the Swiss National Science Foundation. In April 2017, Prof. Manuel Haschke with his research group will join the institute and will facilitate our research in the field of Clinical Pharmacology. We are convinced that both groups will strengthen our institute 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 different research institutes of the University. In doing so, we hope to strengthen both translational research and teaching at 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 2016. All our current activities are summarized in this report below.

Besides the regular teaching in the third 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 is additionally involved in Immunology M.Sc. programmes within the Natural Science Faculty of our university. At the moment, 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 is a member of the tutoring committee “Cell Biology” within that school. Currently, 21 PhD students work at the PKI, and seven PhD students successfully completed their doctoral studies in 2016. 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 2016, staff members of the PKI published 30 original and 16 review articles in international peer-reviewed journals (the sum of the "impact factors" is more than 200). Co-workers of the institute were invited to present 25 lectures or seminars. Several PKI members received research prizes. The research projects of 7 co-workers are currently supported by grants from the Swiss National Science Foundation. Several internationally prominent researchers visited the institute and presented 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), organized an international congress (9th Swiss Apoptosis Meeting; September 8-9, 2016), which attracted approximately 200 scientists interested in the field of "Cell Death". 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 serves as Dean of the Medical Faculty of the University of Bern (starting date was August 1, 2016). 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 2016. I am grateful to all the sponsors and friends of the institute for their support.

Prof. Hans-Uwe Simon, MD, PhD
Director

Bern, January 2017

2. Staff 2016

Director

Prof. Dr.	Simon, Hans-Uwe	MD, PhD

Deputy Director

Prof. Dr.	Huwiler, Andrea	PhD

Principal Investigators

Prof. Dr.	Huwiler, Andrea	PhD
Prof. Dr.	Kaufmann, Thomas	PhD
SNF-Prof.	Konstantinidou, Georgia	PhD* (since Aug 2016)
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

	Aeschlimann, Salome	Lab technician (until Aug 2016)
Dr.	Amini, Poorya	PhD student
	April, Simon	M.Sc. student*
	Bachmann, Daniel	Research assistant
	Bänninger, Liliane	M.Sc. pharm. student* (Jan - June 2016)
	Blanchard, Olivier	PhD student
	Brandl, Fabian	PhD student*
	Büchler, Flavia	Lab technician*
	Burkhard, Fabian	M.Sc. biomed. student* (since July 2016)
Dr.	de Graauw, Elisabeth Lousia	PhD student*
	Fallegger, Angela	M.Sc. biomed. student (since July 2016)
	Fernandez Marrero, Yuniel	PhD student*
	Frangez, Ziva	PhD student*
Dr.	Frias Boligan, Kayluz	Postdoctoral fellow*
	Fuchs, Katharina	MMed student*
	Ganguin, Aymar Abel	B.Sc. biochem. student (Feb – May 2016)
	Germic, Nina	PhD student
	Graeter, Stefanie	PhD student* (since April 2016)
	Grosek, Martin	M.Sc. pharm. student* (April – Aug 2016)
	György, Hamvas	M.Sc. student
	Haas, Quentin	PhD student* (since July 2016)
	Haxholli, Deis	PhD student* (since Sep 2016)
Dr.	He, Zhaoyue	Postdoctoral fellow
	Jenni, Aurelio Leandro	PhD student
	Kozlowski, Evelyne	Lab technician
	Krähenbühl, Debora	M.Sc. pharm. student* (Jan - June 2016)
Dr.	Liu, He	Postdoctoral fellow*
	Lutz, Sarah	M.Sc. biomed. student* (since July 2016)
	Maillard-van Laer, Marianne	Lab technician
	Maneva Timcheva, Tankica	Lab technician* (since Dec 2016)
	Marro, Céline	M.Sc. pharm. student* (until June 2016)

	Meister, Ariane	MMed student* (until April 2016)
	Oberson, Kevin	Lab technician
Dr.	Rabachini de Almeida, T.	Postdoctoral fellow* (until July 2016)
	Reali, Luca	PhD student
	Reinhart, Ramona	PhD student*
	Ris, Raphael	M.Sc. pharm. student* (Jan - June 2016)
	Rossi Sebastiano, Matteo	PhD student (since Aug 2016)
	Scherer, Melanie	B.Sc. biochem. student* (Feb – May 2016)
	Schneider, Christoph	PhD student (until Sept 2016)
	Schorer, Myriam Fabiola	PhD student* (until Dec 2016)
	Sekeres, Nina	M.Sc. pharm. student* (until Feb 2016)
	Sever, Ema	M.Sc. pharm. student* (until Feb 2016)
	Srajner, Luka	M.Sc. pharm. student* (April – Aug 2016)
	Stepanovska, Bisera	PhD student (since Feb 2016)
	Stojkov, Darko	PhD student
	Trefny, Marcel	M.Sc. student* (until Jan 2016)
	Wang, Xiaoliang	Postdoctoral fellow
	Wicki, Simone	PhD student*
	Zimmermann, Monika	M.Sc. pharm. student* (Jan - June 2016)
	Zürcher, Marc	B.Sc. biochem. student* (Feb – May 2016)

External University Teachers

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

Guest scientists

	Dorvignit Pedroso, Denise	PhD student*, University of Havanna (Cuba)
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
Dr.	Surmiak, Marcin	PhD*, Jagiellonian University, Kraków (Poland)
	Vrbek, Sanja	PhD student*, University of Ljubliana (Slovenia)

External Computer Support

Wyss Anne*

Office

Berger, Jana	Secretary, 70% (since Aug 2016)
Krebs, Aniko	Secretary, 80% (until Aug 2016)
Scherrer, Debora	Secretary, 80%
Schranz, José	Secretary, 80% (until July 2016)

Workshop

Andres Hans

House Keeping

Conforti Isa

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

Meeting of the Swiss Society of Pharmacology and Toxicology (SSPT): Progress in Pharmacology - Personalized Medicine, Bern, January 28, 2016

Summer School 2016

Members of the Institute of Pharmacology of the University of Bern together with participants of our International Summer School in Bönigen; August 7 - 9, 2016.
Our guest speakers from Slovenia (Prof. Irena Mlinaric-Rascan) and Germany (Prof. Peter Ruth) are seen.

3. Teaching Activities

3.1. Lectures

Lectures for Medical Students: Pharmacology

Date	Lecturer	Titel of the lecture
Mar 16, 2016	Prof. Stephan von Gunten	Hormone aus pharmakol. Sicht (Teil 1)
Mar 21, 2016	Prof. Stephan von Gunten	Hormone aus pharmakol. Sicht (Teil 2)
Mar 23, 2016	Prof. Stephan von Gunten	Lipidsenker + Behandlung der Gicht
Mar 23, 2016	Prof. Stephan von Gunten	Antidiabetika
Apr 06, 2016	Prof. Andrea Huwiler	Pharmakologie von Narkosemitteln und Muskelrelaxantien I
Apr 06, 2016	Prof. Andrea Huwiler	Pharmakologie von Narkosemitteln und Muskelrelaxantien II
Apr 20, 2016	Prof. Andrea Huwiler	Antiepileptika
Apr 27, 2016	Prof. Andrea Huwiler	Therapie von M. Parkinson und Demenz
Apr 27, 2016	Prof. Andrea Huwiler	Lokalanästhetika
May 04, 2016	Prof. Andrea Huwiler	Psychopharmakologie
May 09, 2016	Prof. Andrea Huwiler	Antidepressiva, Anxiolytika und Stimmungsstabilisatoren
May 09, 2016	Prof. Andrea Huwiler	Antipsychotika
May 11, 2016	Prof. Andrea Huwiler	Schmerz und Analgesiologie (Teil 1)
May 11, 2016	Prof. Andrea Huwiler	Schmerz und Analgesiologie (Teil 2)
May 30, 2016	Prof. Hans-Uwe Simon	Immunmodulation
Sep 21, 2016	Prof. Hans-Uwe Simon	Pharmakodynamik (Teil 1)
Sep 21, 2016	Prof. Hans-Uwe Simon	Pharmakodynamik (Teil 2)
Sep 26, 2016	Prof. Hans-Uwe Simon	Entzündungshemmung
Sep 26, 2016	Prof. Hans-Uwe Simon	Einführung in die Toxikologie
Oct 25, 2016	Prof. Hans-Uwe Simon	Pharmakotherapie bei Lungenkrankheiten
Nov 01, 2016	PD Dr. David Spirk	Pharmakologie der Hämostase
Nov 02, 2016	Prof. U. Zangemeister-Wittke	Pharmakologie des vegetativen Nervensystems
Nov 02, 2016	Prof. U. Zangemeister-Wittke	Antihypertensiva
Nov 07, 2016	PD Dr. David Spirk	Behandlung der Herzinsuffizienz und Angina pectoris
Nov 16, 2016	Prof. U. Zangemeister-Wittke	Antiarrhythmika
Dec 12, 2016	Prof. U. Zangemeister-Wittke	Diuretika (Teil 1)
Dec 12, 2016	Prof. U. Zangemeister-Wittke	Diuretika (Teil 2)

All lecturers additionally participated in the “Wochensynthese”.

