Annual Report 2014

Institut für Pharmakologie (PKI)

der Universität Bern

Institute of Pharmacology,

University of Bern

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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 vierzehnte umfassende Jahresbericht des Instituts für Pharmakologie (PKI) der Universität Bern. Das PKI hat auch im Jahr 2014 seine Aufgaben in Lehre und Forschung innerhalb der Medizinischen Fakultät vorbildlich erfüllt. Die Pharmakologie besitzt eine Brückenfunktion zwischen biologischer Grundlagen- und klinischer Forschung. Das PKI arbeitet deshalb eng mit den verschiedensten 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 2014 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. Die DozentInnen des PKI sind ausserdem innerhalb der interfakultären Graduate School for Cellular and Biomedical Sciences aktiv tätig. Prof. Kaufmann ist Mitglied einer Betreuungskommission innerhalb dieses Ausbildungsprogramms für Doktorandinnen und Doktoranden. Dazu kommen zusätzliche Bildungsangebote in Form von Seminaren (Fortschritte in der Pharmakologie) und einer Summer School (Prof. Simon). Diese Bildungsangebote werden weitgehend aus eigenen finanziellen Mitteln und Sponsorengeldern bestritten. Im Institut arbeiten gegenwärtig 21 DoktorandInnen (19 PhD, 2 MD), und 2 DoktorandInnen (2 PhD) haben im Berichtsjahr ihre Arbeit erfolgreich abgeschlossen.

Die Mitarbeiter und Mitarbeiterinnen des Instituts für Pharmakologie publizierten im Jahr 2014 insgesamt 29 Originalarbeiten sowie 19 Übersichtsartikel in internationalen Fachzeitschriften (Summe der „impact factors“ >300). MitarbeiterInnen des Instituts wurden zu insgesamt 37 Vorträgen bzw. Seminaren eingeladen. Mehrere MitarbeiterInnen des PKI wurden mit Forschungspreisen ausgezeichnet. Gegenwärtig werden 6 MitarbeiterInnen mit

namhaften Beiträgen des Schweizerischen Nationalfonds unterstützt. Zahlreiche Persönlichkeiten besuchten das Institut und hielten Forschungsseminare. Der Berner Immunologie-Club erfreut sich, auch durch die aktive Hilfe aus dem PKI, einer grossen Beliebtheit. Prof. Simon und Prof. Kaufmann organisierten gemeinsam mit PD Dr. Tschan (Institut für Pathologie, Universität Bern) und Prof. Brunner (Lehrstuhl Biochemische Pharmakologie, Universität Konstanz, Deutschland) das „8th Swiss Apoptosis Meeting (SAM)“ (10.-12.09.2014), zu dem wir ca. 200 TeilnehmerInnen aus dem In- und Ausland begrüssen durften. Weiterhin ist das Institut für Pharmakologie seit 2014 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.

Prof. Simon ist seit 01.08.2012 als Forschungsdekan der Medizinischen Fakultät der Universität Bern tätig. Daneben nimmt das PKI auch ausserhalb der Universität wissenschaftspolitische Verantwortung für die Medizin und die Biowissenschaften wahr. Prof. Simon amtet gegenwärtig als Präsident der International Eosinophil Society (IES) und als Vice-Chair der Immunopharmacology Section der International Union of Basic and Clinical Pharmacology (IUPHAR). Ebenso ist er der Vorsitzende des Wissenschaftlichen Beirats des HELMHOLTZ-Zentrums für Umweltforschung in Leipzig. PD Dr. Stephan von Gunten ist Sekretär der Schweizerischen Gesellschaft für Experimentelle Pharmakologie (SGEP).

Ich danke allen Mitarbeiterinnen und Mitarbeitern für ihren Einsatz, welcher auch im Jahr 2014 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 2015

1.2. Foreword

This is the fourteenth comprehensive annual report of the Institute of Pharmacology of the University of Bern. Our institute has worked hard to fulfil optimally its tasks in teaching and research within the Medical Faculty in 2014. Pharmacology plays important roles in both basic biological science and clinical research. The Institute of Pharmacology wants to succeed in both areas and, therefore, maintains close contacts with several clinics at the University Hospital (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. Furthermore, we are very much interested in collaborating with the industry on new developments. Current activities are listed in this report. In addition, we also worked to promote communication between scientists and the public in 2014.

In addition to the regular teaching in the third year medical student curriculum and 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 Sciences Faculty of our university. 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 this school. Furthermore, additional teaching activities outside the medical curriculum, such as seminars (Progress in Pharmacology) and a Summer School (Prof. Simon) were provided. Importantly, these additional events were financed exclusively by external sponsors. Currently, 19 PhD students and 2 MD students work at the PKI, and two students (2 PhD) successfully completed their doctoral studies in 2014.

Research is our second important activity. In 2014, staff members of the PKI published 29 original and 19 review articles in international peer-reviewed journals (the sum of the “impact factors” is more than 300). Co-workers of the institute were invited to present 37 lectures or seminars. Several PKI members received research prizes. Six co-workers are currently supported by grants of the Swiss National Science Foundation. Several internationally prominent researchers visited the institute and presented seminars. The Bern Immunology Club (BIC) is, thanks in part to our contribution, highly active and successful. Prof. Simon and Prof. Kaufmann, together with PD Dr. Tschan (Institute of Pathology, University of Bern) and Prof. Brunner (Department of Biochemical Pharmacology, Univ. of

Konstanz, Germany), organized an international congress (8th Swiss Apoptosis Meeting; September 10-12, 2014), which attracted approximately 200 scientists interested in the field of “Cell Death”. Moreover, since 2014, the Institute of Pharmakology has been part of a Training Network for PhD students within the EU Framework Program for Research and Innovation „HORIZON 2020“. In summary, research plays a very important role at the PKI and is carried out at a high level.

Prof. Simon serves as Vice-Dean for Research in the Medical Faculty of the University of Bern (since August 1, 2012). He is the President of the International Eosinophil Society (IES), the Vice-Chair of the Immunopharmacology Section of the International Union of Basic and Clinical Pharmacology (IUPHAR), and the chairman of the Scientific Advisory Board of the HELMHOLTZ Center for Environmental Research in Leipzig. PD Dr. Stephan von Gunten is secretary 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 2014. I am grateful to all the sponsors and friends of the institute for their support.

Prof. Hans-Uwe Simon, MD, PhD
Director

Bern, January 2015

2. Staff 2014

Director

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

Deputy Director

Prof. Dr. Andrea Huwiler, PhD

Principal Investigators

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

Scientific Staff

Hyrije Ademi, M.Sc. student*
Dr. Poorya Amini, PhD student
Fabian Brandl, PhD student (since April 2014)
Daniel Bachmann, research assistant
Olivier Blanchard, PhD student (since July 2014)
Jonathan Eastline, MMed student* (August 2014)
Michael Eastline, MMed student* (August 2014)
Dr. Elisabeth Louisa de Graauw, PhD student*
Dr. Denise Dorvignit Pedroso, PhD* (May – July 2014)
Daniel Fallegger, PhD student (until October 2014)
Yuniel Fernandez Marrero, PhD student* (since March 2014)
Iuliia Filipenko, PhD student
Ziva Frangez, M.Sc. student*
Kayluz Frias Boligan, PhD student*
Nina Germic, PhD student* (since September 2014)
Dr. Zhaoyue He, PhD*
Faik Imeri, PhD student
Aurelio Lendro Jenni, PhD student (since November 2014)
Evelyne Kozlowski, technician
Emanuel Lauber, M.Sc. student* (since May 2014)
Dr. He Liu, PhD*
Marianne Maillard-van Laer, technician
Tankica Maneva - Timcheva, PhD student*
Nina Meienberger, Research fellow* (since October 2014)
Dr. Christina Merz - Stöckle, PhD*
Dr. Erika Moravcikova, PhD* (since July 2014)
Kevin Oberson, technician
Olexsandr Pastukhov, PhD student (until March 2014)

Dr. Tatiana Rabachini de Almeida, PhD*
Dr. Susanne Radonjic-Hösli, MD-PhD student (until September 2014)
Ramona Reinhart, PhD student* (since March 2014)
Saša Rožman, PhD student
Inès Schmid, head technician
Christoph Schneider, PhD student
Myriam Fabiola Schorer-Cortinas, PhD student*
Dr. Nikolas Stefan, PhD (February 2014 – March 2014)
Darko Stojkov, PhD student*
Sabrina Traxel, B.Sc. student* (April – May 2014)
Marcel Trefny, M.Sc. student* (since September 2014)
Tatiana Vogel, M.Sc. student* (January – June 2014)
Xiaoliang Wang, PhD student*
Simone Wicki, PhD student*
Matthias Widmer, M.Sc. student (January – June 2014)
Christin Wuensche, PhD student (May – September 2014)

External University Teachers

Dr. Sibylle Bürgi, PhD*
PD Dr. Armand Cachelin, MD, PhD*
PD Dr. David Spirk, MD*
Prof. Dr. Irena Mlinaric, PhD* (Visiting Professor of the University of Bern)

Guest scientists

Prof. Dr. Dagmar Simon, MD*, Dept. of Dermatology, Inselspital, University of Bern
Dr. Alice Soragni, PhD*, UCLA-DOE, Los Angeles, USA
Prof. Dr. Alex Straumann, MD*, Dept. of Gastroenterology, University of Basel
Dr. Doriano Fabbro, PhD*
Dr. Christiane Sokollik, MD*, Dept. of Pediatrics, Inselspital, University of Bern

External Computer Support

Anne Wyss*****

Office

Sandra Suter, secretary
Anita Dähler, secretary

Workshop

Hans Andres

House Keeping

Isa Conforti and Elisa Piccirilli

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

Meeting of the Swiss Society of Pharmacology and Toxicology (SSPT):
Progress in Pharmacology – Tumor Pharmacology, Bern, January 30th 2014

Members of the Institute of Pharmacology of the University of Bern together with participants of an international summer school in Stein am Rhein; July 27 – 29, 2014. Our guest speakers from Germany (Dr. Robert Lukowski), USA (Dr. Alice Soragni) and Slovenia (Prof. Irena Mlinaric-Rascan) are seen.

