Annual Report 2013

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 dreizehnte umfassende Jahresbericht des Instituts für Pharmakologie (PKI) der Universität Bern. Das PKI hat auch im Jahr 2013 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 2013 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. PD Dr. 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 20 DoktorandInnen (18 PhD, 2 MD), und 5 DoktorandInnen (4 PhD, 1 MD) haben im Berichtsjahr ihre Arbeit erfolgreich abgeschlossen.

Die Mitarbeiter und Mitarbeiterinnen des Instituts für Pharmakologie publizierten im Jahr 2013 insgesamt 33 Originalarbeiten sowie 17 Übersichtsartikel in internationalen Fachzeitschriften (Summe der „impact factors“ >300). MitarbeiterInnen des Instituts wurden zu insgesamt 33 Vorträgen bzw. Seminaren eingeladen. Mehrere MitarbeiterInnen des PKI wurden mit Forschungspreisen ausgezeichnet. Gegenwärtig werden 8 MitarbeiterInnen mit

namhaften Beiträgen des Schweizerischen Nationalfonds unterstützt. Zahlreiche Persönlichkeiten besuchten das Institut und hielten Forschungsseminare. Der Berner Immunologie-Club erfreut sich, auch durch die aktive Hilfe aus dem PKI, einer grossen Beliebtheit. Prof. Simon und PD Dr. Kaufmann organisieren in 2014 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 erwarten. 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.

Ich danke allen Mitarbeiterinnen und Mitarbeitern für ihren Einsatz, welcher auch im Jahr 2013 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 2014

1.2. Foreword

This is the thirteenth 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 2013. 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 2013.

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). PD Dr. 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, 18 PhD students and 2 MD students work at the PKI, and five students (4 PhD, 1 MD) successfully completed their doctoral studies in 2013.

Research is our second important activity. In 2013, staff members of the PKI published 33 original and 17 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 33 lectures or seminars. Several PKI members received research prizes. Eight 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 PD Dr. Kaufmann, together with PD Dr. Tschan (Institute of Pathology, University of Bern) and Prof. Brunner (Department of Biochemical Pharmacology, Univ. of

Konstanz, Germany), are currently organizing an international congress (8th Swiss Apoptosis Meeting; September 10-12, 2014), which will attract approximately 200 scientists interested in the field of “Cell Death”. 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.

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 2013. I am grateful to all the sponsors and friends of the institute for their support.

Prof. Hans-Uwe Simon, MD, PhD
Director

Bern, January 2014

2. Staff 2013

Director

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

Deputy Director

Prof. Dr. Andrea Huwiler, PhD

Principal Investigators

Prof. Dr. Andrea Huwiler, PhD
PD 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

Dr. Poorya Amini, PhD student
Daniel Bachmann, research assistant*
Florence Charrière, M.Sc. student* (January – June 2013)
Dr. Elisabeth Louisa de Graauw, PhD student*
Nohemy Echeverry, PhD student (until January 2013)
Daniel Fallegger, PhD student
Iuliia Filipenko, PhD student
Kayluz Frias Boligan, PhD student*
Nathalie Friedli, M.Sc. student* (October 2012 – February 2013)
Ziva Frangez, ERASMUS student* (October 2013 – January 2014)
Katharina Fuchs, MMed student*
Christine Gallasz, MMed student* (Sept. – Nov. 2013; MD student since Dec. 1, 2013)
Nina Germic, ERASMUS student* (February – June 2013)
Dominic Guillet, M.Sc. student* (January – June 2013)
Ursina Gurzeler, PhD student* (until June 2013)
Dr. Zhaoyue He, PhD
Tobias Horn, MMed student* (February – April 2013)
Faik Imeri, PhD student
Fabiana Jakob, technician (until June 2013)
Dr. Nataliya Kotelevets, PhD (until January 2013)
Evelyne Kozlowski, technician
Evelin Krajnc, ERASMUS student* (until February 2013)
Dr. He Liu, PhD
Morshed Mahbubul, PhD student*
Marianne Maillard-van Laer, technician
Tankica Maneva - Timcheva, PhD student*
Ariane Meister, MMed student*
Dr. Christina Merz - Stöckle, PhD

Kevin Oberson, technician
Muriel Ott, MMed student* (June – August 2013)
Olexsandr Pastukhov, PhD student
Dr. Tatiana Rabachini de Almeida, PhD*
Dr. Susanne Radonjic-Hösli, MD-PhD student*
Ramona Reinhart, M.Sc. student* (July – January 2014)
Saša Rožman, PhD student
Inès Schmid, head technician
Christoph Schneider, PhD student* (since May 2013)
Myriam Fabiola Schorer-Cortinas, PhD student*
Dr. Manuel Simon, PhD* (until June 2013)
Dr. Nikolas Stefan, PhD (since September 2013)
Darko Stojkov, PhD student*
Rebecca Strässle, MMed student*
Eliane Stucki, M.Sc. student* (January – June 2013)
Nicole Tochtermann, MMed student* (March - September 2013)
Xiaoliang Wang, PhD student*
Dr. Marc Wehrli, MD-PhD student* (until July 2013)
Simone Wicki, PhD student* (since March 2013)
Manon Widmer, M.Sc. student* (January – June 2013)

External University Teachers

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

Guest scientists

Prof. Dr. Francesca Levi-Schaffer, PhD*, The Hebrew University of Jerusalem, Israel
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. Thomas Demoulin, PhD*, Inst. of Virology and Immunoprophylaxis (IVI), Mittelhäusern
Dr. Doriano Fabbro, PhD*

External Computer Support

Dominik Wyss* and Anne Simon*****

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 - Gastroenterological Pharmacology, Bern, Jan. 31, 2013

Members of the Institute of Pharmacology of the University of Bern together with participants of an international summer school in Jongny; August 4 - 6, 2013. Our guest speakers from Germany (Prof. Peter Ruth) and Slovenia (Prof. Irena Mlinaric-Rascan) are seen.

3. Teaching Activities
3.1. Lectures

Lectures for Medical Students: Pharmacology

Date	Lecturer	Titel of the lecture
March 11, 2013	PD Dr. Stephan von Gunten	Antidiabetika
March 13, 2013	PD Dr. Stephan von Gunten	Lipidsenker, Behandlung der Gicht
April 8, 2013	Prof. Andrea Huwiler	Antiepileptika
April 8, 2013	Prof. Andrea Huwiler	Therapie von M.Parkinson und Demenz
April 10, 2013	Prof. Andrea Huwiler	Lokalanästhetika
April 22, 2013	PD Dr. Stephan von Gunten	Hormone aus pharmakologischer Sicht (Teil 1)
April 22, 2013	PD Dr. Stephan von Gunten	Hormone aus pharmakologischer Sicht (Teil 2)
April 24, 2013	Prof. Andrea Huwiler	Pharmakologie von Narkosemitteln und Muskelrelaxantien 1
April 24, 2013	Prof. Andrea Huwiler	Pharmakologie von Narkosemitteln und Muskelrelaxantien 2
May 1, 2013	Prof. Andrea Huwiler	Psychopharmakologie
May 6, 2013	Prof. Andrea Huwiler	Antidepressiva, Anxiolythika und Stimmungsstabilisatoren
May 8, 2013	Prof. Andrea Huwiler	Antipsychotika
May 15, 2013	Prof. Andrea Huwiler	Schmerz und Analgesiologie 1
May 15, 2013	Prof. Andrea Huwiler	Schmerz und Analgesiologie 2
May 15, 2013	Prof. Andrea Huwiler	Pharmakologie bei speziellen Patientengruppen
June 5, 2013	Prof. Hans-Uwe Simon	Immunmodulation
Sept. 18, 2013	Prof. Hans-Uwe Simon	Pharmakodynamik 1
Sept. 18, 2013	Prof. Hans-Uwe Simon	Pharmakodynamik 2
Sept. 18, 2013	PD Dr. Thomas Kaufmann	Adaptation und Zellschäden

Sept. 23, 2013	Prof. Hans-Uwe Simon	Entzündungshemmung
Sept. 23, 2013	Prof. Hans-Uwe Simon	Einführung in die Toxikologie
Oct. 28, 2013	Prof. Hans-Uwe Simon	Pharmakotherapie bei Lungenkrankheiten
Nov. 5, 2013	Dr. David Spirk	Pharmakologie der Hämostase
Nov. 5, 2013	Prof. Uwe Zangemeister-Wittke	Pharmakologie des vegetativen Nervensystems
Nov. 5, 2013	Prof. Uwe Zangemeister-Wittke	Antihypertensiva
Nov. 20, 2013	Prof. Uwe Zangemeister-Wittke	Antiarrhythmika
Nov. 20, 2013	Dr. David Spirk	Behandlung der Herzinsuffizienz und Angina Pectoris
Dec. 9, 2013	Prof. Uwe Zangemeister-Wittke	Diuretika

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

Date	**Lecturer**	**Title of the lecture**
Febr. 4, 2013	Prof. Uwe Zangemeister-Wittke	Einführung in die Pharmakogenetik
Febr. 6, 2013	PD Dr. Thomas Kaufmann	Pharmakogenetik, Interaktionen
Febr. 13, 2013	Prof. Hans-Uwe Simon	Rezeptoren, Dosis-Wirkungskurven
Febr. 13, 2013	Prof. Hans-Uwe Simon	Antagonisten, Applikationsarten
Febr. 18, 2013	Prof. Andrea Huwiler	Narkose-/Beruhigungsmittel
Febr. 18, 2013	Prof. Andrea Huwiler	Pharmakologie der Atemwege
Febr. 20, 2013	Dr. Sibylle Bürgi	Lokalanästhetika
Febr. 27, 2013	Prof. Uwe Zangemeister-Wittke	Phamakologie des vegetativen Nervensystems
March 18, 2013	PD Dr. Stephan von Gunten	Psychopharmaka
March 18, 2013	PD Dr. Stephan von Gunten	Magensäurehemmung

