# Annual Report 2019

# Institut für Pharmakologie (PKI)
# der Universität Bern

# Institute of Pharmacology
# University of Bern

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# Inhaltsverzeichnis

# 1. Introduction

## *1.1. Vorwort*

Dies ist der neunzehnte umfassende Jahresbericht des Instituts für Pharmakologie (PKI) der Universität Bern. Das PKI hat auch im Jahr 2019 seine Aufgaben in Lehre und Forschung innerhalb der Medizinischen Fakultät vorbildlich erfüllt. Nach unserem Umzug im Jahr 2015 bietet uns das INO-Gebäude des Inselspitals hervorragende Bedingungen für eine erfolgreiche Forschungstätigkeit. Mit dem Zentrum für Labormedizin teilen wir uns den Stock F und nutzen gemeinsam die vorhandene Infrastruktur. In Lehre und Forschung wurden inzwischen zahlreiche neue Projekte gestartet, mit dem Ziel die personalisierte Medizin weiter zu entwickeln. Im April 2017 startete Prof. Dr. Manuel Haschke mit seiner Forschungsgruppe für Klinische Pharmakologie in unser Institut und seine zwei aus Basel mitgebrachten Massenspektrometer sind installiert. Mit der Rekrutierung von Prof. Haschke haben sich neue Möglichkeiten der Zusammenarbeit eröffnet, sowohl in der *biologischen Grundlagen*- als auch in der *klinischen Forschung*, beides Kernaufgaben der Pharmakologie, bzw. klinischen Pharmakologie.

Das PKI arbeitet eng mit verschiedenen Kliniken des Inselspitals und mit anderen Forschungseinrichtungen der Universität Bern zusammen. Damit wollen wir helfen, die translationale Forschung sowie die Aus-, Weiter- und Fortbildung an der Medizinischen Fakultät zu stärken. Zum anderen sind wir an der Zusammenarbeit mit Firmen interessiert, wie die weiter hinten aufgeführten gegenwärtigen Kontakte der einzelnen Forschungsgruppen zeigen. Auch im Jahr 2019 trugen wir dazu bei, die Kommunikation zwischen WissenschaftlerInnen und Öffentlichkeit zu fördern.

Neben unserer regulären Lehrtätigkeit im 3. und 6. Studienjahr Medizin sowie der Ausbildung der ZahnmedizinerInnen sind einige DozentInnen des Instituts zusätzlich in die Immunologie-Ausbildung von StudentInnen der Biologie (Naturwissenschaftliche Fakultät der Universität Bern) einbezogen. Weiterhin sind wir auch für die Pharmakologie-Ausbildung in B.Sc.- und M.Sc.-Kursen für Biomedizin der Universität Bern verantwortlich. Ebenso führen wir seit September 2019 die Pharmakologie-Ausbildung im 3. Studienjahr Pharmazie an unserer Universität durch, die neu ein Vollstudium für Pharmazie anbietet. Die DozentInnen des PKI sind ausserdem innerhalb der interfakultären Graduate School for Cellular and Biomedical Sciences der Universität Bern aktiv tätig. Prof. Kaufmann, Prof. von Gunten und Prof. Konstantinidou sind Mitglieder einer Betreuungskommission innerhalb dieses Ausbildungsprogramms für Doktorandinnen und Doktoranden. Dazu kommen zu-

sätzliche Bildungsangebote in Form von Seminaren (Current Topics in Pharmacology and Theranostics; gemeinsam organisiert mit dem Zentrum für Labormedizin) und einer Summer School, die durch mich organisiert wird. Diese Bildungsangebote werden weitgehend aus eigenen finanziellen Mitteln und Sponsorengeldern bestritten. Im Institut arbeiten gegenwärtig 22 DoktorandInnen, und 2 Doktorandinnen (PhD) haben im Berichtsjahr ihre Arbeiten erfolgreich abgeschlossen.

Die Mitarbeiter und Mitarbeiterinnen des PKI (ohne Klinische Pharmakologie) publizierten im Jahr 2019 insgesamt 43 Originalarbeiten sowie 17 Übersichtsartikel in internationalen Fachzeitschriften (Summe der „impact factors“ >200). MitarbeiterInnen des Instituts wurden zu insgesamt 35 Vorträgen bzw. Seminaren eingeladen. Mehrere MitarbeiterInnen des PKI wurden mit Forschungspreisen ausgezeichnet. Gegenwärtig werden 9 MitarbeiterInnen mit namhaften Beiträgen des Schweizerischen Nationalfonds unterstützt. Seit 2014 ist das Institut für Pharmakologie Bestandteil eines Europäischen Netzwerks für Doktoranden innerhalb des EU-Programms für Forschung und Innovation „HORIZON 2020“. Unser Institut ist ebenso mit einem Projekt von Herrn Prof. von Gunten im interfakultären Berner Zentrum für Präzisionsmedizin vertreten. Zahlreiche Persönlichkeiten besuchten das Institut und hielten Forschungsseminare. Prof. von Gunten war Mitorganisator des Jahreskongresses der Schweizerischen Gesellschaft für Pharmakologie und Toxikologie (SGPT). Prof. Kaufmann organisiert gegenwärtig gemeinsam mit Prof. Tschan (Institut für Pathologie, Universität Bern) und Prof. Brunner (Lehrstuhl Biochemische Pharmakologie, Universität Konstanz, Deutschland) das „11$^{th}$ Swiss Apoptosis and Autophagy Meeting (SA$^2$M)“ (9.-11.9.2020), 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.

Ich bin gegenwärtig als Dekan der Medizinischen Fakultät der Universität Bern tätig. Zusätzlich nimmt das PKI auch ausserhalb der Universität wissenschaftspolitische Verantwortung für die Medizin und die Biowissenschaften wahr. Zum Beispiel amtet Prof. von Gunten als Präsident der Schweizerischen Gesellschaft für Experimentelle Pharmakologie (SGEP).

Ich danke allen Mitarbeiterinnen und Mitarbeitern für ihren Einsatz, welcher auch im Jahr 2019 zu einer Bilanz beitrug, die internationalen Massstäben gerecht wird. Ebenso danke ich allen Sponsoren und Freunden des Instituts.

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

Bern, Februar 2020

## *1.2. Foreword*

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

The PKI wants to succeed in both areas and, therefore, maintains close contacts with several clinics at the Inselspital as well as with other research institutes of the University. In doing so, we hope to strengthen both translational research and teaching in the Medical Faculty. In addition, we are very much interested in collaborating with industry on new developments. Finally, we have also made an effort to promote communication between scientists and the public in 2019. All our current activities are summarized here below.

Besides the regular teaching in the third and sixth year medical student curriculum and in the teaching of dental students, we are responsible for teaching Pharmacology in both B.Sc. and M.Sc. courses in Biomedicine. Some of the PKI staff are additionally involved in the Immunology M.Sc. programmes within the Natural Science Faculty of our university. In September 2019, we also started teaching Pharmacology to students of Pharmacy of our University, which newly offers a full study in Pharmacy. Of course, we also actively participate in the graduate program for MD/PhD students of the University of Bern (Graduate School for Cellular and Biomedical Sciences). Prof. Kaufmann, Prof. von Gunten and Prof. Konstantinidou are members of the tutoring committee “Cell Biology” within that school. Currently, 22 PhD students work at the PKI, and in 2019, two PhD student successfully completed their doctoral studies. Also important for the institute are additional teaching activities outside the medical curriculum, such as seminars (Current Topics in Pharmacology and Theranostics; jointly organized with the Center of Laboratory Medicine) and the

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

Research is our other main activity. In 2019, staff members of the PKI (without Clinical Pharmacology) published 43 original and 17 review articles in international peer-reviewed journals (the sum of the "impact factors" is above 200). Co-workers of the institute were invited to present 35 lectures or seminars. Several PKI members received research prizes. The research projects of 9 co-workers are currently supported by grants from the Swiss National Science Foundation. Moreover, since 2014, the Institute of Pharmacology has been part of a Training Network for PhD students within the EU Framework Program for Research and Innovation „HORIZON 2020". With a project of Prof. von Gunten, we are also integrated in the Interfaculty Center for Precision Medicine of the University of Bern. Several internationally prominent researchers visited our institute to present seminars. Prof. von Gunten was a member of the organizing committee for the annual meeting of the Swiss Society of Pharmacology and Toxicology (SSPT). Prof. Kaufmann, together with Prof. Tschan (Institute of Pathology, University of Bern) and Prof. Brunner (Department of Biochemical Pharmacology, Univ. of Constance, Germany), are in the process of organizing an international congress (11$^{th}$ Swiss Apoptosis and Autophagy Meeting; September 9-11, 2020), which will attract approximately 200 scientists interested in the fields of "Cell Death and Autophagy". In summary, we carry out research of a high standard which plays a very important role at the PKI.

I am the Dean of the Medical Faculty of the University of Bern. Prof. von Gunten currently serves as president of the Swiss Society of Experimental Pharmacology (SSEP).

I thank all co-workers in the institute for their hard work. These efforts have contributed in an important way to the success of the PKI in 2019. I am grateful to all the sponsors and friends of the institute for their support.

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

Bern, February 2020

# 2. Staff 2019

**Director**

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

**Deputy Director**

| | | |
|---|---|---|
| Prof. Dr. | Huwiler, Andrea | PhD |

**Principal Investigators**

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

**Scientific Staff**

| | | |
|---|---|---|
| | Bachmann, Daniel | Lab Technican |
| | Brandl, Fabian | PhD student* (until March 2019) |
| | Chen, Yihe | PhD student* (since Oct 2019) |
| | Christen, Mira | Lab Technican (since July 2019) |
| | Claus, Mike | Lab Technican |
| | Erhardt, Martin | PhD student |
| Dr. | Fernandez Marrero, Yuniel | Postdoctoral fellow* (until Aug 2019) |
| | Fartelj, David | M.Sc. student* (since Oct 2019) |
| | Frangez, Ziva | PhD student* |
| Dr. | Frias Boligan, Kayluz | Postdoctoral fellow* (until Aug 2019) |
| | Furer, Alexander | Technician (since Sep 2019) |
| | Germic, Nina | PhD student |
| | Gigon, Lea | M.Sc. student* (since Sep 2019) |
| | Graeter, Stefanie | PhD student* (until Oct 2019) |
| | Haas, Quentin | PhD student* |
| | Hafizi, Redona | PhD student* (since Jan 2019) |
| Dr. | He, Zhaoyue | Postdoctoral fellow |
| | Hevia Hernandez, Giselle | PhD student* (since Oct 2019) |
| | Hugonnet Marjolaine, Claire | PhD student* (since Sep 2019) |
| | Imeri, Faik | Postdoctoral fellow* |
| | JeanRichard, Philippe | M.Sc. pharm. student* (since Aug 2019) |
| | Klapan, Kim | PhD student* |
| | Kozlowski, Evelyne | Lab Technician |
| Dr. | Liu, He | Postdoctoral fellow* (until March 2019) |
| | Maillard-van Laer, Marianne | Lab Technician |
| | Maneva Timcheva, Tankica | Lab Technician* |
| | Markov, Nikita | PhD student |
| | Mürner, Lukas | M.Sc. student* (since Feb 2019) |
| | Naim, Samara | PhD student* |
| | Nasser, Riim | Lab Technician* |

| | | |
|---|---|---|
| | Oberson, Kevin | Lab Technician |
| | Peng, Shuang | PhD student* |
| | Pozzato, Chiara | PhD student* |
| | Rossi Sebastiano, Matteo | PhD student |
| | Saliakoura, Maria | PhD student* |
| | Schnüriger, Noah | M.Sc. student* (until Sep 2019) |
| | Stepanovska, Bisera | PhD student |
| Dr. | Stojkov, Darko | Postdoctoral fellow |
| | Toledo Darien | PhD student* (since Nov 2019) |
| | Valente, Eleonora | M.Sc. pharm. student* (until May 2019) |
| | Verschoor, Daniëlle | PhD student* |
| | Von Gunten, Aldona | PhD student* |
| Dr. | Wang, Xiaoliang | Postdoctoral fellow |
| | Weiss, Fabian | PhD student* (since Apr 2019) |
| | Wu, Yancheng | PhD student* (since Oct 2019) |
| | Zahiroddini, Peymaneh | M.Sc. student* (since Feb 2019) |

**Principal Investigator – Clinical Pharmacology**

| | | |
|---|---|---|
| Prof. Dr. | Haschke, Manuel | MD |

**Scientific Staff – Clinical Pharmacology**

| | | |
|---|---|---|
| Dr. | Liakoni, Evangelia | MD |
| Dr. | Geiling, Katharina | MD |
| | Scholz, Irene | med. pract. |
| | Hammann, Felix | MD, PhD |

**External University Teachers**

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

**Guest Scientists**

| | | |
|---|---|---|
| Prof. Dr. | Simon, Dagmar | MD*, Dept. Dermatology, Inselspital, Univ. Bern |
| Dr. | Schwalm, Stephanie | PhD*, Dept. of Pharmacology, Univ. Frankfurt |
| Prof. Dr. | Spirk, David | MD*, Sanofi-Aventis AG |
| | Lewis, Bonnie | PhD student*, University of Toronto |
| | Medvedev, German Y. | PhD student*, I.M. Sechenoc Medical University |

**Office**

| | | |
|---|---|---|
| | Scherrer, Debora | Secretary, 80% |
| | Cookman, Sabrina | Secretary, 60% |
| | Joray, Celine | Apprentice, 100% (since Aug 2019) |

**Workshop / House Keeping**

Conforti, Isa

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

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

Progress in Pharmacology, Treatment of Skin Diseases, Bern, January 23, 2019

## Summer School

Members of the Institute of Pharmacology of the University of Bern together with participants of our International Summer School in Bönigen; July 28 - 30, 2019.