Seminars for Medical Students: Pharmacology

Date	Lecturer	Titel of the lecture
Apr 14, 2016	Prof. Stephan von Gunten	Functional Glycomics - Neue Optionen für die Tumor- und Entzündungspharmakologie
Apr 14, 2016	Prof. Thomas Kaufmann	Modulation des Zelltodes - aktueller Stand und neue Entwicklungen
Apr 28, 2016	Prof. Hans-Uwe Simon	Personalisierte Arzneimitteltherapie
Apr 28, 2016	Prof. U. Zangemeister-Wittke	Gezielte Tumortherapie mit Antikörpern und Immunkonjugaten

Lectures for Medical Students: Pathology

Date	Lecturer	Title of the lecture
Sep 19, 2016	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 08, 2016	Prof. Hans-Uwe Simon	Rezeptoren, Dosis-Wirkungskurven
Feb 08, 2016	Prof. Hans-Uwe Simon	Antagonisten, Applikationsarten
Feb 22, 2016	Prof. U. Zangemeister-Wittke	Einführung in die Pharmakokinetik
Feb 24, 2016	Prof. Thomas Kaufmann	Pharmakogenetik, Interaktionen
Mar 02, 2016	Prof. U. Zangemeister-Wittke	Pharmakologie des VNS
Mar 14, 2016	PD Dr. Armand Cachelin	Analgetika
Mar 16, 2016	Prof. Stephan von Gunten	Magensäurehemmung
Mar 23, 2016	Prof. Stephan von Gunten	Psychopharmaka
Apr 04, 2016	PD Dr. David Spirk	Pharmakologie der Hämostase
Apr 04, 2016	PD Dr. David Spirk	Pharmakologie der Herzerkrankungen
Apr 06, 2016	Prof. Andrea Huwiler	Pharmakol. von Atemwegserkrankungen
Apr 13, 2016	Prof. Andrea Huwiler	Narkose, Beruhigungsmittel
Apr 18, 2016	Dr. Sibylle Bürgi	Antidiabetika, Lokalanästhetika
May 02, 2016	Dr. Sibylle Bürgi	Antibiotika

Oral examinations: Prof. Zangemeister-Wittke, Prof. Huwiler, Prof. Simon

Lecture for Dental Medicine students: Pathology (Coordinator: Dr. Anja Schmitt-Kurrer)

Date	Lecturer	Title of the lecture
Oct 04, 2016	Prof. Thomas Kaufmann	Zellschäden

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

Date	Lecturer	Title of the lecture
Feb 25, 2016	Prof. Stephan von Gunten	Introduction
Feb 25, 2016	Prof. Stephan von Gunten	Immunopharmacology
May 26, 2016	Prof. Stephan von Gunten	Glycoimmunology

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 17, 2016	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 14, 2016	Dr. Stephanie Schwalm	Lipid mediators in inflammation
May 19, 2016	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 08, 2016	Prof. Shida Yousefi Prof. Stephan von Gunten Prof. Thomas Kaufmann	Immunological Methods (1 day)
Dec 09, 2016	Prof. Shida Yousefi Prof. Stephan von Gunten Prof. Thomas Kaufmann	Immunological Methods (1 day)
Dec 15, 2016	Prof. Shida Yousefi Prof. Stephan von Gunten Prof. Thomas Kaufmann	Immunological Methods (1 day)
Dec 16, 2016	Prof. Shida Yousefi Prof. Stephan von Gunten Prof. Thomas Kaufmann	Immunological Methods (1 day)
Dec 22, 2016	Prof. Shida Yousefi Prof. Stephan von Gunten Prof. Thomas Kaufmann	Immunological Methods (1 day)
Dec 23, 2016	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
May 19, 2016	Prof. Shida Yousefi	Molecular Biology of inflammation
May 26, 2016	Prof. Stephan von Gunten	Selected topics in clinical immunology
Sep 30, 2016	PD Dr. David Spirk	Haemopoietic system and haemostasis
Oct 07, 2016	Prof. Thomas Kaufmann	Immune system
Oct 14, 2016	Prof. Shida Yousefi	Antiinfectious therapy
Oct 21, 2016	Prof. U. Zangemeister-Wittke	Heart and vascular system
Oct 28, 2016	Prof. Stephan von Gunten	Gastrointestinal tract
Nov 04, 2016	Prof. Stephan von Gunten	Endocrine and reproductive system
Nov 11, 2016	Prof. Andrea Huwiler	Nervous system
Nov 18, 2016	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 26, 2016	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 21, 2016	Prof. Shida Yousefi	Laser scanning microscopy and specific applications (FRET, FRAP, spectral unmixing) and digital image restoration (Huygen and Imaris software)

Lectures for clinicians at the Department of Orthodontics and Dentofacial Orthopedics (Coordinator: Prof. Christos Katsaros)

Date	Lecturer	Title of the lecture
Feb 09, 2016	Prof. Stephan von Gunten	Pharmacology Part 1
Feb 22, 2016	Prof. Stephan von Gunten	Pharmacology Part 2

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

Date	Lecturer	Title of the lecture
Sep 20, 2016	Prof. Hans-Uwe Simon	Pharmakodynamik 1
Sep 20, 2016	Prof. Hans-Uwe Simon	Pharmakodynamik 2
Sep 20, 2016	Prof. Hans-Uwe Simon	Entzündungspharmakologie
Sep 20, 2016	Prof. Hans-Uwe Simon	Toxikologie
Sep 27, 2016	Prof. Carlo Largiadèr	Pharmakogenetik
Sep 27, 2016	Prof. U. Zangemeister-Wittke	Pharmakokinetik 1
Sep 27, 2016	Prof. U. Zangemeister-Wittke	Pharmakokinetik 2

Sep 27, 2016 Prof. U. Zangemeister-Wittke Tumorpharmakologie

Written examination: Prof. Simon

External teaching activities: University of Zurich (Molecular Medicine)

Date	Lecturer	Title of the lecture
May 2016 (Total 6h)	Prof. U. Zangemeister-Wittke	Molecular Cell Biology for students of human and dental medicine

3.2. Coordination PBL Medical Students, 3rd year (2016/2017)

Core group:
Prof. Andrea Huwiler

Representatives of Pharmacology in 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 2016/2017)

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

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

3.4. Elective Module Supervision

Biomedical Sciences students:
Isabel Büchi (Prof. Hans-Uwe Simon)
Moran Morelli (Prof. Hans-Uwe Simon)
Priska Zenhäusern (Prof. Hans-Uwe Simon)
Fabian Burkhard (Prof. Hans-Uwe Simon)
Stoffel Jonas (Prof. Hans-Uwe Simon)
Sarah Lutz (Prof. Stephan von Gunten)
Györgyi Hamvas (Prof. Stephan von Gunten)
Angela Fallegger (Prof. Thomas Kaufmann, Prof. Stephan von Gunten)
Andrea Marelli (Prof. Thomas Kaufmann)
Petra Polakova (Prof. Thomas Kaufmann)
Quiowa Rytter (Prof. Shida Yousefi)
Vivianne Schallenberg (Prof. Stephan von Gunten)
Manuel Schüpbach (Prof. Shida Yousefi)

3.5. Seminars of Invited Speakers

Date	Teacher	Title of the seminar	Host
Jan 08, 2016	Prof. Dr. Petr Broz, Biozentrum, University of Basel	Molecular mechanisms of inflammasome assembly and signalling	H.-U. Simon
Jan 20, 2016	Prof. Fabienne Tacchini-Cottier, University of Lausanne, Department of Biochemistry	The importance of neutrophils in cutaneous Leishmaniasis	H.-U. Simon
Feb 17, 2016	Dr. Bruno M. Humbel, Electron Microscopy Facility, University of Lausanne	Correlative Light and Electron Microscopy	H.-U. Simon
Feb 24, 2016	Dr. Tamas Dolowschiak, ETH Zürich, Institut für Mikrobiologie	Dissecting the mucosal immune modules that orchestrate inflammation during Salmonella gut infection	H.-U. Simon
Mar 02, 2016	Prof. Christoph Borner, Albert-Ludwig-Universität Freiburg (D), Institute of Molecular Medicine and Cell Research	Gliotoxin, the major pathogen for Aspergillosis, modulates the integrin/RhoA signaling pathway in lung epithelial cells	T. Kaufmann

Mar 23, 2016	Dr. Sonja Lüer, Universitätsklinik für Kinderheilkunde, Inselspital	Curcumin – could a spice help fighting side effects of cancer therapy?	H.-U. Simon
April 20, 2016	Prof. Dr. Benjamin Gantenbein, Institute for Surgical Technology and Biomechanics, University of Bern	Understanding Mechano-Biology to develop Regenerative Therapy for the Intervertrebral Disc	H.-U. Simon
May 11, 2016	Prof. Dr. Andrew Chan Universitäres ambulantes Neurozentrum, Inselspital	Translational Neuroimmunology: myth or fact?	H.-U. Simon
June 01, 2016	Prof. Dr. Jörn Dengjel, Department of Biology, University of Fribourg	Selective protein degradation by stress-induced macroautophagy	H.-U. Simon
June 8, 2016	Dr. Mohamed Bentires-Alj (Momo), Friedrich Miescher Institute for Biomedical Research (FMI), Basel	Cancer targeted therapy and tumor heterogeneity: Act locally, think globally	S. von Gunten
July 12, 2016	Dr. Ursula Amstutz, Center for Laboratory Medicine, Inselspital, Bern	High-throughput sequencing applications for Biomedical Research	A. Huwiler
Aug 10, 2016	Prof. Dr. Angela Haczku, Translational Lung Biology Center, Pulmonary, Critical Care and Sleep Medicine, University of California, Davis (CA, USA)	Innate lymphoid cells and ozone-induced airway inflammation	H.-U. Simon
Nov 30, 2016	Prof. Dr. Stephen Leib Institut für Infektions-krankheiten, Universität Bern	Experimental approaches to prevention and repair of brain damage in bacterial meningitis	H.-U. Simon
Dec 07, 2016	Prof. Dr. Zhihong Yang Dep. of Medicine/ Physiology, University of Fribourg	L-arginine metabolism and arginase in health and disease	S. von Gunten
Dec 21, 2016	Prof. Dr. Stephan Krähenbühl, Klinische Pharmakologie & Toxikologie, Universitäts-spital Basel	Mechanisms of statin-associated myotoxicity	H.-U. Simon

3.6. Inaugural Lecture (Associate Professor)

Date	Lecturer	Title
Mar 11, 2016	Prof. Dr. Stephan von Gunten	Glycoimmunology: paradigm shift and novel treatment opportunities

