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Institut für Pathologie

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Jahresbericht 2015

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>>> Editorial

Liebe Leserin, lieber Leser

Willkommen zum Jahresbericht 2015 des Institut für Pathologie! In diesem Jahr konnten wir den Neubau unseres LEAN-Labors endlich beginnen, was naturgemäss von Umzügen, Staub und Lärm begleitet war. Trotz dieser zum Teil erschwerten Bedingungen haben wir uns auf verschiedensten Ebenen weiterentwickelt.

Mit der Abteilung für Zytopathologie hat sich der letzte klinische Bereich systematisch nach LEAN-Prinzipien neu aufgestellt, die Resultate können sich bereits sehen lassen.

In der Molekularen Pathologie haben wir unser Angebotsspektrum mit der Anschaffung eines Nano-Strings auf Expressionsanalysen erweitert. So bieten wir jetzt für unsere Kunden, einschliesslich des Mammazentrums, die PAM50-Untersuchung an. Diese erlaubt eine bessere Risiko-Einschätzung von Östrogen-Rezeptor-positiven Mammakarzinomen und dadurch eine weniger aggressive Indikation von adjuvanten Chemotherapien für unsere Patientinnen.

Auch in den Bereichen Lehre und Forschung waren wir aktiv. Studierende nutzen inzwischen unser Angebot an Masterarbeiten so stark, dass wir leider nicht mehr für alle Interessenten ein Projekt anbieten können.

2015 haben Mitarbeitende des Instituts für Pathologie zahlreiche Forschungspreise nach Bern holen können, diese sind auf unserer Website (www.pathology.unibe.ch) in neuem Kleid dargestellt.

Sie sehen, unser Institut ist in Bewegung, wir wollen gemeinsam «the place to go» werden.

Damit wünsche ich Ihnen viel Vergnügen bei der Lektüre!

Ihr Aurel Perren

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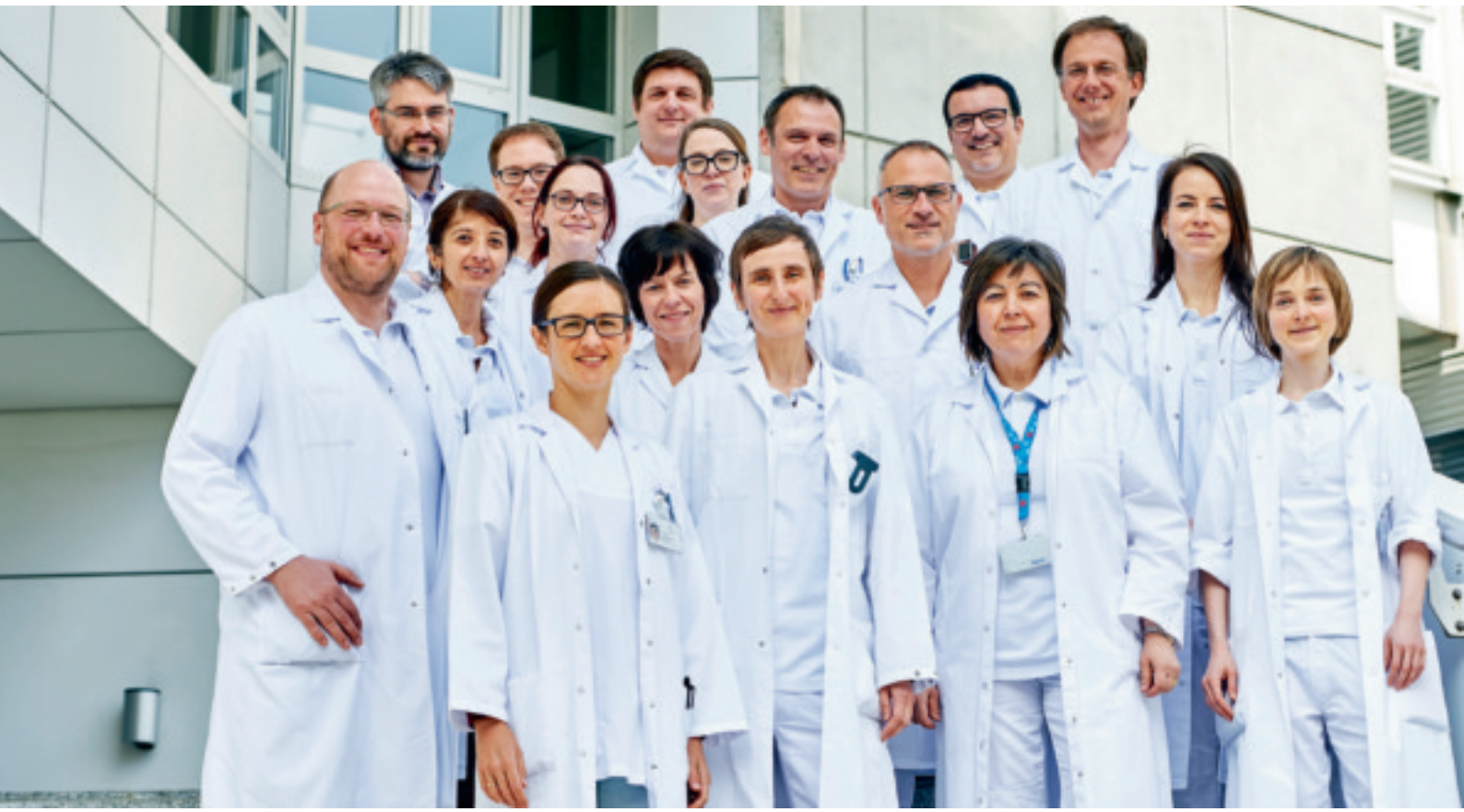
>>> Organigramm



Ärzteteam Klinische Pathologie.

Team Postmortale Diagnostik.

>>> Dienstleistung

1 Klinische Pathologie

Leiter: Prof. Dr. med. Alessandro Lugli

Die Klinische Pathologie (KPath) besteht aus den Einheiten Ärzteschaft, Labor (Histopathologie und Immunhistochemie) und Berichtswesen (Befundsekretariat und Archiv). Die Arbeitsprozesse sowie die Schnittstellen zwischen den Einheiten werden nach dem LEAN-Prinzip gestaltet und dadurch kontinuierlich optimiert. Zusätzlich wurden für das Jahr 2016 auf Abteilungsebene folgende Ziele festgelegt: 1) Im Rahmen des 2015 begonnenen Umbaus koordinierter Umzug in die neuen Räumlichkeiten im ersten und zweiten Stockwerk; 2) Akkreditierung und 3) Modernisierung des Block- und Schnittarchivs.

1.1 Ärzteschaft

In der KPath sind 16 Fachärztinnen und Fachärzte in 19 Fachgruppen eingeteilt, welche jeweils aus 2 bis 6 Mitgliedern bestehen. Diese Fachgruppen arbeiten eng mit der klinischen Kundschaft zusammen und vertreten die Pathologie an den zahlreichen wöchentlichen Tumorboards/Fallbesprechungen innerhalb des Inselspitals. Zusätzlich werden 10 Assistierende in der KPath weitergebildet.

Die Ärzte betätigen sich alle auf den Gebieten Lehre und Forschung. Durch den Besuch nationaler und internationaler Kongresse, die Analyse aktueller Literatur und die Forschungstätigkeit in der Einheit Translational Research Unit (TRU) wird auch das Fachwissen auf dem neuesten Stand gehalten.

1.2 Neuropathologie

Im Jahr 2015 untersuchte die Neuropathologie knapp 1200 neurochirurgische Einsendungen, schwerpunktmässig Resektate und Biopsie von Hirntumoren. Darunter wurden in 300 Fällen intraoperative Schnellschnittuntersuchungen durchgeführt. Wir zählen damit im Hinblick auf die Tumordiagnostik zu den aktivsten Neuropathologien in der Schweiz. Aufgrund des im Schweizer Vergleich grossen Einzugsgebiets und der Ausrichtung der Neurochirurgischen Klinik des Inselspitals besteht der diagnostische Schwerpunkt in der Tumordiagnostik, umfasst jedoch das gesamte Spektrum der «Surgical Neuropathology» einschliesslich vaskulärer und pädiatrischer Neurochirurgie sowie Proben aus der Epilepsie-Chirurgie. Hinzu kommen zahlreiche Einsendungen weiterer Disziplinen aus dem Bereich des peripheren Nervensystems. In Zusammenarbeit mit dem Neuromorphologischen Labor (Leiter: Prof. K. Rösler) der Neurologischen Klinik des Inselspitals wurden rund 70 Muskelbiopsien untersucht. Im Bereich der Postmortalen Diagnostik führten wir 90 Hirnsektionen durch.

Die hohe Spezialisierung spiegelte sich wie in den Vorjahren in einer regen diagnostisch orientierten Publikationstätigkeit wider. Entsprechend dem Charakter der Neuropathologie als Schnittstelle zwischen den klinischen Neurofächern, der Labordiagnostik und der translationalen Forschung war der Fachbereich Neuropathologie auch im Jahr 2015 in zahlreichen Veranstaltungen, insbesondere in Zusammenarbeit mit Kliniken des Inselspitals, engagiert.

1.3 Postmortale Diagnostik

Im Jahr 2015 wurden insgesamt 152 Autopsien durchgeführt, davon 52 für das Inselspital. Die im Vorjahr begonnene und bereits in anderen Abteilungen der Dienstleistung erfolgreich umgesetzte Arbeitsplatz- und Prozessoptimierung nach dem LEAN-Prinzip wurde weiter fortgesetzt. Wesentlicher Punkt war hier die Finalisierung der räumlichen Umbauten und der Modernisierung, mit Neueinrichtung von zwei Autopsietischen. Ebenso wurde mit dem Spot-Imaging-System ein zukunftsorientiertes Bild- und Kommunikationssystem implementiert. Dadurch ist es nun möglich, aus dem Autopsiesaal heraus mit anderen Kollegen an deren Arbeitsplatz zu kommunizieren und digital in Echtzeit fotodokumentierte Befunde zu diskutieren. Zuletzt wurde auch der Zuschnittplatz für die postmortalen Präparate als Prototyp eines voll funktionsfähigen «Ein-Personen»-Zuschnittplatzes eingerichtet. Diese Rahmenbedingungen werden es nun erlauben, den künftigen Fokus auf die weitere inhaltliche Optimierung der Arbeitsprozesse zu legen.

1.4 Labor Histopathologie und Immunhistochemie

Im Jahr 2015 konnte das Labor Histopathologie mit 37'200 Einsendungen einen erneuten Zuwachs verzeichnen. Insgesamt wurden 70'300 Proben untersucht. In diesem Jahr standen die Vorbereitungen für den geplanten Laborumzug und die Akkreditierung im Jahr 2016 im Fokus. Für die 1650 Schnellschnittuntersuchungen wurde eine Durchschnittszeit von 20 Minuten verbucht. Die Zahlen reflektieren die kontinuierlichen Verbesserungsprozesse in der KPath.

2015 wurden an 7843 Fällen rund 48'000 immunhistochemische Färbungen vorgenommen. Zusätzlich verarbeitete das Team der Immunhistochemie 208 native Nierenbiopsien mit je 10 Immunfluoreszenzfärbungen. Die In-situ Hybridisierungen (EBER) haben mit 228 Färbungen gegenüber dem Vorjahr leicht zugenommen. Das Labor Immunhistochemie hat im Verlaufe des Jahres die Aufarbeitung des Autopsiematerials für die Postmortale Diagnostik übernommen und laufend an die neuen Anforderungen angepasst. Es wurden 9 neue Primärantikörper etabliert und eine weitere Doppelfärbung eingeführt. Aktuell stehen der Routine-Diagnostik 240 Antikörper zur Verfügung.

1.5 Berichtswesen

Die Synergien in den Sekretariaten Histopathologie und Zytopathologie werden gemäss LEAN Management System optimal genutzt, sodass die Durchlaufzeiten der Diagnosen in beiden Bereichen sehr kurz gehalten werden können. Als Schnittstelle zwischen der Ärzteschaft und den Labors tragen beide Sekretariate einen erheblichen Teil zum reibungslosen Arbeitsprozess bei. Im Rahmen des Umbaus ist für das Jahr 2016 im Sekretariat der Klinischen Pathologie eine Renovation der Räumlichkeiten geplant.

Laborteam Histopathologie.