8th Swiss Apoptosis Meeting (SAM). Bern, September 10 – 12, 2014

3. Teaching Activities
3.1. Lectures

Lectures for Medical Students: Pharmacology

Date	Lecturer	Titel of the lecture
March 10, 2014	PD Dr. Stephan von Gunten	Antidiabetika
March 12, 2014	PD Dr. Stephan von Gunten	Lipidsenker, Behandlung der Gicht
March 31, 2014	Prof. Andrea Huwiler	Antiepileptika
March 31, 2014	Prof. Andrea Huwiler	Therapie von M.Parkinson und Demenz
April 2, 2014	Prof. Andrea Huwiler	Lokalanästhetika
April 14, 2014	PD Dr. Stephan von Gunten	Hormone aus pharmakologischer Sicht (Teil 1)
April 14, 2014	PD Dr. Stephan von Gunten	Hormone aus pharmakologischer Sicht (Teil 2)
April 16, 2014	Prof. Andrea Huwiler	Pharmakologie von Narkosemitteln und Muskelrelaxantien 1
April 16, 2014	Prof. Andrea Huwiler	Pharmakologie von Narkosemitteln und Muskelrelaxantien 2
April 30, 2014	Prof. Andrea Huwiler	Psychopharmakologie
May 5, 2014	Prof. Andrea Huwiler	Antidepressiva, Anxiolythika und Stimmungsstabilisatoren
May 7, 2014	Prof. Andrea Huwiler	Antipsychotika
May 14, 2014	Prof. Andrea Huwiler	Schmerz und Analgesiologie 1
May 14, 2014	Prof. Andrea Huwiler	Schmerz und Analgesiologie 2
May 14, 2014	Prof. Andrea Huwiler	Pharmakologie bei speziellen Patientengruppen
June 4, 2014	Prof. Hans-Uwe Simon	Immunmodulation
Sept. 17, 2014	Prof. Hans-Uwe Simon	Pharmakodynamik 1
Sept. 17, 2014	Prof. Hans-Uwe Simon	Pharmakodynamik 2
Sept. 17, 2014	Prof. Hans-Uwe Simon	Entzündungshemmung

Sept. 17, 2014	Prof. Hans-Uwe Simon	Einführung in die Toxikologie
Oct. 27, 2014	Prof. Hans-Uwe Simon	Pharmakotherapie bei Lungenkrankheiten
Nov. 3, 2014	PD Dr. David Spirk	Pharmakologie der Hämostase
Nov. 5, 2014	Prof. Uwe Zangemeister-Wittke	Pharmakologie des vegetativen Nervensystems
Nov. 5, 2014	Prof. Uwe Zangemeister-Wittke	Antihypertensiva
Nov. 10, 2014	Prof. Uwe Zangemeister-Wittke	Antiarrhythmika
Nov. 16, 2014	PD Dr. David Spirk	Behandlung der Herzinsuffizienz und Angina Pectoris
Dec. 17, 2014	Prof. Uwe Zangemeister-Wittke	Diuretika

Lectures for Medical Students: Pathology

Date	Lecturer	Title of the lecture
Sept. 22, 2014	Prof. Thomas Kaufmann	Adaptation und Zellschäden

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

Date	Lecturer	Title of the lecture
Febr. 3, 2014	Prof. Uwe Zangemeister-Wittke	Einführung in die Pharmakogenetik
Febr. 17, 2014	Prof. Hans-Uwe Simon	Rezeptoren, Dosis-Wirkungskurven Antagonisten, Applikationsarten
Febr. 19, 2014	PD Dr. Stephan von Gunten	Psychopharmaka
Febr. 26, 2014	Prof. Uwe Zangemeister-Wittke	Phamakologie des vegetativen Nervensystems
March 05, 2014	PD Dr. Stephan von Gunten	Magensäurehemmung
March 12, 2014	Prof. Thomas Kaufmann	Pharmakogenetik, Interaktionen

March 17, 2014	PD Dr. David Spirk	Herz-Kreislauf Medikamente und Antithrombotika
March 19, 2014	Prof. Andrea Huwiler	Narkose-/Beruhigungsmittel
March 26, 2014	Prof. Andrea Huwiler	Pharmakologie der Atemwege
April 7, 2014	Dr. Sibylle Bürgi	Antibiotika I
April 7, 2014	Dr. Sibylle Bürgi	Antibiotika II
April 9, 2014	Dr. Sibylle Bürgi	Antidiabetika
April 16, 2014	Dr. Sibylle Bürgi	Lokalanästhetika
May 5, 2014	PD Dr. Armand Cachelin	Schwache Analgetika, Starke Analgetika
Oral examinations:	Prof. Zangemeister-Wittke, Prof. Huwiler, PD Dr. von Gunten, Prof. Simon	

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

Date	Lecturer	Title of the lecture
Sept. 30, 2014	Dr. Christina Merz-Stöckle	Zellschäden

Lectures for Natural Sciences Faculty and Biomedical Sciences students: Clinical Immunology (Coordinator: Prof. Hans-Uwe Simon)

Date	Lecturer	Title of the lecture
Febr. 20, 2014	Prof. Hans-Uwe Simon	Introduction
Febr. 20, 2014	Prof. Hans-Uwe Simon	Immunopharmacology
May 22, 2014	Prof. Hans-Uwe Simon	Eosinophilic diseases

Written examination and oral tests: Prof. Simon

Lecture for Natural Sciences Faculty: Cellular and Molecular Immunology (Coordinator: Prof. Beda Stadler)

Date	Lecturer	Title of the lecture
Nov. 20, 2014	Prof. Thomas Kaufmann	Cell Death in the Immune System

Lectures for Natural Sciences Faculty: Molecular Biology of Inflammation (Coordinator: Prof. Britta Engelhardt)

Date	Lecturer	Title of the lecture
April 3, 2014	Prof. Andrea Huwiler Dr. Stephanie Schwalm	Lipid mediators in tissue trafficking
May 8, 2014	Prof. Shida Yousefi	Inflammation – good or bad? Resolution of inflammation - apoptosis

Practical work for Natural Science Faculty: Immunology II (Coordinator: PD Dr. Andreas Marti)

Date	Lecturer	Title of the lecture
Dec. 4, 2014	Prof. Hans-Uwe Simon PD Dr. Stephan von Gunten Prof. Thomas Kaufmann Dr. Christina Merz-Stöckle	Immunological Methods (1 day)
Dec. 5, 2014	Prof. Hans-Uwe Simon PD Dr. Stephan von Gunten Prof. Thomas Kaufmann Dr. Christina Merz-Stöckle	Immunological Methods (1 day)
Dec. 11, 2014	Prof. Hans-Uwe Simon PD Dr. Stephan von Gunten Prof. Thomas Kaufmann Dr. Christina Merz-Stöckle	Immunological Methods (1 day)
Dec. 12, 2014	Prof. Hans-Uwe Simon PD Dr. Stephan von Gunten Prof. Thomas Kaufmann Dr. Christina Merz-Stöckle	Immunological Methods (1 day)
Dec. 18, 2014	Prof. Hans-Uwe Simon PD Dr. Stephan von Gunten Prof. Thomas Kaufmann Dr. Christina Merz-Stöckle	Immunological Methods (1 day)

Dec. 19, 2014	Prof. Hans-Uwe Simon PD Dr. Stephan von Gunten Prof. Thomas Kaufmann Dr. Christina Merz-Stöckle	Evaluation (4 h)

Lectures for Biomedical Sciences Students (B.Sc. program, Fribourg): General Pharmacology (Coordination by the University of Fribourg)

Date	Lecturer	Title of the lecture
Nov. 13, 2014	Dr. Christina Merz-Stöckle	Pharmacogenetics
Nov. 13, 2014	Dr. Christina Merz-Stöckle	Personalized Medicine

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
Sept. 26, 2014	Prof. Uwe Zangemeister-Wittke	Heart and vascular system
Oct. 10, 2014	Prof. Thomas Kaufmann	Immune system
Oct. 3, 2014	Prof. Shida Yousefi	Antiinfectious therapy
Sept. 19, 2014	PD Dr. Stephan von Gunten	Pharmacology of the Gastrointestinal System
Oct. 24, 2014	PD Dr. Stephan von Gunten	Endocrine and Reproductive system
Oct. 30, 2014	Prof. Andrea Huwiler	Nervous system
Nov. 14, 2014	Prof. Shida Yousefi	Lungs and kidneys
Nov. 7, 2014	PD Dr. David Spirk	Haemopoietic system and haemostasis

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
Sept. 22, 2014	Prof. Thomas Kaufmann	Cell damage

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

Date	Lecturer	Title of the lecture
Nov. 14, 2014	Prof. Shida Yousefi	Laser scanning microscopy and applications

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

Date	Lecturer	Title of the lecture
Jan. 27, 2014	PD Dr. Stephan von Gunten	Pharmacology Part 1
Febr. 2, 2014	PD Dr. Stephan von Gunten	Pharmacology Part 2

External teaching activities: University of Fribourg (Biochemistry); M.Sc. program and PhD students Biochemistry

Date	Lecturer	Title of the lecture
Febr. & March 2014 (total 8h)	Prof. Thomas Kaufmann	Apoptosis: Mechanisms, Techniques & Therapeutic Targets

External teaching activities: University of Zurich (Molecular Medicine)

Date	Lecturer	Title of the lecture
May 2014 (total 6h)	Prof. Uwe Zangemeister-Wittke	Molecular Cell Biology for students of human and dental medicine

External teaching activities: University of Ljubljana (Swiss-European Mobility Program, Pharmacy)

Date	Lecturer	Title of the lecture
April 2014	Prof. Hans-Uwe Simon	Pharmacology, Cell Biology, and Immunology for Pharmacy students
Sept. 2014 (total 16h)	Prof. Hans-Uwe Simon	Pharmacology, Cell Biology, and Immunology for Pharmacy students

3.2. Coordination PBL Medical Students, 3rd year (2014/2015)

Core group:
Prof. Andrea Huwiler

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

3.3. Tutorials (study year 2014/2015)

Medical students 3rd year:

PD Dr. David Spirk	PD Dr. Stephan von Gunten
Prof. Thomas Kaufmann	Dr. Christina Merz-Stöckle
Dr. Zhaoyue He	Dr. He Liu

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

3.4. Seminars of Invited Speakers

Date	Teacher	Title of the seminar
Jan. 29, 2014	Miro Eigenmann M.Sc. student of Biomedicine, University of Bern (CH)	Mechanism-based PK/PD modeling to quantitatively compare the anticancer effect of erlotinib versus gefitinib in A431 xenograft mice
Febr. 12, 2014	Prof. Dr. Benoît Zuber Institute of Anatomy, University of Bern (CH)	An introduction to serial block face scanning electron microscopy: obtaining 3-dimensional reconstruction of large biological samples with high resolution
Febr. 19, 2014	Prof. Dr. Liliana Schäfer Institute of General Pharmacology and Toxicology, University of Frankfurt/Main (D)	Proteoglycan signaling in inflammation
April 2, 2014	Prof. Dr. Donald R. Branch Toronto General Research Inst. and Canadian Blood Services, University of Toronto (CAN)	HIV infection: Who ya gonna call? Srcman

April 9, 2014	Dr. Nima Etemadi The Walter and Eliza Hall Institute of Medical Research, Melbourne (AUS)	The role of TRAF2 in skin homeostasis
June 4, 2014	Dr. Martina Mattii, Zentrum Allergie & Umwelt, Technical University and Helmholtz Zentrum Munich (D)	Inflammatory skin disorders as a model to study immune functions
July 2, 2014	Prof. Dr. Jan Lünemann, Institute of Exp. Immunology University of Zurich (CH)	IgG-Glycoforms and disease activity in patients with peripheral nervous system autoimmunity
Nov. 7, 2014	Dr. Laurent Gelman Friedrich Miescher Institute, Basel (CH)	Image analysis: ImageJ / FIJI workshop
Nov. 19, 2014	Prof. Dr. Robert Feil Interfaculty Institute of Bio-Chemistry, University Tübingen (D)	cGMP signaling in cell growth and plasticity

3.5. Inaugural Lecture **(Venia docendi)**

Date	**Lecturer**	**Title**
June 24, 2014	Prof. Dr. Thomas Kaufmann Institute of Pharmacology, University of Bern (CH)	Only happy when the cells die

3.6. Bern Immunology Club (BIC)

Date	**Teacher**	**Title of the seminar**
Jan. 29, 2014	Prof. Dr. Anjte Prasse University Medical Center, Freiburg (D)	Defining new pathomechanisms for idiopathic pulmonary fibrosis