March 27, 2013	Dr. David Spirk	Antikoagulantien und Herz-Kreislauf Medikamente
April 8, 2013	PD Dr. Armand Cachelin	Schwache Analgetika, Starke Analgetika
April 10, 2013	Dr. David Spirk	Antithrombotika
April 17, 2013	Dr. Sibylle Bürgi	Antidiabetika
May 6, 2013	PD Dr. Parham Sendi	Mechanismen der Antibiotika und der antiviralen Therapie
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
Oct. 1, 2013	PD Dr. Thomas Kaufmann	Zellschäden

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

Date	Lecturer	Title of the lecture
Febr. 21, 2013	Prof. Hans-Uwe Simon	Introduction
Febr. 21, 2013	Prof. Hans-Uwe Simon	Immunopharmacology
May 30, 2013	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. 28, 2013	PD Dr. 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
March 28, 2013	Prof. Andrea Huwiler	Lipid mediators in tissue trafficking
May 2, 2013	Prof. Shida Yousefi	Inflammation – good or bad? Resolution of inflammation - apoptosis

Practical work for Natural Science Faculty: Immunology II (Coordinator: PD Dr. Nadia Corazza)

Date	Lecturer	Title of the lecture
Oct. 15, 2013	PD Dr. Thomas Kaufmann	Isolation of leukocytes (4 h)
Oct. 15, 2013	Dr. Christina Merz-Stöckle	Isolation of leukocytes (4 h)
Nov. 19, 2013	PD Dr. Thomas Kaufmann	Isolation of leukocytes (4 h)
Nov. 19, 2013	Dr. Christina Merz-Stöckle	Isolation of leukocytes (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
May 23, 2013	Dr. Christina Merz-Stöckle	Pharmacogenetics
Nov. 14, 2013	Dr. Christina Merz-Stöckle	Personalized Medicine
Nov. 14, 2013	Dr. Christina Merz-Stöckle	Pharmacogenetics

Lectures for Biomedical Sciences Students (M.Sc. program, Bern): Pharmacology of major organ systems (Coordinator: PD Dr. Thomas Kaufmann)

Date	Lecturer	Title of the lecture
Sept. 27, 2013	Prof. Uwe Zangemeister-Wittke	Heart and vascular system
Sept. 20, 2013	PD Dr. Thomas Kaufmann	Immune system

Oct. 4, 2013	Prof. Shida Yousefi	Antiinfectious therapy
Oct. 11, 2013	PD Dr. Stephan von Gunten	Pharmacology of the Gastrointestinal System
Oct. 18, 2013	PD Dr. Stephan von Gunten	Endocrine and Reproductive system
Oct. 25, 2013	Prof. Andrea Huwiler	Nervous system
Nov. 8, 2013	Prof. Shida Yousefi	Lungs and kidneys
Nov. 1, 2013	Dr. David Spirk	Haemopoietic system and haemostasis

Lecture for Natural Sciences Faculty and Biomedical Sciences students (M.Sc. program, Bern): General Pathology (Coordinator: Prof. Christoph Müller)

Date	Lecturer	Title of the lecture
Sept. 23, 2013	PD Dr. 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
Oct. 18, 2013	Prof. Shida Yousefi	Laser scanning microscopy and applications

External teaching activities: University of Zurich (Molecular Medicine)

Date	Lecturer	Title of the lecture
May 2013 (total 6h)	Prof. Uwe Zangemeister-Wittke	Molecular Cell Biology for students of human and dental medicine

External teaching activities: University of Ljubljana (ERASMUS, Pharmacy)

Date	Lecturer	Title of the lecture
April 2013 (total 2h)	Prof. Hans-Uwe Simon	Biopharmaceuticals – drugs of the future?

3.2. Coordination PBL Medical Students, 3rd year (2013/2014)

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 2013/2014)

Medical students 3rd year:
Dr. David Spirk
PD Dr. Thomas Kaufmann
PD Dr. Stephan von Gunten
Dr. Susanne Radonjic-Hösli

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

3.4. Seminars of Invited Speakers

Date	Teacher	Title of the seminar
Jan. 16, 2013	Dr. Alexander Eggel Institute of Immunology, Inselspital, Bern (CH)	Basophils and eosinophils in inflammation - from licence to kill to die another day
Jan. 23, 2013	Dr. Gabriela Brumatti The Walter and Eliza Hall Institute of Medical Research, Melbourne (AUS)	Hox Genes: From cell death to differentiation
Febr. 21, 2013	Prof. Thomas Magin Institute for Biology & Translation, Center for Regenerative Medicine, Univ. of Leipzig (D)	Update on epidermolysis bullosa simplex – insights from therapy approaches and fly genetics
March 27, 2013	Dr. Remo Perozzo Dept. Pharmaceutical Sci., University of Geneva (CH)	From compound to target: Chemical proteomics and in silico screening for target identification in *Plasmodium falciparum*

April 16, 2013	Dr. Paul Kubes Dept. of Physiology & Pharmacology, University of Calgary, Alberta (Canada)	Imaging immunity in infection and sterile injury in vivo
April 24, 2013	Dr. Alejandro López-Requena Immunobiology Division, Center of Molecular Immunol., Havana (Cuba)	N-glycolyl-sialic acid (Neu5Gc) in cancer: anti-GM3(Neu5Gc) ganglioside cytotoxic antibodies and tumorigenicity of a mouse lymphocytic leukemia cell line devoid of Neu5Gc-sialoconjugates
May 15, 2013	Dr. Alexander E. Lang Institute of Pharmacology and Toxicology, Univ. of Freiburg (D)	Function and structure of *Photorhabdus* toxin complexes
May 22, 2013	Dr. Christian Appenzeller Pharmazentrum, Universität Basel (CH)	Redox processes in the mammalian endoplasmic reticulum: Sensors, mechanisms, and consequences
Sept. 4, 2013	Prof. Francesca Levi-Schaffer Faculty of Medicine The Hebrew University of Jerusalem (Israel)	All what you would like to know about the effector allergic unit and you never dared to ask
Sept. 30, 2013	Prof. Marco A. Cassatella Department of Pathology and Diagnostics Division of General Pathology University of Verona (I)	Uncovering the regulation of cytokine expression in human neutrophils
Oct. 9, 2013	Dr. Martin Binggeli Unitectra, Univ. of Bern (CH)	From lab to market - why should the University file patents
Oct. 16, 2013	Prof. Nicolai Bovin Shemyakin-Ovchinnikov Institute of Bioorganic Chem. Russian Academy of Sciences Moscow (Russia)	Natural anti-glycan Abs: repertoire, plasticity, and prospects in medicine

3.5. Bern Immunology Club (BIC)

Date	Teacher	Title of the seminar
Febr. 13, 2013	Dr. Martijn A. Nolte Department of Hematopoiesis Sanquin Research and Land-steiner Laboratory Amsterdam (NED)	The impact of immune activation on hematopoiesis
Febr. 27, 2013	Prof. Carole Bourquin Universität Fribourg (CH)	Timing is everything: improving the outcome of cancer immunotherapy
March 27, 2013	Prof. Werner J. Pichler and Dr. Oliver Hausmann Inselspital, Bern (CH)	Clinical Immunological Conference: Drug hypersensitivity - new insights
April 24, 2013	Prof. Michel Gilliet Departement of Dermatology CHUV, Lausanne (CH)	Innate and adaptive immune responses in inflammatory skin diseases
May 29, 2013	Prof. Siegfried Hapfelmeier Institute for Infectious Diseases	Microbes on a short leash: novel bacterial tools to probe intestinal immunity and ecology
	and	
	Dr. Wendy Shaw Institute of Art History University Bern (CH)	Between Lady Montague and the Veiled Islamic Lady: an Immunological Model for the Discourse of Islam in Europe
June 26, 2013	Dr. Onur Boyman Department of Dermatology, University Hospital Zurich (CH)	Regulatory cytokines and cells dampening inflammation and autoimmunity
Sept. 25, 2013	PD Dr. Volker Thiel Institute of Immunobiology, St.Gallen (CH)	Coronaviruses: large RNA viruses with growing impact
Oct. 30, 2013	Clinical Immunological Conference: Regulatory immune cells and disease (Organizer: Prof. Thomas Geiser, Inselspital)	
	Dr. Federica Sallustro (Bellinzona)	Effector, regulatory and memory T cell subsets in humans
	Dr. Fabian Blank (Bern)	Delivery of antigens for pulmonary vaccination: recent advances and challenges

	Prof. Eliane Marti (Bern)	Characterization of equine CD4+CD25high lymphocytes expressing FoxP3 and their role in insect bite hypersensitivity
Nov. 28, 2013	PD Dr. Thomas Kaufmann (chair) Prof. Werner Pichler Dr. Sabine Höpner Dr. Yasmin Köller	Highlights of the Year
Dec. 19, 2013	Dr. Saul A. Villeda The Eli & Edythe Broad Center of Regeneration Medicine & Stem Cell Research University of California, San Francisco (CA, USA)	Systemic regulation of adult neurogenesis and novel approaches to rejuvenate old brains

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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_2014/index_eng.html

3.6. Academic Degrees

Ursina Regula Gurzeler, PhD, University of Bern
Thesis: Regulation of cell death in murine granulocytes (April 2013)
Supervisor: PD Dr. Thomas Kaufmann