3.7. Bern Immunology Club (BIC)

Date	Teacher	Title of the seminar
Feb 24, 2016	Prof. Roxane Tussiwand Department of Biomedicine University of Basel	Dendritic Cells at the Cross-road of Innate and Adaptive Immunity
Mar 23, 2016	Prof. Manfred Kopf, ETH Zürich	Redox biology of T cell responses
Apr 27, 2016	Dr. Curdin Conrad, Dermatologie, CHUV	Immunopathogenesis of paradoxical reactions to TNF-antagonists in psoriasis
May 25, 2016	Prof. César Nombela-Arrieta, Hämatol., Zürich	Structural and functional dynamics of the bone marrow microenvironment
June 29, 2016	Prof. Burkhard Ludewig Kantonsspital St. Gallen	BIC BBQ: Regulation of Intestinal Immunity by Fibroblastic Stromal Cells
Sep 28, 2016	Mirjam Schenk, PhD Pathology, Bern	Immunotherapy in melanoma: Novel DC-based strategies
Oct 26, 2016	*CIC: Autoinflammation* Organizer: Prof. P. Villiger Prof. L. Borradori	
Nov 30, 2016	Drs. Abe, Alves, Ruckstuhl, Eggel, University of Bern	Highlights of the year: four 10 min. presentations

After more than a decade, on August 1, 2016, Prof. Simon handed over the responsibility to coordinate the BIC to Prof. Bachmann.
For the current program of the Bern Immunology Club (BIC) please consult the following website: http://www.bic.unibe.ch/teaching/bic_lectures/index_eng.html

3.8. Academic Degrees

von Gunten, Stephan, Associate Professor, University of Bern
(since Feb 1, 2016)

Cortinas Elizondo, Myriam Fabiola, PhD, University of Bern
Thesis: Innate immune system crosstalk: Eosinophils mediate immune modulation of dendritic cells through exosomes as shuttle vectors of miRNA (May 2016)
Supervisor: Prof. Stephan von Gunten

Schneider, Christoph Jürg, PhD, University of Bern
Thesis: Protein-carbohydrate interactions in the human immune system (September 2016)
Supervisor: Prof. Stephan von Gunten

Stojkov, Darko, PhD, University of Bern
Thesis: Actin polymerization and its glutathionylation are required for NET formation (October 2016)
Supervisor: Prof. Shida Yousefi, Prof. Hans-Uwe Simon

Filipenko, Iuliia, PhD, University of Bern
Thesis: The role of the S1P3 receptor in inflammation-associated proliferative disorders (November 2016)
Supervisor: Prof. Uwe Zangemeister-Wittke, Prof. Andrea Huwiler

de Graauw, Elisabeth Lousia, PhD, University of Bern
Thesis: The requirements of eosinophil activation and monocyte-neutrophil interactions for blister formation in a human *ex vivo* skin model of bullous pemphigoid (November 2016)
Supervisor: Prof. Hans-Uwe Simon, Prof. Dagmar Simon

Wicki, Simone Katharina, PhD, University of Bern
Thesis: Regulation of cell death and innate immune signaling in mouse neutrophils (December 2016)
Supervisor: Prof. Thomas Kaufmann

Amini, Poorya, PhD, University of Bern
Thesis: Optic atrophy 1 (OPA1) is essential for NET formation and antibacterial functions in neutrophils (December 2016)
Supervisor: Prof. Hans-Uwe Simon, Prof. Shida Yousefi

Trefny, Marcel Philipp, M.Sc., University of Bern
Thesis: Mitochondria and cellular energetics of human dermal stem cells (Jan. 2016)
Supervisor: Prof. Hans-Uwe Simon, Dr. He Liu

Meister, Ariane, MMed, University of Bern
Thesis: Aktualisierung der Medikamentendatenbank MediOnline (April 2016)
Supervisor: Prof. Stephan von Gunten, Dr. med. Ulrich Woermann

Tochtermann, Nicole, MMed, University of Bern
Thesis: Effects of BOK downregulation in colorectal cancer (May 2016)
Supervisor: Prof. Thomas Kaufmann, Dr. Tatiana Rabachini de Almeida

Boss, Noémie, MMed, University of Bern
Thesis: Role of the HGMB1/CXCL12 heterocomplex in the migration of B cells within the germinal center (June 2016)
Supervisor: Prof. Stephan von Gunten, Prof. Carole Bourquin

Sansonnens, Caroline, MMed, University of Bern
Thesis: Kinetic analysis of the immune cell infiltration in gastric tumors of CEA424 SV40 T Ag mice (June 2016)
Supervisor: Prof. Stephan von Gunten, Prof. Carole Bourquin, PhD Nathalie Steinhoff

Bänniger, Liliane, M.Sc. pharm., University of Basel
Thesis: The effect of an anti-IL-5 antibody-therapy in bullous pemphigoid (June 2016)
Supervisor: Prof. Hans-Uwe Simon, Prof. Dagmar Simon

Marro, Céline, M.Sc. pharm., University of Basel
Thesis: The role of autophagy-related protein 12 (ATG12) on cell growth and mitochondrial function (June 2016)
Supervisor: Prof. Hans-Uwe Simon, Dr. He Liu, Dr. Zhaoyue He

Krähenbühl, Debora, M.Sc. pharm., University of Basel
Thesis: Eosinophilic esophagitis and epithelial barrier function (May 2016)
Supervisor: Prof. Hans-Uwe Simon, Prof. Dagmar Simon

Ris, Raphael, M.Sc. pharm., University of Basel
Thesis: qRT-PCR analysis of 24 proteins, which are potentially regulated by autophagy (June 2016)
Supervisor: Prof. Hans-Uwe Simon

Zimmermann, Monika, M.Sc. pharm., University of Basel
Thesis: Expression of autophagy-regulating proteins in inflammatory skin diseases (June 2016)
Supervisor: Prof. Hans-Uwe Simon

Sekeres, Nina, M.Sc. pharm., University of Ljubljana
Thesis: The role of nardilysin and lymphocyte phosphatase-associated phosphoprotein in autophagy of cancer cells (September 2016)
Supervisor: Prof. Hans-Uwe Simon, Prof. Irena Mlinaric-Rascan

Ema Sever, M.Sc. pharm., University of Ljubljana
Thesis: Autophagy in intestinal epithelial cells (September 2016)
Supervisor: Prof. Hans-Uwe Simon, Prof. Irena Mlinaric-Rascan

Ganguin, Aymar Abel, B.Sc., University of Bern
Thesis: Evaluation of anti-Siglec-7 and -9 therapeutic antibodies (May 2016)
Supervisor: Prof. Stephan von Gunten, Dr. Kayluz Frias Boligan

Scherer, Melanie, B.Sc., University of Bern
Thesis: Immune regulation in human platelets and neutrophils (May 2016)
Supervisor: Prof. Stephan von Gunten, Dr. Christoph Schneider

Zürcher, Marc, B.Sc., University of Bern
Thesis: Role of Siglec-7 and Siglec-9 in formation and characterization of immunological synapses (June 2016)
Supervisor: Prof. Stephan von Gunten, Dr. Kayluz Frias Boligan

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]
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 growth and death, inflammation and autoimmune diseases, and fibrotic processes.

Sphingosine kinase 2 deficient mice exhibit reduced experimental autoimmune encephalomyelitis: Resistance to FTY720 but not ST-968 treatments
Imeri F, Schwalm S, Lyck R, Zivkovic A, Stark H, Engelhardt B, Pfeilschifter J, Huwiler A
Abstract: The immunomodulatory drug FTY720 is presently approved for the treatment of relapsing-remitting multiple sclerosis. It is a prodrug that requires activation by sphingosine kinase 2 (SK-2) to induce T cell homing to secondary lymphoid tissue. In this study, we have investigated the role of SK-2 in experimental autoimmune encephalomyelitis (EAE) in C57BL/6 mice. We show that SK-2 deficiency reduced clinical symptoms of EAE. Furthermore, in SK-2-deficient mice, the protective effect of FTY720 on EAE was abolished, while the non-prodrug FTY720-derivative ST-968 was still fully active. Protection was paralleled by reduced numbers of T-lymphocytes in blood and a reduced blood-brain-barrier leakage. This correlated with reduced mRNA expression of ICAM-1, VCAM-1, but enhanced expression of PECAM-1. A similar regulation of permeability and of PECAM-1 was seen in primary cultures of isolated mouse brain vascular endothelial cells and in a human immortalized cell line upon SK-2 knockdown. In summary, these data demonstrated that deletion of SK-2 exerts a protective effect on the pathogenesis of EAE in C57BL/6 mice and

that SK-2 is essential for the protective effect of FTY720 but not of ST-968. Thus, ST-968 is a promising novel immunomodulatory compound that may be a valuable alternative to FTY720 under conditions where SK-2 activity is limited.
See original publication No. 1

Original publications

1. Imeri F, Schwalm S, Lyck R, Zivkovic A, Stark H, Engelhardt B, Pfeilschifter J, **Huwiler A**: Sphingosine kinase 2 deficient mice exhibit reduced experimental autoimmune encephalomyelitis: Resistance to FTY720 but not ST-968 treatments. Neuropharmacology 105 (2016), 341-350.

2. Filipenko I, Schwalm S, Reali L, Pfeilschifter J, Fabbro D, **Huwiler A**, Zangemeister-Wittke U: Upregulation of the S1P3 receptor in metastatic breast cancer cells increases migration and invasion by induction of PGE2 and EP2/EP4 activation. Biochim Biophys Acta 11 (2016), 1840-1851.

3. Vasilakaki S, Barbayianni E, Magrioti V, Pastukhov O, Constantinou-Kokotou V, **Huwiler A**, Kokotos G: Inhibitors of secreted phospholipase A2 suppress the release of PGE2 in renal mesangial cells. Bioorg Med Chem 24 (2016), 3029-34.

4. Coldewey SM, Benetti E, Collino M, Pfeilschifter J, Sponholz C, Bauer M, **Huwiler A**, Thiemermann C: Elevation of serum sphingosine-1-phosphate attenuates impaired cardiac function in experimental sepsis. Sci Rep. 6 (2016), doi: 10.1038/srep27594.