# 3. Teaching Activities

## *3.1. Lectures*

### *Lectures for Medical Students: Pharmacology*

| Date | Lecturer | Titel of the lecture |
|---|---|---|
| Mar 18, 2019 | Prof. Stephan von Gunten | Hormone aus pharmakol. Sicht (Teil 1) |
| Mar 18, 2019 | Prof. Stephan von Gunten | Hormone aus pharmakol. Sicht (Teil 2) |
| Mar 20, 2019 | Prof. Stephan von Gunten | Lipidsenker + Behandlung der Gicht |
| Mar 20, 2019 | Prof. Stephan von Gunten | Antidiabetika |
| Mar 27, 2019 | Prof. Andrea Huwiler | Pharmakologie von Narkosemitteln und Muskelrelaxantien I |
| Mar 27, 2019 | Prof. Andrea Huwiler | Pharmakologie von Narkosemitteln und Muskelrelaxantien II |
| Apr 10, 2019 | Prof. Andrea Huwiler | Antiepileptika |
| Apr 17, 2019 | Prof. Andrea Huwiler | Therapie von M. Parkinson und Demenz |
| Apr 25, 2019 | Prof. Andrea Huwiler | Lokalanästhetika |
| Apr 25, 2019 | Prof. Andrea Huwiler | Neurologie-Blocksynthese |
| Apr 29, 2019 | Prof. Andrea Huwiler | Psychopharmakologie |
| May 01, 2019 | Prof. Andrea Huwiler | Antidepressiva, Anxiolytika |
| May 06, 2019 | Prof. Andrea Huwiler | Antipsychotika und Stimmungsstabilisatoren |
| May 08, 2019 | Dr. F. Hammann | Schmerz und Analgesiologie (Teil 1) |
| May 08, 2019 | Dr. E. Liakoni | Schmerz und Analgesiologie (Teil 2) |
| May 22, 2019 | Prof. Hans-Uwe Simon | Immunmodulation |
| Sep 18, 2019 | Prof. Hans-Uwe Simon | Pharmakodynamik (Teil 1) |
| Sep 18, 2019 | Prof. Hans-Uwe Simon | Pharmakodynamik (Teil 2) |
| Sep 25, 2019 | Prof. Hans-Uwe Simon | Entzündungshemmung |
| Sep 25, 2019 | Prof. Hans-Uwe Simon | Einführung in die Toxikologie |
| Oct 08, 2019 | Prof. Hans-Uwe Simon | Pharmakotherapie bei Lungenkrankheiten |
| Oct 22, 2019 | Prof. David Spirk | Pharmakologie der Hämostase |
| Oct 29, 2019 | Prof. U. Zangemeister-Wittke | Pharmakologie des vegetativen Nervensystems |
| Nov 05, 20198 | Prof. David Spirk | Behandlung der Herzinsuffizienz und Angina pectoris |
| Nov 06, 2019 | Prof. U. Zangemeister-Wittke | Antihypertensiva, Antiarrhythmika |
| Nov 26, 2019 | Prof. U. Zangemeister-Wittke | Diuretika (Teil 1), Diuretika (Teil 2) |

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

***Lectures for Medical Students: Cell Biology***

| Date | Lecturer | Titel of the lecture |
|---|---|---|
| Sep 26, 2019 | Prof. Thomas Kaufmann | Entwicklung des Lebens |
| Oct 10, 2019 | Prof. Thomas Kaufmann | Zellstoffwechsel |
| Oct 31, 2019 | Prof. Thomas Kaufmann | Zelltod 2 |

***Seminars for Medical Students: Pharmacology***

| Date | Lecturer | Titel of the lecture |
|---|---|---|
| Mar 21, 2019 | Prof. U. Zangemeister-Wittke | Gezielte Tumortherapie mit Antikörpern und Immunkonjugaten |
| Mar 28, 2019 | Prof. Thomas Kaufmann | Modulation des Zelltodes - aktueller Stand und neue Entwicklungen |
| Apr 04, 2019 | Prof. Stephan von Gunten | Functional Glycomics - Neue Optionen für die Tumor- und Entzündungspharmakologie |
| Apr 04, 2019 | Prof. Hans-Uwe Simon | Personalisierte Arzneimitteltherapie |

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

| Date | Lecturer | Title of the lecture |
|---|---|---|
| Feb 04, 2019 | Prof. U. Zangemeister-Wittke | Einführung in die Pharmakokinetik |
| Feb 18, 2019 | Prof. Hans-Uwe Simon | Rezeptoren, Dosis-Wirkungskurven, |
| Feb 18, 2019 | Prof. Hans-Uwe Simon | Antagonisten, Applikationsarten |
| Feb 20, 2019 | Prof. Thomas Kaufmann | Pharmakogenetik, Interaktionen |
| Feb 27, 2019 | Prof. U. Zangemeister-Wittke | Pharmakologie des vegetativen Nervensys-tems |
| Mar 06, 2019 | Prof. Andrea Huwiler | Pharmakologie der Atemwege |
| Mar 13, 2019 | Prof. Andrea Huwiler | Narkose, Beruhigungsmittel |
| Mar 25, 2019 | PD Dr. Armand Cachelin | Analgetika |
| Mar 27, 2019 | Prof. Stephan von Gunten | Pharmakologie des Knochens |
| Apr 03, 2019 | Prof. Stephan von Gunten | Magensäurehemmung |
| Apr 10, 2019 | Dr. Sibylle Bürgi | Antidiabetika |
| Apr 15, 2019 | Prof. David Spirk | Herz-Kreislauf Medikamente, Antithrombotika |
| Apr 17, 2019 | Dr. Sibylle Bürgi | Lokalanästhetika |
| May 06, 2019 | Dr. Sibylle Bürgi | Antibiotika |

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

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

| Date | Lecturer | Title of the lecture |
|---|---|---|
| Sep 17, 2019 | Prof. Hans-Uwe Simon | Pharmakodynamik 1 |
| Sep 17, 2019 | Prof. Hans-Uwe Simon | Pharmakodynamik 2 |
| Sep 19, 2019 | Prof. Hans-Uwe Simon | Pharmakodynamik 3 |
| Sep 19, 2019 | Prof. Hans-Uwe Simon | Arzneimittelallergien |
| Sep 24, 2019 | Prof. Hans-Uwe Simon | Experimentelle Toxikologie 1 |
| Sep 24, 2019 | Prof. Hans-Uwe Simon | Experimentelle Toxikologie 2 |
| Oct 31, 2019 | Prof. Stephan von Gunten | Säureassoziierte KH / Erbrechen |
| Nov 5, 2019 | Prof. Stephan von Gunten | Motilitätsstörungen / Entzündliche Darmerkrankungen |
| Nov 26, 2019 | Prof. Thomas Kaufmann | Anämien |
| Nov 28, 2019 | Prof. Thomas Kaufmann | Leukämien |
| Dec 3, 2019 | Prof. Thomas Kaufmann | Lymphome |
| Dec 10, 2019 | Prof. Georgia Konstantinidou | Zytostatika, Teil 1 |
| Dec 12, 2019 | Prof. Georgia Konstantinidou | Zytostatika, Teil 2 |

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

| Date | Lecturer | Title of the lecture |
|---|---|---|
| Feb 21, 2019 | Prof. Stephan von Gunten | Introduction |
| Feb 21, 2019 | Dr. Kayluz Frias Boligan | Glycoimmunology |
| May 23, 2019 | Prof. Stephan von Gunten | Immunopharmacology |

Written examination and oral tests: Prof. Stefan von Gunten

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

| Date | Lecturer | Title of the lecture |
|---|---|---|
| Oct 10, 2019 | Prof. Thomas Kaufmann | Cell death in the immune system |

***Lectures for Biomedical Sciences students (M.Sc. program, Bern) and Natural Sciences Faculty: Molecular Biology of Inflammation (Coordinator: Prof. Britta Engelhardt)***

| Date | Lecturer | Title of the lecture |
|---|---|---|
| April 04, 2019 | Prof. Georgia Konstantinidou | Lipid mediators in inflammation |
| May 09, 2019 | Prof. Shida Yousefi | Inflammation - good or bad? |
| | | Resolution of inflammation - apoptosis |

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

| Date | Lecturer | Title of the lecture |
|---|---|---|
| Dec 05, 2019 | Prof. Shida Yousefi<br>Prof. Stephan von Gunten<br>Prof. Thomas Kaufmann | Immunological Methods (1 day) |
| Dec 06, 2019 | Prof. Shida Yousefi<br>Prof. Stephan von Gunten<br>Prof. Thomas Kaufmann | Immunological Methods (1 day) |
| Dec 12, 2019 | Prof. Shida Yousefi<br>Prof. Stephan von Gunten<br>Prof. Thomas Kaufmann | Immunological Methods (1 day) |
| Dec 13, 2019 | Prof. Shida Yousefi<br>Prof. Stephan von Gunten<br>Prof. Thomas Kaufmann | Immunological Methods (1 day) |
| Dec 19, 2019 | Prof. Shida Yousefi<br>Prof. Stephan von Gunten<br>Prof. Thomas Kaufmann | Immunological Methods (1 day) |
| Dec 20, 2019 | Prof. Shida Yousefi<br>Prof. Stephan von Gunten<br>Prof. Thomas Kaufmann | Evaluation (4 h) |

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

| Date | Lecturer | Title of the lecture |
|---|---|---|
| Sep 20, 2019 | Prof. Stephan von Gunten | Gastrointestinal tract |
| Sep 27, 2019 | Prof. David Spirk | Haemopoietic system and haemostasis |
| Oct 04, 2019 | Prof. Shida Yousefi | Lungs and kidneys |
| Oct 11, 2019 | Prof. Stephan von Gunten | Endocrine and reproductive system |
| Oct 18, 2019 | Prof. Georgia Konstantinidou | Immune system |
| Oct 25, 2019 | Prof. Thomas Kaufmann | Antiinfectious therapy |
| Nov 01, 2019 | Prof. U. Zangemeister-Wittke | Heart and vascular system |
| Nov 08, 2019 | Prof. Andrea Huwiler | Nervous system |

***Lecture for Biomedical Sciences Students (M.Sc. program, Bern) and Graduate School for Cellular and Biomedical Sciences: Topics in Tumor Biology (Coordinator: Prof. Deborah Stroka)***

| Date | Lecturer | Title of the lecture |
|---|---|---|
| Feb 27, 2019 | Prof. Georgia Konstantinidou | Oncogenes – how to target them |

***Lecture for Natural Sciences Faculty and Biomedical Sciences students (M.Sc. program, Cell Biology, Bern) and Graduate School for Cellular and Biomedical Sciences: General Pathology & Histology (Coordinator: PD Dr. Philippe Krebs)***

| Date | Lecturer | Title of the lecture |
|---|---|---|
| Sep 17, 2019 | Prof. Thomas Kaufmann | Cell damage |

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

| Date | Lecturer | Title of the lecture |
|---|---|---|
| Oct 18, 2019 | Prof. Shida Yousefi | Laser scanning microscopy and specific applications (FRET, FRAP, spectral unmixing) and digital image restoration (Huygen and Imaris software) |

***Cell Biology tutorial "Happy Cell" 2019 (5.0 ECTS), CTS/KSL 7606"***

| Date | Lecturer | Title of the lecture |
|---|---|---|
| Oct 16, 2019<br>2 hours | Prof. Thomas Kaufmann | Chapter 15 (Cell signaling) |