Febr. 26, 2014	Prof. Dr. Pedro Romero Ludwig Center for Cancer Res. Department of Oncology, University of Lausanne (CH)	Regulation of tumor antigen-specific CD8 T cell-mediated immunity
March 26, 2014	Dr. Stefan Freigang Institute of Pathology, University of Bern (CH)	Mitochondrial control of chronic vascular inflammation in atherosclerosis
April 30, 2014	PD Dr. Stephan von Gunten Institute of Pharmacology, University of Bern (CH)	Sweet - and sometimes fatal: glycans from an immunological perspective
May 21, 2014	Prof. Dr. Rudolf Valenta Medical University Institute of Pathophysiology and Allergy Research, Wien (A)	From allergen genes to new forms of diagnosis and treatment of allergy
June 25, 2014	Prof. Dr. Urs Dahinden Institute of Mass Communi-cation and Media Research, University of Zurich (CH)	Science on the media radar – Opportunities, threats and some suggestions for a productive relationship
Sept. 24, 2014	Clinical Immunological Conference: Tumorimmunology (Organizer: Prof. Dr. Adrian Ochsenbein, Inselspital)	
	Prof. Dr. Alfred Zippelius (Basel)	Harnessing the immune system to treat cancer: from mouse models to patients and vice versa
	Prof. Dr. Maries van den Broek (Zürich)	Complement is a central mediator of radiotherapy-induced tumor-specific immunity and clinical response
	Prof. Dr. Daniel Speiser Lausanne	CD8 T cells target both pillars of malignant tumors
Nov. 26, 2014	Prof. Dr. A. Ochsenbein, chair Dr. Stefan Kuchen, RIA PD Dr. Charaf Benarafa, TKI Dr. Carsten Riether, DKF Dr. Leslie Saurer, Pathology	Highlights of the Year
Dec. 1, 2014	Prof. Dr. Antonio Lanzavecchia Institute for Research in Biomedicine (IRB), Bellinzona (CH)	Dissecting the antibody response to pathogens and self antigens

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For the current program of the Bern Immunology Club (BIC), please consult the following website: http://www.bic.unibe.ch/content/teaching/bic_lectures_2015/index_eng.html

3.8. Academic Degrees

David Spirk, PD Dr. med. (Habilitation), University of Bern

Faik Imeri, PhD, University of Bern
Thesis: Novel oxazolo-oxazole derivatives of FTY720 reduce endothelial cell permeability, immune cell chemotaxis and symptoms of experimental autoimmune encephalomyelitis in mice (October 2014)
Supervisor: Prof. Andrea Huwiler

Saša Rožman, PhD, University of Bern
Thesis: The role of autophagy in neutrophil differentiation and function (December 2014)
Supervisor: Prof. Hans-Uwe Simon

Ramona Reinhart, M.Sc., University of Bern
Thesis: Regulation of cell survival and cell death in mouse basophils (January 2014)
Supervisor: Prof. Thomas Kaufmann

Tatiana Vogel, M.Sc. pharm., University of Basel
Thesis: Hypoxia – induced effets in atopic dermatitis (Juni 2014)
Supervisors: Prof. Dagmar Simon, Prof. Hans-Uwe Simon

Matthias Widmer, M.Sc. pharm., University of Basel
Thesis: Impact of autophagy-related protein 12 (ATG12) on mitochondrial biogenesis (Juni 2014)
Supervisors: Prof. Hans-Uwe Simon, Dr. He Liu

Nina Germic, M.Sc. pharm., University of Ljubljana
Thesis: Subcellular localization of autophagy-related protein 12 (Sept. 2014)
Supervisor: Prof. Hans-Uwe Simon, Prof. Irena Mlinaric-Rascan

Muriel Ott, MMed, University of Bern
Thesis: Expression of Siglecs on dendritic cells (February 2014)
Supervisors: PD Dr. Stephan von Gunten, Fabiola Schorer

Research Activities

4.1. Research Projects and Publications

Group Prof. Andrea Huwiler

Group members: Olivier Blanchard, PhD student[1]
Daniel Fallegger, PhD student[1]
Iuliia Filipenko, PhD student[1]
Faik Imeri, PhD student[1]
Aurelio Lendro Jenni, PhD student
Oleksandr Pastukhov, PhD student[1]
Marianne Maillard-van Laer, technician[1]
Dr. Doriano Fabbro, PhD, guest senior scientist[1]
Dr. Stephanie Schwalm, Postdoc[2]
Isolde Römer, technician[2]
Svetlana Kokin, technician[2]

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

Our research is focused on sphingolipids and their contribution to physiological processes and pathological diseases. On the one side sphingolipids including ceramide, sphingosine 1-phosphate, sphingosylphosphorylcholine and the therapeutically used FTY720 are used to identify signal transduction pathways mediated by these lipids which may point to novel functions of these lipids. On the other side the regulation of sphingolipid-generating and -degrading enzymes (ceramidases, sphingosine kinases, ceramide kinase) are investigated 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/or death.

The ceramide kinase inhibitor NVP-231 inhibits breast and lung cancer cell proliferation by inducing M phase arrest and subsequent cell death

O. Pastukhov, S. Schwalm, U. Zangemeister-Wittke, D. Fabbro, F. Bornancin, L. Japtok, B. Kleuser, J. Pfeilschifter, A. Huwiler

BACKGROUND AND PURPOSE: Ceramide kinase (CerK) catalyzes the generation of ceramide-1-phosphate which may regulate various cellular functions, including inflammatory reactions and cell growth. Here, we studied the effect of a recently developed CerK inhibitor, NVP-231, on cancer cell proliferation and viability and investigated the role of cell cycle regulators implicated in these responses.
EXPERIMENTAL APPROACH: The breast and lung cancer cell lines MCF-7 and NCI-H358 were treated with increasing concentrations of NVP-231 and DNA synthesis, colony formation and cell death were determined. Flow cytometry was performed to analyse cell

cycle distribution of cells and Western blot analysis was used to detect changes in cell cycle regulator expression and activation.
KEY RESULTS: In both cell lines, NVP-231 concentration-dependently reduced cell viability, DNA synthesis and colony formation. Moreover it induced apoptosis, as measured by increased DNA fragmentation and caspase-3 and caspase-9 cleavage. Cell cycle analysis revealed that NVP-231 decreased the number of cells in S phase and induced M phase arrest with an increased mitotic index, as determined by increased histone H3 phosphorylation. The effect on the cell cycle was even more pronounced when NVP-231 treatment was combined with staurosporine. Finally, overexpression of CerK protected, whereas down-regulation of CerK with siRNA sensitized, cells for staurosporine-induced apoptosis.
CONCLUSIONS AND IMPLICATIONS: Our data demonstrate for the first time a crucial role for CerK in the M phase control in cancer cells and suggest its targeted inhibition, using drugs such as NVP-231, in combination with conventional pro-apoptotic chemotherapy.
See original publication No. 1

Ceramide kinase contributes to proliferation but not to prostaglandin E2 formation in renal mesangial cells and fibroblasts
O. Pastukhov, S. Schwalm, I. Römer, U. Zangemeister-Wittke, J. Pfeilschifter,
A. Huwiler
BACKGROUND/AIMS: Ceramide kinase (CerK) catalyzes the generation of the sphingolipid ceramide-1-phosphate (C1P) which regulates various cellular functions including cell growth and death, and inflammation. Here, we used a novel catalytic inhibitor of CerK, NVP-231, and CerK knockout cells to investigate the contribution of CerK to proliferation and inflammation in renal mesangial cells and fibroblasts.
METHODS: Cells were treated with NVP-231 and [(3)H]-thymidine incorporation into DNA, [(3)H]-arachidonic acid release, prostaglandin E2 (PGE2) synthesis, cell cycle distribution, and apoptosis were determined.
RESULTS: Treatment of rat mesangial cells and mouse renal fibroblasts with NVP-231 decreased DNA synthesis, but not of agonist-stimulated arachidonic acid release or PGE2 synthesis. Similarly, proliferation but not arachidonic acid release or PGE2 synthesis was reduced in CERK knockout renal fibroblasts. The anti-proliferative effect of NVP-231 on mesangial cells was due to M phase arrest as determined using the mitosis markers phospho-histone H3, cdc2 and polo-like kinase-1, and induction of apoptosis. Moreover, loss of CerK sensitized cells towards stress-induced apoptosis.
CONCLUSIONS: Our data demonstrate that CerK induces proliferation but not PGE2 formation of renal mesangial cells and fibroblasts, and suggest that targeted CerK inhibition has potential for treating mesangioproliferative kidney diseases.
See original publication No. 2

Novel oxazolo-oxazole derivatives of FTY720 reduce endothelial cell permeability, immune cell chemotaxis and symptoms of experimental autoimmune encephalomyelitis in mice
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D. Meyer zu Heringdorf, T. Homann, B. Kleuser, J. Pfeilschifter, B. Engelhardt,
H. Stark, A. Huwiler
The immunomodulatory FTY720 (fingolimod) is presently approved for the treatment of relapsing-remitting multiple sclerosis. It is a prodrug that acts by modulating sphingosine 1-phosphate (S1P) receptor signaling. In this study, we have developed and characterized two novel oxazolo-oxazole derivatives of FTY720, ST-968 and the oxy analog ST-1071, which require no preceding activating phosphorylation, and proved to be active in intact cells and triggered S1P1 and S1P3, but not S1P2, receptor internalization as a result of receptor

activation. Functionally, ST-968 and ST-1071 acted similar to FTY720 to abrogate S1P-triggered chemotaxis of mouse splenocytes, mouse T cells and human U937 cells, and reduced TNFa- and LPS-stimulated endothelial cell permeability. The compounds also reduced TNFα-induced ICAM-1 and VCAM-1 mRNA expression, but restored TNFα-mediated downregulation of PECAM-1 mRNA expression. In an in vivo setting, the application of ST-968 or ST-1071 to mice resulted in a reduction of blood lymphocytes and significantly reduced the clinical symptoms of experimental autoimmune encephalomyelitis (EAE) in C57BL/6 mice comparable to FTY720 either by prophylactic or therapeutic treatment. In parallel to the reduced clinical symptoms, infiltration of immune cells in the brain was strongly reduced, and in isolated tissues of brain and spinal cord, the mRNA and protein expressions of ICAM-1 and VCAM-1, as well as of matrix metalloproteinase-9 were reduced by all compounds, whereas PECAM-1 and tissue inhibitor of metalloproteinase TIMP-1 were upregulated. In summary, the data suggest that these novel butterfly derivatives of FTY720 could have considerable implication for future therapies of multiple sclerosis and other autoimmune diseases.

See original publication No. 3

Synthesis and cellular characterization of novel isoxazolo- and thiazolohydrazinylidene-chroman-2,4-diones on cancer and non-cancer cell growth and death

A. Jashari, F. Imeri, L. Ballazhi, A. Shabani, B. Mikhova, G. Dräger, E. Popovski, A. Huwiler

Coumarins are extensively studied anticoagulants that exert additional effects such as anticancerogenic and even anti-inflammatory. In order to find new drugs with anticancer activities, we report here the synthesis and the structural analysis of new coumarin derivatives which combine the coumarin core and five member heterocycles in hydrazinylidene-chroman-2,4-diones. The derivatives were prepared by derivatization of the appropriate heterocyclic amines which were used as electrophiles to attack the coumarin ring. The structures were characterized by spectroscopic techniques including IR, NMR, 2D-NMR and MS. These derivatives were further characterized especially in terms of a potential cytotoxic and apoptogenic effect in several cancer cell lines including the breast and prostate cancer cell lines MCF-7, MDA-MB-231, PC-3, LNCaP, and the monocytic leukemia cell line U937. Cell viability was determined after 48 h and 72 h of treatment with the novel compounds by MTT assay and the 50% inhibitory concentrations (EC50 values) were determined. Out of the 8 novel compounds screened for reduced cell viability, 4c, 4d and 4e were found to be the most promising and effective ones having EC50 values that were several fold reduced when compared to the reference substance 4-hydroxycoumarin. However, the effects were cancer cell line dependent. The breast cancer MDA-MB-231 cells, the prostate cancer LNCaP cells, and U937 cells were most sensitive, MCF-7 cells were less sensitive, and PC-3 cells were more resistant. Reduced cell viability was accompanied by increased apoptosis as shown by PARP-1 cleavage and reduced activity of the survival protein kinase Akt. In summary, this study has identified three novel coumarin derivatives that in comparison to 4-hydroxycoumarin have a higher efficiency to reduce cancer cell viability and trigger apoptosis and therefore may represent interesting novel drug candidates.