2 Molekularpathologie

Molekularpathologie (PCR-, FISH- und EM-Labor)

Technischer Leiter: Prof. Dr. pharm. Erik Vassella
Medizinischer Leiter: Prof. Dr. med. Aurel Perren

In der Molekularpathologie verwenden wir die Methoden der PCR-Analyse und Sequenzierung (PCR-Labor), Fluoreszenz-In-situ-Hybridisierung (FISH-Labor) sowie Elektronenmikroskopie (EM-Labor). Das Analysenspektrum des PCR-Labors umfasst Mutationsanalysen, Erregernachweise, Klonalitätsnachweise, Methylierungsnachweise sowie Untersuchung von Mikrosatelliten. Die Tests haben diagnostische oder prädiktive Implikation und können an Formalin-fixiertem und Paraffin-eingebettetem Gewebe durchgeführt werden. Seit dem letzten Jahr haben die im PCR-Labor durchgeführten Tests um 10% zugenommen. Insbesondere erfuhr das «Next-Generation Sequencing» (NGS) eine deutliche Zunahme. Die auf NGS basierende BRCA1/2-Mutationsanalyse bei Therapieentscheid mit PARP-Inhibitoren wurde etabliert und mittels Ringversuch verifiziert. Seit September letzten Jahres bieten wir die PAM50-Analyse an, ein auf der Nanostring-Technologie basierender Genexpressionstest beim Mammakarzinom. Dieser Test, der das FDA -Gütesiegel trägt, erlaubt eine zuverlässige Einschätzung des Risikos von Patientinnen, Fernmetastasen zu entwickeln.

Auch die Zahl der FISH- sowie elektronisch-mikroskopisch durchgeführten Analysen ist in den letzten Jahren deutlich angestiegen. Gewichtige FISH-Analysen sind der Nachweis der ALK-Translokation beim Lungenkarzinom sowie die HER2-Amplifikation beim Mammakarzinom. Ende letzten Jahres haben wir einen Allegro Plus, ein automatisiertes Scanning-system, anschaffen können, welches die Auswertung sowie die Archivierung der FISH-Analysen deutlich vereinfachen wird.

Das Molekularpathologie-Labor nimmt regelmässig an Ringversuchen im Rahmen der Qualitätssicherung teil. Im letzten Jahr stand die Einführung der Akkreditierung an, welche uns auch in diesem Jahr beschäftigen wird. Das Molekularpathologie-Labor dient auch als Ausbildungsstätte für Assistenzärzte sowie für Pathologen zur Erlangung des FMH-Subtitels in Molekularpathologie. Eine Vorlesungsreihe in Molekularpathologie im Rahmen des Masterprogramms Molecular Life Sciences sowie der Graduate School wird jährlich durchgeführt.

Ab 2016 wird PD Dr. med. et phil. T. Grob die Stelle als medizinischer Leiter des Molekularpathologie-Labors antreten.

Mitarbeitende der Abteilung Zytopathologie.

3 Klinische Zytopathologie

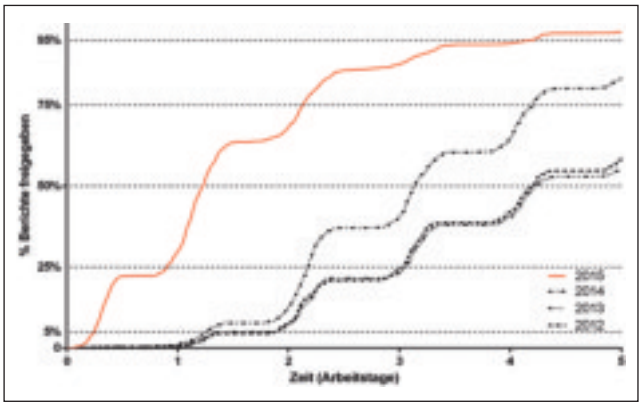
Leiterin: Dr. med. A. Schmitt

Kundenorientierung, Geschwindigkeit und eine hohe diagnostische Qualität haben auch in der Abteilung für Zytologie höchsten Stellenwert.

Das Jahr 2015 stand ganz unter dem Motto «Same Day Cytology» mit dem Ziel einer Berichterstattung innerhalb 24 Stunden nach Probeneingang. Im Rahmen der Reorganisation nach LEAN-Prinzipien konnten wir nach sorgfältiger Analyse des Ist-Zustandes durch verschiedene Anpassungen unserer Arbeitsabläufe eine deutliche Beschleunigung der Berichterstattung bei gleichzeitiger Modernisierung der Berichtsstruktur mit verbesserter Lesbarkeit und Übersichtlichkeit erreichen (siehe Grafik). Eine deutliche Steigerung der Einsendungen sowohl in der gynäkologischen (Anzahl Proben 2014: 7726, 2015: 9421; +22%) als auch in der extragynäkologischen Zytologie (Anzahl Proben 2014: 8418, 2015: 9042; +7%) zeigt uns, dass wir mit diesem Prozess den Bedürfnissen unserer Kunden entsprechen.

Auch im direkten Kontakt mit unseren Kunden ist es unser Ziel, mit unserer Expertise substanziell zu einem schnellen und somit kunden- und patientenorientierten diagnostischen Prozess beizutragen. So konnten wir im Jahre 2015 im Auftrag externer Kunden erneut mehr Feinnadelpunktionen von Lymphknoten, Schilddrüse und Weichteilen im abteilungseigenen Punktionsambulatorium durchführen. Auch spitalintern ist das immer auf Abruf bereite Zytologie-Team vor allem im Rahmen von «rapid on-site evaluations» (ROSE; ein Zytologe führt vor Ort eine Schnellbeurteilung des entweder selbst mittels Feinnadelpunktion oder endoskopisch gewonnenen Materials durch) für mehrere Kliniken des Inselspitals zu einem unabkömmlichen diagnostischen Partner geworden.

Nicht zuletzt ist es ein Ziel der Abteilung für Zytologie, ihre Expertise an Lernende weiterzugeben. So schloss auch 2015 eine Schülerin des Abschlussjahrgangs der Berner Laborschule ihr Praktikum mit einer Diplomarbeit erfolgreich ab. Zusätzlich begann eine biomedizinische Analytikerin die zweijährige berufsbegleitende Ausbildung zur Zytotechnikerin.



Bearbeitungszeiten Gynäkologische Zytologie (Vorsorgeuntersuchungen).

4 Fachgruppen des Instituts für Pathologie der Universität Bern

Stand Februar 2016

Dermatopathologie	
H. Dawson	031 632 99 60
Y. Banz	031 632 88 75
S. Berezowska	031 632 49 37

Endokrinopathologie	
A. Perren	031 632 32 22
M. Dettmer	031 632 99 69
A. Blank	031 632 99 01
A. Schmitt	031 632 32 48

Gastrointestinalpathologie	
A. Lugli	031 632 99 58
R. Langer	031 632 32 47
H. Dawson	031 632 99 60
E. Diamantis	031 632 87 68
M. Montani	031 632 32 67
T. Rau	031 632 87 56

Mamma- und Gynäkopathologie	
T. Rau	031 632 87 56
M. Trippel	031 632 32 76
Y. Banz	031 632 88 75
A. Blank	031 632 99 01
H. Dawson	031 632 99 60
M. Montani	031 632 32 67

Hämatopathologie	
Y. Banz	031 632 88 75
A. Schmitt	031 632 32 48
E. Hewer	031 632 99 51
A. Perren	031 632 32 22

Herz-, Gefäss- und Rheumapathologie	
Y. Banz	031 632 88 75
M. Montani	031 632 32 67
V. Genitsch	031 632 99 22

HNO-Pathologie	
M. Dettmer	031 632 99 69
E. Diamantis	031 632 87 68
E. Hewer	031 632 99 51
T. Rau	031 632 87 56

Leberpathologie	
M. Montani	031 632 32 67
E. Diamantis	031 632 87 68
R. Langer	031 632 32 47

Lungenpathologie	
S. Berezowska	031 632 49 37
E. Hewer	031 632 99 51
Y. Banz	031 632 88 75

Nephropathologie	
V. Genitsch	031 632 99 22
E. Diamantis	031 632 87 68
R. Langer	031 632 32 47

Neuropathologie	
E. Hewer	031 632 99 51
S. Berezowska	031 632 49 37

Ophthalmopathologie	
A. Schmitt	031 632 32 48
E. Hewer	031 632 99 51

Pädopathologie	
M. Trippel	031 632 32 76
M. Montani	031 632 32 67
S. Berezowska	031 632 49 37

Pankreaspathologie	
E. Diamantis	031 632 87 68
M. Montani	031 632 32 67
R. Langer	031 632 32 47
A. Perren	031 632 32 22

Uropathologie	
V. Genitsch	031 632 99 22
E. Diamantis	031 632 87 68
M. Dettmer	031 632 99 69
M. Montani	031 632 32 67

Weichteil- und Knochenpathologie	
R. Langer	031 632 32 47
A. Schmitt	031 632 32 48
H. Dawson	031 632 99 60

Postmortale Diagnostik	
R. Langer	031 632 32 47
A. Lugli	031 632 99 58
A. Blank	031 632 99 01
M. Trippel	031 632 32 76

Zytologie	
A. Schmitt	031 632 32 48
E. Hewer	031 632 99 51
Y. Banz	031 632 88 75

Molekularpathologie	
E. Vassella	031 632 99 43
T. Grob	031 632 82 37
M. Dettmer	031 632 99 69

5 Dienstleistungsstatistik

Klinische Pathologie

Histopathologie	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**
Anzahl Einsendungen	34‘532	35‘001	33‘805	32‘710	35‘293	**37‘232**
Anzahl Lokalisationen	59‘291	61‘693	61‘015	58‘795	66‘420	**70‘286**
Anzahl Einsendungen Schnellschnitte	–	–	1‘220	1‘472	1‘673	**1‘647**
Anzahl Proben Schnellschnitte	2‘049	2‘937	1‘792	1‘997	2‘307	**2‘252**
Autopsie						
Anzahl durchgeführte Autopsien	198	170	195	155	156	**152**
Zytopathologie						
Total Anzahl Einsendungen	–	–	16‘946	14‘237	13‘788	**16‘040**
Anzahl Proben Klinische Zytologie	7‘844	8‘849	8‘218	8‘361	8‘418	**9‘042**
Anzahl Proben Gynäkologische Zytologie	8‘697	8‘697	8‘724	8‘054	7‘726	**9‘421**
Total Anzahl Einsendungen Proben	16‘541	16‘996	16‘942	16‘415	16‘144	**18‘463**
Anzahl Zellblöcke	1‘216	1‘705	1‘830	2‘277	2‘324	**2‘748**
Immunhistochemie						
Anzahl Fälle (Blöcke) Diagnostik (Paraffin)	6‘777	7‘472	6‘692	7‘104	8‘313	**7‘843**
Anzahl Färbungen Immunfluoreszenz (Nierenbiopsien)	2‘712	2‘820	2‘844	2‘101	2‘280	**2‘079**
Anzahl Fälle Immunzytologie am Ausstrich	388	359	302	302	372	**197**
Anzahl Färbungen Immunzytologie am Ausstrich	967	777	672	586	–	**240**
Anzahl Färbungen Diagnostik (Paraffin)	48‘613	50‘535	43‘436	–	52‘532	**47‘944**
Molekularpathologie						
Anzahl Fälle PCR-basierende Tests	1‘042	1‘325	1‘235	1‘420	1‘304	**1‘444**
Anzahl Fälle Lymphome	139	200	171	214	218	**216**
Anzahl Fälle Methylierungsnachweis	133	156	155	180	128	**88**
Anzahl Fälle Mutationsanalysen (EGFR, kRAS, BRAF, IH1/2 + weitere)	493	708	755	818	902	**870**
Anzahl Fälle NGS-Analysen	–	–	–	–	–	**87**
Anzahl Fälle PAM50 (Nanostring)	–	–	–	–	–	**18**
Anzahl Fälle FISH	254	259	206	287	554	**627**
Anzahl Hybridisierungen FISH	328	354	304	391	683	**839**

Tumorbank

Anzahl Einsendungen Tumorbank	880	803	727	831	894	**1‘030**
Anzahl Eingänge TRU	–	–	–	166	465	**457**

>>> Forschung/Research

1 Research at the Institute of Pathology

Research groups Experimental Pathology:
Stefan Freigang, MD
Philippe Krebs, PhD
Christoph Mueller, PhD
Mario Noti, PhD
Jean Claude Reubi, MD
Mario Tschan, PhD
Erik Vassella, PhD

Research groups Clinical Pathology (Translational Research Unit TRU):
Sabina Berezowska, MD
Eva Diamantis-Karamitopoulou, MD
Rupert Langer, MD
Alessandro Lugli, MD
Aurel Perren, MD
Inti Zlobec, PhD

1.1 The Division of Experimental Pathology

Head: Prof. Christoph Mueller, PhD

Administrative support:
Christine Feller (40%)
Christa Hagert (50%)
Martina Häusler (40%)
Cornelia Mileto 40% (since November 2015)

Thematically the research activities of the current 7 research groups in the Division of Experimental Pathology are focused on two main topics, i.e.
– immunopathology and inflammation, and
– experimental tumor pathology and tumor biology

Most of the research groups in the Division of Experimental Pathology address questions related to the fundamental aspects of cell biology and to the etiopathogenesis of neoplastic or inflammatory disorders. Nevertheless, translational aspects are also considered in our research activities. Notably, the research group of Professor Reubi is substantially financed by license fees obtained from their current patents in the field of peptide receptor targeting of tumors.