5. Chen B, Roy SG, McMonigle RJ, Keebaugh A, McCracken AN, Selwan E, Fransson R, Fallegger D, **Huwiler A**, Kleinman MT, Edinger AL, Hanessian S: Azacyclic FTY720 analogues that limit nutrient transporter expression but lack S1P receptor activity and negative chronotropic effects offer a novel and effective strategy to kill cancer cells in vivo. ACS Chem Biol. 11 (2016), 409-414.

6. McCracken AN, McMonigle RJ, Tessier J, Fransson R, Perryman M, Chen B, Keebaugh A, Selwan E, Barr SA, Kim SM, Roy SG, Liu G, Fallegger D, Sernissi L, Brandt C, Moitessier N, Snider AJ, Clare S, Müschen M, **Huwiler A**, Kleinman MT, Hanessian S, Edinger AL: Phosphorylation of a constrained azacyclic FTY720 analog enhances anti-leukemic activity without inducing S1P receptor activation. Leukemia (2016), doi: 10.1038/leu.2016.244.

Group Prof. Thomas Kaufmann

Group members: Dr. Tatiana Rabachini de Almeida, Postdoc
Simone Wicki, PhD student
Ramona Reinhart, PhD student
Yuniel Fernandez Marrero, PhD student
Daniel Bachmann, research assistant
Angela Fallegger, M.Sc. student (BMSc)

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 that apoptosis suppresses necroptosis, the latter is hypothesized to serve as backup, proinflammatory, PCD upon infection with pathogens that actively block apoptosis.

We observed that upon activation of death receptors (Fas/CD95 or TNF-R1) on the surface of neutrophils the outcome ranges from activation of the cells and production of proinflammatory cytokines to PCD by apoptosis or by necroptosis. This outcome is tightly regulated and - among others - depends on the so-called inhibitor of apoptosis (IAPs) family. Our ongoing projects in the lab identify the IAP member XIAP as an antagonist of necroptosis downstream of death receptors. Interestingly, XIAP, which was initially identified as an inhibitor of apoptotic caspases and also carries E3 ligase activity (RING domain), clearly has important functions beyond blocking caspases. Our data indicate that XIAP may act more upstream in death receptor signaling pathways than previously assumed; the exact molecular functions of XIAP's E3 ligase activity are under investigation. Taken together, XIAP can be placed at the intersection of cell death and inflammation.

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. 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. 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.

Loss of XIAP facilitates switch to TNFα-induced necroptosis in mouse neutrophils
Wicki S, Gurzeler U, Wei-Lynn Wong W, Jost PJ, Bachmann D, Kaufmann T
Abstract: Neutrophils are essential players in the first-line defense against invading bacteria and fungi. Besides its antiapoptotic role, the inhibitor of apoptosis protein (IAP) family member X-linked IAP (XIAP) has been shown to regulate innate immune signaling. Whereas the role of XIAP in innate signaling pathways is derived mostly from work in macrophages and dendritic cells, it is not known if and how XIAP contributes to these pathways in neutrophils. Here we show that in response to bacterial lipopolysaccharides (LPS), mouse neutrophils secreted considerable amounts of tumor necrosis factor-α (TNFα) and interleukin-1β (IL-1β) and, in accordance with earlier reports, XIAP prevented LPS-induced hypersecretion of IL-1β also in neutrophils. Interestingly, and in contrast to macrophages or dendritic cells, Xiap-deficient neutrophils were insensitive to LPS-induced cell death. However, combined loss of function of XIAP and cIAP1/-2 resulted in rapid neutrophil cell death in response to LPS. This cell death occurred by classical apoptosis initiated by a TNFα- and RIPK1-dependent, but RIPK3- and MLKL-independent, pathway. Inhibition of caspases under the same experimental conditions caused a shift to RIPK3-dependent cell death. Accordingly, we demonstrate that treatment of neutrophils with high concentrations of TNFα induced apoptotic cell death, which was fully blockable by pancaspase inhibition in wild-type neutrophils. However, in the absence of XIAP, caspase inhibition resulted in a shift from apoptosis to RIPK3- and MLKL-dependent necroptosis. Loss of XIAP further sensitized granulocyte–macrophage colony-stimulating factor (GM-CSF)-primed neutrophils to TNFα-

induced killing. These data suggest that XIAP antagonizes the switch from TNFα-induced apoptosis to necroptosis in mouse neutrophils. Moreover, our data may implicate an important role of neutrophils in the development of hyperinflammation and disease progression of patients diagnosed with X-linked lymphoproliferative syndrome type 2, which are deficient in XIAP.
See original publication No. 1

Original publications

1. Wicki S, Gurzeler U, Wei-Lynn Wong W, Jost PJ, Bachmann D, **Kaufmann T**: Loss of XIAP facilitates switch to TNFα-induced necroptosis in mouse neutrophils.
   Cell Death Dis 7 (2016), doi: 10.1038/cddis.2016.311.

2. Hagmann BR, Odermatt A, **Kaufmann T**, Dahinden CA, Fu 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 (2016), 71-84.

3. Fernandez-Marrero Y, Ke F, Echeverry N, Bouillet P, Bachmann D, Strasser A, **Kaufmann T**: Is BOK required for apoptosis induced by endoplasmic reticulum stress?
   PNAS 113 (2016), 492-493.

4. D'Orsi B, Engel T, Pfeiffer S, Nandi S, **Kaufmann T**, Henshall DC, Prehn JH: Bok is not pro-apoptotic but suppresses poly ADP-ribose polymerase-dependent cell death pathways and protects against excitotoxic and seizure-induced neuronal injury.
   J Neurosci 36 (2016), 4564-4578.

5. Amini P, Stojkov D, Wang X, Wicki S, **Kaufmann T**, Wong WW, Simon HU, Yousefi S: NET formation can occur independently of RIPK3 and MLKL signaling.
   Eur J Immunol 46 (2016), 178-184.

Review articles/Editorials

1. Tuzlak S, **Kaufmann T**, Villunger A: Interrogating the relevance of mitochondrial apoptosis for vertebrate development and postnatal tissue homeostasi.
   Genes Dev (2016), 2133-2151.

2. Fernandez-Marrero Y, Spinner S, **Kaufmann T**, Jost PJ: Survival control of malignant lymphocytes by anti-apoptotic MCL-1.
   Leukemia (2016), 2152-2159.

3. Sharma S, **Kaufmann T**, Biswas S: Impact of inhibitor of apoptosis proteins on immune modulation and inflammation.
   Immunol Cell Biol (2016), doi: 10.1038/icb.2016.101.

Book chapter

1. Reinhart R, Wicki S, **Kaufmann T:** In vitro differentiation of mouse granulocytes, Methods Mol Biol (2016), 95-107.

Group Prof. Georgia Konstantinidou

Group members: Deis Haxholli, PhD student
Matteo Rossi Sebastiano, 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

Padanad MS, **Konstantinidou G**, Venkateswaran N, Melegari M, Rindhe S, Mitsche M, Yang C, Batten K, Huffman KE, Liu J, Tang X, Rodriguez-Canales J, Kalhor N, Shay JW, Minna JD, McDonald J, Wistuba II, DeBerardinis RJ, Scaglioni PP: Fatty acid oxidation mediated by Acyl-CoA synthetase long chain 3 is required for mutant KRAS lung tumorigenesis.
Cell Rep 16 (2016), 1614-1628.

Group Prof. Hans-Uwe Simon

Group members:
Salome Aeschlimann, Technician (80%)*
Dr. Poorya Amini, PhD student*
Simon April, M.Sc. student
Liliane Bänninger, M.Sc. pharm. student**
Flavia Büchler, Technician*,***
Dr. Elisabeth Louisa de Graauw, PhD student**
Ziva Frangez, PhD student
Nina Germic, PhD student
Martin Grosek, M.Sc. pharm. student*
Céline Marro, M.Sc. pharm. student**
Dr. Zhaoyue He, Postdoc
Evelyne Kozlowski, Technician (60%)*
Debora Krähenbühl, M.Sc. pharm. student**
Dr. He Liu, Postdoc
Kevin Oberson, Technician
Raphael Ris, M.Sc. pharm. student**
Nina Sekeres, M.Sc. student
Ema Sever, M.Sc. student***
Luka Srajner, M.Sc. pharm. student*
Marcel Trefny, M.Sc. student
Xiaoliang Wang, Postdoc
Monika Zimmermann, M.Sc. pharm. 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, and malignant melanoma. Our research goal is the identification of new drug targets for future therapeutic approaches in these diseases. Besides the pathogenic aspects of our research, 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 are seen in the following abstracts, which briefly describe our research activities in 2016.

Neutrophil necroptosis is triggered by ligation of adhesion molecules following GM-CSF priming

Wang X, He Z, Liu H, Yousefi S, Simon HU

Abstract: Apoptosis is the most common form of neutrophil death under both physiological and inflammatory conditions. However, forms of nonapoptotic neutrophil death have also been observed. In the current study, we report that human neutrophils undergo necroptosis after exposure to GM-CSF followed by the ligation of adhesion receptors such as CD44, CD11b, CD18, or CD15. Using a pharmacological approach, we demonstrate the presence of a receptor-interacting protein kinase-3 (RIPK3)-a mixed lineage kinase-like (MLKL) signaling pathway in neutrophils which, following these treatments, first activates p38 MAPK and PI3K, that finally leads to the production of high levels of reactive oxygen species (ROS). All these steps are required for necroptosis to occur. Moreover, we show that MLKL undergoes phosphorylation in neutrophils in vivo under inflammatory conditions. This newly identified necrosis pathway in neutrophils would imply that targeting adhesion molecules could be beneficial for preventing exacerbation of disease in the neutrophilic inflammatory response.