See original publication No. 4

Original publications

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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 (patho-)physiologically most relevant form of PCD, whereas the physiological role of necroptosis is far less well understood. Given that apoptosis suppresses necroptotic pathways, necroptosis is hypothesized as a backup strategy for a cell to die by a proinflammatory form of 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 varies from activation of the cells and production of proinflammatory cytokines to cell death by apoptosis or by necroptosis. This outcome is tightly regulated and complex and - among others - depends on the so-called inhibitor of apoptosis family (IAPs). Our ongoing projects in the lab identify the IAP member XIAP as an important inhibitor of necroptotic cell death downstream of death receptors. XIAP, which was initially identified as an inhibitor of apoptotic caspases and also carries an E3 ligase conferring RING domain, clearly has important functions other than blocking caspases. Our data indicate that XIAP may act much more upstream in death receptor signalling than previously assumed; the exact molecular functions of XIAP's E3 ligase activity are under investigation. Interestingly, XIAP also keeps overreaction of inflammatory responses upon encounter with danger signals (such as exuberant production of IL-1beta in response to bacterial LPS) in check, thereby placing XIAP 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 therefore invested time to establish conditionally immortalized progenitor cell lines ("Hoxb8 cells") that are committed to the macrophage/neutrophil- or the basophil lineages and can be differentiated *in vitro* in nearly unlimited numbers. Another great advantage over primary granulocytes is the easy genetic manipulation of these Hoxb8 cells, 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 IgE receptors by antigen, activate these cells, and if/how those stimuli increase basophils/ mast cells 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 (BH3-mimetics) are tested in our lab for their potential to kill activated leukocyte populations selectively.

Classical apoptosis is strongly regulated in most cells by the BCL-2 protein family, which regulates the mitochondrial integrity. Currently of great interest to our research lab is the pro-apoptotic member BOK. BOK has raised much interest recently, as it was show to be deleted in human cancers with surprisingly high frequency. Several cancer models with a newly developed *Bok*-deficient mouse are ongoing in our lab and in collaboration with others to test the tumour suppressor potential of *Bok*. Other projects focus on the molecular function of this still rather enigmatic BCL-2 family member. 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 defects of *Bok*-deficient cells in some forms of ER stress response. Interestingly, BOK is by far the BCL-2 family member most clearly and strongly 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 on the ER/Golgi and the role of BOK in the nucleus, for which we hypothesize a role in the regulation cellular proliferation.

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6. S. Rozman, S. Yousefi, K. Oberson, **T. Kaufmann**, C. Benarafa, H.-U. Simon: The generation of neutrophils in the bone marrow is controlled by autophagy.
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Review articles/Editorials

1. L. Galluzzi, J.M. Bravo-San Pedro, I. Vitale, …..**T. Kaufmann**, …., G. Kroemer: Essential versus accessory aspects of cell death: recommendations of the NCCD 2015.
Cell Death Differ. 22 (2015), 58-73

2. **T. Kaufmann**, H.-U. Simon: Targeting disease by immunomodulation.
Cell Death Diff. 22 (2015), 185-186.

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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, cystic fibrosis, sepsis, 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 2014.

DAPK2 positively regulates motility of neutrophils and eosinophils in response to intermediary chemoattractants

B. Geering, C. Stoeckle, S. Rozman, K. Oberson, C. Benarafa, H.-U. Simon

The tight regulation of granulocyte chemotaxis is crucial for initiation and resolution of inflammation. Here, we show that death-associated protein kinase-2 (DAPK2), a Ca^{2+}/CaM-sensitive serine/threonine kinase known to modulate cell death in various cell types, is a novel regulator of migration in granulocytes. We demonstrate that both human neutrophils and eosinophils express DAPK2, but, unlike other leukocytes, no DAPK1 or DAPK3 protein. When DAPK activities were blocked by inhibitors, we found that neither granulocyte life span nor phagocytosis were affected. However, such pharmacological inactivation of DAPK activity abolished motility of granulocytes in response to intermediary, but not end-target chemoattractants *ex vivo*. The defect in chemotaxis in DAPK2-inactive granulocytes is likely due to reduced polarization of the cells, mediated by a lack of myosin light chain phosphorylation resulting in radial F-actin and pseudopod formation. Because neutrophils treated with DAPK inhibitors also showed reduced recruitment to the site of inflammation in a mouse peritonitis model, DAPK2 may be a novel target for anti-inflammatory therapies.

See original publication No. 1

The generation of neutrophils in the bone marrow is controlled by autophagy

S. Rozman, S. Yousefi, K. Oberson, T. Kaufmann, C. Benarafa, H.-U. Simon

Autophagy has been demonstrated to play an essential function in several cellular hematopoietic differentiation processes, e.g. the differentiation of reticulocytes. In order to investigate the role of autophagy in neutrophil granulopoiesis, we studied neutrophils lacking *autophagy-related (Atg) 5*, a gene encoding a protein essential for autophagosome formation. Using Cre-recombinase mediated gene deletion, *Atg5*-deficient neutrophils showed no evidence of abnormalities in morphology, granule protein content, apoptosis regulation, migration, or effector functions. In such mice, however, we observed an increased proliferation rate in the neutrophil precursor cells of the bone marrow as well as an accelerated process of neutrophil differentiation, resulting in an accumulation of mature neutrophils in the bone marrow, blood, spleen, and lymph nodes. To directly study the role of autophagy in neutrophils, we employed an *in vitro* model of differentiating neutrophils that allowed modulating the levels of ATG5 expression, or, alternatively, intervening pharmacologically with autophagy-regulating drugs. We could show that autophagic activity correlated inversely with the rate of neutrophil differentiation. Moreover, pharmacological inhibition of p38 MAPK or mTORC1 induced autophagy in neutrophilic precursor cells and blocked their differentiation, suggesting that autophagy is negatively controlled by the p38 MAPK – mTORC1 signaling pathway. On the other hand, we obtained no evidence for an involvement of the PI3K-AKT or ERK1/2 signaling pathways in the regulation of neutrophil differentiation. Taken together, these findings show that, in contrast to erythropoiesis, autophagy is not essential for neutrophil granulopoiesis, having instead a negative impact on the generation of neutrophils. Thus, autophagy and differentiation exhibit a reciprocal regulation by the p38 – mTORC1 axis.

See original publication No. 4

Toxicity of eosinophil MBP is repressed by intracellular crystallization and promoted by extracellular aggregation

A. Soragni, S. Yousefi, C. Stoeckle, A.B. Soriaga, M.R. Sawaya, E. Kozlowski, I. Schmid, S. Radonjic-Hoesli, S. Boutet, G.J. Williams, M. Messerschmidt, M.M. Seibert, D. Cascio, N.A. Zatsepin, M. Burghammer, C. Riekel, J.-P. Colletier, R. Riek, D. Eisenberg, H.-U. Simon

Eosinophils are white blood cells that function in innate immunity and participate in the pathogenesis of various inflammatory and neoplastic disorders. Their secretory granules contain four cytotoxic proteins, including the eosinophil major basic protein (MBP-1). How

MBP-1 toxicity is controlled within the eosinophil itself yet activated upon extracellular release is unknown. Here we show how intragranular MBP-1 nanocrystals restrain toxicity enabling its safe storage and characterize them with an x-ray free electron laser. Following eosinophil activation, MBP-1 toxicity is triggered by granule acidification followed by extracellular aggregation which mediates damage to pathogens and host cells. Larger non-toxic amyloid plaques are also present in tissues of eosinophilic patients, in a feedback mechanism which likely limits tissue damage under pathological conditions of MBP-1 oversecretion. Our results suggest that MBP-1 aggregation is important for innate immunity and immunopathology mediated by eosinophils and clarify how its polymorphic self-association pathways regulate toxicity intra- and extracellularly.
See original publication No. 5

Original publications

1. B. Geering, C. Stoeckle, S. Rozman, K. Oberson, C. Benarafa, **H.-U. Simon**: DAPK2 positively regulates motility of neutrophils and eosinophils in response to intermediary chemoattractants.
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4. D. Simon, A. Straumann, **H.-U. Simon**: Eosinophilic esophagitis and allergy.
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5. C. Houriet, **H.-U. Simon**, D. Simon: Hypereosinophiliesyndrome.
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6. S. Radonjic-Hoesli, **H.-U. Simon:** Eosinophils.
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10. L. Galluzzi, J.M. Bravo-San Pedro, I. Vitale, …..**H.-U. Simon**, …., G. Kroemer: Essential versus accessory aspects of cell death: recommendations of the NCCD 2015.
Cell Death Differ. 22 (2015), 58-73

11. T. Kaufmann, **H.-U. Simon**: Targeting disease by immunomodulation.
Cell Death Diff. 22 (2015), 185-186.

12. H. Liu, Z. He, **H.-U. Simon**: Protective role of autophagy and autophagy related protein 5 in early tumorigenesis.
J. Mol. Med., in press.

13. L. Galluzzi, F. Pietrocola, J.M. Bravo-San Pedro, ..., **H.-U. Simon**, ..., G. Kroemer: Multifaceted impact of autophagy on malignant transformation and tumor progression.
EMBO J., in press.

Book chapters

1. S. Radonjic-Hoesli, **H.-U. Simon:** Eosinophils. In: History of Allergy. Chem Immunol Allergy (Eds. K.-C. Bergmann and J. Ring). Karger, Basel (CH), 2014, p. 193-204.

2. **H.-U. Simon:** Eosinophils. In: Global Atlas of Allergy (Eds. C.A. Akdis and I. Agache). European Academy of Allergy and Clinical Immunology (EAACI), 2014, p. 58-59.

3. D. Simon, **H.-U. Simon**, S. Yousefi: Eosinophil extracellular trap formation in response to thymic stromal lymphopoietin stimulation. In: Allergic Diseases: from Mechanisms to Cures (Eds. S.J. Galli and Y.-Y. Kim); Pacini Editore S.p.A., Pisa, 2014, p. 83-86.

4. S. Yousefi, D. Simon, **H.-U. Simon**: Eosinophil extracellular traps: potential role(s) in eosinophilic diseases. In: Allergic Diseases: from Mechanisms to Cures (Eds. S.J. Galli and Y.-Y. Kim); Pacini Editore S.p.A., Pisa, 2014, p. 87-89.

5. S. Radonjic-Hoesli, **H.-U. Simon:** Eosinophile Granulozyten. In: Allergologie (Eds. T. Biedermann, W. Heppt, H. Renz, M. Röcken); 2. Auflage. Springer-Verlag, Heidelberg-Berlin, in press.