***External teaching activities: University of Zurich (Molecular Medicine)***

| Date | Lecturer | Title of the lecture |
|---|---|---|
| Nov 2019<br><br>(total 4h) | Prof. U. Zangemeister-Wittke | Seminars in cardiovascular diseases for students of human medicine (2nd year) |

***Lectures for Medical Students: Clinical Pharmacology***

| Date | Lecturer | Titel of the lecture |
|---|---|---|
| Feb 20, 2019 | Prof. Manuel Haschke | GI Motilitätsstörungen, Laxantien, Antidiarrhoika, Antiemetika |
| Feb 25, 2019 | Dr. Felix Hammann | Pharmakokinetik 3&4 (2 Lekt.) |
| Feb 26, 2019 | Prof. Manuel Haschke | Analgetika SJ6 |
| Feb 26, 2019 | Prof. Manuel Haschke | Antiinfektiva SJ6 |
| Feb 26, 2019 | Dr. Felix Hammann | Arterielle Hypertonie u. Herzinsuffizienz |
| Feb 26, 2019 | Dr. Felix Hammann | Diabetes u. Dyslipidämie |
| Feb 28, 2019 | Prof. Manuel Haschke | Antikoagulantien & Thrombozytenhemmer |
| Feb 28, 2019 | Prof. Manuel Haschke | Notfallmedikamente |
| Mai 08, 2019 | Dr. Evangelia Liakoni | Schmerzmittel 1 |
| Mai 08, 2019 | Dr. Felix Hammann | Schmerzmittel 2 |
| Sep 24, 2019 | Dr. Felix Hammann | Pharmakokinetik 1&2 (2 Lekt.) |
| Nov 13, 2019 | Dr. Evangelia Liakoni | Interaktionen |
| Nov 13, 2019 | Dr. Evangelia Liakoni | Unerwünschte Arzneimittelwirkungen |

***Lectures for Dental Medicine Students: Clinical Pharmacology***

| Date | Lecturer | Titel of the lecture |
|---|---|---|
| Oct 23, 2019 | Dr. Felix Hammann | Pat. mit akuten med. Problemen |
| Oct 30, 2019 | Dr. Felix Hammann | Pat. mit chronischen med. Problem |
| Nov 06, 2019 | Dr. Evangelia Liakoni | Antikoagulation |
| Nov 13, 2019 | Dr. Irene Scholz | UAW im Mund |
| Nov 20, 2019 | Dr. Evangelia Liakoni | Analgetika 1 |
| Nov 27, 2019 | Dr. Evangelia Liakoni | Analgetika 2 |
| Dec 04, 2019 | Dr. Irene Scholz | Antibiotika 1 |
| Dec 11, 2019 | Dr. Irene Scholz | Antibiotika 2 |

***Lectures for Pharmacy Students: Clinical Pharmacology***

| Date | Lecturer | Titel of the lecture |
|---|---|---|
| Sep 26, 2019 | Dr. Evangelia Liakoni | Klinische Toxikologie |
| Oct 01, 2019 | Dr. Evangelia Liakoni | Pharmakokinetik I |
| Oct 03, 2019 | Dr. Evangelia Liakoni | Pharmakokinetik II |
| Oct 10, 2019 | Dr. Felix Hammann | Hypertonie |
| Oct 15, 2019 | Dr. Felix Hammann | Herzinsuffizienz, Rhythmusstörungen |
| Oct 17, 2019 | Dr. Evangelia Liakoni | Venöse KH |
| Oct 22, 2019 | Dr. Evangelia Liakoni | Arterielle KH |
| Oct 24, 2019 | Sarah Banholzer | Drug safety/pharmacovigilance |
| Nov 07, 2019 | Prof. M. Haschke | Virale und retrovirale KH |
| Nov 12, 2019 | Prof. M. Haschke | Pilzerkrankungen Mycobacterielle KH |

| | | |
|---|---|---|
| Nov 14, 2019 | Prof. M. Haschke | Bakterielle Infektionen I |
| Nov 19, 2019 | Prof. M. Haschke | Bakterielle Infektionen II |
| Nov 21, 2019 | Prof. M. Haschke | Parasiten / Malaria |
| Dec 17, 2019 | Dr. Felix Hammann | Nierenkrankheiten, Dialyse, Dosis-anpassung, Nieren-/Lebererkrankungen |
| Dec 19, 2019 | Dr. Irene Scholz | HWI, Inkontinenz |

***Clinical Pharmacology Lectures: University Hospital/Inselspital Bern***

| **Date** | **Lecturer** | **Titel of the lecture** |
|---|---|---|
| Jan 11, 2019 | Prof. Manuel Haschke | DOAC antidotes (KAIM) |
| Feb 05, 2019 | Prof. Manuel Haschke | Thrombozytenaggregationshemmer 1 (KAIM) |
| March 05, 2019 | Prof. Manuel Haschke | Thrombozytenaggregationshemmer 2 (KAIM) |
| Apr 03, 201 | Prof. Manuel Haschke | Nicht-Opioid-Analgetika (Schmerzforum Anästhesie) |
| Apr 09, 2019 | Prof. Manuel Haschke | Statine 1 (KAIM) |
| May 02, 2019 | Liakoni/Hammann/Haschke | Arzneimittelinteraktionen (KAIM, skills) |
| May 17, 2019 | Prof. Manuel Haschke | Statine 2 (KAIM) |
| Jun 14, 2019 | Irene Scholz | Intoxikationen im Kindesalter (Kinderklinik) |
| Jul 02, 2019 | Prof. Manuel Haschke | Pharmakokinetik (KAIM) |
| Jul 09, 2019 | Prof. Manuel Haschke | NSAR, Coxibe (KAIM) |
| Aug 08, 2019 | Prof. Manuel Haschke | Opioide (KAIM) |
| Sept 26, 2019 | Liakoni/Hammann/Haschke | Dosisanpassungen (KAIM skills training) |
| Oct 16, 2019 | Scholz/Banholzer | UAWs und Meldungen (Radio-Onkologie) |
| Oct 22, 2019 | Prof. Manuel Haschke | Tc Aggregationshemmer (KAIM) |
| Oct 29, 2019 | Prof. Manuel Haschke | Arzneimittelinteraktionen (KAIM WBC) |
| Dec 10, 2019 | Prof. Manuel Haschke | Antidepressiva (KAIM) |

***External Lectures: Clinical Pharmacology***

| **Date** | **Lecturer** | **Titel of the lecture** |
|---|---|---|
| May 22, 2019 | Prof. Manuel Haschke | Interaktionen Antiepileptika (CAP) |
| Jun 05, 2019 | Dr. Evangelia Liakoni | Innovative formulations for nicotine self-administration: Advantages and risks of “e-cigarettes” (SGAIM, Basel) |
| Jun 28, 2019 | Dr. Felix Hammann | Co-/Analgetika (CAS Basel) |
| Aug 22, 2019 | Sarah Banholzer | MEGRA StartUp Pharmacovigilance CH |
| Sept 12, 2019 | Prof. Manuel Haschke | Betablocker bei Herzinsuffizienz (Pharma-themen Basel) |
| Nov 08, 2019 | Prof. Manuel Haschke | Phase I studies (RC Congress, Olten) |
| Dec 05, 2019 | Prof. Manuel Haschke | Eliglustat Pharmacogenetics (Sanofi) |

## *3.2. Coordination PBL Medical Students, 3rd year (2019/2020)*

***Core group member:***
Prof. Andrea Huwiler

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

## *3.3. Tutorials (study year 2019/2020)*

***For Medical students 3rd year:***
Prof. Georgia Konstantinidou
Dr. Zhaoyue He
Kim Klapan
Quentin Haas
Prof. Thomas Kaufmann
Dr. Darko Stojkov
Samara Naim

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

***Graduate School for Cellular and Biomedical Sciences, Training course on "Concepts and Methods in Programmed Cell Death and Autophagy"***
Prof. Thomas Kaufmann

## *3.4. Elective Module Supervision*

***For Biomedical Sciences students:***
Marjolaine Hugonnet (Prof. Thomas Kaufmann)
Sara-Jessica Camerin (Prof. Thomas Kaufmann)
Leonie Lara Weber (Prof. Thomas Kaufmann)
Sarah Wicki (Prof. Thomas Kaufmann)

## *3.5. Seminars of Invited Speakers*

| Date | Teacher | Title of the seminar | Host |
|---|---|---|---|
| Feb 6, 2019 | Prof. Dr. De Virgilio Claudio, Department of Biology, University of Fribourg | Regulation of TORC1 by amino acids: a central role for Rag GTPases within the EGO complex | H.-U. Simon |
| Feb 8, 2019 | Prof. Dr. Véronique Witko-Sarsat, Département Immunologie-Infection-Inflammation, Paris | Proliferating Cell Nuclear Antigen: a key regulator of neutrophil survival and activation | H.-U. Simon |
| Mar 13, 2019 | Prof. Dr. Thierry Hennet, Universität Zürich | Prebiotic and immunoregulatory functions of milk oligosaccharides | S. von Gunten |
| Apr 10, 2019 | Prof. Dr. Curzio Ruegg, Department of Oncology, Microbiology and Immunology, University of Fribourg | Chemotherapy induced breast cancer dormancy: a new function for old drugs? | G. Konstantinidou |
| Apr 23, 2019 | Prof. Dr. Deborah Keogh-Stroka, Department for BioMedical Research (DBMR), University of Bern | PKM2 and macrophage polarization during liver regeneration | H.-U. Simon |
| Apr 24, 2019 | Prof. Dr. Mirjam Schenk, Institute of Pathology, University of Bern | IL32: a treatment to convert tumors from “cold” to “hot” | S. von Gunten |
| May 1, 2019 | Prof. Dr. Carsten Riether, Department for BioMedical Research (DBMR), University of Bern | Immune control of cancer stem cells | H.-U. Simon |
| May 3, 2019 | Prof. Dr. Peter Ruth, Institut für Pharmazie, Universität Tübingen | Cysteine-rich protein 4-negative mice: amplified pathogenic actions of angiotensin II in the heart | H.-U. Simon |
| May 7, 2019 | Prof. Dr. Lutz Nolte, Vizerektorat Forschung, University of Bern | Swiss Federal Innovation Promotion Instruments | H.-U. Simon |
| May 22, 2019 | Prof. Dr. Christian Widmann, Department of Physiology, University of Lausanne | Cell-permeable peptides enter cells in multiple (and unusual) ways | G. Konstantinidou |

| | | | |
|---|---|---|---|
| May 27, 2019 | Prof. Dr. Bruce Carleton, Department of Pediatrics, University of British Columbia | Using Pharmacogenomics to Explore the Variability in Response to Drugs | U. Amstutz |
| May 28, 2019 | Prof. Dr. med. David Spirk, Sanofi-Aventis (Suisse) SA and Institute of Pharmacology, University of Bern | PCSK-9 inhibition: Reset of atherosclerosis? | H.-U. Simon |
| June 5, 2019 | PD Dr. Manuela Funke-Chambour, Universitätsklinik für Pneumologie, Inselspital Bern | Search for new antifibrotic drugs | A. Huwiler |
| June 12, 2019 | PhD, Masoodi, Pharm. D, Institut für Klinische Chemie, Inselspital Bern | Investigating the role of lipid metabolism: From patient phenotyping to personalized treatment | A. Huwiler |
| June 19, 2019 | Prof. Dr. Howard Riezman, Department of Biochemistry, University of Geneva | Novel approaches to study lipid homeostasis and function in physiology | G. Konstantinidou |
| Oct 16, 2019 | Prof. Dr. Jörg Huwyler, Dept. of Pharmacy, Pharmaceutical Technologies, University of Basel | Drug targeting to hepatocytes | A. Huwiler |
| Oct 23, 2019 | Dr. Pedro Henrique Imenez Silva, Institute of Physiology, University of Zürich | The role of proton-activated GPCRs in kidney disease | A. Huwiler |
| Nov 4, 2019 | Dr. Christopher Jackson, Biomedicum Helsinki, Finland | Cellular stress responses to mitochondrial dysfunction | H.-U. Simon |
| Nov 27, 2019 | Prof. Dr. Jean-Claude Martinou, University of Geneva | Mitochondrial metabolism and cancer | G. Konstantinidou |

## *3.6. Academic Degrees*

**Graeter Stefanie Rebecca, PhD, University of Bern**
Thesis: Death-inducing properties of intravenous immunoglobulin (IVIG) in neutrophil populations during severe inflammatory conditions (Jan. 2019)
Supervisor: Prof. Stephan von Gunten