Marc Wehrli, PhD, University of Bern
Thesis: Neutrophil death regulation by IgA and its receptor FcαRI (June 2013)
Supervisor: PD Dr. Stephan von Gunten

Manuel Simon, PhD, University of Bern
Thesis: Engineering and preclinical investigation of designed ankyrin repeat proteins as a versatile platform of binding proteins for tumor targeting (August 2013)
Supervisors: Prof. Uwe Zangemeister-Wittke, Prof. Andreas Plückthun

Mahbubul Moshed, PhD, University of Bern
Thesis: Eosinophils and basophils form extracellular DNA traps (November 2013)
Supervisors: Prof. Hans-Uwe Simon, Prof. Dagmar Simon

Thomas Adrian von Rütte, Dr. med. (MD), University of Bern
Thesis: Reduced expression of ATG5 in melanoma (November 2013)
Supervisor: Prof. Hans-Uwe Simon

Christoph Schneider, M.Sc., University of Bern
Thesis: Siglecs as potential targets in enhancing anti-tumor immunity (February 2013)
Supervisors: PD Dr. Stephan von Gunten, Kayluz Frias Boligan

Tobias Horn, MMed, University of Bern
Thesis: Neutrophil death induced by Siglec-9 and Fc-alpha receptor I (April 2013)
Supervisors: PD Dr. Stephan von Gunten, Dr. Marc Wehrli

Christine Gallasz, MMed, University of Bern
Thesis: Siglec-7 and -9: Quantification of their ligands on differnet types of cancer cells and their impact on natural killer cells (November 2013)
Supervisors: PD Dr. Stephan von Gunten, Kayluz Frias Boligan

Nathalie Friedli, M.Sc. pharm., University of Basel
Thesis: Epithelial barrier function in eosinophilic esophagitis (February 2013)
Supervisors: Prof. Hans-Uwe Simon, Prof. Dr. Dagmar Simon

Manon Widmer,* M.Sc. *pharm.*, *University of Basel
Thesis: Basophil responses to extracellular ATP (June 2013)
Supervisors: Prof. Hans-Uwe Simon, Dr. Christina Merz-Stöckle

Florence Charrière, M.Sc. pharm., University of Basel
Thesis: New insights into esophageal barrier function in eosinophilic esophagitis (June 2013)
Supervisors: Prof. Hans-Uwe Simon, Dr. Susanne Radonjic-Hösli

Eliane Stucki, M.Sc. pharm., University of Basel
Thesis: Molecular mechanism required for NET formation (June 2013)
Supervisors: Prof. Hans-Uwe Simon, Prof. Shida Yousefi

Dominic Guillet, M.Sc. pharm., University of Basel
Thesis: Photorhapdus luminescens toxin: Cytotoxic activity on human and mouse neutrophils (June 2013)
Supervisors: Prof. Hans-Uwe Simon, Prof. Shida Yousefi, Dr. Poorya Amini

Evelin Krajnc, M.Sc. pharm., University of Ljubljana
Thesis: Mitochondria in neutrophils: Regulation of their localization (April 2013)
Supervisors: Prof. Hans-Uwe Simon, Prof. Irena Mlinaric-Rascan

4. Research Activities

4.1. Research Projects and Publications

Group Prof. Andrea Huwiler

Group members: Daniel Fallegger, PhD student[1]
Iuliia Filipenko, PhD student[1]
Faik Imeri, PhD student[1]
Oleksandr Pastukhov, PhD student[1]
Marianne Maillard-van Laer, technician[1]
Dr. Doriano Fabbro, PhD, guest senior scientist[1]
Elin Huwiler, high school graduate[1]
Dr. Stephanie Schwalm, Postdoc[2]
Isolde Römer, technician[2]
Svetlana Kokin, technician[2]

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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.

Effective inhibition of acid and neutral ceramidases by novel B-13 and LCL-464 analogues

K.P. Bhabak, B. Kleuser, A. Huwiler, C. Arenz

Induction of apoptosis mediated by the inhibition of ceramidases has been shown to enhance the efficacy of conventional chemotherapy in several cancer models. Among the inhibitors of ceramidases reported in the literature, B-13 is considered as a lead compound having good in vitro potency towards acid ceramidase. Furthermore, owing to the poor activity of B-13 on lysosoamal acid ceramidase in living cells, LCL-464 a modified derivative of B-13 containing a basic ω-amino group at the fatty acid was reported to have higher potency towards lysosomal acid ceramidase in living cells. In a search for more potent inhibitors of ceramidases, we have designed a series of compounds with structural modifications of B-13 and LCL-464. In this study, we show that the efficacy of B-13 in vitro as well as in intact cells can be enhanced by suitable modification of functional groups. Furthermore, a detailed SAR investigation on LCL-464 analogues revealed novel promising inhibitors of aCDase and

nCDase. In cell culture studies using the breast cancer cell line MDA-MB-231, some of the newly developed compounds elevated endogenous ceramide levels and in parallel, also induced apoptotic cell death. In summary, this study shows that structural modification of the known ceramidase inhibitors B-13 and LCL-464 generates more potent ceramidase inhibitors that are active in intact cells and not only elevates the cellular ceramide levels, but also enhances cell death.

See original publication No. 1

PPARγ agonists upregulate sphingosine 1-phosphate (S1P) receptor 1 expression, which in turn reduces S1P-induced $[Ca_{2+}]_i$ increases in renal mesangial cells

A. Koch, A. Völzke, B. Puff, K. Blankenbach, D. Meyer zu Heringdorf, A. Huwiler, J. Pfeilschifter

We previously identified peroxisome proliferator-activated receptor gamma (PPARγ) agonists (thiazolidinediones, TZDs) as modulators of the sphingolipid metabolism in renal mesangial cells. TZDs upregulated sphingosine kinase 1 (SK-1) and increased the formation of intracellular sphingosine 1-phosphate (S1P), which in turn reduced the expression of pro-fibrotic connective tissue growth factor. Since S1P also acts as extracellular ligand at specific S1P receptors (S1PR, $S1P_{1-5}$), we investigated here the effect of TZDs on S1PR expression in mesangial cells and evaluated the functional consequences by measuring S1P-induced increases in intracellular free Ca^{2+} concentration ($[Ca^{2+}]_i$). Treatment with two different TZDs, troglitazone and rosiglitazone, enhanced $S1P_1$ mRNA and protein expression in rat mesangial cells, whereas $S1P_{2-5}$ expression levels were not altered. Upregulation of $S1P_1$ mRNA upon TZD treatment was also detected in human mesangial cells and mouse glomeruli. PPARγ antagonism and promoter studies revealed that the TZD-dependent $S1P_1$ mRNA induction involved a functional PPAR response element in the $S1P_1$ promoter. Pharmacological approaches disclosed that S1P-induced $[Ca^{2+}]_i$ increases in rat mesangial cells were predominantly mediated by $S1P_2$ and $S1P_3$. Interestingly, the transcriptional upregulation of $S1P_1$ by TZDs resulted in a reduction of S1P-induced $[Ca^{2+}]_i$ increases, which was reversed by the $S1P_{1/3}$ antagonist VPC-23019, the protein kinase C (PKC) inhibitor PKC-412, and by $S1P_1$ siRNA. These data suggest that PPARγ-dependent upregulation of $S1P_1$ leads to an inhibition of S1P-induced Ca^{2+} signaling in a PKC-dependent manner. Overall, these results reveal that TZDs not only modulate intracellular S1P levels but also regulate S1PR signaling by increasing $S1P_1$ expression in mesangial cells.

See original publication No. 2

Sphingosine 1-phosphate (S1P) induces COX-2 expression and PGE_2 formation via S1P receptor 2 in renal mesangial cells

A. Völzke, A. Koch, D. Meyer zu Heringdorf, A. Huwiler, J. Pfeilschifter

Understanding the mechanisms of sphingosine 1-phosphate (S1P)-induced cyclooxygenase (COX)-2 expression and prostaglandin E_2 (PGE_2) formation in renal mesangial cells may provide potential therapeutic targets to treat inflammatory glomerular diseases. Thus, we evaluated the S1P-dependent signaling mechanisms which are responsible for enhanced COX-2 expression and PGE_2 formation in rat mesangial cells under basal conditions. Furthermore, we investigated whether these mechanisms are operative in the presence of angiotensin II (Ang II) and of the pro-inflammatory cytokine interleukin-1β (IL-1β). Treatment of rat and human mesangial cells with S1P led to concentration-dependent enhanced expression of COX-2. Pharmacological and molecular biology approaches revealed that the S1P-dependent increase of COX-2 mRNA and protein expression was mediated via activation of S1P receptor 2 ($S1P_2$). Further, inhibition of G_i and p42/p44 MAPK signaling, both downstream of $S1P_2$, abolished the S1P-induced COX-2 expression. In addition, S1P/$S1P_2$-dependent upregulation of COX-2 led to significantly elevated PGE_2 levels, which

were further potentiated in the presence of Ang II and IL-1β. A functional consequence downstream of S1P/$S1P_2$ signaling is mesangial cell migration that is stimulated by S1P. Interestingly, inhibition of COX-2 by celecoxib and SC-236 completely abolished the migratory response. Overall, our results demonstrate that extracellular S1P induces COX-2 expression via activation of $S1P_2$ and subsequent G_i and p42/p44 MAPK-dependent signaling in renal mesangial cells leading to enhanced PGE_2 formation and cell migration that essentially requires COX-2. Thus, targeting S1P/$S1P_2$ signaling pathways might be a novel strategy to treat renal inflammatory diseases.
See original publication No. 3