Group PD Dr. Stephan von Gunten

Group members: Dr. Denise Dorvignit Pedroso, guest scientist
Kayluz Frias Boligan, PhD student
Christoph Schneider, PhD student
Fabiola Schorer, PhD student
Katharina Fuchs, MMed student
Christine Gallasz, MD student
Ariane Meister, MMed student
Jonathan Eastline, MMed student
Michael Eastline, MMed student
Muriel Ott, MMed student
Rebecca Strässle, MMed student
Sinuhe Nussbaum, MMed student

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

Human IgA Fc receptor FcαRI (CD89) triggers different forms of neutrophil death depending on the inflammatory microenvironment

M. Wehrli, F. Cortinas-Elizondo, R. Hlushchuk, F. Daudel, P.M. Villiger, S. Miescher, A.W. Zuercher, V. Djonov, H.-U. Simon, S. von Gunten

Despite the paradigm that carbohydrates are T cell–independent antigens, isotype-switched glycan-specificimmunoglobulin G (IgG) antibodies and polysaccharide-specific T cells are found in humans. We used a systems level approach combined with glycan array technology to decipher the repertoire of carbohydrate-specific IgG antibodies in intravenous and subcutaneous immunoglobulin preparations. A strikingly universal architecture of this repertoire with modular organization among different donor populations revealed an association between immunogenicity or tolerance and particular structural features of glycans. Antibodies were identified with specificity not only for microbial antigens but also for a broad spectrum of host glycans that serve as attachment sites for viral and bacterial pathogens and/or exotoxins. Tumor-associated carbohydrate antigens were differentially detected by IgG antibodies, whereas non-IgG2 reactivity was predominantly absent. Our study highlights the power of systems biology approaches to analyze immune responses and reveals potential glycan antigen determinants that are relevant to vaccine design, diagnostic assays, and antibody-based therapies.

See original publication No. 1

Interactions between Siglec-7/9 receptors and ligands influence NK cell-dependent tumor immunosurveillance

C. Jandus, K. Frias Boligan, O. Chijioke, H. Liu, M. Dahlhaus, T. Démoulins, C. Schneider, M. Wehrli, R.E. Hunger, G.M. Baerlocher, H.-U. Simon, P. Romero, C. Münz, S. von Gunten

Alteration of the surface glycosylation pattern on malignant cells potentially affects tumor immunity by directly influencing interactions with glycan-binding proteins (lectins) on the surface of immunomodulatory cells. The sialic acid-binding Ig-like lectins Siglec-7 and -9 are MHC class I-independent inhibitory receptors on human NK cells that recognize sialic acid-containing carbohydrates. Here, we found that the presence of Siglec-9 defined a subset of cytotoxic NK cells with a mature phenotype and enhanced chemotactic potential. Interestingly, this Siglec-9+ NK cell population was reduced in the peripheral blood of cancer patients. Broad analysis of primary tumor samples revealed that ligands of Siglec-7 and -9 were expressed on human cancer cells of different histological types. Expression of Siglec-7 and -9 ligands was associated with susceptibility of NK cell-sensitive tumor cells and, unexpectedly, of presumably NK cell-resistant tumor cells to NK cell-mediated cytotoxicity. Together, these observations have direct implications for NK cell-based therapies and highlight the requirement to consider both MHC class I haplotype and tumor-specific glycosylation.

See original publication No. 3

The human IgG anti-carbohydrate repertoire exhibits a universal architecture and contains specificity for microbial attachment sites

C. Schneider, D.F. Smith, R.D. Cummings, K. Frias Boligan, R.G. Hamilton, B.S. Bochner, S. Miescher, H.-U. Simon, A. Pashov, T. Vassilev, S. von Gunten

Despite the paradigm that carbohydrates are T cell-independent antigens, isotype-switched glycan-specific immunoglobulin G (IgG) antibodies and polysaccharide-specific T cells are found in humans. We used a systems-level approach combined with glycan array technology to decipher the repertoire of carbohydrate-specific IgG antibodies in intravenous and subcutaneous immunoglobulin preparations. A strikingly universal architecture of this repertoire with modular organization among different donor populations revealed an association between immunogenicity or tolerance and particular structural features of glycans. Antibodies were identified with specificity not only for microbial antigens but also for a broad spectrum of host glycans that serve as attachment sites for viral and bacterial pathogens and/or exotoxins. Tumor-associated carbohydrate antigens were differentially detected by IgG antibodies, whereas non-IgG2 reactivity was predominantly absent. Our study highlights the power of systems biology approaches to analyze immune responses and reveals potential glycan antigen determinants that are relevant to vaccine design, diagnostic assays, and antibody-based therapies.

See original publication No. 4

Original publications

1. M. Wehrli, F. Cortinas-Elizondo, R. Hlushchuk, F. Daudel, P.M. Villiger, S. Miescher, AW Zuercher, V. Djonov, H.-U. Simon, **S. von Gunten**: Human IgA Fc receptor FcaRI (CD89) triggers different forms of neutrophil death depending on the inflammatory microenvironment.
J. Immunol. 193 2014, 5649-59.

2. S.R. Stowell, C.M. Arthur, R. McBride, O. Berger, N. Razi, J. Heimburg-Molinaro, L.C. Rodrigues, J.P. Gourdine, A.J. Noll, **S. von Gunten**, D.F. Smith, Y.A. Knirel, J.C. Paulson, R.D. Cummings: Microbial glycan microarrays define key features of host-microbial interactions.
Nat. Chem. Biol. 10 (2014), 470–476.

3. C. Jandus, K. Frias Boligan, O. Chijioke, H. Liu, M. Dahlhaus, T. Démoulins, C. Schneider, M. Wehrli, RE Hunger, GM Baerlocher, H.-U. Simon, P. Romero, C. Münz, **S. von Gunten**: Interactions between Siglec-7/9 receptors and ligands influence NK cell-dependent tumor immunosurveillance.
J Clin Invest. 124 (2014), 1810-1820.

4. C. Schneider, D.F. Smith, R.D. Cummings, K.F. Boligan, R.G. Hamilton, B.S. Bochner, S. Miescher, H.-U. Simon, A. Pashov, T. Vassilev, **S. von Gunten**: The human IgG anti-carbohydrate repertoire exhibits a universal architecture and contains specificity for microbial attachment sites.
Sci. Transl. Med. 7 (2015), 269ra1

Review articles/Editorials

1. **S. von Gunten**, Y. Shoenfeld, M. Blank, D.R. Branch, T. Vassilev, F. Käsermann, J. Bayry, S. Kaveri, H.-U. Simon: IVIG pluripotency and the concept of Fc-sialylation: challenges to the scientist.
Nat. Rev. Immunol. 14 (2014), 349.

2. **S. von Gunten**: Protein-glycan interactions as targets of intravenous/subcutaneous immunoglobulin (IVIg/SCIg) preparations.
Clin. Exp. Immunol. 178 (2014) Suppl 1, 151-152.

3. **S. von Gunten:** Targeting Siglecs: Neue potenzielle Strategien zur Immuntherapie entzündlicher oder maligner Erkrankungen.
Leading Opinions in Hämatologie und Onkologie 2 (2014), 82–84.

4. K.F. Boligan, C. Mesa, L.E. Fernandez, **S. von Gunten**: Cancer intelligence acquired (CIA): tumor glycosylation and sialylation codes dismantling antitumor defense.
Cell Mol. Life Sci., in press.

Group Prof. Shida Yousefi

Group members: Poorya Amini, PhD student*
Evelyne Kozlowski, technician*
Kevin Oberson, technician (70%)*
Inès Schmid, head technician*
Darko Stojkov, PhD student*

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

We are interested in molecular mechanisms regulating granulocyte functions, such as the release of inflammatory mediators. This includes cell signaling and death pathways. To understand gene functions, we established a lentiviral gene transfer technology in our institute that can be used to modify the expression of genes in *in vitro* and *in vivo* experimental systems. Moreover, we are specialized in using confocal microscopy and imaging analysis. Recently, we became interested in an exciting new field of granulocyte biology that is the investigation of both mechanism and function of mitochondrial DNA release by eosinophils, neutrophils, and basophils.

Basophils exhibit NADPH oxidase-independent antibacterial activity through elaboration of extracellular DNA traps
M. Morshed, R. Hlushchk, D. Simon, A.F. Walls, K. Obata-Ninomiya, H. Karasuyama, V. Djonov, T. Kaufmann, H.-U. Simon, S. Yousefi
Basophils are primarily associated with a pro-inflammatory and immunoregulatory role in allergic diseases and parasitic infections. Recent studies have shown that basophils can also bind various bacteria both in the presence and the absence of opsonizing antibodies. In this report, we show that both human and mouse basophils are able to produce mitochondrial reactive oxygen species and to form extracellular DNA traps upon IL-3 priming and subsequent activation of the complement factor 5 or high-affinity IgE receptor. Such basophil extracellular traps (BETs) contain mitochondrial, but not nuclear DNA, as well as the granule proteins basogranulin and mouse mast cell protease 8. By means of BET formation, basophils are able to kill bacteria, even though they lack both functional NADPH oxidase and the ability to phagocytose bacteria. BETs can be found in both human and mouse inflamed tissues, suggesting that they also play a role under *in vivo* inflammatory conditions. Taken together, these findings indicate that basophils exert direct innate immune effector functions against bacteria in the extracellular space.
See original publication No. 1

Original publications

1. M. Morshed, R. Hlushchuk, D. Simon, A.F. Walls, K. Obata-Ninomiya, H. Karasuyama, V. Djonov, A. Eggel, T. Kaufmann, H.-U. Simon, **S. Yousefi**: NADPH oxidase-independent formation of extracellular DNA traps by basophils.
J. Immunol. 192 (2014), 5314-5323.
Comment in: J. Immunol. 192 (2014):
www.jimmunol.org/cgi/doi/10.4049/jimmunol.1490018: BET-ing Basophils

2. H.-U. Simon, **S. Yousefi**, I. Schmid, R. Friis: ATG5 can regulate p53 expression and activation.
Cell Death Dis. 5 (2014), e1339.

3. S. Rozman, **S. Yousefi**, K. Oberson, T. Kaufmann, C. Benarafa, H.-U. Simon: The generation of neutrophils in the bone marrow is controlled by autophagy.
Cell Death Differ., in press: doi: 10.1038/cdd.2014.169.

4. A. Soragni, **S. Yousefi**, C. Stoeckle, A.B. Soriaga, M.R. Sawaya, E. Kozlowski, I. Schmid, S. Radonjic-Hoesli, S. Boutet, G.J. Williams, M. Messerschmidt, M.M. Seibert, D. Cascio, N.A. Zatsepin, M. Burghammer, C. Riekel, J.-P. Colletier, R. Riek, D. Eisenberg, H.-U. Simon: Toxicity of eosinophil MBP is repressed by intracellular crystallization and promoted by extracellular aggregation.
Mol. Cell, in press.

5. D. Simon, S. Radonjic-Hoesli, A. Straumann, **S. Yousefi**, H.-U. Simon: Active eosinophilic esophagitis is characterized by epithelial barrier defects and eosinophil extracellular trap formation.
Allergy, in press.

Book chapters

1. D. Simon, H.-U. Simon, **S. Yousefi**: Eosinophil extracellular trap formation in response to thymic stromal lymphopoietin stimulation. In: Allergic Diseases: from Mechanisms to Cures (Eds. S.J. Galli and Y.-Y. Kim); Pacini Editore S.p.A., Pisa, 2014, p. 83-86.