**Frangez Ziva, PhD, University of Bern**
Thesis: Expression and function of autophagy-regulating proteins in primary and metastatic melanomas (Dec. 2019)
Supervisor: Prof. Hans-Uwe Simon

**Karlen Hélène, M.Med., University of Bern**
Thesis: Expression of IL-15 in atopic dermatitis (Jan. 2019)
Supervisor: Prof. Dagmar Simon, Prof. Hans-Uwe Simon

**Schnüriger Noah, M.Sc., University of Bern**
Thesis: Exploring the role of the BCL-2 family member BOK – Novel discoveries on its impact on cell death and mitochondrial metabolism (March 2019)
Supervisor: Prof. Thomas Kaufmann

**Gigon Lea, M.Sc., University of Bern**
Thesis: The role of $Ca^{2+}$ and BK channel in the mechanism of neutrophil extracellular traps (NETs) and neutrophil metabolism (Sep. 2019)
Supervisor: Prof. Hans-Uwe Simon

**Eleonora Valente, M. Sc. pharm., University of Basel**
Thesis: Immunological effects of the interleukin-4/13 inhibitor dupilumab in atopic dermatitis (June 2019)
Supervisors: Prof. Hans-Uwe Simon, Prof. Dagmar Simon

**Baumann Sven, B.Sc., University of Bern**
Thesis: Comparing cell death in neutrophils and eosinophils (May 2019)
Supervisor: Prof. Stephan von Gunten

**Gut Aaron David, B.Sc., University of Bern**
Thesis: Role of Siglec-9 in the natural killer cell immunological synapse (NKIS) formation (May 2019)
Supervisor: Prof. Stephan von Gunten

**Hemmann Mike, B.Sc., University of Bern**
Thesis: Siglec expression and function on lymphocytes in cancer and sepsis (May 2019)
Supervisor: Prof. Stephan von Gunten

**Valentina Pecoraro, B.Sc., University of Bern**
Thesis: Role of focal adhesion kinase in lung cancer progression (May 2019)
Supervisor: Prof. Georgia Konstantinidou

**Rebecca Poonam Brachat, B.Sc., University of Bern**
Thesis: Role of focal adhesion kinase in lung cancer progression (May 2019)
Supervisor: Prof. Georgia Konstantinidou

**Simon Sennhauser, B.Sc., University of Bern**
Thesis: Characterization of T cell populations in pancreatic cancer and their changes upon ACSL3-knockout (May 2019)
Supervisor: Prof. Georgia Konstantinidou

**Nicholas Küng, B.Sc., University of Bern**
Thesis: Characterization of the immune landscape of pancreatic ductal adenocarcinoma and how ACSL3 controls it: Focus on macrophages, neutrophils and dendritic cells (May 2019)
Supervisor: Prof. Georgia Konstantinidou

# 4. Research Activities

## *4.1. Research Projects and Publications*

### *Group Prof. Andrea Huwiler*

Group members: Tankica Maneva Timcheva, Lab Technician[1]
Marianne Maillard-van Laer, Lab Technician[1]
Faik, Imeri, postdoctoral fellow[1]
Bisera Stepanovska, PhD student[1]
Redona Hafizi
Isolde Römer, Technician[2]
Stephanie Schwalm, Dr., postdoctoral fellow[1,2]

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

Our research is focused on sphingolipids and their contribution to physiological and patho-physiological processes that regulate diseases such as cancer, inflammation and fibrosis. A special focus we have put on those sphingolipid species that build the cellular “rheostat”, i.e. ceramide, sphingosine, sphingosine 1-phosphate (S1P), and ceramide 1-phosphate (C1P). We are studying the regulation of the critical sphingolipid-generating and -degrading enzymes including ceramidases, sphingosine kinases, and the ceramide kinase to understand under which conditions a certain sphingolipid is accumulating in the cell to exert a function. The major goal is it to identify novel therapeutic targets within the sphingolipid cascades which may turn useful in the treatment of diseases characterized by abnormal cell growth.

#### *Original publication*

1. Dennhardt S, Finke KR**, Huwiler A**, Coldewey SM: Sphingosine-1-phosphate promotes barrier-stabilizing effects in human microvascular endothelial cells via AMPK-dependent mechanisms. Biochim Biophys Acta 1865 (2019), 774-781.

2. Stepanovska B, Lange AI, Schwalm S, Pfeilschifter J, Coldewey SM, **Huwiler A**: Down-regulation of S1P lyase mediates an improved barrier function in human cerebral microvascular endothelial cells following an inflammatory challenge. Int. J. Mol. Sci. (2020) in press.

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

***Review article***

1. Stepanovska B, **Huwiler A:** Targeting the S1P receptor signaling pathways as a promising approach for treatment of autoimmune and inflammatory diseases. Pharmacol Res. (2019), doi: 10.1016/j.phrs.2019.02.009.

## *Group Prof. Thomas Kaufmann*

Group members: Dr. Yuniel Fernandez Marrero, postdoctoral fellow
Samara Naim, PhD student
Noah Schnüriger, M.Sc. student
Peymaneh Zahiroddini, M.Sc. student
Daniel Bachmann, Lab Technician

Our group is interested in the molecular mechanisms of programmed cell death (PCD), in particular apoptosis and necroptosis, and the link between cell death and innate immune signaling. A focus in the latter lies on myeloid cells, in particular granulocytes (neutrophils and basophils) and mast cells, which are central players of innate immunity. Apoptosis is recognized as the most relevant (patho-) physiological form of PCD, whereas the physiological role of necroptosis is less well understood. Given the fact that apoptosis suppresses necroptosis, the latter is hypothesized to serve as a backup, proinflammatory form of PCD upon infection with pathogens that actively block apoptosis.

Granulocytes isolated from mice can only be obtained in low numbers, which makes biochemical analyses difficult, and – in the case of basophils – almost impossible. We have established a protocol to generate conditionally immortalized progenitor cells (“Hoxb8 cells”) that are committed to the macrophage/neutrophil- or the basophil lineages. Those cells can be differentiated in vitro into mature granulocytes in nearly unlimited numbers. An advantage of “Hoxb8” cells over primary granulocytes lies in the straightforward possibility of further genetic manipulation, such as overexpression of genes of interest reconstitution of gene deficient cells lines with particular mutants of that same gene. Regarding basophils and mast cells, we are interested how cytokines, such as IL-3, or binding of IgE and subsequent cross-linking of the high affinity IgE receptor by antigen, activate these cells, and if/how those stimuli increase cellular viability. On the other hand, selective killing of activated basophils or mast cells (or activated immune cells in general) is an intriguing concept to target immunological disorders, including allergies. Newly developed drugs aiming at inducing apoptosis in cancer cells (so called BH3-mimetics) are tested in our lab for their potential to kill activated leukocyte populations selectively.

Currently of great interest to our group is the pro-apoptotic family member BOK. BOK has raised much interest recently, as it is deleted in human cancers with surprisingly high frequency. Several cancer models with our newly developed Bok-deficient mouse strain are ongoing in our lab and in collaboration with others to test the potential tumour suppressor potential of BOK. Our recent data indicate that BOK may have a previously non-recognized tumor-suppressor function in non-small-cell lung cancer and that BOK is a crucial mediator of

liver damage and carcinogenesis induced by chemical carcinogens. Other BOK related projects focus on the molecular function of this still rather enigmatic protein, as well as its role in cancer development and maintenance. Regarding the latter, we have recently identified a novel function of BOK, linking this cell death regulator to nucleotide metabolism.

**BCL-2 family protein BOK is a positive regulator of uridine metabolism in mammals.**
Srivastava R, Cao Z, Nedeva C, Naim S, Bachmann D, Rabachini T, Gangoda L, Shahi S, Glab J, Menassa J, Osellame L, Nelson T, Fernandez-Marrero Y, Brown F, Wei A, Ke F, O'Reilly L, Doerflinger M, Allison C, Kueh A, Ramsay R, Smith BJ, Mathivanan S, Kaufmann T, Puthalakath H
BCL-2 family proteins regulate the mitochondrial apoptotic pathway. BOK, a multidomain BCL-2 family protein, is generally believed to be an adaptor protein similar to BAK and BAX, regulating the mitochondrial permeability transition during apoptosis. Here we report that BOK is a positive regulator of a key enzyme involved in uridine biosynthesis; namely, uridine monophosphate synthetase (UMPS). Our data suggest that BOK expression enhances UMPS activity, cell proliferation, and chemosensitivity. Genetic deletion of Bok results in chemoresistance to 5-fluorouracil (5-FU) in different cell lines and in mice. Conversely, cancer cells and primary tissues that acquire resistance to 5-FU down-regulate BOK expression. Furthermore, we also provide evidence for a role for BOK in nucleotide metabolism and cell cycle regulation. Our results have implications in developing BOK as a biomarker for 5-FU resistance and have the potential for the development of BOK-mimetics for sensitizing 5-FU-resistant cancers.
**See original publication No 1**

### *Original publications*

1. Srivastava R, Cao Z, Nedeva C, Naim S, Bachmann D, Rabachini T, Gangoda L, Shahi S, Glab J, Menassa J, Osellame L, Nelson T, Fernandez-Marrero Y, Brown F, Wei A, Ke F, O'Reilly L, Doerflinger M, Allison C, Kueh A, Ramsay R, Smith BJ, Mathivanan S, **Kaufmann T**, Puthalakath H: BCL-2 family protein BOK is a positive regulator of uridine metabolism in mammals.
   Proc Natl Acad Sci U S A. 116 (2019), 15469-15474.

2. Knop J, Spilgies LM, Rufli S, Reinhart R, Vasilikos L, Yabal M, Crowley E, Jost PJ, Marsh RA, Wajant H, Robinson MD, **Kaufmann T**, Wong WW: TNFR2 induced priming of the inflammasome leads to a RIPK1-dependent cell death in the absence of XIAP.
   Cell Death Dis. 10 (2019), 700.

## *Group Prof. Georgia Konstantinidou*

Group members: Chiara Pozzato, PhD student
Matteo Rossi Sebastiano, PhD student
Maria Saliakoura, PhD student

Cancer cells undergo oncogene-directed reprogramming in order to meet the energetic and biosynthetic challenges of cell survival, growth and proliferation. Our lab aims at identifying vulnerabilities of cancer cells in order to reveal targets for the development of innovative therapeutic strategies. In particular, we focus on the signaling and lipid metabolic alterations in KRAS-induced lung and pancreatic cancer. We work on cell lines (using a combination of techniques in molecular biology, cell biology and biochemistry), mouse models of lung and pancreatic cancer and human specimens.

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

### *Original publication*

1. Saliakoura M, Reynoso-Moreno I, Pozzato C, Rossi Sebastiano M, Galié M, Gertsch J, **Konstantinidou G:** The ACSL3-LPIAT1 signaling drives prostagladin synthesis in non-small cell lung cancer.
Oncogene 2020 Feb 7. doi: 10.1038/s41388-020-1196-5. [Epub ahead of print]

### *Review article*

1. Rossi Sebastiano M, **Konstantinidou G:** Targeting long chain acyl-CoA synthetases for cancer therapy. Int J Mol Sci. 20 (2019), 1-16.

## *Group Prof. Hans-Uwe Simon*

Group members:
Kevin Oberson, Lab Technician*
Meike Claus, Lab Technician*
Evelyne Kozlowski, Lab Technician*
Riim Naser, Lab Technician**
Dr. Zhaoyue He, Postdoctoral fellow
Dr. He Liu, Postdoctoral fellow
Dr. Darko Stojkov, Postdoctoral fellow*
Dr. Xiaoliang Wang, Postdoctoral fellow
Ziva Frangez, PhD student
Nina Germic, PhD student
Kim Klapan, PhD student**
Peng Shuang, PhD student*
Nikita Markov, PhD student*
Yihe Chen, PhD student*
Yancheng Wu, PhD student*
Philippe JeanRichard, M.Sc. pharm. student*
David Fartelj, M.Sc. student*
Lea Gigon, M.Sc. student*
Eleonora Valente, M.Sc. pharm. student**

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

We are interested in the role of apoptosis and autophagy in inflammatory diseases and cancer. Several diseases serve as models to study such processes. In particular, we investigate pathogenic mechanisms of the following diseases: Atopic dermatitis, hypereosinophilic syndromes, eosinophilic esophagitis, bullous pemphigoid and malignant melanoma. Our research goal is the identification of new drug targets for future therapeutic approaches in these diseases. Besides research into pathogenesis, we have developed several *in vitro* and *in vivo* test systems to determine potential effects of a given drug on the immune system. Moreover, we are involved in several clinical drug studies. Our research requires a network of physician-scientists from many different clinics. Most of the participating groups are located at the Medical Faculty of the University of Bern. Results of these collaborative interactions can be seen in the following abstracts, which briefly describe our research activities in 2019.