Dual role of sphingosine kinase-1 in promoting the differentiation of dermal fibroblasts and the dissemination of melanoma cells
V. Albinet, M.L. Bats, A. Huwiler, P. Rochaix, C. Chevreau, B. Ségui, T. Levade, N. Andrieu-Abadie
Despite progress in the understanding of the biology and genetics of melanoma, no effective treatment against this cancer is available. The adjacent microenvironment has an important role in melanoma progression. Defining the molecular signals that control the bidirectional dialog between malignant cells and the surrounding stroma is crucial for efficient targeted therapy. Our study aimed at defining the role of sphingosine-1-phosphate (S1P) in melanoma-stroma interactions. Transcriptomic analysis of human melanoma cell lines showed increased expression of sphingosine kinase-1 (SPHK1), the enzyme that produces S1P, as compared with normal melanocytes. Such an increase was also observed by immunohistochemistry in melanoma specimens as compared with nevi, and occurred downstream of ERK activation because of BRAF or NRAS mutations. Importantly, migration of melanoma cells was not affected by changes in SPHK1 activity in tumor cells, but was stimulated by comparable modifications of S1P-metabolizing enzymes in cocultured dermal fibroblasts. Reciprocally, incubation of fibroblasts with the conditioned medium from SPHK1-expressing melanoma cells resulted in their differentiation to myofibroblasts, increased production of matrix metalloproteinases and enhanced SPHK1 expression and activity. In vivo tumorigenesis experiments showed that the lack of S1P in the microenvironment prevented the development of orthotopically injected melanoma cells. Finally, local tumor growth and dissemination were enhanced more efficiently by coinjection of wild-type skin fibroblasts than by fibroblasts from $Sphk1^{-/-}$ mice. This report is the first to document that SPHK1/S1P modulates the communication between melanoma cells and dermal fibroblasts. Altogether, our findings highlight SPHK1 as a potential therapeutic target in melanoma progression.
See original publication No. 4

Original publications

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Review articles

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Basic Clin. Pharmacol. Toxicol. 114 (2014), 44-49.

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Our group is interested in the molecular mechanisms of apoptosis, also called programmed cell death. Apoptosis is recognised to be crucial for sculpting the developing embryo, for maintaining tissue homeostasis in the adult, for shaping the immune repertoire, for terminating immune responses and in host responses to infections. Abnormalities in the control of apoptosis have been implicated in a variety of diseases, including cancer, autoimmune and neurodegenerative disorders, AIDS, stroke and sepsis. A deeper understanding of the regulation of apoptosis will thus not only help to clarify significant questions about normal development and physiology but may also provide insight into a number of pathological states.

The generation and use of genetically modified mice allows analysis of the regulation of apoptosis in organs/tissues of the developing and mature organism as well as the development of tumours and autoimmunity in case of a de-regulated apoptotic program. We are using mouse strains lacking important apoptosis regulators, such as pro- and anti-apoptotic members of the Bcl-2 family. Members of the BH3-only subgroup, which acts as sensors of apoptotic stress signals, are of particular interest and there are now mice available lacking one or several BH3-only proteins. On the other hand, we have shown that anti-apoptotic proteins of the 'inhibitor of apoptosis' family (IAP) are crucial in preventing death receptor-induced apoptosis. We have addtionally estalished a system to differentiate *ex vivo* immortalised myeloid progenitor cells (derived from any given genetically modified mouse strain) into mature granulocytes (neutrophils or basophils) or macrophages in near unlimited numbers.

In vitro differentiation of near-unlimited numbers of functional mouse basophils using conditional Hoxb8

U. Gurzeler, T. Rabachini, M. Salmanidis, G. Brumatti, P.G. Ekert, N. Echeverry, D. Bachmann, H.-U. Simon, T. Kaufmann

Background: Basophils constitute a rare leukocyte population known for their effector functions in inflammation and allergy, as well as more recently described immunoregulatory roles. Besides their low frequency, functional analysis of basophils is hindered by a short life

span, inefficient ex vivo differentiation protocols, and lack of suitable cell models. A method to produce large quantities of basophils in vitro would facilitate basophil research and constitute a sought-after tool for diagnostic and drug testing purposes.
Methods: A method is described to massively expand bone marrow–derived basophils in vitro. Myeloid progenitors are conditionally immortalized using Hoxb8 in the presence of interleukin-3 (IL-3) and outgrowing cell lines selected for their potential to differentiate into basophils upon shutdown of Hoxb8 expression.
Results: IL-3-dependent, conditional Hoxb8-immortalized progenitor cell lines can be expanded and maintained in culture for prolonged periods. Upon shutdown of Hoxb8 expression, near-unlimited numbers of mature functional basophils can be differentiated in vitro within six days. The cells are end-differentiated and short-lived and express basophil-specific surface markers and proteases. Upon IgE- as well as C5a-mediated activation, differentiated basophils release granule enzymes and histamine and secrete Th2-type cytokines (IL-4, IL-13) and leukotriene C4. IL-3-deprivation induces apoptosis correlating with upregulation of the BH3-only proteins BCL-2-interacting mediator of cell death (BIM) and p53 upregulated modulator of apoptosis (PUMA) and downregulation of proviral integration site for Moloney murine leukemia virus 1 kinase (PIM-1).
Conclusion: A novel method is presented to generate quantitative amounts of mouse basophils in vitro, which moreover allows genetic manipulation of conditionally immortalized progenitors. This approach may represent a useful alternative method to isolating primary basophils.
See original publication No. 1

Intracellular localization of the BCL-2 family member BOK and functional implications
N. Echeverry, D. Bachmann, F. Ke, A. Strasser, H.-U. Simon, T. Kaufmann
The pro-apoptotic BCL-2 family member BOK is widely expressed and resembles the multi-BH domain proteins BAX and BAK based on its amino acid sequence. The genomic region encoding BOK was reported to be frequently deleted in human cancer and it has therefore been hypothesized that BOK functions as a tumor suppressor. However, little is known about the molecular functions of BOK. We show that enforced expression of BOK activates the intrinsic (mitochondrial) apoptotic pathway in BAX/BAK-proficient cells but fails to kill cells lacking both BAX and BAK or sensitize them to cytotoxic insults. Interestingly, major portions of endogenous BOK are localized to and partially inserted into the membranes of the Golgi apparatus as well as the endoplasmic reticulum (ER) and associated membranes. The C-terminal transmembrane domain of BOK thereby constitutes a ‘tail-anchor’ specific for targeting to the Golgi and ER. Overexpression of full-length BOK causes early fragmentation of ER and Golgi compartments. A role for BOK on the Golgi apparatus and the ER is supported by an abnormal response of Bok-deficient cells to the Golgi/ER stressor brefeldin A. Based on these results, we propose that major functions of BOK are exerted at the Golgi and ER membranes and that BOK induces apoptosis in a manner dependent on BAX and BAK.
See original publication No. 2

Foxo-mediated Bim transcription is dispensable for the apoptosis of hematopoietic cells that is mediated by this BH3-only protein
MJ Herold, L. Rohrbeck, MJ Lang, R. Grumont, S. Gerondakis, L. Tai, P. Bouillet,
T. Kaufmann* and A. Strasser* (*: shared senior authorship)
The BH3-only protein Bim is a critical initiator of apoptosis in hematopoietic cells. Bim is upregulated in response to growth factor withdrawal and in vitro studies have implicated the transcription factor Foxo3a as a critical inducer. To test the importance of this regulation in vivo, we generated mice with mutated Foxo-binding sites within the Bim promoters (BimΔFoxo/ΔFoxo). Contrary to Bim-deficient mice, BimΔFoxo/ΔFoxo mice had a normal

hematopoietic system. Moreover, cytokine-dependent haematopoietic cells from BimΔFoxo/ΔFoxo and wt mice died at similar rates. These results indicate that regulation of Bim by Foxo transcription factors is not critical for the killing of hematopoietic cells.
See original publication No. 3

Original publications

1. U. Gurzeler, T. Rabachini, M. Salmanidis, G. Brumatti, P.G. Ekert, N. Echeverry, D. Bachmann, H.-U. Simon, **T. Kaufmann**: In vitro differentiation of near-unlimited numbers of functional mouse basophils using conditional Hoxb8
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2. N. Echeverry, D. Bachmann, F. Ke, A. Strasser, H.-U. Simon, **T. Kaufmann**: Intracellular Localization of the BCL-2 Family Member BOK and Functional Implications
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3. M.J. Herold, L. Rohrbeck, M.J. Lang, R. Grumont, S. Gerondakis, L. Tai, P. Bouillet, **T. Kaufmann***, A. Strasser*: Foxo-mediated Bim transcription is dispensable for the apoptosis of hematopoietic cells that is mediated by this BH3-only protein.
   EMBO Reports 14 (2013), 992-998. *: shared senior authorship.

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

We are interested in the role of apoptosis and autophagy in inflammatory diseases and cancer. Several diseases serve as models to study such processes. In particular, we investigate pathogenic mechanisms of the following diseases: Atopic dermatitis, hypereosinophilic syndromes, eosinophilic esophagitis, 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 2013.