2. **S. Yousefi**, D. Simon, H.-U. Simon: Eosinophil extracellular traps: potential role(s) in eosinophilic diseases. In: Allergic Diseases: from Mechanisms to Cures (Eds. S.J. Galli and Y.-Y. Kim); Pacini Editore S.p.A., Pisa, 2014, p. 87-89.

Group Prof. Uwe Zangemeister-Wittke

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Tankica Timcheva, PhD student
Kevin Oberson, technician (30%)
Dr. Nikolas Stefan, Postdoc
Fabian Brandl, PhD student
Hannes Merten, PhD student
Oliver Brehmer, M.Sc. student

We are interested in translational aspects of molecular oncology, biomarker validation and tumor targeting with pharmacologically improved drug conjugates.

We focus on tumor targeting with Designed Ankyrin Repeat Proteins (DARPins) as highly stable non-IgG scaffold proteins for drug and biotoxin delivery. To this end, affinity-maturated DARPins with specificity for the pan-carcinoma antigen EpCAM were developed. Using maleimide and the DARPin compatible bioorthogonal click chemistry for site-specific functionalization, we generated nanomedicines equipped with various payloads including domain I-truncated Pseudomonas Aeruginosa Exotoxin A (ETA") and Monomethyl Auristatin F (MMAF). Using appropriate linker chemistry, the conjugates were further equipped with serum albumin or polyethylene glycol (PEG) for half-life extension.

We could demonstrate that the pharmacokinetics of a fusion toxin composed of a DARPin and ETA can be significantly improved by facile bioorthogonal conjugation with a PEG 20kDa polymer at a unique position. Fusion of the anti-EpCAM DARPin Ec1 to ETA" and expression in methionine-auxotrophic *E. coli* enabled introduction of the non-natural amino acid azidohomoalanine at position 1 for strain-promoted click PEGylation. PEGylated Ec1-ETA" was characterized by detailed biochemical analysis and its potential for tumor targeting was assessed in preclinical tumor models *in vitro* and *in vivo*. Pharmacological analysis in mice unveiled an almost 6-fold increase in the elimination half-life (14 vs. 82 min) and a more than 7-fold increase in the AUC compared to non-PEGylated Ec1-ETA", which directly translated in increased and longer-lasting effects on established tumor xenografts. Our data underline the great potential of combining the inherent advantages of the DARPin format with bioorthogonal click chemistry to overcome the limitations of engineering fusion toxins with enhanced efficacy for cancer therapy.

Despite replacement of the natural cell-binding domain of ETA" by tumor-selective antibodies or alternative binding proteins the therapeutic window of such fusion toxins is still limited by target-independent cellular uptake, resulting in normal tissue toxicity. Furthermore, the strong immunogenicity of the bacterial toxin precludes repeated administration in most

patients. Site-specific modification to convert ETA" into a prodrug-like toxin which is reactivated specifically in the tumor, and at the same time has a longer circulation half-life and is less immunogenic, is therefore appealing. To engineer a prodrug-like fusion toxin consisting of the anti-EpCAM DARPin Ec1 and ETA", we used strain-promoted azide alkyne cycloaddition for bioorthogonal conjugation of linear or branched PEG polymers at defined positions within the toxin moiety. Reversibility of the shielding was provided by a designed peptide linker containing the cleavage site for the rhinovirus 3C model protease. We identified two distinct sites, one within the catalytic domain and one close to the C-terminal KDEL sequence of Ec1-ETA", simultaneous PEGylation of which resulted in up to 1000-fold lower cytotoxicity in EpCAM-positive tumor cells. Importantly, the potency of the fusion toxin was fully restored by proteolytic unveiling. Upon systemic administration in mice, PEGylated Ec1-ETA" was much better tolerated than the non-PEGylated fusion toxin, showed a longer circulation half-life and an almost 10-fold increased AUC. Our strategy of engineering prodrug-like fusion toxins by bioorthogonal veiling thus opens new possibilities for targeting tumors with more specificity.

AMR-Me inhibits PI3K/Akt signaling in hormone-dependent MCF-7 breast cancer cells and inactivates NF-κB in hormone-independent MDA-MB-231 cells

R. Thangaiyan, A. Huwiler, U. Zangemeister-Wittke

AMR-Me, a C-28 methylester derivative of triterpenoid compound Amooranin isolated from Amoora rohituka stem bark and the plant has been reported to possess multitude of medicinal properties. Our previous studies have shown that AMR-Me can induce apoptosis through mitochondrial apoptotic and MAPK signaling pathways by regulating the expression of apoptosis related genes in human breast cancer MCF-7 cells. However, the molecular mechanism of AMR-Me induced apoptotic cell death remains unclear. Our results showed that AMR-Me dose-dependently inhibited the proliferation of MCF-7 and MDA-MB-231 cells under serum-free conditions supplemented with 1 nM estrogen (E2) with an IC_{50} value of 0.15 µM, 0.45 µM, respectively. AMR-Me had minimal effects on human normal breast epithelial MCF-10A + ras and MCF-10A cells with IC_{50} value of 6 and 6.5 µM, respectively. AMR-Me downregulated PI3K p85, Akt1, and p-Akt in an ERα-independent manner in MCF-7 cells and no change in expression levels of PI3K p85 and Akt were observed in MDA-MB-231 cells treated under similar conditions. The PI3K inhibitor LY294002 suppressed Akt activation similar to AMR-Me and potentiated AMR-Me induced apoptosis in MCF-7 cells. EMSA revealed that AMR-Me inhibited nuclear factor-kappaB (NF-κB) DNA binding activity in MDA-MB-231 cells in a time-dependent manner and abrogated EGF induced NF-κB activation. From these studies we conclude that AMR-Me decreased ERα expression and effectively inhibited Akt phosphorylation in MCF-7 cells and inactivated constitutive nuclear NF-κB and its regulated proteins in MDA-MB-231 cells. Due to this multifactorial effect in hormone-dependent and independent breast cancer cells AMR-Me deserves attention for use in breast cancer prevention and therapy.

See original publication No. 1

Increasing the anti-tumor effect of an EpCAM-targeting fusion toxin by facile click PEGylation

M. Simon, N. Stefan, L. Borsig, A. Plückthun, U. Zangemeister-Wittke

Fusion toxins used for cancer therapy have demonstrated short circulation half-lives, which impairs tumor localization and hence efficacy. Here, we demonstrate that the pharmacokinetics of a fusion toxin composed of a Designed Ankyrin Repeat Protein (DARPin) and domain I-truncated Pseudomonas Exotoxin A (PE40/ETA") can be significantly improved by facile bioorthogonal conjugation with a polyethylene glycol polymer at a unique position. Fusion of the anti-EpCAM DARPin Ec1 to ETA" and expression in methionine-auxotrophic E. coli enabled introduction of the non-natural amino acid azidohomoalanine at position 1 for strain-promoted click PEGylation. PEGylated Ec1-ETA" was characterized by detailed biochemical analysis, and its potential for tumor targeting was assessed using carcinoma cell lines of various histotypes in vitro, and subcutaneous and orthotopic tumor xenografts in vivo. The mild click reaction resulted in a well-defined mono-PEGylated product, which could be readily purified to homogeneity. Despite an increased hydrodynamic radius resulting from the polymer, the fusion toxin demonstrated high EpCAM-binding activity and retained cytotoxicity in the femtomolar range. Pharmacological analysis in mice unveiled an almost 6-fold increase in the elimination half-life (14 vs. 82 min) and a more than 7-fold increase in the AUC compared to non-PEGylated Ec1-ETA", which directly translated in increased and longer-lasting effects on established tumor xenografts. Our data underline the great potential of combining the inherent advantages of the DARPin format with bioorthogonal click chemistry to overcome the limitations of engineering fusion toxins with enhanced efficacy for cancer therapy.

See original publication No. 2

Original publications

1. R. Thangaiyan, A. Huwiler, **U. Zangemeister-Wittke**: AMR-Me inhibits PI3K/Akt signaling in hormone-dependent MCF-7 breast cancer cells and inactivates NF-kB in hormone-independent MDA-MB-231 breast cancer cells.
   Mol. Carcinog. 53 (2014), 578-588.

2. M. Simon, N. Stefan, A. Plückthun, **U. Zangemeister-Wittke**: Increasing the anti-tumor effect of an EpCAM-targeting fusion toxin by facile click PEGylation.
   Mol. Cancer Ther. 13 (2014), 375–385.

3. O. Pastukhov, S. Schwalm, I. Römer, **U. Zangemeister-Wittke**, J. Pfeilschifter, A. Huwiler: Ceramide kinase contributes to proliferation but not to prostaglandin E_2 formation in renal mesangial cells and fibroblasts.
   Cell Physiol. Biochem. 34 (2014), 119–133.

4. N. Stefan, M. Simon, **U. Zangemeister-Wittke**, A. Plückthun: Novel prodrug-like fusion toxin with protease-sensitive bioorthogonal PEGylation for tumor targeting.
   Bioconjug. Chem. 25 (2014), 2144–2156.

5. O. Pastukhov, S. Schwalm, **U. Zangemeister-Wittke**, D. Fabbro, F. Bornancin, L. Japtok, B. Kleuser, J. Pfeilschifter, A. Huwiler: The ceramide kinase inhibitor NVP-231 inhibits breast and lung cancer cell proliferation by inducing M phase arrest and subsequent cell death.
   Br. J. Pharmacol. 171 (2014), 5829–5844.

Additional Publications by PKI Members

PD Dr. Peter Späth

Original publications

S. Tamburin, K. Borg, X.J. Caro, S. Jann, A.J. Clark, F. Magrinelli, G. Sobue, L. Werhagen, G. Zanette, H. Koike, **P.J. Späth**, A. Vincent, A. Goebel: Immunoglobulin G for the treatment of chronic pain: Report of an Expert Workshop.
Pain Med. 15 (2014), 1072-1082.

M. Sudo, Y. Yamaguchi, **P.J. Späth**, K. Matsumoto-Morita, B.K. Ong, N. Shahrizaila, N. Yuki: Different IVIG glycoforms affect in vitro inhibition of anti-ganglioside antibody-mediated complement deposition.
PLoS One 9 (2014), e107772.

Letters to the Editor

P.J. Späth: A novel use of intravenous immunoglobulin is not restricted to complement hypercatabolism because of factor H deficiency.
Prog. Transplant. 24 (2014), 120.

P.J. Späth: Report from a rare diseases event in Târgu Mures, ROM.
Romanian Review of Laboratory Medicine 22 (2014), 397-398.

Review articles

J. Kerr, I. Quinti, M. Eibl, H. Chapel, **P.J. Späth**, W.A. Sewell, A. Salama, I.N. van Schaik, T.W. Kuijpers, H.H. Peter: Is dosing of therapeutic immunoglobulins optimal? A review of a three-decade long debate in Europe.
Front. Immunol. 5 (2014), 629.

P.J. Späth: A glance on recent progresses in diagnosis and treatment of primary immunodeficiencies.
Romanian Review of Laboratory Medicine 22 (2014), 297-309.

W.A.C. Sewell, J. Kerr, M.E. Behr-Gross, H.H. Peter, on behalf of the Kreuth Ig Working Group (including **P.J. Späth**): European consensus proposal for immunoglobulin therapies.
Eur. J. Immunol. 44 (2014), 2207-2214.

PD Dr. David Spirk

Original publication

R.P. Engelberger, J. Fahrni, T. Willenberg, F. Baumann, **D. Spirk**, N. Diehm, D.-D. Do, I. Baumgartner, N. Kucher: Fixed low-dose ultrasound-assisted catheter-directed thrombolysis followed by routine stenting of residual stenosis for acute ilio-femoral deep-vein thrombosis.
Thromb. Haemost. 111 (2014), 1153-1160.