See original publication No. 1

RhoH is a negative regulator of eosinophilopoiesis

Stoeckle C, Geering B, Yousefi S, Rožman S, Andina N, Benarafa C, Simon HU

Abstract: Eosinophils are frequently elevated in pathological conditions and can cause tissue damage and disease exacerbation. The number of eosinophils in the blood is largely regulated by factors controlling their production in the bone marrow. While several exogenous factors, such as interleukin-5, have been described to promote eosinophil differentiation, comparatively little is known about eosinophil-intrinsic factors that control their de novo generation. Here, we report that the small atypical GTPase RhoH is induced during human eosinophil differentiation, highly expressed in mature blood eosinophils and further upregulated in patients suffering from a hypereosinophilic syndrome. Overexpression of RhoH increases, in a Rho-associated protein kinase-dependent manner, the expression of GATA-2, a transcription factor involved in regulating eosinophil differentiation. In RhoH-/- mice, we observed reduced GATA-2 expression as well as accelerated eosinophil differentiation both in vitro and in vivo. Conversely, RhoH overexpression in bone marrow progenitors reduces eosinophil development in mixed bone marrow chimeras. These results highlight a novel negative regulatory role for RhoH in eosinophil differentiation, most likely in consequence of altered GATA-2 levels.

See original publication No. 2

A new eosinophilic esophagitis (EoE)-like disease without tissue eosinophilia found in EoE families

Straumann A, Blanchard C, Radonjic-Hoesli S, Bussmann C, Hruz P, Safroneeva E, Simon D, Schoepfer AM, Simon HU

Abstract: Eosinophilic esophagitis (EoE) is a rapidly emerging, chronic inflammatory, genetically impacted disease of the esophagus, defined clinically by symptoms of esophageal dysfunction and, pathologically, by an eosinophil-predominant tissue infiltration. However, in four EoE-families, we have identified patients presenting with EoE-typical and corticosteroid-responsive symptoms, but without tissue eosinophilia. It was the aim of this study to clinically and immunologically characterize these patients with EoE-like disease. Five patients suffering from an EoE-like disease were evaluated with endoscopic, histologic, functional and quantitative immunohistologic examinations, and mRNA expression determination. The frequency of first generation offspring of EoE-like disease patients affected by EoE or EoE-like disease was 40%. Immunofluorescence analysis confirmed an almost complete absence of eosinophils in the esophageal tissues of patients with EoE-like disease, but revealed a considerable T cell infiltration, comparable to EoE. In contrast to EoE, eotaxin-3 mRNA and

protein were markedly reduced in EoE-like disease ($P < 0.05$). The mRNA expression levels of three selected EoE genes (eotaxin-3, MUC4 and CDH26) allowed to discriminate between EoE-like disease, EoE and normal epithelium. Patients suffering from "EoE without eosinophilia" do not fulfill formally the diagnostic criteria for EoE. However, their clinical manifestation, immunohistology and gene-expression pattern, plus the fact that they bequeath EoE to their offspring, suggest a uniform underlying pathogenesis. Conventional EoE, with its prominent eosinophilia, therefore appears to be only one phenotype of a broader "inflammatory dysphagia syndrome" spectrum. In this light, the role of the eosinophils, the definition of EoE, and its diagnostic criteria must likely be reconsidered.

See original publication No. 3

Adhesion-induced eosinophil cytolysis requires the RIPK3-MLKL signaling pathway which is counter-regulated 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

Abstract: Eosinophils are a subset of granulocytes which can be involved in the pathogenesis of different diseases, including allergy. Their effector functions are closely linked to their cytotoxic granule proteins. The release takes place by several different mechanisms, one of which is cytolysis, which is associated with the 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.

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.

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.

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. 4

Original publications

1. Wang X, He Z, Liu H, Yousefi S, **Simon HU**: Neutrophil necroptosis is triggered by ligation of adhesion molecules following GM-CSF priming.
   J Immunol 197 (2016), 4090-4100.

2. Stoeckle C, Geering B, Yousefi S, Rožman S, Andina N, Benarafa C, **Simon HU**: RhoH is a negative regulator of eosinophilopoiesis.
   Cell Death Differ 23 (2016), 1961-1972.

3. Straumann A, Blanchard C, Radonjic-Hoesli S, Bussmann C, Hruz P, Safroneeva E, Simon D, Schoepfer AM, **Simon HU**: A new eosinophilic esophagitis (EoE)-like disease without tissue eosinophilia found in EoE families.
   Allergy 71 (2016), 889-900.

4. 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 RIPK3-MLKL signaling pathway which is counter-regulated by autophagy.
   J Allergy Clin Immunol, in press.

5. Amini P, Stojkov D, Wang X, Wicki S, Kaufmann T, Wong WW, **Simon HU**, Yousefi S: NET formation can occur independently of RIPK3 and MLKL signaling.
   Eur J Immunol 46 (2016), 178-184.

6. Bussmann C, Schoepfer AM, Safroneeva E, Haas N, Godat S, Sempoux C, **Simon HU**, Straumann A: Comparison of different biopsy forceps models for tissue sampling in eosinophilic esophagitis.
   Endoscopy 48 (2016), 1069-1075.

7. Leu T, Rauthe S, Wirth C, **Simon HU**, Kunzmann V, Hebestreit H, Kunzmann S: The lymphoid variant of HES (L-HES) as differential diagnose of severe asthma in childhood.
   Klin Padiatr 228 (2016), 319-324.

8. Dhayade S, Kaesler S, Sinnberg T, Dobrowinski H, Peters S, Naumann U, Liu H, Hunger RE, Thunemann M, Biedermann T, Schittek B, **Simon HU**, Feil S, Feil R: Sildenafil potentiates a cGMP-dependent pathway to promote melanoma growth.
   Cell Rep 14 (2016), 2211-1247.

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, doi: 10.1111/jdv.13989, in press.

10. Gevaert E, Zhang N, Krysko O, Lan F, Holtappels G, De Ruyck N, Nauwynck H, Yousefi S, **Simon HU**, Bachert C: Extracellular eosinophilic traps target *Staphylococcus aureus* at the site of epithelial barrier defects in severe airway inflammation.
    J Allergy Clin Immunol, in press.

11. de Graauw E, Sitaru C, Horn M, Borradori L, Yousefi S, **Simon HU**, Simon D: Evidence for a role of eosinophils in blister formation in bullous pemphigoid.
    Allergy, in press.

Review articles/Editorials

1. Simon D, Cianferoni A, Spergel JM, Aceves S, Holbreich M, Venter C, Rothenberg ME, Terreehorst I, Muraro A, Lucendo AJ, Schoepfer A, Straumann A, **Simon HU**: Eosinophilic esophagitis is characterized by a non-IgE-mediated food hypersensitivity. Allergy 71 (2016), 611-620.

2. Yousefi S, **Simon HU**: NETosis - does it really represent nature's "suicide bomber"? Front Immunol 7 (2016), 328.

3. **Simon HU**, Friis R, Tait S, Ryan KM: Retrograde signaling from autophagy modulates stress responses.
Science Signaling, in press.

4. Werfel T, Allam JP, Biedermann T, Eyerich K, Gilles S, Guttman-Yassky E, Hoetzenecker W, Knol E, **Simon HU**, Wollenberg A, Bieber T, Lauener R, Schmid-Grendelmeier P, Traidl-Hoffmann C, Akdis CA: Cellular and molecular immunologic mechanisms in patients with atopic dermatitis.
J Allergy Clin Immunol 138 (2016), 336-349.

5. Muraro A, Lemanske RF Jr, Hellings PW, Akdis CA, Bieber T, Casale TB, Jutel M, Ong PY, Poulsen LK, Schmid-Grendelmeier P, **Simon HU**, Seys SF, Agache I: Precision medicine in patients with allergic diseases: Airway diseases and atopic dermatitis-PRACTALL document of the European Academy of Allergy and Clinical Immunology and the American Academy of Allergy, Asthma & Immunology.
J Allergy Clin Immunol 137 (2016), 1347-58.

6. Carr TF, Berdnikovs S, **Simon HU**, Bochner BS, Rosenwasser LJ: Eosinophilic bioactivities in severe asthma.
World Allergy Organ J (2016), 9-21.

7. Metcalfe DD, Pawankar R, Ackerman SJ, Akin C, Clayton F, Falcone FH, Gleich GJ, Irani AM, Johansson MW, Klion AD, Leiferman KM, Levi-Schaffer F, Nilsson G, Okayama Y, Prussin C, Schroeder JT, Schwartz LB, **Simon HU**, Walls AF, Triggiani M: Biomarkers of the involvement of mast cells, basophils and eosinophils in asthma and allergic diseases.
World Allergy Organ J (2016), 40413-40416.

8. Bieber T, Akdis C, Lauener R, Traidl-Hoffmann C, …. **Simon HU**, …Ring J: Global Allergy Forum and 3rd Davos Declaration 2015: Atopic dermatitis/Eczema: challenges and opportunities toward precision medicine.
Allergy 71 (2016), 588-592.

9. Klionsky DJ, Abdelmohsen K, Abe A, Abedin MJ, **Simon HU**, … Zughaier SM: Guidelines for the use and interpretation of assays for monitoring autophagy (3rd edition).
Autophagy 12 (2016), 1-222.

10. Muraro A, Lemanske R, Agache I, Akdis CA, …. **Simon HU**, …Hellings PW: Precision medicine in allergic disease.
Allergy, in press.

11. Simon D, **Simon HU**: Leserbrief zum Beitrag Hypereosinophilie. Swiss Medical Forum 16 (2016), 104.

Book chapters

1. **Simon HU**, Simon D, Yousefi S: Basophils can form extracelluclar DNA traps independent of a functional NADPH oxidase. In: Allergies: Current challenges and solutions (Eds. M. Maurer, D. Behrendt). Pacini Editore Medicina, Pisa: 2016, p. 67-70.

2. Simon D, Aeberhard C, Erdemoglu Y, **HU Simon**: IL.17, IL-22 and tissue remodeling in atopic and contact dermatitis. In: Allergies: Current challenges and solutions (Eds. M. Maurer, D. Behrendt). Pacini Editore Medicina, Pisa: 2016, p. 183-186.

3. Liu H, He Z, **Simon HU**: The role of autophagy in cancer and chemotherapy. In: Autophagy (Eds. M. Hayat); 8. Auflage. Academic Press, 2016, p. 253-265. DOI 10.1016/B978-0-12-802937-4.00014-4

4. Zangemeister-Wittke U, **Simon HU**: Myelosuppression. In: Encyclopedia of Cancer (Ed.: Schwab M): Springer-Verlag Berlin Heidelberg 2016, p. 3940-3942.