**Biochemical re-programming of human dermal stem cells to neurons by increasing mitochondrial membrane potential.**
Liu H, He Z, Leonhard April S, Trefny MP, Rougier JS, Salemi S, Olariu R, Widmer HR, Simon HU
Stem cells are generally believed to contain a small number of mitochondria, thus accounting for their glycolytic phenotype. We demonstrate here, however, that despite an indispensable glucose dependency, human dermal stem cells (hDSCs) contain very numerous mitochondria. Interestingly, these stem cells segregate into two distinct subpopulations. One exhibits

high, the other low-mitochondrial membrane potentials (Δψm). We have made the same observations with mouse neural stem cells (mNSCs) which serve here as a complementary model to hDSCs. Strikingly, pharmacologic inhibition of phosphoinositide 3-kinase (PI3K) increased the overall Δψm, decreased the dependency on glycolysis and led to formation of TUJ1 positive, electrophysiologically functional neuron-like cells in both mNSCs and hDSCs, even in the absence of any neuronal growth factors. Furthermore, of the two, it was the Δψm-high subpopulation which produced more mitochondrial reactive oxygen species (ROS) and showed an enhanced neuronal differentiation capacity as compared to the Δψm-low subpopulation. These data suggest that the Δψm-low stem cells may function as the dormant stem cell population to sustain future neuronal differentiation by avoiding excessive ROS production. Thus, chemical modulation of PI3K activity, switching the metabotype of hDSCs to neurons, may have potential as an autologous transplantation strategy for neurodegenerative diseases.

**See original publication No 1**

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

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

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

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

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

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

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

**See original publication No 2**

**ATG12 deficiency leads to tumor cell oncosis owing to diminished mitochondrial biogenesis and reduced cellular bioenergetics.**

Liu H, He Z, Germič N, Ademi H, Frangež Ž, Felser A, Peng S, Riether C, Djonov V, Nuoffer JM, Bovet C, Mlinarič-Raščan I, Zlobec I, Fiedler M, Perren A, Simon HU

In contrast to the "Warburg effect" or aerobic glycolysis earlier generalized as a phenomenon in cancer cells, more and more recent evidence indicates that functional mitochondria are pivotal for ensuring the energy supply of cancer cells. Here, we report that cancer cells with reduced autophagy-related protein 12 (ATG12) expression undergo an oncotic cell death, a phenotype distinct from that seen in ATG5-deficient cells described before. In addition, using untargeted metabolomics with ATG12-deficient cancer cells, we observed a global reduction in cellular bioenergetic pathways, such as β-oxidation (FAO), glycolysis, and tricarboxylic acid cycle activity, as well as a decrease in mitochondrial respiration as monitored with Sea-

horse experiments. Analyzing the biogenesis of mitochondria by quantifying mitochondrial DNA content together with several mitochondrion-localizing proteins indicated a reduction in mitochondrial biogenesis in ATG12-deficient cancer cells, which also showed reduced hexokinase II expression and the upregulation of uncoupling protein 2. ATG12, which we observed in normal cells to be partially localized in mitochondria, is upregulated in multiple types of solid tumors in comparison with normal tissues. Strikingly, mouse xenografts of ATG12-deficient cells grew significantly slower as compared with vector control cells. Collectively, our work has revealed a previously unreported role for ATG12 in regulating mitochondrial biogenesis and cellular energy metabolism and points up an essential role for mitochondria as a failsafe mechanism in the growth and survival of glycolysis-dependent cancer cells. Inducing oncosis by imposing an ATG12 deficiency in solid tumors might represent an anticancer therapy preferable to conventional caspase-dependent apoptosis that often leads to undesirable consequences, such as incomplete cancer cell killing and a silencing of the host immune system.

**See original publication No 3**

**Machine learning with autophagy-related proteins for discriminating renal cell carcinoma subtypes.**

He Z, Liu H, Moch H, Simon HU

Machine learning techniques have been previously applied for classification of tumors based largely on morphological features of tumor cells recognized in H&E images. Here, we tested the possibility of using numeric data acquired from software-based quantification of certain marker proteins, i.e. key autophagy proteins (ATGs), obtained from immunohistochemical (IHC) images of renal cell carcinomas (RCC). Using IHC staining and automated image quantification with a tissue microarray (TMA) of RCC, we found ATG1, ATG5 and microtubule-associated proteins 1A/1B light chain 3B (LC3B) were significantly reduced, suggesting a reduction in the basal level of autophagy with RCC. Notably, the levels of the ATG proteins expressed did not correspond to the mRNA levels expressed in these tissues. Applying a supervised machine learning algorithm, the K-Nearest Neighbor (KNN), to our quantified numeric data revealed that LC3B provided a strong measure for discriminating clear cell RCC (ccRCC). ATG5 and sequestosome-1 (SQSTM1/p62) could be used for classification of chromophobe RCC (crRCC). The quantitation of particular combinations of ATG1, ATG16L1, ATG5, LC3B and p62, all of which measure the basal level of autophagy, were able to discriminate among normal tissue, crRCC and ccRCC, suggesting that the basal level of autophagy would be a potentially useful parameter for RCC discrimination. In addition to our observation that the basal level of autophagy is reduced in RCC, our workflow from quantitative IHC analysis to machine learning could be considered as a potential complementary tool for the classification of RCC subtypes and also for other types of tumors for which precision medicine requires a characterization.

**See original publication No 4**

### *Original publications*

1. Liu H, He Z, April S, Trefny MP, Rougier JS, Salemi S, Olariu R, Widmer HR, **Simon HU**: Biochemical re-programming of human dermal stem cells to neurons by increasing mitochondrial membrane potential.
Cell Death Differ. 26 (2019), 1048-1061.

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J Lipid Res. 2020 Jan;61(1):1-9. doi: 10.1194/jlr.M092072. Epub 2019 Nov 18.

***Review articles and Editorials***

1. Germic N, Frangez Z, Yousefi S, **Simon HU**: Regulation of the innate immune system by autophagy: neutrophils, eosinophils, mast cells, NK cells.
Cell Death Differ. 26 (2019), 703-714.

2. Germic N, Frangez Z, Yousefi S, **Simon HU**: Regulation of the innate immune system by autophagy: monocytes, macrophages, dendritic cells and antigen presentation.
Cell Death Differ. 26 (2019), 715-727.

3. Yousefi S, Stojkov D, Germic N, Simon D, Wang X, Benarafa C, **Simon HU**: Untangling "NETosis" from NETs.
Eur J Immunol. 49 (2019), 221-227.

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Int Arch Allergy Immunol. 178 (2019), 207-218.

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Z Rheumatol. 78 (2019), 306-312.

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11. Simon D, **Simon HU**: Relationship of skin barrier breakdown and eosinophilic esophagitis.
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***Book chapter***

1. **Simon HU**, Friis R: Autophagy. In: Encyclopedia of Molecular Pharmacology (Eds. S. Offermanns and W. Rosenthal); Springer, in press.

## *Group Prof. Stephan von Gunten*

Group members: Dr. Kayluz Frias Boligan, Postdoc
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Lukas Mürner, M.Sc. 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.

**The architecture of the IgG anti-carbohydrate repertoire in primary antibody deficiencies (PADs).**
Jandus P, Frias Boligan K, Smith DF, de Graauw E, Grimbacher B, Jandus C, Abdelhafez MM, Despont A, Bovin N, Simon D, Rieben R, Simon HU, Cummings RD, von Gunten S
Immune system failure in primary antibody deficiencies (PADs) has been linked to recurrent infections, autoimmunity and cancer, yet clinical judgment is often based on the reactivity to a restricted panel of antigens. Previously, we demonstrated that the human repertoire of carbohydrate-specific IgG exhibits modular organization related to glycan epitope structure. The current study compares the glycan-specific IgG repertoires among different PAD entities. Distinct repertoire profiles with extensive qualitative glycan-recognition defects were observed, characterized by the common loss of Gala- and GalNAc-reactivity and disease-specific recognition of microbial, self-antigens and tumor-associated carbohydrate antigens. Antibody repertoire analysis may provide a useful tool to elucidate the dimension and clinical implications of the immune system failure in individual patients.
**See original publication No 1**

**Antitumor effects of the GM3(Neu5Gc) ganglioside-specific humanized antibody 14F7hT against Cmah-transfected cancer cells.**

Dorvignit D, Boligan KF, Relova-Hernández E, Clavell M, López A, Labrada M, Simon HU, López-Requena A, Mesa C, von Gunten S

The GM3(Neu5Gc) ganglioside represents a tumor-specific antigen that is considered a promising target for cancer immunotherapy. We previously demonstrated that the humanized antibody 14F7hT, specific for this ganglioside, exhibited significant antitumor effects in preclinical hematological tumor models. As this antibody recognizes human tumor tissues from several origins, we addressed its potential effect on different tumor types. The use of cell lines for testing GM3(Neu5Gc)-targeting strategies, in particular for human malignancies, is complicated by the absence in humans of functional cytidine monophospho-N-acetylneuraminic acid hydroxylase (CMAH), the enzyme required for Neu5Gc sialic acid biosynthesis. Quantitative flow cytometry revealed the absence of surface GM3(Neu5Gc) in several human but also mouse cell lines, in the last case due to low expression of the enzyme. Hypoxia-induced expression of this ganglioside on human SKOV3 cells was observed upon culture in Neu5Gc-containing medium without evidence for CMAH-independent biosynthesis. However, only transfection of the mouse Cmah gene into human SKOV3 and mouse 3LL cells induced a stable expression of GM3(Neu5Gc) on the cancer cell surface, resulting in effective models to evaluate the antitumor responses by 14F7hT in vitro and in vivo. This antibody exerted antibody-dependent cell-mediated cytotoxicity (ADCC) and in vivo antitumor effects on these Cmah-transfected non-hematological tumors from both mouse and human origin. These results contribute to validate GM3(Neu5Gc) as a relevant target for cancer immunotherapy and reinforces the value of 14F7hT as a novel anti-cancer drug.

**See original publication No 2**

**Siglec-9 regulates an effector memory CD8+ T-cell subset that congregates in the melanoma tumor microenvironment.**

Haas Q, Boligan KF, Jandus C, Schneider C, Simillion C, Stanczak MA, Haubitz M, Seyed Jafari SM, Zippelius A, Baerlocher GM, Läubli H, Hunger RE, Romero P, Simon HU, von Gunten S

Emerging evidence suggests an immunosuppressive role of altered tumor glycosylation due to downregulation of innate immune responses via immunoregulatory Siglecs. In contrast, human T cells, a major anticancer effector cell, only rarely express Siglecs. However, here, we report that the majority of intratumoral, but not peripheral blood, cytotoxic CD8+ T cells expressed Siglec-9 in melanoma. We identified Siglec-9+ CD8+ T cells as a subset of effector memory cells with high functional capacity and signatures of clonal expansion. This cytotoxic T-cell subset was functionally inhibited in the presence of Siglec-9 ligands or by Siglec-9 engagement by specific antibodies. TCR signaling pathways and key effector functions (cytotoxicity, cytokine production) of CD8+ T cells were suppressed by Siglec-9 engagement, which was associated with the phosphorylation of the inhibitory protein tyrosine phosphatase SHP-1, but not SHP-2. Expression of cognate Siglec-9 ligands was observed on the majority of tumor cells in primary and metastatic melanoma specimens. Targeting the tumor-restricted, glycosylation-dependent Siglec-9 axis may unleash this intratumoral T-cell subset, while confining T-cell activation to the tumor microenvironment.

**See original publication No 3**

**Xenogeneic Neu5Gc and self-glycan Neu5Ac epitopes are immune targets in multiple sclerosis.**
Boligan KF, Oechtering J, Keller CW, Peschke B, Rieben R, Bovin N, Kappos L, Cummings RD, Kuhle J, von Gunten S*, Lünemann JD*.
*shared last authorship
To explore the repertoire of glycan-specific immunoglobulin G (IgG) antibodies in treatment-naive patients with relapsing-remitting multiple sclerosis (RRMS). A systems-level approach combined with glycan array technologies was used to determine specificities and binding reactivities of glycan-specific IgGs in treatment-naive patients with RRMS compared with patients with noninflammatory and other inflammatory neurologic diseases. We identified a unique signature of glycan-binding IgG in MS with high reactivities to the dietary xenoglycan N-glycolylneuraminic acid (Neu5Gc) and the self-glycan N-acetylneuraminic acid (Neu5Ac). Increased reactivities of serum IgG toward Neu5Gc and Neu5Ac were additionally observed in an independent, treatment-naive cohort of patients with RRMS. Patients with MS show increased IgG reactivities to structurally related xenogeneic and human neuraminic acids. The discovery of these glycan-specific epitopes as immune targets and potential biomarkers in MS merits further investigation.
**See original publication No 6**

### *Original publications*


1. Jandus P, Frias Boligan K, Smith DF, de Graauw E, Grimbacher B, Jandus C, Abdelhafez MM, Despont A, Bovin N, Simon D, Rieben R, Simon HU, Cummings RD, **von Gunten S**: The architecture of the IgG anti-carbohydrate repertoire in primary antibody deficiencies (PADs).
   Blood 134 (2019), 1941-1950.