ATG5 is induced by DNA-damaging agents and promotes mitotic catastrophe independent of autophagy

D. Maskey, S. Yousefi, I. Schmid, I. Zlobec, A. Perren, R. Friis, H.-U. Simon

Anticancer drug therapy activates both molecular cell death and autophagy pathways. Here we show that even sublethal concentrations of DNA-damaging drugs, such as etoposide and cisplatin, induce the expression of autophagy-related protein 5 (ATG5), which is both necessary and sufficient for the subsequent induction of mitotic catastrophe. We demonstrate that ATG5 translocates to the nucleus, where it physically interacts with survivin in response to DNA-damaging agents both in vitro and in carcinoma tissues obtained from patients who had undergone radiotherapy and/or chemotherapy. As a consequence, elements of the chromosomal passenger complex are displaced during mitosis, resulting in chromosome misalignment and segregation defects. Pharmacological inhibition of autophagy does not prevent ATG5-dependent mitotic catastrophe, but shifts the balance to an early caspase-dependent cell death. Our data suggest a dual role for ATG5 in response to drug-induced DNA damage, where it acts in two signalling pathways in two distinct cellular compartments, the cytosol and the nucleus.

See original publication No. 1

Down-regulation of autophagy-related protein 5 (ATG5) contributes to the pathogenesis of early-stage cutaneous melanoma

H. Liu, Z. He, T. von Rütte, S. Yousefi, R.E. Hunger, H.-U. Simon

The role of autophagy in cancer is controversial: Both tumor-suppressing and tumor-promoting functions have been reported. We show that a key regulator of autophagy, autophagy-related protein 5 (ATG5), is often down-regulated in primary melanomas compared to benign nevi, leading to a reduction of basal autophagy as evidenced by a reduced expression of LC3. A follow-up of 158 primary melanoma patients showed that patients with low levels of ATG5 in their tumors had a reduced progression-free survival. In an in vitro model of melanoma tumorigenesis, where the BRAF oncogene was transduced into normal melanocytes, we observed that lowering ATG5 expression promoted proliferation by precluding oncogene-induced senescence. Hence, it appears that down-regulation of ATG5 contributes to tumorigenesis in early-stage cutaneous melanoma, and the expression of ATG5 and LC3 correlates with melanoma diagnosis and prognosis.

See original publication No. 2

p73 regulates autophagy and hepatocellular lipid metabolism through a transcriptional activation of the ATG5 gene

Z. He, H. Liu, M. Agostini, S. Yousefi, A. Perren, M.P. Tschan, T.W. Mak, G. Melino, H.-U. Simon

p73, a member of the p53 tumor suppressor family, is involved in neurogenesis, sensory pathways, immunity, inflammation, and tumorigenesis. How p73 is able to participate in such a broad spectrum of different biological processes is still largely unknown. Here, we report a novel role of p73 in regulating lipid metabolism by direct transactivation of the promoter of autophagy-related protein 5 (ATG5), a gene whose product is required for autophagosome formation. Following nutrient deprivation, the livers of p73-deficient mice demonstrate a massive accumulation of lipid droplets, together with a low level of autophagy, suggesting that triglyceride hydrolysis into fatty acids is blocked owing to deficient autophagy (macrolipophagy). Compared with wild-type mice, mice functionally deficient in all the p73 isoforms exhibit decreased ATG5 expression and lower levels of autophagy in multiple organs. We further show that the TAp73α is the critical p73 isoform responsible for inducing ATG5 expression in a p53-independent manner and demonstrate that ATG5 gene transfer can correct autophagy and macrolipophagy defects in p73-deficient hepatocytes. These data strongly suggest that the p73-ATG5 axis represents a novel, key pathway for regulating lipid

metabolism through autophagy. The identification of p73 as a major regulator of autophagy suggests that it may have an important role in preventing or delaying disease and aging by maintaining a homeostatic control.
See original publication No. 3

Anti-eosinophil activity and clinical efficacy of the CRTH2 antagonist OC000459 in eosinophilic esophagitis

A. Straumann, S. Hoesli, C. Bussmann, M. Stuck, M. Perkins, L.P. Collins, M. Payton, R. Pettipher, M. Hunter, J. Steiner, H.-U. Simon

Background: Eosinophilic esophagitis (EoE) is a chronic, Th2-type inflammatory disease. CRTH2 (chemoattractant receptor-homologous molecule on Th2 cells) is a prostaglandin D_2 (PGD_2) receptor, expressed by Th2 cells and other inflammatory cells, including eosinophils and basophils, that mediates chemotaxis and activation. OC000459 is a selective CRTH2 antagonist and would be expected to suppress eosinophilic tissue inflammation. **Objective:** The purpose of this study was to evaluate the efficacy and safety of an OC000459 monotherapy in adult patients with active, corticosteroid-dependent or corticosteroid-refractory EoE. **Methods:** In this randomized, double-blind, placebo-controlled trial, 26 adult patients (m/f = 22/4; mean age 41 yrs, range 22-69 yrs) with active EoE, dependent or resistant to corticosteroids, were treated either with 100 mg OC000459 (n=14) or placebo (n=12) twice daily. Pre- and post-treatment disease activity was assessed clinically, endoscopically, histologically and via biomarkers. The primary endpoint was the reduction of esophageal eosinophil infiltration. **Results:** After an 8-week OC000459 treatment, the esophageal eosinophil load decreased significantly, from 114.83 to 73.26 eosinophils per high power field (eos/hpf), p=0.0256), whereas no reduction was observed with placebo (102.80 to 99.47 eos/hpf, p=0.870). With OC000459, the physician's global assessment of disease activity improved from 7.13 to 5.18 (p=0.035). OC000459 likewise reduced extracellular deposits of eosinophil peroxidase and tenascin C, effects not seen with placebo. No serious adverse events were observed. **Conclusions:** An 8-week treatment with the CRTH2-antagonist, OC000459, exerts modest, but significant anti-eosinophil and beneficial clinical effects in adult patients with active, corticosteroid-dependent or corticosteroid-refractory EoE, and is well tolerated.
See original publication No. 4

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. 7

Original publications

1. D. Maskey, S. Yousefi, I. Schmid, I. Zlobec, A. Perren, R. Friis, **H.-U. Simon**: A novel role for ATG5 in drug-induced mitotic catastrophe independent of autophagy.
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2. H. Liu, Z. He, T. von Rütte, S. Yousefi, R.E. Hunger, **H.-U. Simon**: Down-regulation of autophagy-related protein 5 (ATG5) contributes to the pathogenesis of early stage cutaneous melanoma.
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   Allergy 68 (2013), 365-375.

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   J. Leukoc. Biol. 95 (2014), in press.

8. D. Simon, C. Aeberhard, Y. Erdemoglu, **H.-U. Simon**: Th17 cells and tissue remodeling in atopic and contact dermatitis.
   Allergy 69 (2014), in press.

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10. N. Echeverry, D. Bachmann, F. Ke, A. Strasser, **H.-U. Simon**, T. Kaufmann: Intracellular localization of the BCL-2 family member BOK and functional implications.
    Cell Death Differ. 20 (2013), 785-799.

11. T. Démoulins, I. Bassi, L. Thomann-Harwood, C. Jandus, P. Kaeuper, **H.-U. Simon**, S. von Gunten, K.C. McCullough: Alginate-coated chitosan nanogel capacity to modulate the effect of TLR ligands on blood dendritic cells.
    Nanomedicine 9 (2013), 806-817.

12. A.M. Schoepfer, E. Safroneeva, C. Bussmann, T. Kuchen, S. Portmann, **H.-U. Simon**, A. Straumann: Delay in diagnosis of eosinophilic esophagitis increases risk for stricture formation, in a time-dependent manner.
Gastroenterology 145 (2013), 1230-1236.

13. M. Humbert, E.A. Federzoni, A. Britschgi, A.M. Schläfli, P.J.M. Valk, T. Kaufmann, T. Haferlach, G. Behre, **H.-U. Simon**, B.E. Torbett, M.F. Fey, M.P. Tschan: The tumor suppressor gene DAPK2 is induced by the myeloid transcription factors PU.1 and C/EBPalpha during granulocytic differentiation but repressed by PML-RARalpha in APL.
J. Leukoc. Biol. 95 (2014), 83-93.

14. C. Jandus, K. Frias Boligan, O. Chijioke, H. Liu, H. Dahlhaus, T. Démoulins, C. Schneider, M. Wehrli, R.E. Hunger, G.M. 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. 2014, in press.

Review articles/Editorials

1. B. Geering, C. Stoeckle, S. Conus, **H.-U. Simon**: Living and dying for inflammation: neutrophils, eosinophils, basophils.
Trends Immunol. 34 (2013), 398-409.

2. H. Liu, Z. He, **H.-U. Simon**: Targeting autophagy as a potential therapeutic approach for melanoma therapy.
Seminars Cancer Biol. 23 (2013), 352-360.

3. Z. He, **H.-U. Simon**: A novel link between p53 and ROS.
Cell Cycle 12 (2013), 201-201.

4. Z. He, **H.-U. Simon**: Autophagy protects from liver injury.
Cell Death Differ. 20 (2013), 850-851.

5. S. von Gunten, M. Wehrli, **H.-U. Simon**: Cell death in immune thrombocytopenia: Novel insights and perspectives.
Sem. Hematol. 50 (2013), Suppl. 1, S109-S115.

6. **H.-U. Simon**: Allergic inflammation: focus on eosinophils.
Allergy 68 (2013), 823-824.

7. D. Simon, L. Borradori, **H.-U. Simon**: Glucocorticoids in autoimmune bullous diseases: Are neutrophils the key cellular target?
J. Invest. Dermatol. 133 (2013), 2314-2315.

8. **H.-U. Simon**, R. Friis: ATG5: A distinct role in the nucleus.
Autophagy 10 (2014), 176-177.

9. **H.-U. Simon**, A. Straumann: Immunopathogenesis of eosinophilic esophagitis.
Dig. Dis. 32 (2014), 11-14.

10. H. Liu, Z. He, **H.-U. Simon**: Autophagy suppresses melanoma tumorigenesis by inducing senescence.
Autophagy 10 (2014), in press.