4.2. Congress Invitations

Dr. Susanne Radonjic-Hoesli

World Immune Regulation Meeting – VIII; Session: „Essentials of immune regulation in the innate immune response“, Davos (CH), March 19-22, 2014;
The death pathway leading to eosinophil cytolysis.

Prof. Thomas Kaufmann

8th European Work Shop on Cell Death (EWCD); Paphos (Cyprus), March 30 – April 4, 2014;
Investigating molecular functions of BOK and its role in cancer.

Dr. Erika Moravcikova

19th World Congress on Advances in Oncology, Athens (GR), October 09-11, 2014;
Differential sensitivity to apoptosome apparatus activation in non-small cell lung carcinoma and the lung.

Prof. Hans-Uwe Simon

Annual Meeting of the European Allergy and Clinical Immunology (EAACI), Copenhagen (Denmark), June 7-11, 2014;
Extracellular DNA traps.

Annual Meeting of the European Allergy and Clinical Immunology (EAACI), Copenhagen (Denmark), June 7-11, 2014;
Ethics in research: The journal editor’s point of view.

Workshop on “Cell Death in Neurodegeneration and Cancer”, Villa Vigoni, Loveno di Menaggio, Como (I), June 25-28, 2014;
ATG5 – a novel tumor suppressor.

17th World Congress of Basic & Clinical Pharmacology (WCP), Cape Town (South Africa), July 13-18, 2014;
CRTH2 antagonism – a new therapeutic principle in allergic diseases.

Summer School für biomedizinische Nachwuchsforscher, Universität Tübingen, Institut für Pharmazie, Kloster Frauenchiemsee (D), July 18-20, 2014;
ATG5 and cancer.

XIVth International Symposium on Proteinases, Inhibitors and Biological Control, Portoroz, Slovenia; September 6-10, 2014;
ATG5 expression and function in cancer.

8th Swiss Apoptosis Meeting, Bern (CH); September 10-12, 2014;
Autophagy and autophagic cell death.

30th Symposium of the Collegium Internationale Allergologicum; Allergies: Current challenges and solutions, Petersberg (D); September 13-18, 2014;
NADPH oxidase-independent formation of extracellular DNA traps by basophils.

53rd Annual Meeting of the Japan Rhinologic Society, Osaka (Japan), Sept. 25-27, 2014;
Innate immunity and immunopathology mediated by eosinophils.

5th Cell Death & Disease Symposium on Immunity, Stem Cells and Diseases, Changzhou (China), October 10-14, 2014;
ATG5 expression and function in cancer.

6th AIO – Symposium der Deutschen Krebsgesellschaft e.V., Berlin (Germany), November 12, 2014;
ATG5: a multitasking molecule.

6th EADV Dermatological Meeting in Ticino 2014: From the Bench to the Clinic, Bellinzona (CH), December 4, 2014;
Regulation of MBP toxicity in eosinophilic diseases.

PD Dr. Stephan von Gunten

11th International Workshop IMMUNOTHERAPY 2014: Chronic inflammation in cancer and autoimmunity: Revisiting the Links, Havanna (CU), November 10-14, 2014;
Altered surface glycosylation with expression of Siglec-7/-9 ligands protects tumors from NK cell immunosurveillance.

19th World Congress on Advances in Oncology, Athens (GR), October 09-11, 2014;
Altered surface glycosylation with expression of Siglec-7/-9 ligands protects tumors from NK cell immunosurveillance.

7th International Immunoglobulin Conference 2014, Interlaken (CH), April 4-5, 2014;
The human IgG repertoire: Glycan array analysis of IVIG/SCIG reveals novel insights for glycovaccination and antiadhesion therapy.

PD Dr. Peter Späth

100th J Project Meeting of the European Society for Immunodeficiencies, Antalya (TUR), March 12–15, 2014;
European consensus proposal for immunoglobulin therapies.

7th International Immunoglobulin Conference, Interlaken (CH), April 4-5, 2014;
Strong but transient anti-inflammatory effect of IVIG in patients with chronic complement hypercatabolism due to dysregulated control (C-CHC-DC).

Hereditary Angioedema & Primary Immunodeficiency Conference – East Meets West & The 102nd J Project Meeting‘, Tirgu Mures (ROM), April 24–26, 2014;
Reasoning about the nature of hereditary angioedema - Is HAE a PID?
Immunoglobulin concentrates - Characteristics and clinical use.

Bradykinin Symposium 2014, Berlin (D), October 15–17, 2014;
Where do we stand, where do we go?

Dr. Christina Merz-Stoeckle

TM's 3rd World Immunology Online Conference, March 25-27, 2014;
Putting brakes on eosinophil development.

Simone Wicki

8th European Work Shop on Cell Death (EWCD); Paphos (Cyprus), March 30 – April 4, 2014;
Role of XIAP in murine neutrophils downstream of death receptors and in response to danger signals.

Prof. Shida Yousefi

LS2 Annual Meeting 2014, Lausanne (CH), Feb. 4, 2014;
Basophils exhibit NADPH oxidase-independent antibacterial activity through elaboration of extracellular DNA traps.

SwissMito Meeting; Kandersteg (CH), Sept. 2-3, 2014;
Molecular mechanisms of mtDNA release by granulocytes.

4th International Symposium on Molecular Technology, Tehran (Iran), Oct. 14-16, 2014;
Molecular mechanisms of mtDNA release by granulocytes.

4.3. Seminar Invitations

Prof. Thomas Kaufmann

Biochemical Pharmacology, University of Konstanz (D), May 28, 2014;
guest of Prof. Thomas Brunner:
The BCL-2 family member BOK: know the unknown, expect the unexpected.

Institute of Pharmacology, University of Bern (CH), June 24, 2014;
Inaugural Lecture (Associate Professor)
Only happy when the cells die.

Institute of Clinical Chemistry, University Hospital Bern (CH), Oct. 23, 2014;
guest of Prof. Carlo Largiadèr:
Regulation of programmed cell death by BCL-2 family proteins.

Prof. Hans-Uwe Simon

Faculty of Pharmacy, University of Ljubljana, Ljubljana (Slovenia), May 19, 2014;
guest of Prof. Irena Mlinaric-Rascan:
ATG5 – update on its role in autophagy and beyond.

Dind Cottier Skin Foundation Lecture Series, University of Lausanne, Lausanne, June 5, 2014; guest of Prof. Daniel Hohl:
Extracellular DNA traps: neutrophils, eosinophils, basophils.

Forschungsseminar „Experimentelle Medizin 2014“, Kantonsspital St. Gallen,
St. Gallen, Dec. 12, 2014; guest of Prof. Burkhard Ludewig:
Molecular mechanisms of innate immunity and immunopathology mediated by eosinophils.

PD Dr. Stephan von Gunten

Department of Hematology, University Hospital of Bern, Bern, Feb 27, 2014;
guest of Prof. Gabriele Baerlocher:
Altered surface glycosylation shields tumor cells from NK cell immunosurveillance.

Bern Immunology Club (BIC), University of Bern, Bern, April 30, 2014;
Sweet - and sometimes fatal: glycans from an immunological perspective.

The Center for Molecular Medicine Cologne, University of Cologne, Cologne (D),
July 22, 2014; guest of Prof. Hinrich Abken:
Siglec ligands protect tumor cells from NK cell immunosurveillance.

Theodor Kocher Institute, University of Bern, Bern, Nov. 24, 2014;
guest of Prof. Britta Engelhardt and PD Dr. Marelene Wolf:
Glycan-protein interactions in cellular and humoral immunity.

4.4. Organization of Meetings and Courses

Prof. Thomas Kaufmann

8th Swiss Apoptosis Meeting (together with H.-U. Simon, M. Tschan, and T. Brunner),
Bern (CH), 10.-12.09.2014

Prof. Hans-Uwe Simon

Symposium of the Swiss Society of Pharmacology and Toxicology (together with task force SSPT): Progress in Pharmacology – Tumorpharmacology,
Bern (CH), Jan. 30, 2014

Workshop on “Cell Death in Neurodegeneration and Cancer” (together with D. Kulms, D. Delia, and P. Krammer),
Villa Vigoni, Loveno di Menaggio, Como (I), June 25-28, 2014

13th III-Bern International Summer School,
Stein am Rhein (CH), July 27-29, 2014

8th Swiss Apoptosis Meeting (together with T. Kaufmann, M. Tschan, and T. Brunner),
Bern (CH), Sept. 10-12, 2014

PD Dr. Stephan von Gunten

Annual Meeting 2014 of the Swiss Society for Pharmacology and Toxicology (SSPT) (*together* with task force SSPT),
Bern (CH), April 4, 2014

Prof. Shida Yousefi

ImageJ / Fiji Workshop at the Institute of Pharmacology, University of Bern,
Bern (CH), November 7, 2014

4.5. Invited Chairperson at Congresses

Prof. Thomas Kaufmann

8th Swiss Apoptosis Meeting; Session: Apoptosis and Immunity;
Bern (CH); September 10-12, 2014.
8th European Work Shop on Cell Death (EWCD);
Paphos (Cyprus), March 30 – April 4, 2014;

Prof. Hans-Uwe Simon

Symposium of the Swiss Society of Pharmacology and Toxicology: Fortschritte in der Pharmakologie – Tumorpharmacology, Morning session;
Bern (CH), Jan. 30, 2014

World Immune Regulation Meeting – VIII; Session: „Essentials of immune regulation in the innate immune response“;
Davos (CH), March 19-22, 2014

80. Jahrestagung der Deutschen Gesellschaft für Experimentelle und Klinische Pharmakologie und Toxikologie e. V. (DGPT); Poster session: „Entzündung und Immunpharmakologie“;
Hannover (D), March 31- April 3, 2014

Annual Meeting of the European Allergy and Clinical Immunology (EAACI);
JMA Educational Session;
Copenhagen (Denmark), June 7-11, 2014

Neuroscience Update Symposium: Neuropharmakologie; Session: Mechanismen;
Bern (CH), September 4, 2014

8th Swiss Apoptosis Meeting; Session: Apoptosis pathways;
Bern (CH); September 10-12, 2014

30th Symposium of the Collegium Internationale Allergologicum; Allergies:
Current challenges and solutions; Session: Lymphocytes & Mediators of Immunoregulation;
Petersberg (D); September 13-18, 2014

PD Dr. Stephan von Gunten

19th World Congress on Advances in Oncology; Session: Immunology/Molecular Oncology;
Athens (GR), October 9-11, 2014

Annual Meeting 2014 of the Swiss Society for Pharmacology and Toxicology;
Session: Young Investigator Research;
Bern (CH), April 4, 2014

PD Dr. Peter Späth

International Plasma Protein Congress: Session 2, Clinical Developments;
Vienna (A), March 11-12, 2014

100th J Project Meeting of the European Society for Immunodeficiencies: Session 2, Immunoglobulin replacement therapy;
Antalya (TUR), March 12–15, 2014

Hereditary Angioedema & Primary Immunodeficiency Conference – ‚East Meets West' & The 102nd J Project Meeting, Session: Angioedema 2;
Tîrgu Mures (ROM), April 24–26, 2014

4.6 Referee Work for Peer-Reviewed Journals

Dr. Zhaoyue He

Allergy
Cell Death Differ.
Cell Death Dis.