The research activities are well integrated on a national and international level, including the Swiss IBD cohort study. In our experimental work we can rely on facilities available at our institute, e.g. Laser Capture Microdissection, confocal microscopy, but also on core facilities, provided by the Dept. of Clinical Research, including the FACS (cytometry) core facility, and the genomics core facility (with access to an Ion Torrent instrument). Those two core facilities are conveniently located in the building of the Institute of Pathology. In addition, access to the microscopy center (MIC), with its instruments for confocal microscopy (including live cell imaging and 2-photon microscopy), and to the proteomic core facility of the Medical Faculty is available. We are also part of the Interfaculty Bioinformatics Unit and are granted unrestricted access to the deep sequencing platform of the University of Bern (equipped with a Roche GS Junior and Illumina HiSeq 2000). Several of our research groups also use the central mouse facility, and more recently, also the germ-free and gnotobiotic mouse facility (Clean Mouse Facility) at the Medical Faculty. An nCounter Analysis System using Nanostring technology was purchased by the Molecular Pathology Laboratory for breast cancer diagnosis (PAM50 panel). The Nanostring technology utilizes digital color-coded barcode hybridization technology to detect and quantify hundreds of unique transcripts in a single reaction. This technology, operated by the trained experts, will be available to all researchers at our institute. In addition to these facilities, through collaborative efforts we also have access to other state-of-the-art facilities, including the genomics facility at the functional genomics center at the ETH Zurich (fgcz) and the metabolomics facilities at the Insitute of Molecular Systems Biology, ETH Zurich (Group of Professor Uwe Sauer).

The spectrum of available and well-established technologies in the Division of Experimental Pathology includes confocal microscopy, fluorescent in situ hybridization (FISH), laser capture microdissection of FFPE, and frozen tissue sections (including immunostained FFPE tissue sections), and autoradiography of tissue sections, including a combined immunohistochemical-receptor autoradiography, but also the entire spectrum of FACS-based techniques in cell sorting and multicolor analysis. Highly sophisticated methodologies are established for the identification of miRs and their target sequences in normal and diseased tissues, and several distinct transfection systems, including lentivirus-based transduction systems, and mRNA expression profiling from small numbers of cells and microdissected tissues are available. The Ion Torrent platform is currently used for 16S rRNA sequencing of intestinal bacte-

Mitarbeitende der Abteilung Experimentelle Pathologie.

ria and for the identification of the Ion Torrent 50 gene cancer panel by ampliseq. Furthermore, several of our research groups have a longstanding expertise in isolating and culturing primary cells, such as immune cells, mesenchymal stromal cells, including liver sinusoidal endothelial cells, and epithelial cells from patient material, but also experimental animals. Experimental protocols for determining the functional capacities of these cell subsets ex vivo and in vitro are established and optimized.

Thanks to the generous support by the University of Bern we are able to replace a substantial portion of the more than 20 year old pieces of equipment, but also to acquire new critical equipment, including a hypoxia incubator for the Seahorse extracellular flux analyzer, a U-Cup bioreactor for 3D cell culture, a NEON transient transfection and a Simple Western detection system. Simple Western is an automated, capillary-based immunoassay that does not require gels, transfer devices or blots. This equipment will be shared among all research groups at the Institute of Pathology.

In 2015 the research groups of the Division of Experimental Pathology were again highly successful in the acquisition of external funding (for details see: Reports of the individual research groups).

Honors

Stefan Freigang is the recipient of the 2015 «Pfizer Forschungspreis», the 2015 «Forschungspreis der Schweizerischen Herzstiftung» and was a top-5 finalist for the 2015 ETH Spark Award. He obtained the Venia docendi in Experimental Pathology, University of Bern (Umhabilitation).

Teaching

In 2015 the Division of Experimental Pathology actively contributed to the teaching at both the Medical Faculty and the Biological Science Faculty. Teaching at the Medical faculties included tutorials in problem-based learning for 1st, 2nd and 3rd year students, and lectures for 3rd year students in general pathology for students in medicine and dentistry as well as lectures in the MSc course Biomedical Sciences.

Members of the Division organized several courses for undergraduate and graduate students in Cell Biology and Biomedical Sciences at the University of Bern, including courses in histology and general pathology, molecular pathology and tumor biology, a MSc course in cellular and molecular immunology, and a practical course in immunology.
Several members of the Division are actively involved in coaching PhD students from the Graduate School for Cellular and Biomedical Sciences, Universtity of Bern, as well as from additional Universities. In 2015 the following individuals successfully completed their academic degrees at the Division of Experimental Pathology:

Stefan Freigang
- PhD (Co-Supervisor): Peter Bretscher (PI: Prof. M. Kopf, ETHZ)

Philippe Krebs
- MSc: Ivonne Köck (Co-Supervisors: Christoph Mueller, Lukas Mager)
- MSc: Marie-Hélène Wasmer (Co-Supervisors: Christoph Mueller, Lukas Mager)
- MD-PhD: Lukas Mager (Co-Supervisor: Christoph Mueller)
- PhD (mentor): Cheong Kwet Choy Kwong Chung (PIs: Andrew Macpherson and Kathy McCoy, Dept. Clinical Research, University of Bern)

Christoph Mueller
- MSc: Diego von Werdt (Co-Supervisor: Nadia Corazza)
- PhD: Daniel Zysset (Co-Supervisor: Leslie Saurer)
- PhD (External Supervisor): Jitka Sulcova (PI: Prof. S. Werner, ETH Zurich), Manuel Coutaz (PI: Prof. F. Tacchini-Cottier, University of Lausanne)

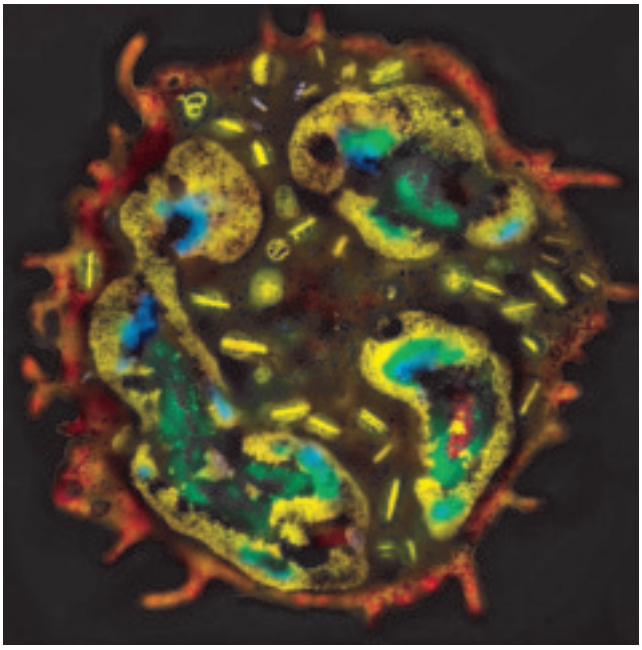
Mario Noti
- MSc: Loïc Borcard

Mario Tschan
- BMA Master: Daniel Schärer, Emilly Auma
- MD Master: Susanne Jutzi, Marielle Hardegger
- MD Thesis: Severin Gloor, Manuela Messikommer
- PhD: Aladin Haimovici
- PhD (Co-advisor): Anna Pham (PI: PD Dr. E. Oppliger, Hematology, Inselspital), Stefan Haemmig (PI: Prof. E. Vassella, Institute of Pathology)
- PhD (Mentor): Oleksandr Pastukhov (PI: Prof. A. Huwiler, Institute of Pharmacology), Paul Burda (PI: Prof. V. Heussler, IZB), Silvan Roethlisberger (PI: Dr. M. Vogel, RIA), Xiaoliang Wang (Prof. H.-U. Simon, Institute of Pharmacology)
- PhD (External Expert): Julia Delgado Tascón (PI: Prof. C. Hauck, University of Konstanz)

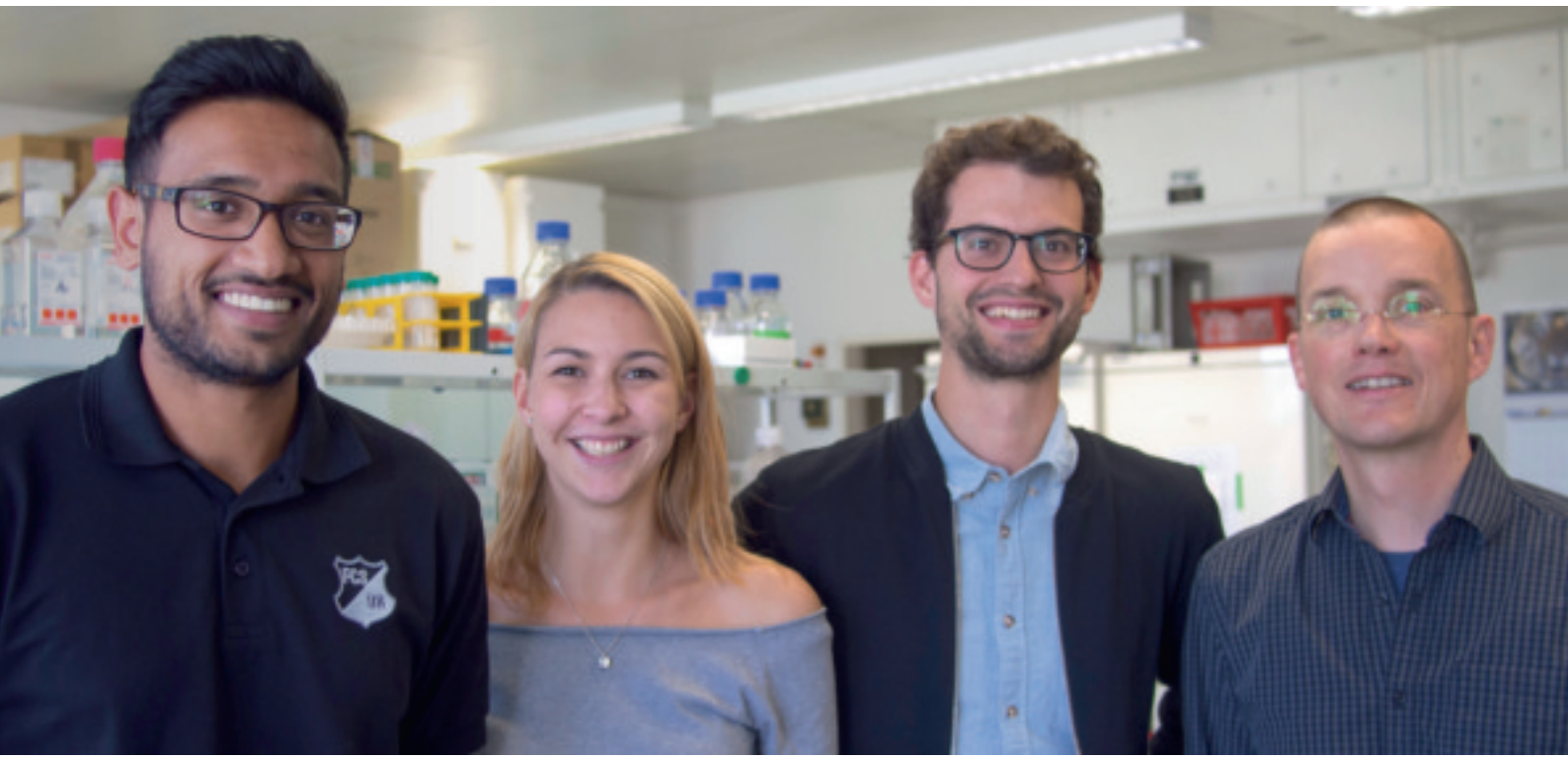
Erik Vassella
- PhD: Stefan Haemmig
- PhD: Stephanie Langsch
- MSc: Nicole Wirth
- PhD (Co-adviser): Philipp Odermatt (PI: Prof. D. Schümperli, Institute of Cell Biology).