11. D. Simon, **H.-U. Simon**, S. Yousefi: Extracellular DNA traps in allergic, infectious, and autoimmune diseases.
Allergy 68 (2013), 409-416.

Book chapters

1. **H.-U. Simon**, S. Yousefi: Eosinophil-mediated antibacterial host defense. In: Eosinophils in Health and Disease (Eds. J.J. Lee and H.F. Rosenberg); Elsevier Inc., London – Waltham, MA – San Diego, CA, 2013, p. 279-281.

2. S. Radonjic-Hoesli, **H.-U. Simon:** History of eosinophils. In: History of Allergy (Eds. K.-C. Bergmann und J. Ring; Series: Chemical Immunology and Allergy). Karger, in press.

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

Group PD Dr. Stephan von Gunten

Group members: Kayluz Frias Boligan, PhD student
Christoph Schneider, PhD student
Fabiola Schorer, PhD student
Dr. Marc Wehrli, MD-PhD student
Katharina Fuchs, MMed student
Christine Gallasz, MMed student (MD student since Dec. 1)
Tobias Horn, MMed student
Ariane Meister, MMed student
Muriel Ott, MMed student
Rebecca Strässle, 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.

Alginate-coated chitosan nanogel capacity to modulate the effect of TLR ligands on blood dendritic cells

T. Démoulins, I. Bassi, L. Thomann-Harwood, C. Jandus, P. Kaeuper, H.-U. Simon, S. von Gunten, K.C. McCullough

Biodegradable nanoparticles have been employed for vaccine delivery, frequently admixed with adjuvants. Surprisingly, there is little information on their modulation of immune responses, speculated to be negligible. We analyzed the immunomodulatory capacity of alginate-coated chitosan nanogels (Ng), on porcine and human blood dendritic cells (DCs), when applied with defined adjuvants targeting different DC subpopulations. DC maturation, cytokine production and cell migration were assessed. Ng differentially influenced the immunomodulatory characteristics of individual Toll-like receptor (TLR) ligands: Pam3Cys-SK4-induced IL-1β was enhanced; CpG-oligodeoxynucleotides (CpG-ODN)-induced IFN-α, IL-6 and TNFα were impaired; CpG-ODN-induced CD86 and CCR7, and cell migration, were diminished-plasmacytoid DCs (pDCs) were particularly sensitive. Therein, the Ng influence on DC endocytosis of the TLR ligands was apparently a major contributory element. This demonstrates the importance of predefining the interplay between delivery vehicles and admixed immunostimulatory moieties, for ensuring appropriate immune activation and efficacious combinations.

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, H. Dahlhaus, T. Démoulins,
C. Schneider, M. Wehrli, R.E. Hunger, G.M. Baerlocher, H.-U. Simon, P. Romero,
C. Münz, S. von Gunten
Altered surface glycosylation on malignant cells may affect tumor immunity by direct interaction with glycan-binding proteins (lectins). Siglec-7 and -9 are MHC class I independent inhibitory receptors on human NK cells that recognize sialic acid containing carbohydrates. We found that Siglec-9 defines a subset of cytotoxic $CD56^{dim}$ NK cells with a more mature phenotype and enhanced chemotactic potential that is reduced in the peripheral blood of cancer patients. A broad analysis revealed that Siglec-7 and -9 ligands are expressed on human cancer cells of different histological types. Siglec-7- and -9 ligand expression determined the susceptibility of NK cell-sensitive and, unexpectedly, of presumably resistant tumor cells for NK cell-mediated cytotoxicity. These observations have direct implications for NK cell-based therapies and highlight the requirement to consider both the MHC-I haplotype and tumor-specific glycosylation.

See original publication No. 2

Original publications

1. T. Démoulins, I. Bassi, L. Thomann-Harwood, C. Jandus, P. Kaeuper, H.-U. Simon, **S. von Gunten,** K.C. McCullough: Alginate-coated chitosan nanogel capacity to modulate the effect of TLR ligands on blood dendritic cells.
Nanomedicine 9 (2013), 806-817.

2. C. Jandus, K. Frias Boligan, O. Chijioke, H. Liu, H. Dahlhaus, T. Démoulins, C. Schneider, M. Wehrli, R.E. Hunger, G.M. 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. 2014, in press

Review articles/Editorials

1. **S. von Gunten**, F. Cortinas-Elizondo, M. Kollarik, C. Beisswenger, P.M. Lepper: Mechanisms and potential therapeutic targets in allergic inflammation: recent insights.
Allergy 68 (2013), 1487-1498.

2. **S. von Gunten**, M. Wehrli, H.-U. Simon: Cell death in immune thrombocytopenia: novel insights and perspectives.
Semin. Hematol. 50, Suppl 1 (2013), 109-115.

Group Prof. Shida Yousefi

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Dominic Guillet, M.Sc. student*
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Inès Schmid, head technician*
Darko Stojkov, PhD student*
Eliane Stucki, M.Sc. 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.

Original publications

1. D. Maskey, **S. Yousefi**, I. Schmid, I. Zlobec, A. Perren, R. Friis, H.-U. Simon: A novel role for ATG5 in drug-induced mitotic catastrophe independent of autophagy.
   Nat. Commun. 4 (2013), 2130.

2. H. Liu, Z. He, T. von Rütte, **S. Yousefi**, R.E. Hunger, H.-U. Simon: Down-regulation of autophagy-related protein 5 (ATG5) contributes to the pathogenesis of early stage cutaneous melanoma.
   Sci. Transl. Med. 5 (2013), 202ra123.

3. Z. He, H. Liu, M. Agostini, **S. Yousefi**, A. Perren, M.P. Tschan, T.W. Mak, G. Melino, H.-U. Simon: p73 regulates autophagy and hepatocellular lipid metabolism through a transcriptional activation of the ATG5 gene.
   Cell Death Differ. 20 (2013), 1415-1424.

Review article

1. D. Simon, H.-U. Simon, **S. Yousefi**: Extracellular DNA traps in allergic, infectious, and autoimmune diseases.
   Allergy 68 (2013), 409-416.

Book chapter

1. H.-U. Simon, **S. Yousefi**: Eosinophil-mediated antibacterial host defense. In: Eosinophils in Health and Disease (Eds. J.J. Lee and H.F. Rosenberg); Elsevier Inc., London – Waltham, MA – San Diego, CA, 2013, p. 279-281.

Group Prof. Uwe Zangemeister-Wittke

Group members Bern/Zürich: Julia Filipenko, PhD student
Tankica Timcheva, PhD student
Dr. Manuel Simon, Postdoc[1,2]
Dr. Nikolas Stefan, Postdoc[1,2]
Kevin Oberson, technician (30%)
Bernd Schumacher, M.Sc. student[2]

[1]Institute of Pharmacology, University of Bern
[2]Institute of Biochemistry, University of Zürich

We are interested in translational aspects of tumor targeting and molecular oncology.

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 have generated state-of-the-art nanomedicines equipped with various payloads comprising bacterial biotoxins, chemotherapeutic agents and therapeutic oligonucleotides. In addition to tumor targeted delivery, in a prodrug-like approach the highly destructive potential of the biotoxin is further harnessed by reversible veiling using a protease cleavable linkage of polymers.

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. T. Rabi, A. Huwiler, **U. Zangemeister-Wittke**: 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.
Mol. Carcinog. 2013 Mar 8. doi: 10.1002/mc.22012 (in press).

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. 2013 Nov 1, in press.

3. A. Wojtalla, B. Fischer, N. Kotelevets, F.A. Mauri, J. Sobek, H. Rehrauer, C. Wotzkow, M.P. Tschan, M.J. Seckl, **U. Zangemeister-Wittke**, A. Arcaro: Targeting the phosphoinositide 3-kinase p110a isoform impairs cell proliferation, survival and tumor growth in small cell lung cancer.
Clin. Cancer Res. 19 (2013), 96-105.

4. M. Simon, R. Frey, **U. Zangemeister-Wittke**, A. Plückthun: Orthogonal assembly of a designed ankyrin repeat protein-cytotoxin conjugate with a clickable serum albumin module for half-life extension.
Bioconjug. Chem. 24 (2013), 1955-1966.

Review article

1. M. Simon, N. Stefan, A. Plückthun, **U. Zangemeister-Wittke**: Epithelial cell adhesion molecule-targeted drug delivery for cancer therapy.
Expert Opin. Drug Deliv. 10 (2013), 451-468.

Additional Publications by PKI Members

Dr. Christina Merz-Stöckle

Original articles

E. Adamopoulou, S. Tenzer, N. Hillen, P. Klug, I.A. Rota, S. Tietz, M. Gebhardt, S. Stevanovic, H. Schild, E. Tolosa, A. Melms, **C. Stoeckle:** Exploring the MHC-peptide matrix of central tolerance in the human thymus.
Nat. Commun. 19 (2013), 2039.

C. Stoeckle, I.A. Rota, E. Tolosa, C. Haller, A. Melms, E. Adamopoulou: Isolation of myeloid dendritic cells and epithelial cells from human thymus.
J. Vis. Exp. 79 (2013), e50951.

Dr. Tatiana Rabachini

Original articles

S.D. Walter, C.A. Riddell, **T. Rabachini**, L.L. Villa, E.L. Franco: Accuracy of p53 codon 72 polymorphism status determined by multiple laboratory methods: a latent class model analysis.
PLoS One 8 (2013), e56430.

G.N. Haij, ..., **T. Rabachini**, ... , et al.: The unconventional secretion of stress-inducible protein 1 by a heterogeneous population of extracellular vesicles.
Cell Mol. Life Sci. 70 (2013), 3211-3227.