5. Radonjic-Hoesli S, **Simon HU**: Eosinophile Granulozyten. In: Allergologie (Eds. Biedermann T, Heppt W, Renz H, Röcken M): Springer-Verlag Berlin Heidelberg 2016, p. 77-85. DOI 10.1007/978-3-642-37203-2_7

6. **Simon HU**, Friis R: Autophagy signalling. In: eLS (Encyclopedia of Life Sciences). John Wiley & Sons, Ltd: Chichester, UK, 2016. DOI 10.1002/9780470015902.a0026792

Group Prof. Stephan von Gunten

Group members: Denise Dorvignit Pedroso, PhD student*
Dr. Kayluz Frias Boligan, Postdoc
Graeter Stefanie, PhD student
Quentin Haas, PhD student
Tankica Maneva Timcheva, Technician
Christoph Schneider, PhD student
Fabiola Schorer, PhD student
Katharina Fuchs, MMed student
Ariane Meister, MMed student
Sarah Lutz, M.Sc. student
György Hamvas, M.Sc. student
Angela Fallegger, M.Sc. student
Marc Zürcher, B.Sc. student
Melanie Scherer, B.Sc. student
Aymar Abel Ganguin, B.Sc. student

*Joint supervision together with Dr. C. Mesa (Center of Mol. Immunology, Univ. Havanna).

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

Original publications

1. Brönnimann D, Bouchet A, Schneider C, Potez M, Serduc R, Bräuer-Krisch E, Graber W, **von Gunten S**, Laissue JA, Djonov V: Synchrotron microbeam irradiation induces neutrophil infiltration, thrombocyte attachment and selective vascular damage in vivo. Sci Rep 6 (2016), 33601.

2. Quast I, Keller CW, Weber P, Schneider C, **von Gunten S**, Lünemann JD: Protection from experimental autoimmune encephalomyelitis by polyclonal IgG requires adjuvant-induced inflammation.
J Neuroinflammation 13 (2016), 42.

Review articles/Editorials

1. Pashova S, Schneider C, **von Gunten S**, Pashov A: Antibody repertoire profiling with mimotope arrays.
   Human Vaccines & Immunotherapeutics (2016), in press.

2. Späth PJ, Schneider C, **von Gunten S**: Clinical use and therapeutic potential of IVIG/SCIG, plasma-derived IgA or IgM, and other alternative immunoglobulin preparations.
   Archivum Immunologiae et Therapiae Experimentalis (2016), in press.

3. Engert A, Balduini C, Brand A, Coiffier B, Cordonnier C, Döhner H, de Wit TD, Eichinger S, Fibbe W, Green T, de Haas F, Iolascon A, Jaffredo T, Rodeghiero F, Salles G, Schuringa JJ,….., **von Gunten S,** …… et al.: The European Hematology Association Roadmap for European Hematology Research: a consensus document.
   Haematologica 101 (2016), 115-208.

Group Prof. Shida Yousefi

Group members: Dr. Poorya Amini, PhD student*
Salome Aeschlimann, Technician (80%)*
Flavia Büchler, Technician*,**
Evelyne Kozlowski, Technician*
Kevin Oberson, Technician *
Darko Stojkov, PhD student

*Joint supervision together with Prof. H.-U. Simon.
**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 cell death, and 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.

NET formation can occur independently of RIPK3 and MLKL signaling.
Amini P, Stojkov D, Wang X, Wicki S, Kaufmann T, Wong WW, Simon HU, Yousefi S.
Abstract: The importance of neutrophil extracellular traps (NETs) in innate immunity is well established but the molecular mechanisms responsible for their formation are still a matter of scientific dispute. Here, we aim to characterize a possible role of the receptor-interacting protein kinase 3 (RIPK3) and the mixed lineage kinase domain-like (MLKL) signaling pathway, which are known to cause necroptosis, in NET formation. Using genetic and pharmacological approaches, we investigated whether this programmed form of necrosis is a prerequisite for NET formation. NETs have been defined as extracellular DNA scaffolds associated with the neutrophil granule protein elastase that are capable of killing bacteria. Neither *Ripk3*-deficient mouse neutrophils nor human neutrophils in which MLKL had been pharmacologically inactivated, exhibited abnormalities in NET formation upon physiological activation or exposure to low concentrations of PMA. These data indicate that NET formation occurs independently of both RIPK3 and MLKL signaling.
See original publication No. 1

Original publications

1. Amini P, Stojkov D, Wang X, Wicki S, Kaufmann T, Wong WW, Simon HU, **Yousefi S**: NET formation can occur independently of RIPK3 and MLKL signaling. Eur J Immunol 46 (2016), 178-184.

2. Wang X, He Z, Liu H, **Yousefi S**, Simon HU: Neutrophil necroptosis is triggered by ligation of adhesion molecules following GM-CSF priming.
J Immunol (2016), 4090-4100.

3. Stoeckle C, Geering B, **Yousefi S**, Rožman S, Andina N, Benarafa C, Simon HU: RhoH is a negative regulator of eosinophilopoiesis.
Cell Death Differ 23 (2016), 1961-1972.

4. Gevaert E, Zhang N, Krysko O, Lan F, Holtappels G, De Ruyck N, Nauwynck H, **Yousefi S**, Simon HU, Bachert C: Extracellular eosinophilic traps target *Staphylococcus aureus* at the site of epithelial barrier defects in severe airway inflammation.
J Allergy Clin Immunol, in press.

5. 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 RIPK3-MLKL signaling pathway which is counter-regulated by autophagy.
J Allergy Clin Immunol, in press.

6. de Graauw E, Sitaru C, Horn M, Borradori L, **Yousefi S**, Simon HU, Simon D: Evidence for a role of eosinophils in blister formation in bullous pemphigoid.
Allergy, in press.

Review article

1. **Yousefi S**, Simon HU: NETosis - Does it really represent nature's "suicide bomber"?
Front Immunol 7 (2016), 328.

Book chapter

1. Simon HU, Simon D, **Yousefi S**: Basophils can form extracellular DNA traps independent of a functional NADPH oxidase. In: Allergies: Current challenges and solutions (Eds. M. Maurer, D. Behrendt). Pacini Editore Medicina, Pisa: 2016, p. 67-70.

Group Prof. Uwe Zangemeister-Wittke

Group members: Fabian Brandl, PhD student[1]
Hannes Merten, PhD student[1]
Luca Reali, PhD student
Claudia Perez, trainee[1]

[1]Institute of Biochemistry, University of Zurich

We are interested in translational aspects of molecular oncology, biomarker validation and tumor targeting with rationally engineered and pharmacologically improved protein-drug conjugates. A main focus is on tumor targeting with Designed Ankyrin Repeat Proteins (DARPins) as highly stable non-IgG scaffold proteins for targeted drug and biotoxin delivery under optimized pharmacokinetic conditions. To this end, affinity-maturated DARPins with specificity for the pan-carcinoma antigen EpCAM were generated and genetically modified to enable site-specific conjugation for functionalization using maleimide and DARPin-compatible bioorthogonal click chemistry together with optimized linker 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 targeting, the serum half-life of the bioconjugates was extended by site-specific conjugation with serum albumin, PEG or the synthetic unstructured polypeptides PAS or XTEN with variable length.

Upregulation of the S1P3 receptor in metastatic breast cancer cells increases migration and invasion by induction of PGE2 and EP2/EP4 activation
Filipenko I, Schwalm S, Reali L1, Pfeilschifter J, Fabbro D, Huwiler A, Zangemeister-Wittke U
Abstract: Breast cancer is one of the most common and devastating malignancies among women worldwide. Recent evidence suggests that malignant progression is also driven by processes involving the sphingolipid molecule sphingosine 1-phosphate (S1P) and its binding to cognate receptor subtypes on the cell surface. To investigate the effect of this interaction on the metastatic phenotype, we used the breast cancer cell line MDA-MB-231 and the sublines 4175 and 1833 derived from lung and bone metastases in nude mice, respectively. In both metastatic cell lines expression of the $S1P_3$ receptor was strongly upregulated compared to the parental cells and correlated with higher S1P-induced intracellular calcium ($[Ca^{2+}]_i$), higher cyclooxygenase (COX)-2 and microsomal prostaglandin (PG) E_2 synthase expression, and consequently with increased PGE_2 synthesis. PGE_2 synthesis was decreased by antagonists and siRNA against $S1P_3$ and $S1P_2$. Moreover, in parental MDA-MB-231 cells overexpression of $S1P_3$ by cDNA transfection also increased PGE_2 synthesis, but only after treatment with the DNA methyltransferase inhibitor 5-aza-2-deoxycytidine, indicating reversible silencing of the COX-2 promoter. Functionally, the metastatic sublines showed enhanced migration and Matrigel invasion in adapted Boyden chamber assays, which further increased by S1P stimulation. This response was abrogated by either $S1P_3$ antagonism, COX-2 inhibition or PGE_2 receptor 2 (EP_2) and 4 (EP_4) antagonism, but not by $S1P_2$ antagonism. Our data demonstrate that in breast cancer cells overexpression of $S1P_3$

and its activation by S1P has pro-inflammatory and pro-metastatic potential by inducing COX-2 expression and PGE_2 signaling via EP_2 and EP_4.
See original publication No. 1

Original publication

1. Filipenko I, Schwalm S, Reali L, Pfeilschifter J, Fabbro D, Huwiler A, **Zangemeister-Wittke U**: Upregulation of the S1P3 receptor in metastatic breast cancer cells increases migration and invasion by induction of PGE2 and EP2/EP4 activation. Biochim Biophys Acta 11 (2016), 1840-1851.

Book chapter

1. **Zangemeister-Wittke U**, Simon HU: Myelosuppression. In: Encyclopedia of Cancer (Ed.: Schwab M): Springer-Verlag Berlin Heidelberg 2016, p. 3940-3942.