Administrative duties

In 2015 members of the Division of Experimental Pathology voluntarily served in several profession-related functions. Since 2013 Nadia Corazza is a member of the committee «Gleichstellung von Frauen und Männern» and was a member in one faculty search committee. Christoph Mueller was member, or Chair, of several faculty committees in 2015, including the task force «Experimental Animal Center», and chaired the steering committee of the program in Certified Advanced Studies (CAS) in Research Management at the University of Bern. He remained an ad hoc research council member in the SNSF «ambizione» program (Division III). He was a board member of the Swiss Society of Allergology and Immunology and member of the subcommittee «Experimental Immunology» of this society, and is also a board member of the Stiftung für klinisch-experimentelle Tumorforschung (Bern) and member of the executive board and the scientific board of the SNSF-funded Swiss IBD cohort study. Mario Tschan is a member of the Interfacultary PhD Committee, which is responsible for the strategic orientation, the administration, and the quality control of the PhD program and of the Expert Committees Cell Biology, Graduate School for Cellular, Biomedical Sciences and Biomedical Analysts. He is a member of the «Vereinigung der Dozentinnen und Dozenten der Medizinischen Fakultät Bern» representing the interests of the lecturers at the Medical Faculty meetings. Stefan Freigang and Philippe Krebs are members of the Expert Commission of the Graduate School for Cellular and Biomedical Sciences of the University of Bern. Philippe Krebs and Stefan Freigang are Biosafety and Radiation Safety Officers of the entire Institute of Pathology.



Computer-enhanced electron microscopic image of a TSLP-elicited mouse basophil.



Research group Stefan Freigang.

Group of Stefan Freigang, MD

Olivier Friedli, PhD student
Marleen Hanelt, PhD student
Abilashan Sithampari, MSc student
Romina Theiler, technician (until July 2015)
Svenja Ewert, technician (since September 2015)

Research activities

Our research focuses on the immune recognition of lipids in inflammation and immunopathology. In particular, we study the molecular mechanisms of lipid-induced inflammation in atherosclerosis, the regulation of immune responses by products of lipid peroxidation, and the sensing of glycolipids by innate-like natural killer T (NKT) cells.

Cardiovascular diseases, particularly atherosclerosis, remain the leading cause of death worldwide. Whereas major risk factors have been identified and provide targets for therapeutic intervention, there is still no effective treatment that directly targets the underlying inflammatory process. We have previously identified a novel pathway that selectively induces IL-1a-driven vascular inflammation in response to metabolic perturbation. Our study identified mitochondrial uncoupling as a metabolic signal that triggers IL-1a secretion but inhibits inflammasome activation. We are currently investigating the role of physiological mitochondrial uncoupling for inflammatory immune responses in metabolic dysfunction and microbial infection.

A second interest of the group are products of lipid peroxidation and their immuno-regulatory bioactivites (Bretscher 2015, Egger 2015, Matsushita 2015). The exposure of cellular lipids to reactive oxygen species creates a broad range of distinct oxidized phospholipid (OxPL) species that actively modulate cellular signaling processes and influence the resulting immune response.

We have characterized an anti-inflammatory bioactivity of OxPL that can be attributed to a specific category of OxPL (Bretscher 2015). This potent anti-inflammatory effect is mediated by the prostanoid-like OxPL component epoxycyclopentenone, which activates the transcription factor Nrf2 to inhibit pro-inflammatory cytokine and chemokine responses in myeloid cells in vitro and in vivo. Thus, our findings provide insight to the essential structural characteristics and signaling of anti-inflammatory OxPL, and demonstrate that both are shared with endogenous, pro-resolving lipid mediators (Bretscher 2015, Egger 2015).

Results demonstrate the potential of targeting OxPL/Nrf2-signaling in inflammation, and suggest a novel class of highly bioactive compounds as promising therapeutic agents for the treatment of inflammatory diseases. In collaboration with the group of Prof. Jan Lünemann, University of Zurich, we are currently investigating the contributions of autophagy to lipid antigen presentation and NKT cell responses.

Internal collaborations

- Christoph Mueller, PhD

External collaborations

National

- Erick Carreira, PhD, ETH Zurich
- Marc Donath, MD, University of Basel
- Olivier Guenat, PhD, University of Bern
- Martin Hersberger, PhD, University Children's Hospital Zurich
- Manfred Kopf, PhD, ETH Zurich
- Jan Lünemann, MD, University of Zurich
- Olivier Pertz, PhD, University of Bern

International

- Harald Köfeler, PhD, Medical University of Graz, Austria
- Paul B. Savage, PhD, Brigham Young University, Provo, USA

Grant support

- SNF 310030_152872 (2015–2017), 510'000 CHF
- SNF R'Equip 316030_157702 (2014–2015), 240'000 CHF
- Vontobel-Stiftung (2014–2017), 120'000 CHF
- Olga-Mayenfisch-Stiftung (2014–2015), 50'000 CHF
- 3R Research Foundation (Co-PI) (2015–2016), 138'000 CHF
- UniBE Interdisciplinary (ID) Grant (2016–2018), 150'000 CHF
- Several smaller grants, 42'000 CHF

Research group Philippe Krebs.

Group of Philippe Krebs, PhD

Michael Berger, MSc student
Ludmila Cardoso Alves, PhD student
Lukas Mager, PhD student
Regula Stuber Roos, technician
Marie-Hélène Wasmer, PhD student

Research activities

We currently work on the following research projects:

Project 1 – Role of cytokine signaling for myeloproliferative disease
Myeloproliferative neoplasms (MPNs) are characterized by the clonal expansion of cells from the myeloid lineage. MPNs are also associated with aberrant expression and activity of multiple cytokines. We have recently shown that IL-33 signaling is important for the development of MPN (Mager LF et al, J Clin Invest., 2015). We currently study the role of IL-33 for the progression of this disease by using mouse models and patient-derived samples.

Project 2 – Role of cytokine signaling for colorectal cancer
Several genetic aberrations in key cellular pathways that underlie colon tumorigenesis have been identified. However, there is now compelling evidence that intestinal tumorigenesis is greatly promoted by chronic inflammation that follows such genetically-driven tumor-initiating events. Recently, we have shown that the IL-33 pathway contributes to intestinal tumorigenesis in humans and mice (Mertz KD, Mager LF et al, OncoImmunology, 2015, in press). We now further investigate the cellular and molecular mechanisms underlying IL-33-dependent colorectal cancer.

Project 3 – Cross-talk between innate and adaptive immunity
The vertebrate immune system comprises the innate immune system, providing the first line of defense, and the adaptive immune system, which is triggered at a later stage and that is responsible for memory. In this project, we use different murine models to better understand how innate immune cells modulate adaptive immune responses in dependence on the inflammatory environment, in infectious (e.g. after infection with a pathogen) or sterile (e.g. for tumor surveillance) situations.

Internal collaborations

- Christoph Mueller, PhD / Leslie Sauer, PhD
- Mario Noti, PhD
- Aurel Perren, MD / Ilaria Marinoni, PhD
- Mario Tschan, PhD
- Inti Zlobec, PhD
- Alessandro Lugli, MD
- Nadia Corazza, PhD
- Viktor Kölzer, MD
- Vera Genitsch, MD
- Yara Banz, MD-PhD
- Christian Schürch, MD-PhD
- Tilman Rau, MD

External collaborations

National

- Andrew Macpherson, MD, Kathy McCoy, PhD, Dept. Clinical Research, University of Bern
- Adrian Ochsenbein, MD, Carsten Riether, PhD, Dept. Clinical Research, University of Bern
- Guido Beldi, MD, Clinics for Visceral Surgery and Medicine, Bern
- Pascal Juillerat, MD, Clinics for Visceral Surgery and Medicine, Bern
- Tobias Junt, PhD, Lab Head, Immunomodulation, Novartis Pharma AG, Basel
- Kirsten D. Mertz, MD, Institute of Surgical Pathology, University Hospital Zurich, Zurich
- Alexandre Theocharides, MD, Division of Hematology, University Hospital Zurich, Zurich

International

- Bruce Beutler, MD, Center for Genetics of Host Defense, UT Southwestern Medical Center, 5323 Harry Hines Boulevard, 8505, Suite NB9-202D, Dallas, TX, 75390, USA
- Daniel Popkin, MD-PhD, Department of Dermatology, Case Western Reserve University, 10900 Euclid Avenue, Cleveland, OH 44106, USA
- Edith Janssen, PhD, & Kasper Hoebe, PhD, Division of Immunobiology, Cincinnati Children's Hospital, 240 Sabin Way, MLS 7021, S5.419, Cincinnati, OH 45244, USA
- Karl Lang, MD, Universitätsklinikum Essen (AöR), Institut für Immunologie, Hufelandstrasse 55, D-45147 Essen, Germany
- Astrid Westendorf, PhD, Infektionsimmunologie, Universitätsklinikum Essen (AöR), Institut für Medizinische Mikrobiologie, Hufelandstrasse 55, D-45122 Essen, Germany

Grant support

- Swiss National Science Foundation_138188 (2012–2015), 377'366 CHF
- Marie Curie Career Integration Grants_X-talk (2014–2017), 100'000 EUR
- Stiftung für klinisch-experimentelle Tumorforschung (2015), 80'000 CHF
- Foundation Johanna Dürmüller-Bol (2015–2016), 20'000 CHF
- Krebsliga Schweiz_KLS-3408-02-2014 (2015–2016), 124'350 CHF
- Olga Mayenfisch Foundation (2015–2016), 23'000 CHF
- Gertrud-Hagmann-Stiftung für Malignom-Forschung (to Lukas Mager) (2015–2017), 241'566 CHF

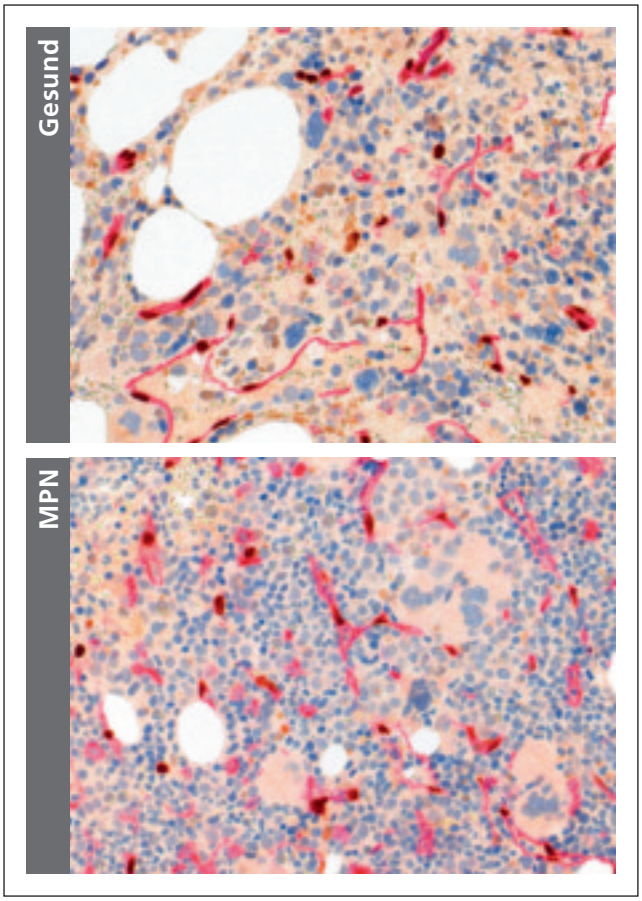


Fig. 1: Erhöhte Expression von IL-33 im Knochenmark von MPN-Patienten. Immunhistochemie zeigt die Expression von IL-33 (braun) und CD34 (rot; Endothelzellen) in MPN- und gesunden Patienten.