M.L. Baggio, …, **T. Rabachini**, … , et al.: Polymorphism in the promoter region of the Toll-like receptor 9 gene and cervical human papillomavirus infection.
J. Gen. Virol. 94 (2013), 1858-1864.

M. Chevarie-Davis, ... , **T. Rabachini**, ... , et al.: Assessment of the performance of algorithms for cervical cancer screening: evidence from the Ludwig-McGill cohort study. Gynecol. Oncol. 128 (2013), 415-419.

PD Dr. Peter Späth

Review article

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 Medicine 2014, in press.

Book chapter

P.J. Späth, R.W. Van Holten, C. Kempf: Pathogen safety of immunoglobulin preparations. In: Wahn, V. and Orange, J. (eds) Clinical Use of Immunoglobulins. 2nd edn. UNI-MED Verlag, Bremen - London - Boston, 2013, p. 26-50.

4.2. Congress Invitations

PD Dr. Thomas Kaufmann

8th Tuscany Retreat on Cancer Research and Apoptosis: Genetic profiling, resistance mechanism and novel treatment concepts in cancer; Sarteano-Siena (IT), Aug. 3-8, 2013;
Investigating the molecular functions of the BCL-2 family member BOK.

Joint Annual Meeting of the Swiss Society for Allergology and Immunology and the Swiss Respiratory Society; Bern (CH), April 17-19, 2013;
Regulation of programmed cell death by BCL-2 family members.

Prof. Hans-Uwe Simon

Annual Meeting of the American Academy of Allergy Asthma and Immunology (AAAAI); San Antonio, TX (USA), February 22-26, 2013;
How to get your manuscript published.

Annual Meeting of the American Academy of Allergy Asthma and Immunology (AAAAI); San Antonio, TX (USA), February 22-26, 2013;
Extracellular eosinophil DNA traps: How to assess and their role in disease.

Annual Meeting of the American Academy of Allergy Asthma and Immunology (AAAAI); San Antonio, TX (USA), February 22-26, 2013;
Eosinophilic esophagitis: Lessons learned from investigator-initiated trials.

Joint Annual Meeting of the Swiss Society for Allergology and Immunology and the Swiss Respiratory Society; Bern (CH), April 17-19, 2013;
New insights into eosinophil biology.

2nd Global Allergy Forum (GAF) – Davos; Allergy and allergic diseases: Barriers to cure and possible interventions; Davos (CH), June 16-19, 2013;
Education in allergy – how to close the information gap.

EAACI-WAO: World Allergy & Asthma Congress; Milan (I), June 22-26, 2013;
Treatment of eosinophil-related disorders.

8th Biennial Symposium of the International Eosinophil Society; Oxford (UK),
July 13-17, 2013;
State of the art: Eosinophil effector function.

Falk Symposium on Eosinophilic Esophagitis: A Novel Chronic-Inflammatory Disease of the GI Tract; Graz (A), September 6-7, 2013;
Effector functions of eosinophils and immunopathology.

Falk Symposium on Eosinophilic Esophagitis: A Novel Chronic-Inflammatory Disease of the GI Tract; Graz (A), September 6-7, 2013;
Treatment of EoE with drugs 2: Non-corticosteroid drugs.

21st European Cell Death Organization (ECDO) Euroconference on Apoptosis;
Paris (F), September 25-28, 2013;
Role of ATG5 in cancer.

22nd European Academy of Dermatology and Venereology (EADV) Congress;
Istanbul (TR), October 2-6, 2013;
Eosinophils: Friend or foe.

EADV Dermatological Meeting in Ticino: From the Bench to the Clinic;
Bellinzona (CH), November 28, 2013;
ATG5: A novel tumour suppressor.

International Symposium "Cell Death and Immunity", Cologne Excellence on Cellular Stress Responses in Aging Associated Diseases (CECAD) Research Center, University of Cologne; Cologne (D), December 11, 2013;
New insights into granulocyte biology.

Kick-off follow up: new horizons; SCRM Platform, University of Bern;
Bern (CH), December 13, 2013;
ATG5 is induced by DNA-damaging agents and promotes mitotic catastrophe independent of autophagy.

PD Dr. Peter Späth

8th C1 Inhibitor Deficiency Workshop; Budapest (H), May 23-26, 2013;
"Closing remarks" http://www.haenet2013.hu/img/nicedit/closing_remarks.pdf.

Dr. Christina Merz-Stoeckle

Joint Annual Meeting of the Swiss Society for Allergology and Immunology and the Swiss Respiratory Society; Bern (CH), April 17-19, 2013;
The role of the small GTPase RhoH in eosinophil development and eosinophilic disorders.

TM's 2nd World Immunology Online Conference, March 19-21, 2013;
Antigen processing and presentation in the human thymus.

Prof. Shida Yousefi

22th Cytomeet; Bern (CH), January 29, 2013;
Mechanism of mitochondrial DNA release.

Carl Zeiss Workshop (user meeting); Munich (D), October 30-31, 2013;
Confocal microscopy.

4.3. Seminar Invitations

PD Dr. Thomas Kaufmann

Institute of Experimental Immunology, University of Zurich, June 4, 2013;
guest of Dr. Lynn Wong:
New insights into the regulation of cell death by BCL-2 and IAP family members.

Saša Rožman

Theodor Kocher Institute, University of Bern, March 12, 2013;
guest of Prof. Britta Engelhardt:
Role of ATG5 in neutrophil differentiation.

Dr. Christina Merz-Stoeckle

University Medical Center Hamburg-Eppendorf, Institut für Immunologie, Jan. 10, 2013;
guest of PD Dr. Eva Tolosa:
Putting brakes on eosinophil development.

Prof. Hans-Uwe Simon

Department of Cell Biology, University of Geneva, Jan. 11, 2013; guest of Prof. Jean-Claude Martinou:
The p73-ATG5 axis in hepatocellular lipid metabolism.

Institute for Genomics and Proteomics, University of California, Los Angeles (CA, USA), Febr. 27, 2013; guest of Prof. David Eisenberg:
The p73-ATG5 axis: A key pathway regulating autophagy and hepatocellular lipid metabolism.

Department of Dermatology, University of Bonn, SFB 704, Bonn (D), April 10, 2013;
guest of Prof. Thomas Bieber:
Epigenetic silencing of ATG5 in melanoma.

Faculty of Pharmacy, University of Ljubljana, Ljubljana (Slovenia), April 26, 2013;
guest of Prof. Irena Mlinaric-Rascan:
Autophagy and epigenetics in melanoma pathogenesis.

Department of Biochemistry, University of Lausanne, Lausanne, May 31, 2013;
guest of Prof. Fabienne Tacchini-Cottier:
Novel insights into innate immune mechanisms mediated by eosinophils.

Novartis Institutes for BioMedical Research, Basel, July 11, 2013;
guest of Dr. Andreas Billich:
Programmed cell death pathways in neutrophils.

Department of Clinical Immunology and Allergy, University Hospital Geneva, Geneva, Nov. 1, 2013; guest of Prof. Jörg Seebach:
Innate immunity and immunopathology mediated by eosinophils.

Institute of Pathophysiology and Allergy Research, Medical University Vienna, Vienna (A), Nov. 15, 2013; guest of Prof. Rudolf Valenta:
New insights in eosinophil biology.

PD Dr. Stephan von Gunten

Department of Internal Medicine, Cantonal Hospital of Baden, Baden (CH), July 11, 2013; guest of Prof. Hans-Jürg Beer:
Update on IVIG: indications, mechanisms, results.

4.4. Organization of Meetings and Courses

Prof. Hans-Uwe Simon

Symposium of the Swiss Society of Pharmacology and Toxicology (together with task force SSPT): Progress in Pharmacology – Gastroenterological Pharmacology,
Bern (CH), Jan. 31, 2013.

Mitglied der Programmkommission: 79. Jahrestagung der Deutschen Gesellschaft für Experimentelle und Klinische Pharmakologie und Toxikologie e.V. (DGPT),
Halle (D), March 5-7, 2013.

Member of the Local Organizing Board: Joint Annual Meeting of the Swiss Society for Allergology and Immunology (SSAI) and Swiss Respiratory Society (SRS), Bern (CH), April 17-19, 2013.

Workshop on Cell Death and Disease (together with E. Candi, D. Delia, and P. Krammer), Villa Vigoni, Loveno di Menaggio, Como (I), June 19-22, 2013.

12th III-Bern International Summer School, Jongny (CH), August 04-06, 2013.

Falk Symposium on Eosinophilic Esophagitis: A Novel Chronic-Inflammatory Disease of the GI Tract (together with A. Straumann and A. Schoepfer),
Graz (A), September 6-7, 2013.

4.5. Invited Chairperson at Congresses

PD Dr. Thomas Kaufmann

Joint Annual Meeting of the Swiss Society for Allergology and Immunology and the Swiss Respiratory Society; Session: “Development and death in the immune system”; Bern (CH), April 17-19, 2013.

Prof. Hans-Uwe Simon

Symposium of the Swiss Society of Pharmacology and Toxicology: Fortschritte in der Pharmakologie – Gastroenterological Pharmacology, Morning session; Bern (CH), Jan. 31, 2013.

79. Jahrestagung der Deutschen Gesellschaft für Experimentelle und Klinische Pharmakologie und Toxikologie e. V. (DGPT); Poster session: „Session E“; Halle (D), March 5-7, 2013.

World Immune Regulation Meeting – VII; Session: „Control of inflammation“; Davos (CH), March 13-16, 2013.