2. Dorvignit D, Boligan KF, Relova-Hernández E, Clavell M, López A, Labrada M, Simon HU, López-Requena A, Mesa C, **von Gunten S**: Antitumor effects of the GM3(Neu5Gc) ganglioside-specific humanized antibody 14F7hT against Cmah-transfected cancer cells.
   Sci Rep. 9 (2019), 9921.

3. Haas Q, Boligan KF, Jandus C, Schneider C, Simillion C, Stanczak MA, Haubitz M, Seyed Jafari SM, Zippelius A, Baerlocher GM, Läubli H, Hunger RE, Romero P, Simon HU, **von Gunten S**: Siglec-9 regulates an effector memory CD8+ T-cell subset that congregates in the melanoma tumor microenvironment.
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   J Exp Med. (2020), in press.

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

***Review articles and Editorials***

1. **Gunten S**: The future of Pharmacology: Towards more personalized pharmacotherapy and reverse translational research.
Pharmacology 105 (2019), 1-2.

2. Verschoor D, **von Gunten S:** Allergy and atopic diseases: An update on experimental evidence.
Int Arch Allergy Immunol. 180 (2019), 235-243.

3. Graeter S, Simon HU, **von Gunten S:** Granulocyte death mediated by specific antibodies in intravenous immunoglobulin (IVIG).
Pharmacol Res. 2019 Feb 6:104168. doi: 10.1016/j.phrs.2019.02.007. [Epub ahead of print]

## *Group Prof. Shida Yousefi*

Group members: Meike Claus, Technician*
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Philippe JeanRichard, M.Sc. student*
David Fartelj, M.Sc. student*
Lea Gigon, M.Sc. student*

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

We are interested in mechanisms regulating granulocyte functions, such as the release of inflammatory mediators and anti-microbial defense mechanisms. Extracellular DNA trap formation by granulocytes is a newly defined anti-microbial mechanism. Previous reports from our group revealed that extracellular DNA trap formation by neutrophils, eosinophils, and basophils does not require their death, and that DNA traps are composed of mitochondrial DNA and granule proteins. Our aim is to investigate mouse and human neutrophils with respect to their extracellular DNA trap formation and the molecular events required.

**Oxidative damage of SP-D abolishes control of eosinophil extracellular DNA trap formation.**
Yadav SK, Stojkov D, Feigelson SW, Roncato F, Simon HU, Yousefi S, Alon R
Microtubules (MTs) are critically involved in the transport of material within cells, but their roles in chemotactic leukocyte motility and effector functions are still obscure. Resting neutrophils contain few MTs assembled in an MT organizing center (MTOC) behind their multilobular nuclei. Using a probe of real-time tubulin polymerization, SiR-tubulin, we found that neutrophils elongated their MTs within minutes in response to signals from the two prototypic chemotactic peptides, CXCL1 and fMLP. Taxol, a beta-tubulin binding and MT stabilizing drug, was found to abolish this CXCL1- and fMLP-stimulated MT polymerization. Nevertheless, taxol treatment as well as disruption of existing and de novo generated MTs did not impair neutrophil protrusion and squeezing through IL-1β-stimulated endothelial monolayers mediated by endothelial deposited CXCL1 and neutrophil CXCR2. Notably, CXCL1-dependent neutrophil TEM was not associated with neutrophil MT polymerization. Chemokinetic neutrophil motility on immobilized CXCL1 was also not associated with MT polymerization, and taxol treatment did not interfere with this motility. Nevertheless, and consistent with its ability to suppress MT polymerization induced by soluble CXCL1 and fMLP, taxol treatment inhibited neutrophil chemotaxis toward both chemotactic peptides. Taxol treatment also suppressed CXCL1- and fMLP-triggered elastase-dependent neutrophil invasion through collagen I barriers. Collectively, our results highlight de novo chemoattractant-triggered MT polymerization as key for neutrophil chemotaxis and elastase-dependent invasion but not for chemotactic neutrophil crossing of inflamed endothelial barriers.
**See publication No 1**

***Original publications***

1. Yadav SK, Stojkov D, Feigelson SW, Roncato F, Simon HU, **Yousefi S**, Alon R: Chemokine-triggered microtubule polymerization promotes neutrophil chemotaxis and **invasion** but not transendothelial migration.
J Leukoc Biol. 105 (2019), 755-766.

2. Simon D, **Yousefi S**, Cazzaniga S, Bürgler C, Radonjic S, Houriet C, Heidemeyer K, Klötgen HW, Kozlowski E, Borradori L, Simon HU: Mepolizumab failed to affect bullous pemphigoid: a randomized, placebo-controlled, double-blind phase 2 pilot study.
Allergy 2019 Jun 22. doi: 10.1111/all.13950. [Epub ahead of print]

3. Surmiak M, Gielicz A, Stojkov D, Szatanek R, Wawrzycka-Adamczyk K, **Yousefi S**, Simon HU, Sanak M: LTB4 and 5-oxo-ETE from extracellular vesicles stimulate neutrophils in granulomatosis with polyangiitis.
J Lipid Res. 2020 Jan;61(1):1-9. doi: 10.1194/jlr.M092072. Epub 2019 Nov 18.

***Review articles***

1. **Yousefi S**, Stojkov D, Germic N, Simon D, Wang X, Benarafa C, Simon HU: Untangling "NETosis" from NETs.
Eur J Immunol. 49 (2019), 221-227.

2. Germic N, Frangez Z, **Yousefi S**, Simon HU: Regulation of the innate immune system by autophagy: neutrophils, eosinophils, mast cells, NK cells.
Cell Death Differ. 26 (2019), 703-714.

3. Germic N, Frangez Z, **Yousefi S**, Simon HU: Regulation of the innate immune system by autophagy: monocytes, macrophages, dendritic cells and antigen presentation.
Cell Death Differ. 26 (2019), 715-727.

4. Boeltz S, Amini P, Anders HJ, Andrade F, Bilyy R, Chatfield S, Cichon I, Clancy DM, Desai J, Dumych T, Dwivedi N, Gordon RA, Hahn J, Hidalgo A, Hoffmann MH, Kaplan MJ, Knight JS, Kolaczkowska E, Kubes P, Leppkes M, Manfredi AA, Martin SJ, Maueröder C, Maugeri N, Mitroulis I, Munoz LE, Nakazawa D, Neeli I, Nizet V, Pieterse E, Radic MZ, Reinwald C, Ritis K, Rovere-Querini P, Santocki M, Schauer C, Schett G, Shlomchik MJ, Simon HU, Skendros P, Stojkov D, Vandenabeele P, Berghe TV, van der Vlag J, Vitkov L, von Köckritz-Blickwede M, **Yousefi S**, Zarbock A, Herrmann M: To NET or not to NET:current opinions and state of the science regarding the formation of neutrophil extracellular traps.
Cell Death Differ. 26 (2019), 395-408.

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

## *Group Prof. Uwe Zangemeister-Wittke*

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

### *Original publications*

1. Brandl F, Merten H, Zimmermann M, Béhé M, **Zangemeister-Wittke U**, Plückthun A: Influence of size and charge of unstructured polypeptides on pharmacokinetics and biodistribution of targeted fusion proteins. J Control Release. 307 (2019), 379-392.
2. Lorenzer C, Streußnig S, Tot E, Winkler AM, Merten H, Brandl F, Sayers EJ, Watson P, Jones AT, **Zangemeister-Wittke U**, Plückthun A, Winkler J: Targeted delivery and endosomal cellular uptake of DARPin-siRNA bioconjugates: Influence of linker stability on gene silencing. Eur J Pharm Biopharm. 141 (2019), 37-50.

### *Book chapter*

1. Merten H, Schaefer JV, Brandl F, **Zangemeister-Wittke U**, Plückthun A: Facile site-specific multiconjugation strategies in recombinant proteins produced in bacteria. Methods Mol Biol. 2033 (2019), 253-273.

## *Group Prof. Manuel Haschke (Clinical Pharmacology)*

Group members: Dr. Evangelia Liakoni, MD
Dr. Felix Hammann, MD, PhD
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Dr. Katharina Grafinger, PhD

We are interested in mechanisms of drug toxicity and factors responsible for variations in the metabolism of xenobiotics. Exogenous and endogenous compounds used as biomarkers for toxicity or variations in metabolism of xenobiotics are quantified using liquid chromatography tandem mass spectrometry (LC-MS/MS). To investigate variations in phase I metabolism, we developed a cocktail of low-dose probe drugs combined in a single capsule. To search for potential genetic risk factors for metamizole-induced agranulocytosis, patients with this adverse drug reaction are compared with metamizole-tolerant and never-exposed subjects in a genome-wide association study. In a clinical study, the effect of the CYP- and P-gp-inducer hypericum perforatum (a component of St. John's wort preparations used as antidepressant) on the pharmacokinetics and pharmacodynamics of the direct oral factor Xa inhibitor rivaroxaban is studied in healthy volunteers. As part of the European Drug Emergency Network (EuroDEN) data on toxicity of recreational drugs and novel psychoactive substances is collected and analyzed. In another project, arthropods are investigated as new pharmacokinetic model organisms in the framework of an endectocide-based malaria intervention trial in Africa.

**Metamizole-associated neutropenia: Comparison of patients with neutropenia and metamizole-tolerant patients.**
Rudin D, Spoendlin J, Cismaru A, Liakoni E, Bonadies N, Amstutz U, Meier CR, Krähenbühl S, Haschke M
Metamizole (dipyrone) is a non-opioid analgesic and antipyretic drug with good efficacy and low gastrointestinal toxicity. However, susceptible patients may experience neutropenia or agranulocytosis, a severe and potentially fatal decrease in circulating neutrophil granulocytes. To date, there are no effective strategies to identify patients at increased risk for this rare adverse effect. Characteristics of patients with metamizole-induced neutropenia were compared with metamizole-tolerant patients. Median latency until diagnosis of neutropenia was shorter in inpatients compared to outpatients. There was no association with cumulative metamizole dose or treatment duration and no evidence was found for non-myelotoxic and non-immunosuppressive co-medication, history of drug allergy or preexisting auto-immune diseases as individual risk factors for metamizole-associated neutropenia.
**See original publication No 1**

### *Original publications*

1. Rudin D, Spoendlin J, Cismaru A, Liakoni E, Bonadies N, Amstutz U, Meier CR, Krähenbühl S, **Haschke M**: Metamizole-associated neutropenia: Comparison of patients with neutropenia and metamizole-tolerant patients. Eur J Int Med. 68 (2019), 36-43.

2. Boschung-Pasquier L, Atkinson A, Kastner LK, Banholzer S, **Haschke M**, Buetti N, Furrer DI, Hauser C, Jent P, Que YA, Furrer H, Babouee Flury B: Cefepime neurotoxicity:

thresholds and risk factors. A retrospective cohort study. Clin Microbiol Infect. 2019. Jul 5. pii: S1198-743X(19)30379-9. doi: 10.1016/j.cmi.2019.06.028. [Epub ahead of print]

3. Hoemme A, Barth H, **Haschke MM**, Krähenbühl S, Strasser F, Lehner C, von Kameke A, Wälti T, Thürlimann B, Früh M, Driessen C, Joerger M: Prognostic impact of polypharmacy and drug interactions in patients with advanced cancer. Cancer Chemother Pharmacol. 83 (2019), 763-774.

4. Leuppi-Taegtmeyer A, Duthaler U, Hammann F, Schmid Yasmin, Dickenmann M, Amico P, Jehle AW, Kalbermatter S, Lenherr C, Meyer zu Schwabedissen HE, **Haschke MM**, Liechti ME, Krähenbühl S: (2019). Pharmacokinetics of oxycodone/naloxone and its metabolites in patients with end-stage renal disease during and between haemodialysis sessions. Nephrol Dialysis Transplant. 34(2019), 692-702.