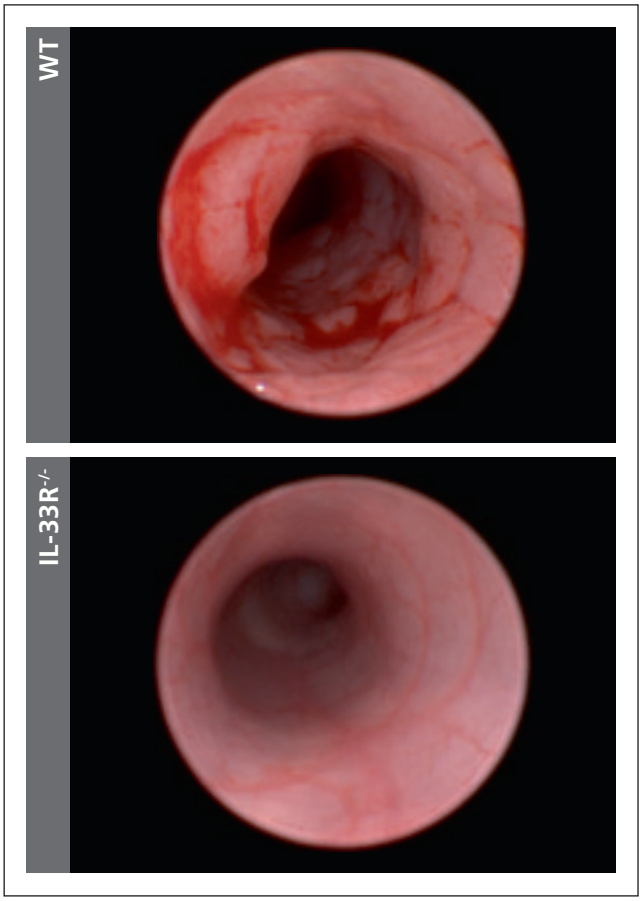


Fig. 2: Blockade des IL-33-Signalwegs verzögert die Darmkrebsentstehung im Mausmodell. Das Tumorwachstum in Wildtyp-(WT-) Mäusen und Tieren ohne funktionierenden IL-33-Rezeptor (IL-33R-/-) wurde mittels Endoskopie evaluiert.

Group of Prof. Christoph Mueller, PhD

Jennifer Brasseit, PhD, postdoc
Nadia Corazza, PhD, staff scientist (60%)
Martin Faderl, PhD student
Kwong Chung Cheong Kwet Choy, PhD, postdoc
Silvia Rihs, technician (90%)
Leslie Saurer, PhD, staff scientist (60%)
Alexandra Suter, technician (SIBDCS biobank)
Diego von Werdt, MSc student
Daniel Zysset, PhD student, since October 2015: PhD, postdoc

Research activities

The intestinal mucosa is constantly exposed to a vast array of antigens. Hence, the numerous immune effector cells present within the intestinal epithelium and in the underlying lamina propria face a difficult task in mounting appropriate responses against invading pathogens while tolerating the commensal microflora and harmless antigens.
The main research activities of our group are aimed at a better understanding of the immunoregulatory mechanisms that are operative in the intestinal mucosa under homeostatic conditions and the potentially dysregulated immune responses that may contribute to chronic inflammatory disorders such as seen in inflammatory bowel diseases (IBD). To this end, we are analyzing various mouse mutant and/or transgenic lines in different models of experimental colitis. A longstanding interest lies in the improved characterization of intestinal intraepithelial lymphocytes (IEL) that represent a major, but still very enigmatic population of T cells in the mouse. Besides studying the functional responses of conventional (CD8$\alpha\beta$) and unconventional (CD8$\alpha\alpha$) IEL subsets in homeostasis and models of intestinal inflammation, we are specifically looking at the role of the regulator of G protein signaling (RGS) proteins in governing IEL functions. IEL highly express RGS1 which likely contributes to their noncirculating, tissue-resident memory phenotype. We are interested how the intestinal milieu shapes expression of RGS1 and how intestinal inflammation may potentially disrupt RGS1 expression leading to altered IEL responses.
A major part of research is dedicated to the investigation of mechanisms that are operative in the resolution of intestinal inflammation (Sinergia grant with the research teams of Prof. Andrew Macpherson (Gastroenterology, Bern), W.D. Hardt (ETH Zurich) and U. Sauer (ETH Zurich). We recently established a reversible mouse model of colitis that allows for a timed and deliberate induction of remission. Indeed, shortly after remission induction a rapid clinical recovery can be observed that is followed by mucosal healing on a molecular and cellular level within a few days (Brasseit et al, Mucosal Immunol 2015). In continuation of the Sinergia grant, we are currently studying the dynamics of mucosal healing focusing on the distinct mutualistic interactions between host and microbial communities during induction and recovery from intestinal inflammation.

Our previous finding that in distinct models of colitis and bona fide infections mice deficient in the immune-amplifying receptor TREM-1 (Trem1-/- mice) showed reduced immune-associated pathologies while they retained their capacity for microbial control (Weber B et al, PLoS Pathog. 2014) has sustained our interest in the role (as well as the prognostic and therapeutic potential) of TREM-1 in noninfectious chronic inflammatory diseases.

Currently, we are investigating the impact of TREM-1 in experimental models of atherosclerosis and colitis-associated cancer. We aim to substantiate our findings on TREM-1 by extending our analyses to human tissues and making use of the state-of-art equipment and expertise that is available at the Institute of Pathology.

Internal collaborations

- Stefan Freigang, MD
- Vera Genitsch, MD
- Philippe Krebs, PhD
- Mario Noti, PhD
- Mario Tschan, PhD

External collaborations

National
- Andrew Macpherson, Kathy McCoy, Markus Geuking, Department of Clinical Research, University of Bern
- Wolf Hardt, Institute of Microbiology, ETH Zurich
- Uwe Sauer, Ruben Mars, Institute of Molecular Systems Biology, ETH Zurich
- Fabienne Tacchini-Cottier, Department of Biochemistry, WHO Immunology Research and Training Center, University of Lausanne
- Walter Reith, Department of Pathology and Immunology, University of Geneva
- Carsten Riether, Department of Clinical Research, University of Bern

International
- Katrin Andreasson, Stanford University Medical Center, USA
- Adelheid Cerwenka, DKFZ, Heidelberg, Germany
- John Kerl, NIAID, Bethesda, MD, USA
- Markus P. Radsak, Institute of Immunology, University of Mainz, Germany
- Martina Seiffert, DKFZ, Heidelberg, Germany

Grant support

- SNF 310030_138392 /1 (3 years), 623'000 CHF
- SNF CRSII3_136286 / 1 (Sinergia) (3 years), 456'531 CHF
- SNF 33CS30_134274 / 1 (SIBDCS) (per year), ca. 65' 000 CHF
- Bern. Krebsliga (to Dr. Leslie Saurer) (1 year), 45'000 CHF
- Novartis Foundation for medical-biological research, 60'000 CHF (to Dr. Leslie Saurer)

Group of Mario Noti, PhD

Loïc Borcard, MSc student (till December 2015)
Maryam Hussain, PhD student (since December 2015)
Maria Pena Rodriguez, technician (SIBDCS biobank, since January 2016), 40%

Research activities

Recent studies have highlighted that differential colonization of the body's barrier surfaces by defined commensal bacterial communities can have a profound effect on the development and function of distinct T helper cell populations. Dysregulation in the balance of these helper T cell populations can profoundly alter susceptibility to a number of chronic inflammatory disorders including allergy, asthma, arthritis, multiple sclerosis, psoriasis and inflammatory bowel disease.

Research in the Noti lab is focusing on how host factors including expression of cytokines and cytokine receptors influence innate and adaptive immune responses in the context of allergic inflammation. In addition to host-derived factors, an emerging hypothesis is that alterations in the acquisition and/or composition of beneficial commensal bacteria can profoundly impact innate and adaptive immune cell responses resulting in susceptibility to multiple infectious and inflammatory diseases. Metagenomic sequencing approaches in patient populations have revealed alterations of commensal bacterial communities in patients suffering from multiple inflammatory diseases.

Studies in murine model systems support a causal relationship between alterations in commensal bacteria and chronic inflammation. We are employing germ-free or gnotobiotic mouse models and/or selective antibiotic treatment, coupled with pyrosequencing of bacterial communities, to interrogate the mechanisms through which signals derived from commensal bacteria can influence expression of proinflammatory cytokines and the pathogenesis of allergic inflammation at multiple barrier surfaces. In a second line of research, we investigate immune cell-derived factors in the plasma of humans and mice that positively correlate with ageing. Employing murine model systems, we are currently investigating whether targeting age-related changes in immune cell-derived factors can alter metabolic, physical and/or cognitive signatures associated with ageing.

Internal collaborations

- Christoph Mueller, PhD
- Nadia Corazza, PhD
- Philippe Krebs, PhD
- Inti Zlobec, PhD

External collaborations

National

- Alexander Eggel, PhD, Institute of Immunology, University of Bern
- Carsten Riether, PhD, DKF, University of Bern
- Andrew Macpherson, PhD, University of Bern
- Kathy McCoy, PhD, University of Bern
- Johan Auwerx, PhD, EPFL Lausanne
- Stephen Leib, MD, PhD, IFIK, University of Bern
- Ingrid Böhm, MD, PhD, Department of Diagnostic, Interventional and Pediatric Radiology, University of Bern

International

- David Artis, PhD, Weill Cornell University, New York, USA
- Jonathan Spergel, MD, PhD, Children's Hospital of Philadelphia, Philadelphia, USA
- Brian S. Kim, MD, PhD Washington University, St Louis, USA
- Thomas Brunner, PhD, University of Konstanz, Konstanz, Germany
- Saul Villeda, PhD, University of California, San Francisco, USA

Grant support

- SSNF Ambizione PZ00P3_154777/1 (2014–2017), 599'156 CHF
- Olga Mayenfisch Stiftung (2015–2016), 25'000 CHF
- Novartis Foundation for medical-biological research (2015–2016), 60'000 CHF
- Project Pool Mittelbau Unibe (2015), 3000 CHF

Group of Prof. Jean Claude Reubi, MD

Beatrice Waser, technician
International collaborators

Research activities

Peptide receptor targeting of tumors is currently investigated at 3 different levels: 1) target definition, 2) tools, 3) clinical applications. In the reporting year, we have focused on the following peptide receptors: somatostatin receptors, gastrin-releasing peptide (GRP) receptors, GLP-1 receptors, GIP receptors, neurotensin receptors and CCK receptors.

ad 1) Target definition includes the identification of human pathological tissues, in particular tumors, which overexpress peptide receptors. We show, for the first time, the immunohistochemical distribution of GLP-1 receptors in normal and diseased thyroid and pancreas, resolving a conflicting issue in the current literature. We also identified the presence of neurotensin receptors, not only in primaries, but also in liver metastases of pancreatic adenocarcinomas. Further, we evaluated in NET to which extent SS-R and GIP-R correlated with tumor grade and stage. Finally, we could demonstrate that the use of triple radiolabeling (SS-R, GLP1-R and GIP-R) in NET allows detecting all tumors with no exception.

ad 2) We have designed and characterized a number of new tools for peptide receptor targeting: several new GRP receptor antagonists with N-terminal modifications and/or spacers of various lengths; novel CCK analogs with various spacers.

ad 3) On the clinical side, localization of hidden insulinomas and of adult nesidioblastosis in patients were successfully performed using Ga-DOTA excentin-4 PET/CT.

External collaborations

National
- E. Christ, MD, PhD, Univ. Hospital Bern
- D. Wild, MD, Univ. Hospital Basel

International
- H. Mäcke, PhD, Nucl. Med., Univ. Freiburg, Germany
- T. Maina, PhD, Demokritos, Athen, Greece
- D. Fourmy, PhD, INSERM, Toulouse, France
- J. Rivier, PhD, Salk Institute, San Diego, CA, USA

Grant support

- Patent licence fees

Research group Mario P. Tschan.