Additional Publications by PKI Members

Original publications

Sudo M, Miyaji K, **Späth P**, Morita-Matsumoto K, Yamaguchi Y, Yuki N: Polyclonal IgM and IgA block in vitro complement deposition mediated by anti-ganglioside antibodies in autoimmune neuropathies.
Int Immunopharmacol 40 (2016), 11-15.

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 (2017), in press.

Silbernagel G, **Spirk D**, Hager A, Baumgartner I, Kucher N: Electronic alert system for improving stroke prevention among hospitalized oral-anticoagulation-naive patients with atrial fibrillation: A randomized trial.
J Am Heart Assoc 5 (2016), doi: 10.1161/JAHA.116.003776.

Kucher N, Aujesky D, Beer JH, Mazzolai L, Baldi T, Banyai M, Hayoz D, Kaeslin T, Korte W, Escher R, Husmann M, Frauchiger B, Baumgartner I, **Spirk D**: Rivaroxaban for the treatment of venous thromboembolism. The SWIss Venous ThromboEmbolism Registry (SWIVTER).
Thromb Haemost 116 (2016), 472-479.

Spirk D, Aujesky D, Stuck AK, Beer JH, Mazzolai L, Baldi T, Banyai M, Hayoz D, Kaeslin T, Korte W, Escher R, Husmann M, Frauchiger B, Baumgartner I, Kucher N: Clinical outcomes of venous thromboembolism in patients with and without cancer: The SWIss Venous ThromboEmbolism Registry (SWIVTER).
Semin Thromb Hemost 42 (2016), doi: 10.1055/s-0036-1584131.

Review articles/Editorials

Späth PJ, Schneider C, von Gunten S: Clinical use and therapeutic potential of IVIG/SCIG, plasma-derived IgA or IgM, and other alternative immunoglobulin preparations.
Arch. Immunol Ther. Exp. (2016), in press.

Wuillemin WA, **Spirk D**, Beer JH, Baumgartner I: Schweizer Expertenkommentare zum Update der ACCP-Guidelines.
Swiss Med Forum 16 (2016), 1059-1060.

4.2. Congress Invitations

Prof. Hans-Uwe Simon
Annual Meeting of the American Academy of Allergy Asthma and Immunology (AAAAI);
Los Angeles, CA (USA), February 4-8, 2016;
Eosinophil cytolysis: Programmed death pathways and significance in disease.

31st Symposium of the Collegium Internationale Allergologicum;
Charleston, South Carolina (USA), April 3-8, 2016;
Eosinophil cytolysis occurs through necroptosis.

Nobel Conference: The Cell Cycle and Cell Death in Disease; Stockholm (Sweden),
June 8-11, 2016;
Neutrophils and eosinophils undergo necroptosis under inflammatory conditions.

Annual Meeting of the European Allergy and Clinical Immunology (EAACI),
Vienna (A), June 11-15, 2016;
Understanding the process of publishing.

Workshop on “Cell Death in Neurodegeneration and Cancer”, Villa Vigoni,
Loveno di Menaggio, Como (I), June 22-25, 2016;
Necroptosis in granulocytes: Triggers, pathways, and in vivo relevance.

9th Swiss Apoptosis Meeting, Bern (CH); September 8-9, 2016;
Autophagy in health and disease.

XVth International Symposium on Proteinases, Inhibitors and Biological Control,
Portoroz (Slovenia); September 17-21, 2016;
Mechanism of eosinophil cytolysis.

11. Deutscher Allergiekongress, Berlin (D); Sept. 29 – Oct. 1, 2016;
Eosinophile und IgE als Partner: Szenen einer Ehe.

4th Food Allergy and Anaphylaxis Meeting, Rome (Italy); Oct. 13-15, 2016;
Pathogenesis of eosinophilic esophagitis.

4th Food Allergy and Anaphylaxis Meeting, Rome (Italy); Oct. 13-15, 2016;
Tips for successfully publishing.

Annual Congress of the National Society of Allergy and Clinical Immunology,
San Sebastian (Spain); Oct. 19-22, 2016;
Biological evidences of eosinophilic asthma.

EAACI Master Class on Translational Immunology in Allergic Diseases. When and how to use biologicals, Zurich (CH); Oct. 21-22, 2016;
Using anti – IL-5 in the clinic.

8th Dermatological Meeting in Ticino 2016: From the bench to the clinic, Bellinzona (CH);
Dec. 1, 2016;
Neutrophils and eosinophils undergo necroptosis under inflammatory conditions.

Prof. Stephan von Gunten
10th World Congress on Vaccines, Immunization and Immunotherapy, Bern (CH), June 1-2, 2016;
The human anti-carbohydrate IgG antibody repertoire – implications for glycovaccination.

German Pharm-Tox Summit, Berlin (Germany), February 29 - March 3, 2016;
Anti-inflammatory effects of intravenous immunoglobulins.

PD Dr. Peter Späth
23rd International Plasma Protein Congress, Plasma Protein Therapeutic Association, Barcelona (E), March 22-23, 2016;
IVIG/SCIG and secondary immunodeficiencies - New developments.

Annual Conference, Romanian Society of Allergology and Clinical Immunology, Bucharest (RO), May 13-15, 2016;
Concise overview of HAE knowledge progress.

30ies Anniversary of R & D at CSL Behring in Bern, Bern (CH), September 9, 2016;
History of the plasma industry - A ZLB perspective: Roots of & roads to research & development in Bern / First infusions of Sandoglobulin liquid.

Prof. Shida Yousefi
NETs consensus meeting, Erlangen (D), September 21-23, 2016;
Mechanism of NET formation.

4.3. Seminar Invitations

Prof. Hans-Uwe Simon
Clinic of Hematology, University Hospital Bern, Bern (CH), Feb 18, 2016; guest of Prof. Johanna Kremer:
Die Rolle von Autophagie bei Tumorerkrankungen.

Genomic Center, University of California, Los Angeles (UCLA), Los Angeles (CA, USA), March 4, 2016; guest of Dr. Alice Soragni:
Eosinophils and neutrophils can undergo necroptosis – mechanism and consequences.

Department of Clinical Science, Lund University, Lund (Sweden), Sept 2, 2016; guest of Prof. Arne Egesten:
Mechanism of eosinophil cytolysis.

Institute of Biomedicine and Molecular Immunology – National Research Council (IBIM-NRC), Palermo (I), Oct 28, 2016; guest of Dr. Andreina Bruno:
Mechanism of eosinophil cytolysis.

Prof. Stephan von Gunten
Department of Chemistry, University of Athens, Athens (GR), January 27, 2016; guest of Prof. George Kokotos and Prof. Thanasis Gimisis: Altered surface glycosylation with expression of Siglec-7/-9 ligands protects tumors from NK cell immunosurveillance.

Department of Medicine, University of Fribourg, Fribourg (CH), January 13, 2016; guest of Prof. Caroline Bourquin: The multifaceted role of carbohydrates in disease.

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 – Personalized Medicine;
Bern (CH), January 28, 2016

Workshop on "Cell Death in Neurodegeneration and Cancer" (together with C. Brancolini, K.-M. Debatin and P.H. Krammer),
Villa Vigoni, Loveno di Menaggio, Como (I), June 22-25, 2016

15th III-Bern International Summer School,
Bönigen/Interlaken (CH), August 7-9, 2016

Prof. Thomas Kaufmann
9th Swiss Apoptosis Meeting (SAM) (together with T. Brunner and M. Tschan)
Bern (CH), September 8-9, 2016

Prof. Stephan von Gunten
Annual Meeting 2016 of the Swiss Society for Pharmacology and Toxicology (together with task force SSPT), Bern (CH), April 21, 2016

4.5. Invited Chairperson at Congresses

Prof. Hans-Uwe Simon

Symposium of the Swiss Society of Pharmacology and Toxicology:
Progress in Pharmacology – Personalized Medicine, Morning session;
Bern (CH), January 28, 2016

82. Jahrestagung der Deutschen Gesellschaft für experimentelle und klinische Pharmakologie und Toxikologie (DGPT) und 18. Jahrestagung der Klinischen Pharmakologie (VKliPha) in Zusammenarbeit mit der AGAH;
Symposium of the Swiss Society of Pharmacology and Toxicology: Novel therapeutic approaches in inflammation and cancer.
Berlin (D), Feb. 29 – March 3, 2016.

31st Symposium of the Collegium Internationale Allergologicum; Session: "IgE: Its discovery and roles in allergy";
Charleston, South Carolina (USA), April 3-8, 2016.

Eröffnungsfeier Liquid Biobank Bern; Scientific Session;
Bern, May 31, 2016.

Annual Meeting of the European Allergy and Clinical Immunology (EAACI);
Session: “Late braking poster session”;
Vienna (A), June 11-15, 2016.

Workshop on “Cell Death in Neurodegeneration and Cancer”; Session 1:
Role of the immune system;
Villa Vigoni, Loveno di Menaggio, Como (I), June 22-25, 2016.

9th Swiss Apoptosis Meeting; Session: Apoptosis pathways;
Bern (CH); September 8-9, 2016.

XVth International Symposium on Proteinases, Inhibitors and Biological Control;
Session: Programmed necrosis pathways and inflammation;
Portoroz (Slovenia), September 17-21, 2016.

4th Food Allergy and Anaphylaxis Meeting; Session: Food allergy and the gut: EoE;
Rome (Italy); Oct. 13-15, 2016.

PD Dr. Peter Späth
23th International Plasma Protein Congress, Plasma Protein Therapeutic Association, 3rd
Session: Innovation & Developments; Barcelona (E), March 22-23, 2016.

Prof. Stephan von Gunten
Joint Swiss Society for Allergology and Immunology (SSAI) / Swiss Society of Oto-Rhino-Laryngology (SSORL) Meeting 2016, chair and jury member, Session “Posterwalk Clinical Immunology/Translational Immunology/Diagnostic Laboratory Immunology” Montreux (CH), April 28-29, 2016.