5. Liakoni E, Berger F, Klukowska-Rötzler J, Kupferschmidt H, **Haschke MM**, Exadaktylos A: Characteristics of emergency department presentations requiring consultation of the national Poisons Information Centre. Swiss Medical Weekly 149 (2019), w20164.

6. Piotrowska N, Klukowska-Rötzler J, Lehmann B, Krummrey G, **Haschke M**, Exadaktylos AK, Liakoni E: (2019). Presentations related to acute paracetamol intoxication in an urban emergency department in Switzerland. Emerg Med Int. 2019 Dec 6;2019:3130843. doi: 10.1155/2019/3130843. eCollection 2019.

7. Rudin D, Lanzilotto A, Bachmann F, Housecroft CE, Constable EC; Drewe J, **Haschke MM**, Krähenbühl S: (2019). Non-immunological toxicological mechanisms of metamizole-associated neutropenia in HL60 cells. Biochem Pharmacol 163 (2019), 345-356.

8. Scholz I, Schmid Y, Exadaktylos A, **Haschke MM**, Liechti ME, Liakoni E: Emergency department presentations related to abuse of prescription and over-the-counter drugs in Switzerland: time trends, sex and age distribution. Swiss Medical Weekly 149 (2019), w20056.

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

10. Ziesenitz VC, Rodieux F, Atkinson A, Borter C, Bielicki JA, **Haschke M**, Duthaler U, Bachmann F, Thomas O, Gürtler N, Holland-Cunz S, van den Anker JN, Gotta V, Pfister M: Dose evaluation of intravenous metamizole (dipyrone) in infants and children: a prospective population pharmacokinetic study. Eur J Clin Pharmacol. 75 (2019), 1491-1502.

11. Duthaler U, Leisegang R, Karlsson MO, Krähenbühl S, Hammann F: The effect of food on the pharmacokinetics of oral ivermectin. J Antimicrob Chemother. 75 (2020), 438-440.

12. Schmid Y, Scholz I, Mueller L, Exadaktylos AK, Ceschi A, Liechti ME, Liakoni E: Emergency department presentations related to acute toxicity following recreational use of cannabis products in Switzerland. Drug Alcohol Depend. 206 (2020), 107726.

***Review article***

13. Grafinger KE, Liechti ME, Liakoni E: Clinical value of analytical testing in patients presenting with New Psychoactive Substances intoxication. Br J Clin Pharmacol. 2019 Sep 4. doi: 10.1111/bcp.14115. [Epub ahead of print]

## *Additional Publications by PKI Members*

***Original publications***

Sebastian T, **Spirk D**, Engelberger RP, Dopheide JF, Baumann FA, Barco S, Spescha R, Leeger C, Kucher N. Incidence of Stent Thrombosis after Endovascular Treatment of Iliofemoral or Caval Veins in Patients with the Postthrombotic Syndrome. Thromb Haemost. 119 (2019), 2064-73.

**Spirk D**, Sebastian T, Banyai M, Beer JH, Mazzolai L, Baldi T, Aujesky D, Hayoz D, Engelberger RP, Kaeslin T, Korte W, Escher R, Husmann M, Mollet A, Szucs TD, Kucher N. Venous Thromboembolism and Renal Impairment: Insights from the SWIss Venous Thrombo-Embolism Registry (SWIVTER). Semin Thromb Hemost. 45 (2019), 851-8.

Schnetzler G, Bremgartner MF, Grossmann Straessle R, **Spirk D**, Tay F, Troxler Saxer R, Traber M. Evolution to a Competency-Based Training Curriculum for Pharmaceutical Medicine Physicians in Switzerland. Front Pharmacol. 27 (2019), 10:164.

Sebastian T, Engelberger RP, **Spirk D**, Hakki LO, Baumann FA, Spescha RS, Kucher N: Cessation of anticoagulation therapy following endovascular thrombus removal and stent placement for acute iliofemoral deep vein thrombosis. Vasa 48 (2019), 331-339.

## *4.2. Congress Invitations*

**Prof. Hans-Uwe Simon**
21st Meeting: Allergy and Immunology Update 2019,
Grindelwald (CH), Jan. 25-27, 2019;
Recent advances in eosinophil physiology and pathophysiology.

Scientific Workshop: Role of Eosinophils – from Science to Patient Experience,
Zurich (CH), Febr. 7, 2019;
Role of eosinophils in the immune system and in pathology of eosinophil-mediated diseases.

Annual Meeting of the American Academy of Allergy Asthma and Immunology (AAAAI);
San Francisco, CA (USA), February 22-25, 2019;
Barrier dysfunction in eosinophilic esophagitis.

4th German Pharm-Tox Summit; 85th Annual Meeting of the German Society for Experimental and Clinical Pharmacology and Toxicology (DGPT) and 21st Annual Meeting of the Association of the Clinical Pharmacology (VKliPha) with contribution of the AGAH;
Stuttgart (D), February 25-28, 2019;
Molecular mechanism of NET formation.

Workshop on “Cell Death and Disease”, Villa Vigoni, Loveno di Menaggio,
Como (I), June 26-29, 2019;
Eosinophilic esophagitis-like disease: description of a new disease entity.

50 Shades of Immunology, Celebrating 50 Years of Department of Immunology,
Zurich (CH), July 2-3, 2019;
Neutrophil extracellular traps and cytolysis.

11th Biennial Symposium of the International Eosinophil Society,
Portland (Oregon, USA), July 9-13, 2019;
Eosinophilic esophagitis-like disease: Description of a new disease entity.

SSAI Annual Congress 2019; Immunomodulation: from basic to clinical aspects,
Lugano (CH), September 5-6, 2019;
The role of eosinophils in the immune system and in the pathophysiology.

CDD Conference: Cancer, Immunity & Inflammation, Cambridge (UK), Sept. 9-11, 2019:
The resurrection of an ion channel in neutrophils.

Swiss Institute of Allergy and Asthma Research: Opening symposium of the new campus building, Davos (CH), Sept. 27, 2019:
Novel aspects of eosinophil biology.

18ème Journée d’automne d’actualités en Gastro-entérologie et Hépatologie,
Lausanne (CH), Oct. 3, 2019:
Novel aspects of the pathogenesis of eosinophilic esophagitis.

International Conference: The Regulation of Proteostasis in Cancer,
St. Petersburg (RU), Oct. 11-12, 2019:
ATG12 deficiency leads to tumor cell oncosis owing to diminished mitochondrial biogenesis and reduced cellular bioenergetics.

The Wuxi International Bioforum 2019, Wuxi (China), Nov. 4-6, 2019;
Extracellular DNA traps formed by granulocytes: Essential roles for ROS, ATP and calcium.

11th EADV Dermatological Meeting in Ticino, Bellinzona (CH), Nov. 21, 2019;
Molecular and immunological characterization of inflammatory responses of the esophagus.

**Prof. Thomas Kaufmann**
CDD Conference – Cancer, Immunity & Inflammation, Cambridge (UK), Sep 9-11 2019;
The BCL-2 family member BOK is a positive regulator of uridine metabolism.

**Prof. Stephan von Gunten**
13th Jenner Glyobiology and Medicine Symposium, Boston MA (USA), May 4-7, 2019;
Glycosylation of the tumor cell surface: Impact and opportunities for cancer immunotherapy

Langenargener Symposium des Bodenseeforums, Langenargen (Germany), December 4-5, 2019;
Bedrohung durch Bioterrorismus – Notwendigkeit zur vermehrten interinstitutionellen Zusammenarbeit.

**Prof. Georgia Konstantinidou**
1st Bern Cancer Research Cluster (BCRC) retreat, Univ. of Bern, Bern (CH), June 13, 2019;
Targeting KRAS-driven tumors.

**Dr. Zhaoyue He**
Annual Meeting of the Swiss Metabolomics Society 2019,
Bern (CH), Nov. 6, 2019;
Facilitating interpretation of metabolomics data using KEGG and HMDB databases.

**Bisera Stepanovska**
FEBS Special Meeting in Sphingolipid Biology, Sphingolipids in Physiology and Pathology, Cascais (Portugal), May 6-10, 2019;
In vivo validation of two novel S1P1-selective compounds, ST-1893 and ST-1894, in the experimental autoimmune encephalomyelitis model in mice.

Annual Meeting 2019 of the Swiss Society for Pharmacology and Toxicology, Bern (CH), April 11, 2019;
A regulatory role of S1P lyase in brain endothelial cell barrier function.

## *4.3. Seminar Invitations*

**Prof. Hans-Uwe Simon**
Karolinska Institutet, Institute of Environmental Medicine, Stockholm (S); Jan. 17, 2019;
Guest of Prof. Boris Zhivotovsky:
Molecular mechanisms of extracellular DNA trap formation by granulocytes.

Karolinska Institutet, Institute of Environmental Medicine, Stockholm (S); Jan. 18. 2019;
Opponent of the PhD thesis of Kadri Valter:
Induction of death in cancer cells.

National Institutes of Health (NIH), Bethesda (MD, USA); February 21, 2019;
Guest of Dr. Amy Klion:
Molecular mechanisms of extracellular DNA trap formation by granulocytes.

National Cheng Kung University (NCKU), College of Medicine, Tainan (Taiwan);
March 3, 2019; guest of Prof. Jang-Yang Chang:
The role of eosinophils in health and disease.

Department of Pharmaceutical Sciences, University of Basel, Basel (CH); April 24, 2019;
Guest of Prof. Stephan Krähenbühl:
Extracellular DNA trap formation by granulocytes.

Department of Clinical Immunology and Allergology, Sechenov University, Moscow (Ru);
April 26, 2019; guest of Prof. Alexander Karaulov:
The role of eosinophils in health and disease.

DACH Respiratory Journal Club, AstraZeneca AG, Baar (CH); May 6, 2019;
Guest of Dr. Gunther Pendl:
Licht und Schatten der Immunabwehr durch Eosinophile.

Department of Clinical Immunology and Allergology, Sechenov University, Moscow (Ru);
October 14, 2019; guest of Prof. Alexander Karaulov:
Neutrophils and extracellular DNA trap formation.

**Prof. Thomas Kaufmann**
RIA – Immunology lunch meeting, Inselspital Bern, Feb 13, 2019;
Guest of Prof. M. Bachmann;
Regulation of programmed cell death in granulocytes.

**Prof. Stephan von Gunten**
Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA (USA), February 26, 2019; guest of Prof. Richard D. Cummings;
Aspects of humoral and cellular glycoimmunology.

RIA - Immunology lunch meeting, Inselspital Bern (CH), April 17, 2019;
Guest of Prof. M. Bachmann;
The role of sugars in immunodecifiency, inflammation and cancer.

Palleon Pharmaceuticals Inc., Waltham MA (USA), May 2, 2019: Sweet escape by tumor glycosylation.

LimmaTech Research Conference, Schlieren (CH), October 2, 2019;
Glycoimmunology: biological implications and opportunities.

Seminar, Regensburg Center for Interventional Immunology (RCI), Regensburg (Germany), October 15, 2019; guest of Prof. Hinrich Abken: Glycans as tumor markers and immune checkpoints.

KomABC Meeting, Bern (CH), October 29, 2019;
Risikoszenarien im Gesundheitswesen.

## *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 - Die Arzneimittelabgabe durch Apotheker aufgrund von Leitsymptomen;
Bern (CH), Jan. 23, 2019

Journée de reflexion 2019 (together with Dr. Werner Bauer): Meeting of the Swiss Institute for Medical and Continuing Education (SIWF);
Lucerne (CH), Jan. 25-26, 2019

Workshop on “Cell Death and Disease” (together with C. Brancolini, K.-M. Debatin and P.H. Krammer), Villa Vigoni, Loveno di Menaggio, Como (I), June 26-29, 2019

18$^{th}$ III-Bern International Summer School,
Bönigen (CH), July 28-30, 2019

**Prof. Stephan von Gunten**
Annual Meeting 2019 of the Swiss Society for Pharmacology and Toxicology, Bern (CH), April 11, 2019.

## *4.5. Invited Chairperson at Congresses*

**Prof. Hans-Uwe Simon**
Symposium of the Swiss Society of Pharmacology and Toxicology (together with task force SSPT): Progress in Pharmacology - Die Arzneimittelabgabe durch Apotheker aufgrund von Leitsymptomen; Bern (CH), Jan. 23, 2019

4$^{th}$ German Pharm-Tox Summit; 85$^{th}$ Annual Meeting of the German Society for Experimental and Clinical Pharmacology and Toxicology (DGPT) and 21$^{st}$ Annual Meeting of the Association of the Clinical Pharmacology (VKliPha) with contribution of the AGAH, Symposium 12: Novel drug targets in the immune system; Stuttgart (D), February 25-28, 2019.