Joint Annual Meeting of the Swiss Society for Allergology and Immunology and the Swiss Respiratory Society; Session: “Eosinophils in inflammation”; Bern (CH), April 17-19, 2013.

2nd Global Allergy Forum (GAF) – Davos; Allergy and allergic diseases: Barriers to cure and possible interventions; Plenary session: “Education in allergy”; Davos (CH), June 16-19, 2013.

8th Biennial Symposium of the International Eosinophil Society; Poster session II: “Eosinophils as effector cells”; Oxford (UK), July 13-17, 2013.

Falk Symposium on Eosinophilic Esophagitis: A Novel Chronic-Inflammatory Disease of the GI Tract; Session: “Basics II: Genetic-environmental interactions”; Graz (A), September 6-7, 2013.

21st ECDO Euroconference on Apoptosis; Session: “Death & Disease”; Paris (F), September 25-28, 2013.

PD Dr. Peter Späth

International Plasma Protein Congress, Session 7: **“**Clinical Developments”; Dublin (Ireland), March 5-6, 2013.

CSL Behring Summer School for Pediatricians, Charité, Campus Virchow-Klinikum; Pediatric immunology – Basic concepts and presentation of new cases form the daily clinical practice, Chairing the Friday afternoon sessions; Berlin (D), August 30-31, 2013.

4.6 Referee Work for Peer-Reviewed Journals

Dr. Zhaoyue He

Allergy
Cell Death Dis.
Cell Death Differ.

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.
FEBS Lett.
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

Prof. Thomas Kaufmann

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

Dr. He Liu

Cell Death Differ.
Cell Death Dis.

Dr. Christina Merz-Stöckle

Allergy
Drug Design, Development and Therapy

Prof. Hans-Uwe Simon

Allergy
Apoptosis
Autophagy
Biochem. Biophys. Acta
Blood
J. Cell Cycle
Clin. Exp. Allergy
EMBO Journal
EMBO Reports
Science Signaling
Eur. J. Immunol.
FASEB J.
Cell Death Differ.
Frontiers Oncology
Gut
J. Allergy Clin. Immunol.
J. Antioxid. Redox Signal.
J. Exp. Med.
J. Immunol.
J. Leukoc. Biol.
J. Cell Sci.
Oncogene
Int. J. Cancer
FEBS letters
PloS One
Nat. Med.
Cell Death Dis.
Mol. Cell. Oncol.

PD Dr. Peter Späth

Clinical Investigation
Expert Review of Clinical Immunology
Journal of Allergy and Clincal Immunology
Journal of Clinical Immunology
Journal of the Peripheral Nervous System
Nature Review in Neurology
Neurology
PloS One

PD Dr. Stephan von Gunten

Allergy
Am. J. Respir. Cell Mol. Biol.
Front. Mol. Cell. Oncol.
Cell Death Differ.
Cell Death Dis.
Immunol. Lett.
J. Allergy Clin. Immunol.
J. Invest. Dermatol.
J. Immunol.
J. Immunotoxicol.
Med. Inflamm.
Respiration
Pathobiology

Prof. Shida Yousefi

Allergy
Cell Biochem. Biophys.
Cell. Mol. Neurobiol.
Int. J. Biochem. Cell Biol.
Arch. Biochem. Biophys.
Cell Death Differ.
Frontiers Immunol.
PloS One

Prof. Uwe Zangemeister-Wittke

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

4.7. Referee Work for Grant Bodies

Prof. Andrea Huwiler

Deutsche Forschungsgemeinschaft (DFG)

Dr. Christina Merz-Stöckle

National Science Center (NCN), Poland

Prof. Thomas Kaufmann

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

Prof. Hans-Uwe Simon

Swiss National Science Foundation (SNF)
Deutsche Forschungsgemeinschaft (DFG)
Italian Association for Cancer Res.
Swiss Cancer League
European Research Council (ERC)
HELMHOLTZ-Gemeinschaft

PD Dr. Stephan von Gunten

Swiss National Science Foundation (SNF)
Swiss Cancer League
Bernese Cancer League
Association for Int. Cancer Res. (AICR)

Prof. Uwe Zangemeister-Wittke

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

4.8. Awards

Elin Huwiler

Anerkennungspreis 2013 des Gymnasiums Altdorf
Maturaarbeit: *Die Wirkung verschiedener Nahrungsinhaltstoffen aus Tomate, Heidelbeere, Curry und Berberitze auf das Wachstum von Brustkrebszellen*.

Dr. Stephanie Schwalm

Elevated Abstract Award
Pharmacology Meeting “Novel drugs and drug targets to treat inflammation”, Ylläs, Finland, March 2013.

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

Coordinator for FACS and Chemicals at the PKI

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

ERASMUS-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);
http://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)

Member of Council of the Collegium International Allergologicum (CIA)

Fellow of the American Academy of Allergy, Asthma and Immunology (AAAAI)

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 Cells and Cytokine Committee (Workshops) of the American Academy of Allergy, Asthma and Immunology (AAAAI)

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

Member of the Scientific Advisory Board “Pharmacology” of Pfizer AG, Switzerland

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

Member of the Advisory Board of the Max and Elsa Beer-Brawand-Fonds

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

Member of the Scientific Board, 8th C1 Inhibitor Deficiency Workshop, Budapest (H), May 23-26, 2013

Head Jury awarding the “Grant for Young Investigators”, 8th C1 Inhibitor Deficiency Workshop, Budapest (H), May 23-26, 2013

Nominated expert, responsible in Switzerland for the survey on immunoglobulins by the European Directorate for the Quality of Medicines & HealthCare (EDQM) – Questionnaire on clinical use of coagulation factors/immunoglobulins

Member of the Kreuth Immunoglobulin Working Group 'European Consensus Proposal for Immunoglobulin Therapies'

PD Dr. Stephan von Gunten

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 Centro Genética Humana, 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 Exhibitions

Vera Liechti, Thun, Switzerland
Vernissage: March 21, 2013

Daniella Guidali, Widen, Switzerland
Vernissage: May 30, 2013

8. Sponsors

8.1. Research Grants

Nina Germic
Fellowship, ERASMUS program (February - June 2013)

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

Prof. Andrea Huwiler

Swiss National Science Foundation (grant No. 310030-135619)
Deutsche Forschungsgemeinschaft
Schweizerische Multiple Sklerose Gesellschaft

Prof. Thomas Kaufmann

Swiss National Science Foundation, SNF-Professorship (grant No. PP0033_119203)
Swiss Cancer League (KFS-3014-08-2012)
3R Foundation Switzerland (No. 127-11)
Novartis Stiftung für medizinisch-biologische Forschung

Evelin Krajnc

Fellowship, ERASMUS program (October 2012 – January 2013)

Dr. Susanne Radonjic-Hösli

Stipend, Swiss National Science Foundation and Swiss Academy of Medical Sciences
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)

PD Dr. Stephan von Gunten

Swiss National Science Foundation (grant No. 310030-135734)
Swiss National Science Foundation, Bulgarian-Swiss Research Programme (grant No. IZEBZO_142967/1)
Bernese Cancer League
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)

Dr. Marc Wehrli

Stipend, Swiss National Science Foundation and Swiss Academy of Medical Sciences

Prof. Uwe Zangemeister-Wittke

Swiss National Science Foundation (grant No. 310030E_132762)
Swiss National Science Foundation (grant No. 310030E_138201)
Sasella-Stiftung (Zürcher Kantonalbank)
UniBern Forschungsstiftung

8.2. Meetings

Swiss Society of Pharmacology and Toxicology (SSPT): Progress in Pharmacology – Gastroenterological Pharmacology, Bern (CH), Jan. 31, 2013
Pfizer AG, Zurich
Roche Pharma (Schweiz) AG, Reinach

12th III-International Summer School, Hôtel du Léman, 1805 Jongny (CH), Aug. 4 – 6, 2013
BD Biosciences, Allschwil
Carl Zeiss AG, Feldbach
CSL Behring AG, Bern
Members companies of the Kontaktgruppe für Forschungsfragen (KGF: Novartis, F. Hoffmann-La Roche, and Merck Serono), Basel
Novartis Pharma AG, Bern
Pfizer AG, Zurich
LS2 - Life Sciences Switzerland (former USGEB)

8.3. Seminars „Progress in Pharmacology“

2013:
ASTELLAS Pharma AG, Wallisellen
CSL Behring AG, Bern
Pfizer AG, Zurich

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

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

Dr. Marc Wehrli
Graduate School for Cellular and Biomedial Sciences, Univ. Bern (World Immune Regulation Meeting, Davos, CH, March 13 -16, 2013)

Dr. Susanne Radonjic-Hösli
Graduate School for Cellular and Biomedial Sciences, Univ. Bern (8th Biennial Symposium of the International Eosinophil Society, Oxford, UK, July 13 - 17, 2013)

Dr. Christina Merz-Stöckle

International Eosinophil Society (IES), Inc. (8th Biennial Symposium of the International Eosinophil Society, Oxford, UK, July 13 - 17, 2013)

Kayluz Frias Boligan
Swiss Society of Pharmacology and Toxicology (15th International Congress of Immunology, Milan, I, August 22 - 27, 2013)

Mahbubul Morshed
Graduate School for Cellular and Biomedial Sciences, Univ. Bern (15th International Congress of Immunology, Milan, I, August 22 - 27, 2013)

Fabiola Schorer-Cortinas
Graduate School for Cellular and Biomedial Sciences, Univ. Bern (5th International Conference on Crossroads between Innate and Adaptive Immunity, Corfu, Greece, September 21 - 26, 2013)

8.6. Other Support

Bürgi Fonds Seminar series of the institute