Group of Mario P. Tschan, PhD

Olivia Adams, PhD student (Co-supervision: PD Dr. R. Langer)
Priska auf der Maur, Master student (BIO)
Aladin Hamoivici, PhD postdoc
Magali Humbert, PhD postdoc
Jing Jin, PhD student
Susanne Jutzi, Master student (MED)
Nicolas Niklaus, Master student (BIO)
Sarah Parejo, Master student (BIO)
Julia Parts, PhD student
Vreni Rentsch, Master student (BMA) (since November 2015 to May 2016)
Daniel Schärer, technician
Anna Schläfli, PhD postdoc
Deborah Shan, technician
Stefanie Trueb, Master student (BMA) (since November 2015 to May 2016)
Tabea Wiedmer, PhD student (Co-supervision: Prof. A. Perren)

Research activities

Acute myeloid leukemia (AML) is characterized by an impairment of normal myeloid differentiation that leads to a clonal expansion of early immature myeloid progenitor cells. This block in differentiation is among others caused by loss-of-function mutations in hematopoietic transcription factors that govern the orderly commitment of a cell to a particular hematopoietic lineage. Focusing on the myeloid transcription factor PU.1, we identified additional downstream targets of this transcription factor important for neutrophil differentiation and cell survival including the death-associated protein kinase 2 (DAPK2) and several autophagy genes (MAP1S, WIPI1, ATG16L2). Autophagy is a catabolic self-degradation process characterized by the formation of double-membraned autophagosomes adopted by cells to maintain cellular homeostasis during conditions of stress. Projects aiming at deciphering the function of autophagy in leukemogenesis and in metabolism during normal as well as leukemic myeloid differentiation are on their way.

Current literature suggests that cancer cells may use autophagy for cytoprotection in adverse conditions such as during anti-cancer therapy. In general, the role of autophagy varies depending on the particular type of tumor and the stage of disease progression. Therefore, our current collaborative projects with clinical pathologists aim at investigating whether activation of autophagy contributes to therapy resistance in a variety of solid tumors. We found that combinations therapies using tyrosine kinase inhibitors or retinoic acid in combina-

tion with autophagy inhibitors increase cell death responses in a variety of cancer cell models. We are in the process to develop a series of 3D cell culture models for cancer cell lines and primary lung and breast tumors to validate our findings of beneficial combination therapies with autophagy inhibitors from our 2D cell culture systems.

Internal collaborations

- Rupert Langer, MD
- Aurel Perren, MD
- Erik Vassella, PhD
- Inti Zlobec, PhD
- Sabina Beresowska, MD

External collaborations

National

- Hans-Uwe Simon, MD, Institute of Pharmacology, University of Bern
- Thomas Kaufmann, PhD, Institute of Pharmacology, University of Bern
- Volker Heussler, PhD, Institute of Cell Biology, University of Bern
- Deborah Stroka, PhD, Dpt. of Clinical Research, University of Bern
- Yitzhak Zimmer, PhD, Dpt. of Clinical Research, University of Bern
- Urban Novak, MD, Medical Oncology, University of Bern

International

- Bruce E. Torbett, PhD, TSRI, La Jolla, CA, USA
- Anne Simonsen, PhD, Dpt. of Biochemistry, University of Oslo, Norway
- Gerhard Behre, MD, Dpt. of Internal Medicine, University Hospital Leipzig, Germany
- Sharon McKenna, PhD, Biosciencies Institute, University College Cork, Cork, Ireland
- Philipp Jost, MD, Dpt. of Hematology/Oncology, TUM, Munich, Germany
- Enrico Garattini, MD, Istituto di Ricerche Farmacologiche Mario Negri, Milano, Italy
- Mojgan Djavaheri-Mergny, PhD, INSERM U916 VINCO, Bordeaux Cedex, France
- Valeria Bertagnolo, PhD, DMCMS, University of Ferrara, Ferrara, Italy
- Thomas Brunner, PhD, Dpt. of Biology, University of Konstanz, Germany
- Christof R. Hauck, PhD Dpt. of Biology, University of Konstanz, Germany

Grant support

- SNF 31003A_143739 (2012–2016), 390'000 CHF
- KFS-3409-02-2014 (2014–2017), 370'000 CHF
- Berger-Janser 9/2014 (2015–2016), 30'000 CHF
- Stiftung Klin. Exp. Tumorforschung (2015–2016), 81'000 CHF
- KLS-3360-02-2014 (2014–2016), Co-PI, 287'000 CHF
- BKL (2015–2016), Co-PI, 60'000 CHF

Group of Prof. Erik Vassella, Dr. pharm.

Ulrich Baumgartner, PhD student
Nicole Wirth, Master student (since September 2014 to December 2015)
Stephanie Langsch, PhD student (since September 2012 to December 2015)
Alexander Zulliger, Master student (BIO)
Fabienne Chantal Berger, Master student (BIO)
Claudia Zurbuchen, technician
Cornelia Schlup, technician
Maja Neuenschwander, technician
Brigitte Jossen, technician
Nicole Klaus, technician

Research activities

microRNAs are short regulatory RNAs at the post-transcriptional level that are implicated in a wide variety of basic biological processes. They play an important role in cancer where they act as tumor suppressing or oncogenic microRNAs. We are interested in the role of miRNAs in cell cycle control, apoptosis and drug-resistance in two tumor systems, non-small cell lung cancer (NSCLC) and gliomas. We have shown previously that miR-15a, miR-16 and miR-34a act together to induce cell cycle arrest in a synergistic and Rb-dependent manner and have identified physiologically relevant targets in NSCLC cells (Bandi et al, Cancer Res. 2009, Bandi and Vassella, Mol Cancer 2011). In addition we showed that miR-125b, which is upregulated in glioblastomas, is significantly associated with shorter overall survival of patients treated with temozolomide. TNFAIP3 and NKIRAS2 are the most relevant targets of this miRNA. Glioblastoma cells overexpressing miR-125b showed increased NF-κB activity and resistance TMZ. Our results provide a new mechanism of TMZ resistance in glioblastomas (Haemmig et al. Cell, Death Disease 2014).

We are currently investigating miRNAs that are regulated by EGFR signaling for their role in conferring chemoresistance, apoptosis, invasion and proliferation of NSCLC cells. In addition, we performed a lentiviral screen for miRNAs conferring temozolomide resistance in glioblastoma cell lines. We have identified several interesting candidates which are currently tested for their role in tumorigenic processes as well as chemoresistance. In a further project, we identified the mutational profile in the adenocarcinoma and squamous cell carcinoma components of adenosquamous carcinoma of the lung by NGS using an Ion Torrent PGM (Vassella et al, Oncotarget 2015) and are currently assessing epigenetic differences as well as differences in the microRNA expression profile in each component.

Internal collaborations

- Ekkehard Hewer
- Sabina Berezowska
- Mario Tschan
- Ilaria Marinoni and Aurel Perren
- Inti Zlobec
- Eva Diamantis
- Rupert Langer

External collaborations

National

- Jean-Louis Boulay, PhD, and Luigi Mariani, MD, University Hospital, Basel
- Rolf Jaggi, PhD, DKF, Bern
- Peng Ren-Wang, PhD and Thomas Marti, PhD, Universitätsklinik für Thoraxchirurgie
- Michael Reinert, MD, Ospedale regionale di Lugano, Lugano

International

- Stephan Schäfer, MD, Universitätsspital Köln, Germany

Grant support

- SNF (#138129) (2012–2015), 290'066 CHF
- Krebsliga Schweiz (Project KFS-2826-08-2011) (2012–2015), 204'400 CHF
- Bernische Krebsliga (2014–2016), 70'000 CHF

Team Translational Research Unit (TRU).

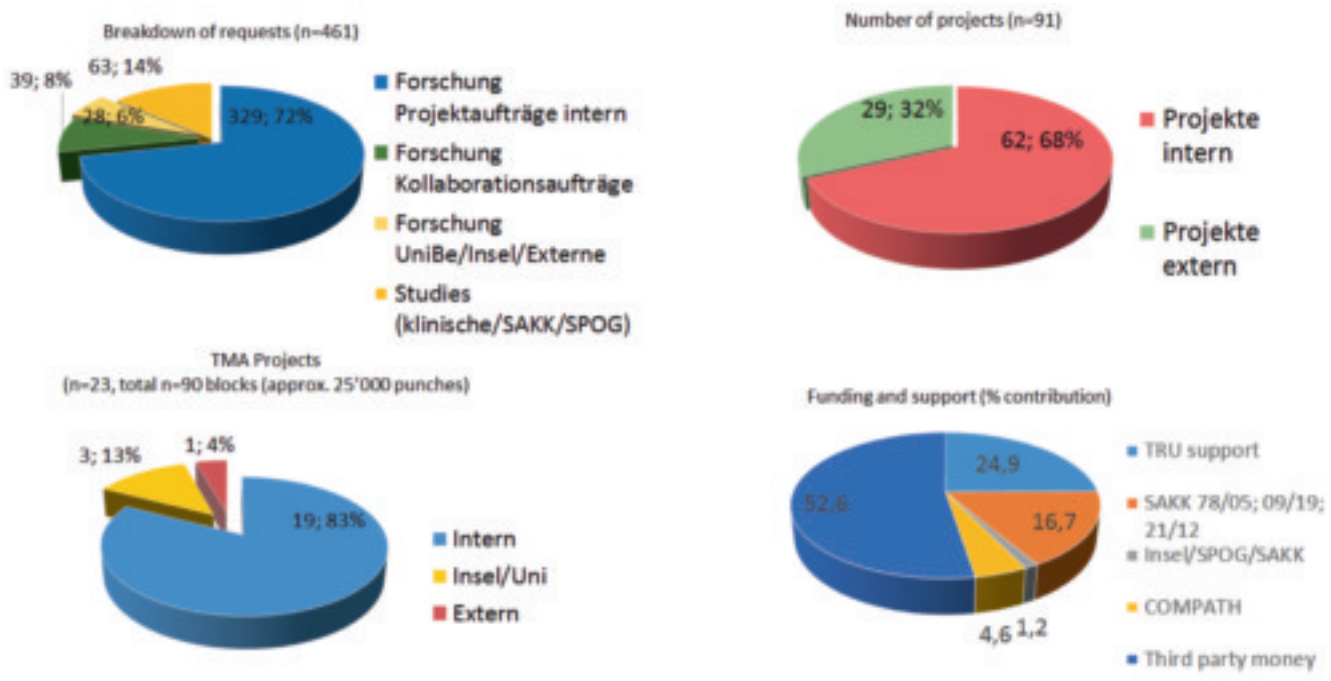
1.2 Translational Research Unit (TRU)

TRU Staff
Prof. Inti Zlobec, Head of Unit
Caroline Hammer, Lab administrator
Dr. Irene Centeno-Ramos, Research technician
Dr. José Galván, Research technician
Liliane Schöni, Research technician
Patricia Ney, Research technician

Associated Staff
Joël Kupferschmid, biobank and data manager
Silvia Suardi, Research technician COMPATH

The TRU is a core facility with expertise in tissue-based methods. It provides not only technical know-how but also scientific input to help support pathologists, collaborators and researchers from inside and outside the University of Bern. In addition to histology, we experiment with different visualization methods on tissues including immunohistochemistry (single, double), in situ hybridization (mRNA, miRNA, DNA) and immunofluorescence (single, double). These techniques are now being extended for cells fixed directly onto slides or cell blocks. Slide scanning and access to slides via a virtual platform is also offered. In collaboration with the experimental pathology and molecular pathology divisions, TRU is continuously expanding its palet of molecular techniques to study genetic changes on all levels. 2016 will see the implementation of image analysis for quantification of protein, RNA and DNA within the framework of collaboration and the launch of an institution-wide digital pathology project with the aim of establishing and harmonizing a coordinated platform for digital slides for research, and then later to diagnostics.

Over the last year, the TRU has processed 461 requests related to 91 different projects. Approximately 75% of the costs of TRU are covered by its users. Some statistics regarding the distribution, origin and funding of projects are found below.



Project statistics in the Translational Research Unit.

From its inception in 2012, our next-generation Tissue Microarraying (ngTMA, www.ngtma.com) platform continues to make great strides. With over 71 different projects thus far, TRU has created over 330 ngTMA blocks, totaling over 195'000 punches for internal groups, collaborators and external companies or researchers. The true power of ngTMA will be underlined by biomarker projects coupling the advantages of this technique to image analysis. Thus with more objective quantitation of immunostains and ISH on appropriately powered patient cohorts an ngTMA/image analysis approach will be far-reaching in terms of (re-)investigating, validating and standardizing new (and already established) biomarkers.

This year has also seen the launch of a joint project of the Institute of Pathology and the Institute of Animal Pathology (Vetsuisse Faculty), generously funded by the Medical Faculty to support research being carried out on animal models of human disease. This comparative pathology platform (www.compath.ch) joins human and veterinary pathologists, their fields of expertise and TRU technology to further the investigation of animal models with the goal of better managing and treating of human disease.

The TRU and its staff provide regular support to the following clinically oriented researchers, groups and collaborators.