World Immune Regulation Meeting XIII; Session: Regulation of chronic inflammation;
Davos (CH), April 6-9, 2019.

Workshop on “Cell Death and Disease”; Session 3; Villa Vigoni, Loveno di Menaggio, Como (I), June 26-29, 2019.

11th Biennial Symposium of the International Eosinophil Society; Session 8 – Eosinophils and Cancer; Portland (Oregon, USA), July 9-13, 2019.

**Prof. Stephan von Gunten**
Langenargener Symposium des Bodenseeforums, Langenargen (Germany), December 4-5, 2019; Bedrohung durch Bioterrorismus – Notwendigkeit zur vermehrten interinstitutionellen Zusammenarbeit.

## *4.6. Referee Work for Peer-Reviewed Journals*

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

**Dr. Ziva Frangez**
Cell Death Dis.

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

**Prof. Thomas Kaufmann**
Acta Tropica
Advances in Medicine
Apoptosis
Allergy
BioEssays
Cell Communication and Signaling
Cell Death Differ.
Cell Death Dis.
Cellular & Molecular Immunology
Eur. J. Immunol.
FEBS Letter
FEBS Journal
Frontiers in Molecular and Cellular Oncology
Future Oncology
Hepatology
Immunology and Cell Biology
International Archives of Allergy and Immunologie
International Review of Cell and Molecular Biology
J. Hepatology
J. Molecular Cell Biology
J. Neuroscience
Methods
Molecular Cancer Therapeutics
Mol. Cell. Oncology
Oncogene
PLoS One
Scientific Reports
Trends in Cell Biology

**Prof. Georgia Konstantinidou**
Cell Death Dis.
Oncotarget
eLIFE

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

**Prof. Hans-Uwe Simon**

Allergy
Apoptosis
Autophagy
Blood
FEBS J.
EMBO Reports
Eur. J. Immunol.
Cell Death Differ.
Cell Death Dis.
Gut
J. Allergy Clin. Immunol.
J. Exp. Med.
J. Immunol.
J. Leukoc. Biol.
Oncogene
Clin. Exp. Allergy
N. Engl. J. Med.
Cell Reports

**PD Dr. Peter Späth**

Clin. Exp. Allergy
Immunotherapy

**Prof. Stephan von Gunten**

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

**Prof. Shida Yousefi**

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

**Prof. Uwe Zangemeister-Wittke**

Bioconjug. Chem.
J. Control. Release
Cancers
Proteins

**Prof. Manuel Haschke**

Bioanalysis
British J Clin Pharmacol
Swiss Med Forum
Pediatric Research

## *4.7. Referee Work for Grant Bodies*

**Prof. Andrea Huwiler**

Deutsche Forschungsgemeinschaft (DFG)
Swiss National Science Foundadtion (SNF)

**Prof. Thomas Kaufmann**

Agence Nationale de la Recherche (ANR)
Austrian Science Fund (FWF)
German Research Foundation (DFG)
L'Oréal Österreich
National Science Centre Poland
Swiss Cancer League
Swiss National Science Foundation (SNF)

**Prof. Hans-Uwe Simon**

Swiss National Science Foundation (SNF)
NÖ Forschungs- und Bildungsgesellschaft (NFB)
Novartis Foundation
Swiss Cancer League
European Research Council (ERC)

**Prof. Stephan von Gunten**

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

**Prof. Uwe Zangemeister-Wittke**

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

## *4.8. Awards*

**Prof. Andrea Huwiler**

**British Pharmacology Society Award**
FASEB conference on Lysophospholipids 2019, Lisbon (Portugal),
July 28 – August 2, 2019

**Dr. Darko Stojkov**

**Bern Immunology Club (BIC) Prize «Best paper 2018»**
Bern Immunology Club (BIC), Bern (CH), June 26, 2019

**Prize for best young investigator presentation**
SSPT Spring Meeting, Bern (CH), April 11, 2019

**Quentin Haas**

**Award of the best presentation, MIM retreat (microbiology and immunology retreat)**
ETH Zürich, Grindelwald (CH), August 29-31, 2019

**Bisera Stepanovska**

**Novartis Institutes for Biomedical Research Prize for an excellent poster presentation**
SSPT Spring Meeting, Bern (CH), April 11, 2019

**Dr. Evangelia Liakoni**

**Taylor & Francis best scientific presentation award**
39th EAPCCT Congress in Naples (May 2019) for the talk entitled “Butanediol conversion to gamma-hydroxybutyrate markedly reduced by the alcohol dehydrogenase blocker fomepizole”

# 5. Administrative, Advisory, and Honorary Posts

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

**Prof. Andrea Huwiler**
President of the Ernennungs- und Habilitationskommission (EHK), Medical Faculty, University of Bern (until 31.01.2019)

Member of the Evaluation Committee, Postdoc mobility grants, Swiss National Science Foundation

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

Member of the Editorial Board of the International Journal of Molecular Sciences

Collection Editor of the Topical Collection of “Sphingolipids in health and disease” in Int. J. Mol. Sci.; Section: Mol. Pharmacol.

Guest Editor of the Special Issue “Lipids as a Cancer Therapeutic Target” in Int. J. Mol. Sci.; Section: Mol. Oncol. 2019.

Member of the Editorial Board of Experimental Pharmacology and Drug Discovery, Frontiers in Pharmacology

**Prof. Thomas Kaufmann**
Member of the Supervision commission “Cell Biology” within the Graduate School for Cellular and Biomedical Sciences of the University of Bern, since 2009

Member of the Editorial Board, Cell Death and Disease
Member of the Editorial Board, Frontiers in Molecular and Cellular Oncology

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

Coordinator FPLC (Äkta)

**Prof. Georgia Konstantinidou**
Member of the Supervision commission “Cell Biology” within the Graduate School for Cellular and Biomedical Sciences of the University of Bern.

Member of the doctorate course of Molecular Medicine (role: lecturer from foreign University) at the University of Ferrara, Italy.

Associate Editor, Frontiers in Molecular and Cellular Oncology

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

President, Collegium of the Deans of the Swiss Faculties of Medicine

Vorstandsmitglied, Universitäre Medizin Schweiz

Mitglied der Direktion, Insel Gruppe AG

Member of the German National Academy of Sciences (Deutsche Akademie der Naturforscher Leopoldina)

Member of the Swiss Academy of Medical Sciences (SAMW)

President of the Novartis Foundation for Biomedical Research

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

Editor-in-Chief, Cell Death & Disease

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

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

**PD Dr. Peter Späth**
Member of the Kreuth Immunoglobulin Working Group ‘European Consensus Proposal for Immunoglobulin Therapies’; member of the expert group drafting an update of the ‘core Summary of Product Characteristics’ for human immunoglobulin preparations

Member of the Scientific Board, 11th C1 Inhibitor Deficiency and Angioedema Workshop, Budapest (H), May 23 -26, 2019

Head Jury awarding the “Grant for Young Investigators”, 11th C1 Inhibitor Deficiency Workshop, Budapest, Hungary, May 23 -26, 2019
Member of taskforce for revision and update of the WAO/EAACI HAE guideline - taskforce for the recommendations on „Nomenclature and diagnosis of HAE” (HAE=hereditary angioedema)

**Prof. Stephan von Gunten**
Editor-in-Chief elect (editorial activity from Sept), journal “Pharmacology”

President of the Swiss Society of Experimental Pharmacology (SSEP)

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

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

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

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

Topic Editor, Frontiers Oncology

Coordinator library at the PKI

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

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

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

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

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

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

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

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

*All PKI principal investigators served as tutors in graduation committes of the Graduate School for Cellular and Biomedical Sciences of the University of Bern.*

# 6. Services

## *6.1. Confocal Microscopy*

The facility hosts three laser scanning microscopes (LSM 5 Exciter, LSM 510 and LSM 700, Carl Zeiss Microimaging GmbH, Jena), which may be used by members of the Medical Faculty at a small charge (CHF 50 per h). The facility for confocal microscopy and image analysis in our institute is part of the Microscopy Imaging Center (MIC) of the University of Bern and operated by Prof. S. Yousefi.

## *6.2. Flow Cytometry*

The Institute of Pharmacology is equipped with Becton-Dickinson FACSCalibur (4 color), and FACSVerse 8 color Flow Cytometer instruments and FACSLyric able to detect up to 12 colors. A service is provided for analyzing potential pathogenic mechanisms of eosinophilic disorders and other inflammatory diseases. Monitoring of patients under immunomodulatory therapy is also included. The costs are currently covered by research grants of the coordinator (Prof. H.-U. Simon, FAMH Clinical Immunology), who can also be consulted for scientific support. Usage of the flow cytometer by non-members of the institute within collaborative projects is also possible.

# 7. Public work

## Art Exhibition

**Gabriela Hess**

Vernissage: June 6, 2019
Welcome Prof. H.-U. Simon / Prof. M. Fiedler
Duration of the exhibition: June 6 – Aug 6, 2019

More information:

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

# 8. Sponsors

## *8.1. Research Grants*

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

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

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

**Prof. Hans-Uwe Simon**
Swiss National Science Foundation (grant No. 310030-166473)
Swiss National Science Foundation (grant No. 310030_184816)
Swiss Cancer League (KFS-3703-08-2015)
Novartis Foundation for Biological-Medical Research, Novartis, Basel (CH)
HORIZON 2020, Marie Sklodowska-Curie Actions, MEL-PLEX

**Prof. Stephan von Gunten**
Swiss National Science Foundation (SNSF) Grant Nr. 310030_184757 / 1
Swiss Cancer League (KFS-3941-08-2016)
Palleon Pharmaceuticals Inc., Waltham MA (USA)
Mizutani Foundation for Glycoscience (Japan)

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

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

**Prof. Manuel Haschke**
Swiss National Science Foundation (31003A_160206 / 32003B_179346)

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

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

## *8.2. Meetings*

***Swiss Society of Pharmacology and Toxicology (SSPT): Progress in Pharmacology – Treatment of Skin Diseases, Bern, Jan 24, 2018 - Die Arzneimittelabgabe durch Apotheker aufgrund von Leitsymptomen; Bern (CH), Jan. 23, 2019***
MSD Merck Sharp & Dohme AG, Luzern
Allmirall AG, Wallisellen
Janssen-Cilag AG, Zug
Pierre Fabre Dermo-Cosmétique, Allschwil
Sanofi-Aventis AG, Vernier
Ultrasun AG, Zürich

***18th III-Bern International Summer School***
***Seehotel La Terrasse, CH 3806 - Bönigen, July 28 – 30, 2019***
Bucher Biotec, Basel
Carl Zeiss AG, Feldbach
GSK, Münchenbuchsee
Lucerna Chem AG, Luzern
Mycrosynth AG, Balgach

Pfizer AG, Zürich
Sysmex Suisse AG, Horgen
Zentrum für Labormedizin, Inselspital Bern
Graduate School for Cellular and Biomedical Sciences, Universität Bern

## *8.3. Seminar Series*

***„Current topics in Pharmacology and Theranostics“ (organized together with the Center of Laboratory Medicine and Division of Clinical Pharmacology, University Hospital Bern, Inselspital)***
Astellas Pharma AG, Wallisellen
AstraZeneca AG, Baar

## *8.4. Travel Support*

**Quentin Haas**
The Graduate School for Cellular and Biomedical Sciences (GCB) of the University of Bern
Swiss Society of Pharmacology and Toxicology (SSPT)
(Society for Glycobiology, Annual Meeting 2019, Phoenix, AZ (USA), November 2-5, 2019)

**Martin Erhardt**
The Graduate School for Cellular and Biomedical Sciences (GCB) of the University of Bern
(FEBS Special Meeting 2019, Sphingolipid Biology: Sphingolipids in Physiology and Pathology, Cascais (Portugal), May 6-10, 2019)

**Kim Klapan**
The Graduate School for Cellular and Biomedical Sciences (GCB) of the University of Bern
(GBM/DGZ Fall conference 2019, Tübingen (Germany), Sepember 2-27, 2019)

**Shuang Peng**
The Graduate School for Cellular and Biomedical Sciences (GCB) of the University of Bern
(SSAI Annual Congress 2019, Lugano (CH), September 5-7, 2019)

Swiss Society of Pharmacology and Toxicology (SSPT)
17th International Congress of Immunology, Beijing (China), October 19-23, 2019)

**Bisera Stepanovska**
Federation of European Biochemical Societies (FEBS)
(FEBS Special Meeting in Sphingolipid Biology: Sphingolipids in Physiology and Pathology, Cascais (Portugal), May 6-10, 2019)

## *8.5. Other Support*

***Bürgi Fonds*** Seminar series of the institute