Annual Meeting 2016 of the Swiss Society for Pharmacology and Toxicology; Session “Young Investigator Research”, Bern (CH), April 21, 2016.

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.
Carcinogenesis
Circ. Res.
Clin. Chem. Lab. Med.
Diabetologica
Eur. J. Pharmacol.
Exp. Cell Res.
Hormone Metabol. Res.
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
FEBS letters

Prof. Thomas Kaufmann

Acta Tropica
Advances in Medicine
Apoptosis
Allergy
Cell Communication and Signaling
Cell Death Differ.
Cell Death Dis.
Cell Mol Immunol
Eur. J. Immunol.
FEBS Letter
FEBS Journal
Frontiers in Molecular and Cellular Oncology
Future Oncology
Hepatology
Immunol Cell Biol
Int Arch Allergy Immunol
Int Rev Cell Mol Biol
J. Hepatology
J. Mol Cell Biol
J. Neuroscience
Methods
Mol. Cancer Therapeutics
Mol. Cell. Oncology
Oncogene
PLoS One
Scientific Reports

Dr. He Liu

Allergy
Cell Death Dis.
Cell Death Differ.
Frontiers in Oncology

Prof. Hans-Uwe Simon

Allergy
Apoptosis
Autophagy
Cell Death Differ.
Cell Death Dis.
J. Clin. Invest.
EMBO Journal
EMBO Reports
Science Signaling
Eur. J. Immunol.
FASEB J.
Cell Reports
Gut
J. Allergy Clin. Immunol.
J. Exp. Med.
J. Immunol.
J. Leukoc. Biol.
J. Infect. Dis
Oncogene
Oncotarget
FEBS letters
Mol. Cell. Oncology
Nat. Med.
N. Engl. J. Med.

PD Dr. Peter Späth

Allergy
Current Pediatrics Research
Drugs & Aging
Exp. Rev. Clin. Immunol.
J. Clin. Immunol.
PLoS One

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. Invest. Dermatol.
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.
Front. Immunol.
Eur. J. Immunol.
Exp. Lung Res.
Int. J. Mol. Sci.
Immunology
J. Vasc. Intervent. Radiol.
Respir. Res.
Sci. Rep.
Int. J. Biochem. Cell Biol.
Thorax

Prof. Uwe Zangemeister-Wittke

Bioconjug. Chem.
Cell Death Dis.
Expert Opin. Drug Delivery
Mol. Cell. Biol.
Toxins

4.7. Referee Work for Grant Bodies

Dr. Zhaoyue He

Swiss Cancer League

Prof. Andrea Huwiler

Deutsche Forschungsgemeinschaft (DFG)

Prof. Thomas Kaufmann

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

PD Dr. Peter Späth

Wellcome Trust

Prof. Stephan von Gunten

Swiss Cancer League
Medical Research Council (UK)

Prof. Uwe Zangemeister-Wittke

Swiss Cancer League
Qatar National Research Fund (QNRF)

4.8. Awards

Prof. Georgia Konstantinidou
Förderprofessur
Swiss National Science Foundation (SNF), Bern (CH), March 2, 2016

Fabiola Schorer-Cortinas
Novartis Institute of Biomedical Research Prize 2016 for Best Oral Talk
Spring Meeting of the Swiss Society of Pharmacology and Toxicology (SSPT), Bern (CH), April 21, 2016

Fabiola Schorer-Cortinas
Best Poster Award
Swiss Society for Allergology and Immunology (SSAI), Montreux (CH), April 28-29, 2016

Simone Wicki
FEBS Journal Poster Awards
9th Swiss Apoptosis Meeting (SAM), Bern (CH), September 8-9, 2016

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 Advisory Board, Oncotarget, Section 'Autophagy and Cell Death'
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. Hans-Uwe Simon
Dean, Medical Faculty, University of Bern (2016-2020)

Coordinator Pharmacology/Pharmacy, Swiss-EU mobility program, 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)

Member of the the Scientific Executive Board of SystemsX.ch:
The Swiss Initiative in Systems Biology (2013-2016)

Past-President of the International Eosinophil Society (IES) (2015-2017)

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

Member of the Scientific Committee, Swiss Cancer League

Member of the Scientific Advisory Board of the Novartis Foundation

Member of the Advisory Board, Research Foundation, University of Bern (until June 2016)

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), 2015-2017

Editor-in-Chief, Allergy

Editor-in-Chief, Cell Death & Disease

Section Editor, Apoptosis

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

Member of the Scientific Board, Allergologie

Member of the Editorial Board, Int. Journal of Hygiene and Environmental Health

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 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

Coordinator for FACS and 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

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

Urs Grunder

Vernissage: November 17, 2016, Inselspital, INO- F

Welcome: Prof. H.-U. Simon / Prof. M. Fiedler
Laudatio: Prof. Anselm Ernst

Duration of the exhibition: 17.11.2016 - 15.12.2016

More information:

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

8. Sponsors

8.1. Research Grants

Denise Dorvignit Pedroso
Swiss Government Excellence Scholarship for Foreign Scholars (Sep 2015 – Aug 2016)

Martin Grosek
Erasmus/SEMP-Fellowship at the University of Bern (Apr 2016 – Aug 2016)

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

Luka Srajner
Erasmus/SEMP-Fellowship at the University of Bern (Apr 2016 – Aug 2016)

Prof. Thomas Kaufmann
Swiss National Science Foundation, project grant 31003A_149387
Swiss National Science Foundation, project grant 310030E_150805 (part of FOR2036)
Start-up project grant, Understanding Disease Research Focus Area, La Trobe University (AU), other chief investigator.

Prof. Georgia Konstantinidou
Swiss National Science Foundation, SNF-Professorship (grant No. PP00P3_163929)

Nina Sekeres
Erasmus/SEMP-Fellowship at the University of Bern (Oct 2015 – Feb 2016)

Ema Sever
Erasmus/SEMP-Fellowship at the University of Bern (Oct 2015 – Feb 2016)

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 Cancer Research foundation (KFS-3248-08-2013)
Swiss National Science Foundation (Grant Nr. 310030_162552 / 1)
Allergie-Stiftung Ulrich Müller-Gierock
Novartis Research Foundation (Novartis, Switzerland)
Innate Pharma SA, Marseille (France)

Prof. Shida Yousefi
Swiss National Science Foundation (grant No. 310030-146215)

Prof. Uwe Zangemeister-Wittke
Swiss National Science Foundation (grant No. 31003A-170134)
Swiss National Science Foundation (grant No. 310030A-138201)
Sassella-Stiftung of the Zürcher Kantonalbank

8.2. Meetings

Swiss Society of Pharmacology and Toxicology (SSPT): Progress in Pharmacology – Personalized Medicine, Bern, Jan 28, 2016
Pfizer AG, Zürich
Sanofi Aventis (Schweiz) AG, Vernier
Novartis Pharma Schweiz AG, Rotkreuz
AbbVie AG, Baar
Roche Pharma AG, Reinach
Takeda Pharma AG, Pfäffikon

15th III-International Summer School, Seehotel, CH 3806 – Bönigen/Interlaken, Aug 7-9, 2016
BD Biosciences, Allschwil
Carl Zeiss AG, Feldbach
CSL Behring AG, Bern
Novartis Pharma AG, Rotkreuz
Member companies of the Kontaktgruppe für Forschungsfragen (KGF), Basel:
Novartis and Roche
Lucerna Chem AG, Luzern
Pfizer AG, Zürich
Swiss Committee for Molecular Biology (SKMB), Geneva
Graduate School for Cellular and Biomedical Sciences, Universität Bern

9th Swiss Apoptosis Meeting (SAM)
Bern, Sep 8-9, 2016
Carl Zeiss AG, Feldbach
Lubio, Luzern
LiCOR, Lincoln, Nebraska USA
Lucerna Chem AG, Luzern
Bioconcept, Allschwil
HuberLab, Aesch
AdipoGen AG, Liestal
Member companies of the Kontaktgruppe für Forschungsfragen (KGF), Basel:
Novartis and Roche
Thermo Fisher Scientific (Schweiz) AG, Reinach
AbbVie AG, Baar
Graduate School for Cellular and Biomedical Sciences, University of Bern

8.3. Seminars „Current topics in Pharmacology and Theranostics“

(organized together with the Center of Laboratory Medicine, University Hospital Bern, Inselspital)

Astellas Pharma AG, Wallisellen
Vifor AG, Villars-sur-Glâne
Pfizer AG, Zürich

8.4 Seminars „Bern Immunology Club“

Luca Borradori, Britta Engelhardt, Thomas Geiser, Adrian Ochsenbein, Andrew Macpherson, Christoph Müller, Hans-Uwe Simon, Artur Summerfield, Peter Villiger, Martin Bachmann

8.5 Travel Support

Dr. Poorya Amini
Graduate School for Cellular and Biomedical Sciences, University of Bern (49th Annual Meeting of Society for Leukocyte Biology and Neutro, Verona (Italy), Sep 15-17, 2016)

Swiss Society of Pharmacology and Toxicology (SSPT) (49th Annual Meeting of Society for Leukocyte Biology and Neutro, Verona (Italy), Sep 15-17, 2016)

Christoph Schneider
Swiss Society for Experimental Pharmacology (43rd annual meeting of Scandinavian society for immunology and summer school, Turku (Finland), May 10-13, 2016)

Dr. Elizabeth Louisa de Graauw
Graduate School for Cellular and Biomedical Sciences, University of Bern (49th Annual Meeting of Society for Leukocyte Biology and Neutro, Verona (Italy), Sep 15-17, 2016)

Yuniel Fernandez Marrero
Swiss Society of Pharmacology and Toxicology (SSPT) (10th EWCD Meeting: “Death Never Dies, Fiuggi (Italy), Apr 3-8, 2016)

Darko Stojkov
Graduate School for Cellular and Biomedical Sciences, University of Bern (49th Annual Meeting of Society for Leukocyte Biology and Neutro, Verona (Italy), Sep 15-17, 2016)

8.6 Other Support

Bürgi Fonds Seminar series of the institute