Groups of:

- S. Berezowska
- E. Diamantis-Karamitopoulou
- R. Langer
- A. Lugli
- A. Perren
- I. Zlobec

Group of Dr. Sabina Berezowska, MD

Group members:
Anna Schläfli, PhD (co-affiliation with Experimental Pathology Group Tschan)

Master students / Dissertation candidates:
Yasin Irmak, cand. med.
Manuel Keller, cand. med.
Dennis von Arx, cand. med.

Research activities

Lung cancer remains the leading cause of cancer death worldwide. One of the recent significant practice changers has been the effective therapeutic exploitation of targetable mutations, e.g. ALK inversions. But even after clinical response on tyrosine kinase inhibitors the neoplasms will eventually develop resistance and recur. Tools to overcome those resistance mechanisms are needed for extended remission. Modulation of autophagy – the stress response and homeostasis mechanism in normal and neoplastic cells – may be one possible way to interfere with tumor cell adaptation and viability.

The aim of one of our major projects is therefore to characterize the role of autophagy – a druggable mechanism – in the pathobiology of lung cancer, and in particular in EML4-ALK-positive NSCLC, and to map the autophagy pathway operative in resistance mechanisms to ALK inhibitors. Functional cell culture-based assays and tissue-based immunohistochemical analyses are applied.

Very recently, lung cancer has been surprisingly shown to be amenable to immunotherapeutic approaches. The PD-1 immune checkpoint inhibitor nivolumab has been FDA-approved for the treatment of patients with advanced NSCLC already earlier this year. Predictive biomarkers are not yet established, but PD-L1 expression and tumor-infiltrating lymphocytes are in the focus of many investigators. Mostly, primary tumors are studies. Because 20–40% of all NSCLC patients develop brain metastases, with associated drop in prognosis, we are interested in the characterization of cerebral metastases of lung cancer in comparison to the primary site. We conduct tissue-based research using tissue microarrays. Hereby, one project focuses on the immunohistochemical expression of immune checkpoint marker expression and tumor-infiltrating lymphocytes.

Furthermore, we collaborate with the thoracic surgery research group in the generation of primary cell cultures in 2D and 3D systems. Thus, truly translational research is enabled, where the same tumor can be analyzed in parallel using functional assays, on formalin-fixed and paraffin-embedded tissue or using frozen tissue samples.

Internal collaborations

- Mario Tschan, PhD, Experimental Pathology
- Erik Vassella, PhD, Experimental Pathology
- Rupert Langer, MD, Clinical Pathology
- Thoracic surgery research group DKF (Prof. Dr. R. Schmid, Dr. T. Marti, Dr. S. Hall, Dr. R. Peng, Dr. P. Dorn) thoraxchirurgie.insel.ch/de/forschungslabor/forschungs-arbeit-research/
- Pulmonary Medicine (Adults) research group DKF (Prof. Dr. T. Geiser, Dr. F. Blank, Dr. M. Funke)
- DCR Research Cluster Lung Development Regeneration and Disease
- Urspeter Knecht, MD, Universitätsklinik für Diagnostische und Interventionelle Neuroradiologie, Inselspital

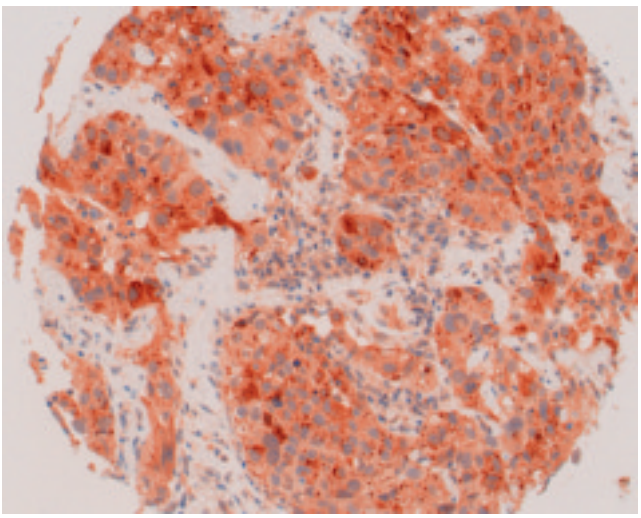
External collaborations

National
- Prof. Dr. Lukas Bubendorf, Institute of Pathology, University of Basel, Switzerland

International
- Dr. Stephan Schäfer, Institute of Pathology, University of Cologne, Germany
- Prof. Dr. Axel Walch, Helmholtz-Zentrum München, Munich, Germany

Grant support

- Bern. Krebsliga (to Dr. Sabina Berezowska), 2015/2016, 30'000 CHF



Die Rolle der Autophagie in Karzinomen der Lunge
Die Autophagie ist ein zellulärer Homöostasemechanismus, der sowohl bei der Zellentartung als auch beim Überleben von Krebszellen in Stresssituationen (z.B. unter Therapie) eine Rolle spielt. Wir haben die Visualisierung von anerkannten Autophagiemarkern am Gewebe etabliert und untersuchen gewebebasiert die Rolle der Autophagie in Karzinomen der Lunge, mit Fokus auf deren Metastasierung und Therapieresistenz.

Group of PD Eva Diamantis-Karamitopoulou, MD

Group members:
Martin Wartenberg MD, PhD

Master students / Dissertation candidates:
Jens Brönnimann
Petra Schmid

Research activities

In the era of personalized medicine pancreatic ductal adenocarcinoma (PDAC) remains a highly lethal malignancy with rising incidence, characterized by a rich stromal component. Its poor prognosis is attributed to the rapid dissemination of cancer cells to the lymphatic system and distant organs and partly also to treatment resistance. To date the management of PDAC remains suboptimal since available conventional and targeted treatments are merely directed against the cancer cells.

Our group is interested in the characterization of the complex cellular interactions in the tumor microenvironment of the invasive front of PDAC. In more detail, we are trying to better characterize the tumor-stroma interactions taking place between the cancer-associated fibroblasts and the cancer cells, ideally represented by an aggressive cancer cell population, in form of dissociated cancer cells with EMT features, called «tumor-budding cells». Our group and others have shown that tumor budding is a strong and independent prognostic factor in PDAC. However, the mechanisms that promote tumor budding are still unknown.

Our recent findings indicate a close interaction of the stromal component with the EMT process and suggest functional heterogeneity of the stromal cells. Moreover, they show that a concomitant loss of tumor suppressors in tumor and stromal cells defines a subpopulation of PDAC with more aggressive behavior and that stromal cells also harbor genetic aberrations in tumor suppressor genes.

A further aim of our group is the identification and characterization of specific microRNAs in PDAC. Our recent experiments in a limited number of cases indicate that tumor and stromal cells differentially regulate microRNAs and this correlates with the expression of proteins known to be targets of these microRNAs.

Furthermore we are interested in the characterization of the peri-tumoral and intra-tumoral immune cell infiltration, especially by cytotoxic T-cells and tumor-associated macrophages (TAMs), which constitute a very important host-related factor. We could recently show that PDAC microenvironment displays a tumor-favoring immune-cell composition in the immediate environment of the EMT-type tumor-budding cells.

The general objective of our research projects is to provide information on the role of different subtypes of stromal and immune cells in the tumor microenvironment of PDAC and their impact on the EMT process and the neoplastic progression through the effect of specific microRNAs. This may provide the basis for the possible use of microRNA interference to prevent the effect on EMT and metastatic spread in PDAC and to improve treatment response thorough personalized targeted therapy.

Internal collaborations

- Aurel Perren, MD
- Erik Vassella, PhD
- Inti Zlobec, PhD
- José Galván, PhD
- Irene Centeno, PhD

External collaborations

National
- Prof. Beat Gloor, MD, Department of Visceral Surgery, Insel University Hospital, Bern
- Prof. Luigi Terracciano, MD, Institute of Pathology, University of Basel

International
- Prof. A. Kondi-Pafiti, University of Athens, Greece

Grant support

- Bernische Krebsliga (2013–2015)
- Werner und Hedy Berger-Janser Stiftung zur Erforschung der Krebskrankheiten (2014–2015)

Group of Prof. Rupert Langer, MD

Group members:
Bastian Dislich, MD, PhD
Olivia Adams, PhD student (Co-supervision: Mario Tschan)

Associated group members
(Gastrointestinal Cancer research group, GIC):
Inti Zlobec, PhD
Alessandro Lugli, MD
Lena Sokol, PhD
Heather Dawson, MD
Stefan Zahnd, PhD student
Gregor Rieger, MD
Viktor Koelzer, MD

Master students / Dissertation candidates:
Lars Guldener
Simon Nobs
Alexandra Stein
Laura Noser
Nicola Blaser

Research activities

Under the umbrella of the Gastrointestinal Cancer (GIC) research group we are investigating histomorphological and molecular characteristics of upper gastrointesinal tract tumors, especially esophageal carcinomas, in correlation with biological and clinical factors, treatment response (e.g. neoadjuvant chemotherapy) and patient prognosis.

We are especially interested on the impact of cellular stress reactions and death mechanisms on tumor behavior and chemotherapy and resistance. In this field we are closely collaborating with Mario Tschan's group of the Experimental Pathology department. One focus lies on the investigation of autophagy, a cellular degradation process that has been described to play an important role not only for the maintenance of normal cellular homeostasis but also for cancer. However, the role in malignant diseases is not completely understood, since it may promote tumor death on the one hand and be benefitial for cell survival on the other hand. We are analyzing the expression of autophagy-related proteins in human biopsy and resection samples and correlate the expression patterns with clinical and pathological parameters, including tumor regression after neoadjuvant chemotherapy. The tissue analyses are complemented by functional cell line experiments that mirror the clinical scenario (i.e. treatment with conventional chemotherapeutics, but also with targeting drugs). Another interesting group of molecules are the so called heat shock proteins (HSPs) that also play a role in cellular stress response. We are investigating a link between these two mechanisms, in specific relation to response to chemotherapy and targeted therapy.

A second focus of our work is the assessment of response to cytoxotic treatment based on histology. We have shown that tumor regression is a reliable prognostic factor after neoadjuvant therapy in adenocarcinomas of the upper gastrointestinal tract, and that grading of tumor regression based on histology can be considered as highly reproducible and feasible. Future studies will also encompass the histopathologic analysis of the effect of targeted treatment.

Moreover, we are investigating morphological features of tumors with potentially prognostic impact such as tumor budding and inflammation, and several immunohistochemical markers for a more comprehensive characterization of esophageal and gastric adenocarcinomas.

Internal collaborations

- Mario Tschan, PhD
- Erik Vassella, PhD
- Sabina Berezowska, MD

External collaborations

National
- Prof. C.A. Seiler and Dr. Dino Kroell, Department of Surgery, Inselspital
- Prof. Dr. Rosenberg, Kantonsspital Liestal

International
- Dr. J. Slotta-Huspenina, Institute of Pathology, Technische Universität München, Germany
- Prof. K.F. Becker, Institute of Pathology, Technische Universität München, Germany
- Prof. A. Walch, Institute of Pathology, Helmholtz-Zentrum Neuherberg, Germany

Grant support

- Schweizerische Krebsliga (2013–2016), 236'000 CHF
- Bernische Krebsliga (2015–2016), 60'000 CHF

Group of Prof. Alessandro Lugli, MD

Group members:
Lena Sokol, PhD
Heather Dawson, MD

Associated group members
(Gastrointestinal Cancer research group, GIC):
Inti Zlobec, PhD
Stefan Zahnd, MSc, PhD student
Viktor Kölzer, MD
Rupert Langer, MD
Olivia Adams, PhD
Bastian Dislich, MD, PhD
Gregor Rieger, MD

Master cand. med. / Dissertation students:
Lucine Christe (2013)
Sandra Burren (2013)
Alexandra Tröhler (2015)
Lynn Richmond (2015)
Carla Schenker (2015)

Research activities

Our research group focuses on the surgical and molecular pathology aspects of tumor buds and the tumor microenvironment in colorectal cancer (CRC).

One of our main goals is the implementation of «tumor budding» in the daily diagnostic practice. Especially three clinical scenarios in CRC need additional prognostic biomarkers which are able to support interdisciplinary decisions, namely if a hemicolectomy is indicated in completely resected malignant polyps (pT1 CRC), if stage II CRC with a high risk for metastases need an adjuvant therapy or if rectal cancer will respond to the neo-adjuvant therapy based on pre-operative biopsies. Many studies have shown the high prognostic potential of tumor budding, but the lack of a standardized scoring system is one of the main reasons why tumor budding is still not reported routinely. Therefore, under the umbrella of the Swiss Association of Gastrointestinal Pathology (SAGIP) our group is planning an international multicentric study that validates the 1HPF (hot spot) method in malignant polyps. Additionally the group organizes an International Tumor Budding Consensus Conference (ITBCC) in Bern in 2016.