Dr. Susanne Radonjic-Hösli

Allergy

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
BioEssays
Cell Communication and Signaling
Cell Death and Differentiation
Cell Death and Disease
Cellular & Molecular Immunology
European Journal of Immunology
FEBS Letter
FEBS Journal
Frontiers in Molecular and Cellular Oncology
Future Oncology
Immunology and Cell Biology
Journal of Hepatology
Journal of Molecular Cell Biology
Journal of Neuroscience
Methods
Molecular Cancer Therapeutics
Molecular & Cellular Oncolog
Oncogene
PLoS One
Hepatology

Dr. He Liu

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

Dr. Christina Merz-Stöckle

Allergy
Cell Death Dis.

Prof. Hans-Uwe Simon

Allergy
Apoptosis
Autophagy
Blood
J. Cell Cycle
Clin. Exp. Allergy
EMBO Journal
EMBO Reports
Science Signaling
Eur. J. Immunol.
FASEB J.
Cell Death Differ.
Gut
J. Allergy Clin. Immunol.
J. Exp. Med.
J. Immunol.
J. Leukoc. Biol.
J. Cell Sci.
Oncogene
Frontiers Oncology
FEBS letters
Mol. Cell. Oncology
Nat. Med.
Cell Death Dis.

PD Dr. Peter Späth

Allergy
Autoimmunity
Int. Arch. Allergy Immunol.
J. Clin. Immunol.
PloS One

PD Dr. Stephan von Gunten

Allergy
Blood
Cell Death Differ.
Cell Death Dis.
J. Allergy Clin. Invest.
Gene Therapy
Frontiers Oncology
J. Invest. Dermatol.
PLoS One

Prof. Shida Yousefi

Cell Death Differ.
Cell Biochem. Biophysics
Int. J. Mol. Sci.
J. Vasc. Intervent.
Radiology
Resp. Res.

Prof. Uwe Zangemeister-Wittke

Bioconjug. Chem.
Biomacromolecules
Cell Death Dis.
Clin Cancer Res.
Expert Opin. Drug Delivery
Int. J. Cancer
J. Drug Targeting
Mol. Cell. Biol.
Nanomedicines

4.7. Referee Work for Grant Bodies

Dr. Zhaoyue He

Swiss Cancer League

Prof. Andrea Huwiler

Deutsche Forschungsgemeinschaft (DFG)
Norwegischer Forschungsrat (NFR)

Prof. Thomas Kaufmann

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

Dr. Christina Merz-Stöckle

National Science Center (NCN), Poland

PD Dr. Stephan von Gunten

Dutch Arthritis Foundation
Medical Research Council (UK)
Swiss Cancer League
Worldwide Cancer Research (formerly AICR)

Prof. Uwe Zangemeister-Wittke

Swiss Cancer League
Catalan Agency for Health Information, Assessment and Quality (CAHIAQ)
Qatar National Research Fund (QNRF)

4.8. Awards

Dr. Elisabeth Louisa de Graauw

Best Poster Award
LS² Annual Meeting of the Swiss Society for Experimental Pharmacology (SSEP);
Lausanne, Febr. 12, 2014

PD Dr. Stephan von Gunten

Best Oral Presentation
7th International Immunoglobulin Conference 2014:
Interlaken, April 4-5, 2014

Dr. Susanne Radonjic-Hösli

Best Abstract Prize
European Academy of Allergy and Clinical Immunology (EAACI) Congress:
Copenhagen, June 7– 11, 2014

Dr. Elisabeth Louisa de Graauw

Poster Prize (1st)
Annual Meeting of the Swiss Society of Dermatology and Venerology (SSDV);
Basel, Sept. 4-6, 2014

Yuniel Fernandez Marrero

Poster Award (2nd)
8th Swiss Apoptosis Meeting (SAM); Bern, Sept. 10-12, 2014

Dr. He Liu

Poster Award (3rd)
8th Swiss Apoptosis Meeting (SAM); Bern, Sept. 10-12, 2014

Dr. He Liu

Dr. Lutz Zwillenberg Price 2014
Bern, Dec 6, 2014

5. Administrative, Advisory, and Honorary Posts

Dr. Zhaoyue He

Coordinator for PC work at the PKI

Webmaster at the PKI

Prof. Andrea Huwiler

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

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

Member of the Collegium generale of the University of Bern

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, Frontiers in Molecular and Cellular Oncology

Member of the Editorial Board, Allergy

Member of the Editorial Board, Cell Death and Disease

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

Coordinator for FACS and Chemicals at the PKI

Coordinator Fluorescence Microscope

Coordinator FPLC (Äkta)

Dr. Christina Merz-Stöckle

Member of the Website Committee of the International Eosinophil Society (IES)

Prof. Hans-Uwe Simon

Vice-Dean for Research, Medical Faculty, University of Bern

Swiss-EU mobility program, Coordinator Pharmacology/Pharmacy, 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 (2013-2015)

President of the International Eosinophil Society (IES); www.eosinophil-society.org

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

Member of the Scientific Committee, Swiss Cancer League

Chairman of Scientific Advisory Board, HELMHOLTZ Zentrum für Umweltforschung (UFZ), Leipzig (D) (until Oct. 2014)

Member of Council of the Collegium International Allergologicum (CIA) (until Sept. 2014)

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

Member of the Advisory Board, Research Foundation, University of Bern

Member of the Advisory Board, Foundation pour la recherche et le traitement des maladies respiratoires, Lausanne

Mentor, junior EAACI member program

Past-President, European Cell Death Society (ECDO)

Past-President, Union of the Swiss Societies for Experimental Biology (USSEB)

Past-President, Swiss Society of Pharmacology and Toxicology (SSPT)

Editor-in-Chief, Allergy

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

Section Editor, Cell Death and Disease

Associate Editor, Frontiers in Oncology

Associate Editor, Molecular & Cellular Oncology

PD Dr. Peter Späth

Advisory activity for preparation of a ‘resolution on principles concerning immunodeficiency therapies’ in function as a member of the Kreuth Immunoglobulin Working Group ‘European Consensus Proposal for Immunoglobulin Therapies’ under the patronage of the European Directorate for the Quality of Medicines & Health Care

PD Dr. Stephan von Gunten

General secretary of the Council of the Swiss Society of Experimental Pharmacology (SSEP)

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

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

Member of the Editorial Board, Allergy

Webmaster at the PKI

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 two laser scanning microscopes (LSM 5 Exciter and LSM 510, 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

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

Anna Karolina Karbownik & Aldona von Gunten
Vernissage: May 15, 2014

8. Sponsors

8.1. Research Grants

Ziva Frangez
Fellowship, ERASMUS program (October 2013 – January 2014)

Prof. Andrea Huwiler

Swiss National Science Foundation (grant No. 310030-135619/1)
Norwegian Research Council and Avexxin AS
Schweizerische Multiple Sklerose Gesellschaft

Prof. Thomas Kaufmann

Swiss National Science Foundation, project grant 31003A_149387
Swiss National Science Foundation, project grant 310030E_150805 (part of FOR2036 research unit)
Swiss Cancer League (KFS-3014-08-2012)
3R Research Foundation Switzerland (No 127-11)

Dr. Christina Merz-Stöckle

Novartis Foundation for medical-biological research (148074)

Dr. Erika Moravcikova
SCIEX PostDoc Fellowship (July 2014 – June 2015)

Dr. Susanne Radonjic-Hösli

Allergie-Stiftung Ulrich Müller-Gierok, Bern (together with Prof. Hans-Uwe Simon)

Prof. Hans-Uwe Simon

Swiss National Science Foundation (grant No. 310030-146181)
Swiss Cancer League (KFS-3099-02-2013)
Allergie-Stiftung Ulrich Müller-Gierok, Bern (together with Dr. Susanne Radonjic-Hösli)
HORIZON 2020, Marie Sklodowska-Curie Actions, MEL-PLEX

PD Dr. Stephan von Gunten

Swiss National Science Foundation (SNSF) Grant Nr. 3100_135734)
Swiss National Science Foundation (SNSF), Bulgarian-Swiss Research Programme, Grant No.IZEBZO_142967/1
CSL Behring AG, Research Agreement
Swiss Cancer League (KFS-3248-08-2013)

Prof. Shida Yousefi

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

Xiaoliang Wang

State Scholarship Fund of China (CSC Scholarship)

Prof. Uwe Zangemeister-Wittke

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

8.2. Meetings

Swiss Society of Pharmacology and Toxicology (SSPT): Progress in Pharmacology – Tumorpharmacology, Bern (CH), Jan. 30, 2014
Pfizer AG, Zurich
Roche Pharma (Schweiz) AG, Reinach

13th III-International Summer School, Hotel Adler, CH-8260 Stein am Rhein, July 27–29, 2014
Jakob und Emma Windler-Stiftung, Stein am Rhein
BD Biosciences, Allschwil
Carl Zeiss AG, Feldbach
Novartis Pharma AG, Rotkreuz
Member companies of the Kontaktgruppe für Forschungsfragen (KGF), Basel:
Novartis, F. Hoffmann-La Roche, and Merck Serono
Lucerna Chem AG, Luzern
Pfizer AG, Zürich
Swiss Committee for Molecular Biology, Geneva
Programm für die Interfakultäre Ausbildung des Forschungsnachwuchses der Universität Bern
Graduate School for Cellular and Biomedical Sciences, Universität Bern

Swiss Apoptosis Meeting (SAM), Bern (CH), Sept. 10–12, 2014

Member companies of the Kontaktgruppe für Forschungsfragen (KGF), Basel:
Novartis, F. Hoffmann-La Roche, and Merck Serono
Graduate School for Cellular and Biomedical Sciences, Universität Bern

8.3. Seminars „Progress in Pharmacology“

2014:
AstraZeneca AG, Zug
CSL Behring AG, Bern
Merck Sharp & Drohme AG, Luzern
Pfizer AG, Zurich

2015:
Merck Sharp & Drohme AG, Luzern
Mepha Pharma AG, Basel
CSL Behring AG, Bern

8.4. Seminars „Bern Immunology Club“

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

8.5. Travel Support

Kayluz Frias Boligan
Swiss Society of Pharmacology and Toxicology (SSPT) (8th Word Immune Regulation Meeting, Davos (CH), March 19-22, 2014)

Kayluz Frias Boligan
Graduate School for Cellular and Biomedical Sciences, Univ. Bern (11th International Workshop Immunotherapy, Havanna (CU), November 10-14, 2014)

Yuniel Fernandez Marrero
FOR2036 research unit; Scientific exchange,
October – December 2014, Tübingen (D)

Dr. Susanne Radonjic-Hösli
Swiss Society of Experimental Pharmacology (SSEP) (8th World Immune Regulation Meeting, Davos (CH), March 19-22, 2014)

Dr. Tatiana Rabachini de Almeida
Keystone Symposia Fellowship (Keystone Symposium 'Cell Death Signaling in Cancer and the Immune System'), Guaruja, Sao Paolo (BRA), October 28 – November 2, 2014

Ramona Reinhart
3R Foundation Switzerland (Cell Symposia: The Multifaced Roles of Type 2 Immunity), Bruges (B), December 10–12, 2014

Saša Rožman
Euroconference on Apoptosis, Cell Death & Rejuvenation,
Crete (GR), October 1–4, 2014

Christoph Schneider
Graduate School for Cellular and Biomedical Sciences, Univ. Bern (11th International Workshop Immunotherapy, Havanna (CU), November 10-14, 2014)

8.6. Other Support

Bürgi Fonds Seminar series of the institute