The immune system plays a crucial role in the development and progression of CRC. We hypothesized that aberrant expression of certain miRNAs contributes to the pathogenesis of CRC by influencing tumor-host interactions. We characterized the microRNA expression in CRC, the correlation with their target proteins, molecular and clinic-pathological factors. This approach could yield new prognostic microRNA profiles, or identify novel potential therapeutic targets. Thus far, we have characterized the expression of 5 microRNAs and 18 target proteins by using a sequential in situ hybridization/immunohistochemistry and digital image analysis approach on a next generation tissue microarray (ngTMA) including 244 CRC patients. Indeed, we were able to determine a multimarker phenotype that can help to identify patients with an activated immune phenotype of CRC. Next, we will investigate whether the selected miRNAs can be targeted in vivo by antagomirs to affect tumor-immune rejection.

In colorectal cancer, epithelial mesenchymal transition (EMT) is considered to be a driving force of tumor dissemination, which occurs via vascular invasion. Tumor budding may be the morphological correlate of this process and is strongly linked to lympho-vascular invasion, nodal and distant metastases. Hypoxia is also critical for tumor progression and has been demonstrated to be an important regulator of EMT and neovascularization of the tumor microenvironment. Therefore, the aim of this study is to examine the roles of 1) hypoxia-related genes in tumor buds and 2) angiogenesis in tumor-associated vasculature. Selected markers will be visualized at the level of protein expression (immunohistochemistry) and mRNA transcripts (in situ hybridization) on a next-generation TMA specifically targeting areas of highest budding/vascular density, enabling the identification of expression profiles most likely to contribute to a pro-angioinvasive and thus particularly aggressive tumor phenotype.

Internal collaborations

- Philippe Krebs, PhD
- Tilman Rau, MD
- Eva Diamantis, MD
- José Galván, PhD

External collaborations

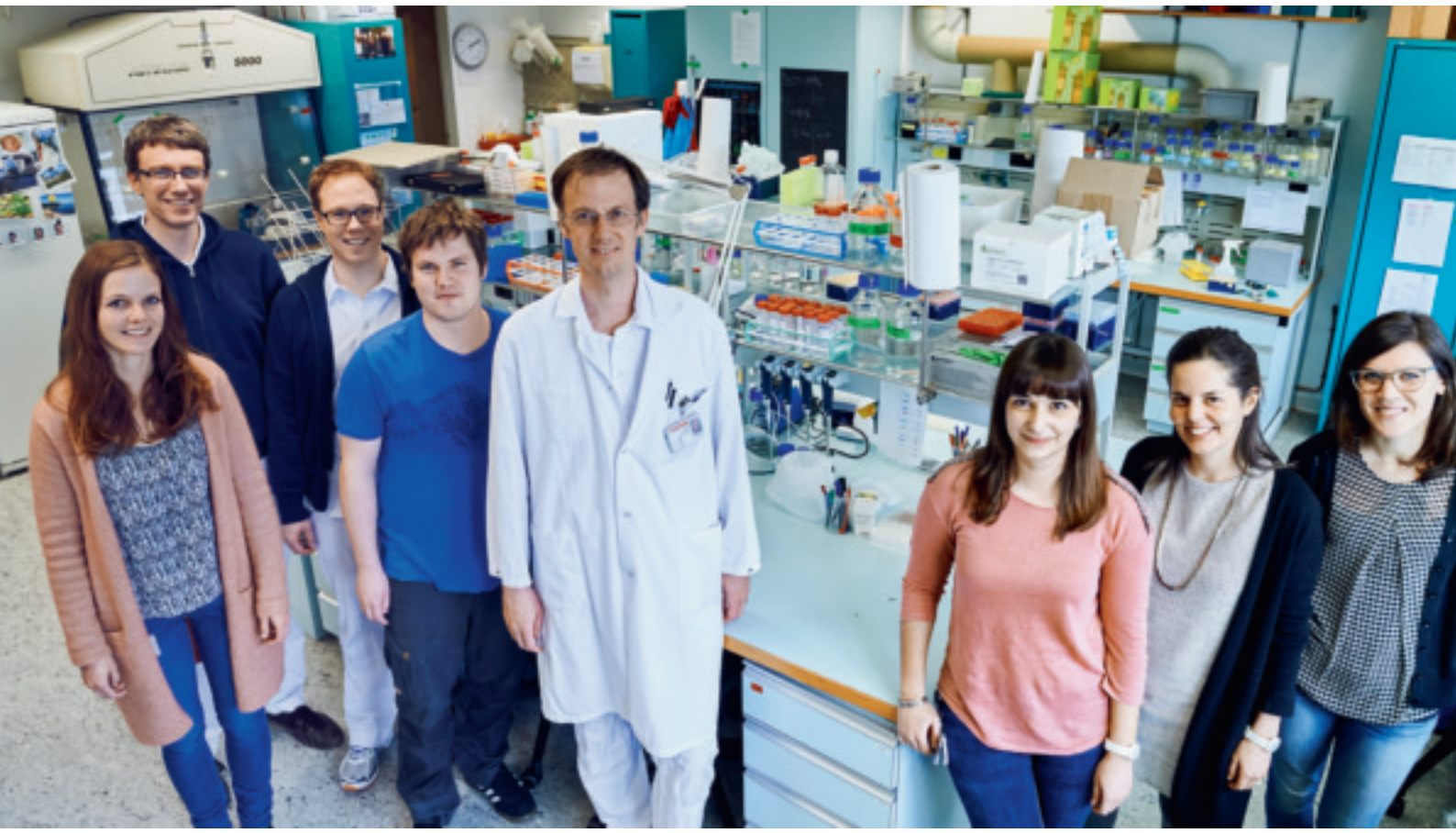
National
- Interdisciplinary research group from Visceral Surgery and Internal Medicine at the Inselspital and Spitalnetz Bern (Prof. Daniel Inderbitzin, Dr. Martin D. Berger, Dr. Marion Hädrich, Dr. Lukas Brügger, Dr. Peter Studer, Dr. Beat Schnüriger)
- Prof. Gieri Cathomas and Prof. Robert Rosenberg (Kantonsspital Baselland, Liestal)
- Prof. Giandomenica Iezzi (ZLF, Universitätsspital Basel)
- Dr. Giacomo Puppa (Institute of Pathology, HUG, Genève)
- PD Dr. Kaspar Truninger (Gastroenterologie, Langenthal)

International
- Prof. Jérôme Galon (INSERM, Paris, France)
- Prof. Franck Pages (INSERM, Paris, France)
- Prof. Ian Tomlinson (University of Oxford, UK)
- Prof. Robert Genta (UT Southwestern Medical Center, Dallas, USA)
- Prof. Robert Riddell (Mount Sinai Hospital, Toronto, Canada)
- Prof. Iris Nagtegaal (Radboudumc, Nijmegen, Netherlands)

- Prof. Motohiro Kojima (National Cancer Center, Tokyo, Japan)
- Prof. Giuseppe Masucci (Karolinska Institutet, Stockholm, Sweden)
- Dr. Parham Minoo (University of Calgary, Alberta, Canada)
- Prof. Kieran Sheahan (University of Dublin, Ireland)
- Prof. Jean-François Fléjou (Hôpital Saint-Antoine, Paris, France)
- Prof. Fatima Carneiro, Ipatimup, Porto, Portugal)

Grant support

- KFS-3294-08-2013: microRNAs in the tumour microenvironment of colorectal cancer: novel targets for therapeutic intervention ?
- KFS-3252-08-2013: Interaction between EMT-like cancer cells («tumor buds») and blood/lymphatic vessel invasion in the tumor microenvironment of colorectal cancer
- Bernische Krebsliga (2015–2016): cDNA library for (mi)RNA detection in distinct cell populations of archived FFPE colorectal cancer tissue (to L. Sokol/V. Kölzer)



Research group Prof. Aurel Perren.

Group of Prof. Aurel Perren, MD, PhD

Group members:
Aurel Perren, MD, group leader
Ilaria Marinoni, PhD, senior research assistant
Anja Schmitt, MD, attending pathologist
Matthias Dettmer, MD, attending pathologist
Annika Blank, MD, attending pathologist
Tabea Wiedmer, MSc, PhD student
Dominik Nann, MD, resident
Astrid Wiederkehr, BSc, master student (until July 2015)
Lea Normand, technician
Sophia Pantasis, MSc, technician
Rahel Klossner BSc, Master student (BMS)
Samara Naim, BSc Master student (BMS)
Mirjam Franzelli, cand. med.

Research activities

Four major projects are currently ongoing:

Dissection of the role of DAXX and ATRX in pNET

DAXX and ATRX expression is lost in 40% of sporadic pNETs. We have shown that DAXX/ATRX loss predicts reduced survival and that DAXX/ATRX loss precedes ALT (Alternative Lengthening Telomeres) activation and CIN (Chromosomal Instability) along tumor progression. We hypothesize that in these tumors CIN drives malignant evolution and ultimately metastasis. Yet the mechanisms by which DAXX/ATRX loss can induce genomic instability, ALT activation and tumor progression are still unknown. We focus on unraveling the mechanism underlying this new cancer-associated pathway and specifically on the epigenetic modification resulting from DAXX/ATRX loss. The possible clinical implications of our findings are then evaluated on pNETs human tissue samples.

The role of hypoxia signaling in pNET

About 10% of patients with VHL syndrome suffer from pNET. These tumors are characterized by active hypoxia signaling. We described in a subset of pNET somatic VHL alterations that also are associated with hypoxia signaling and a poor prognosis. The underlying mechanisms are dissected on pNET cell lines with correlations to pNET tissues.

Autophagy in pNETs – biology and treatment

Autophagy plays a major role in mediating metastasis formation as well as therapy response and resistance. Pancreatic neuroendocrine tumor (pNET) patients often display primary or secondary resistance to the approved treatments. We investigate in vitro and in vivo the role of autophagy in pNET development and in mediating therapy response and resistance.

The relevance of autophagy activation in pNETs progression and the possible effects of combining autophagy inhibition with targeted treatments are then evaluated ex vivo on patient tumor cells.

Micro RNAs in thyroid carcinomas
While morphologically defined subtypes of thyroid carcinomas are genetically well defined, these genetic alterations such as BRAF mutations in a subset of papillary thyroid carcinomas do not accurately predict clinical outcome and response to therapy. Using a genome-wide mircoRNA-screening approach in a large set of clinically well-characterized thyroid carcinomas, we dissect the potential clinical relevance as well as the functional consequences of deregulated microRNAs.

Internal collaborations
- Mario Tschan, PhD, Institute of Pathology, University of Bern
- Philippe Krebs, PhD, Institute of Pathology, University of Bern
- Erik Vassella, PhD, Institute of Pathology, University of Bern

External collaborations
National
- PD Dr. med. Martin Walter, Universitätsklinik für Nuklearmedizin, University of Bern
- Prof. Dr. Roch-Philippe Charles, Institute of Biochemistry & Molecular Medicine, University of Bern
- Prof. Beat Gloor, Department of Visceral Surgery and Medicine, Inselspital, Bern
- Dr. Deborah Stroka, Department of Clinical Research, University of Bern
- Prof. Gerhard Christofori, Department of Biomedicine, University of Basel

International
- Dr. Dr. Chrissie Thirlwell, Department of Cancer Biology, University College London, UK
- Prof. Maria Chiara Zatelli, Department of Medical Science, University of Ferrara, Italy
- Prof. Marianne Pavel, Medizinische Klinik, Hepatologie Gastroenterologie, Campus Virchow-Klinikum, Charité – Universitätsmedizin Berlin, Germany
- Prof. Gunter Klöppel, Department of Pathology, Technical University of Munich, Germany
- Prof. Ernst-Jan Speel, Institute of Pathology Maastricht UMC, Netherlands
- Prof. Dr. Yuri Nikiforow, Department of Pathology, University of Pittsburg, Pittsburg, USA
- PD Natalia Pellegata, Institute of Pathology, Helmholtz-Zentrum, Munich, Germany
- PD Martin Anlauf, Institute of Pathology, University of Düsseldorf, Germany

Grant support
- Bernische Krebsliga Grant to Anja Schmitt Kurrer (2012–2015), 80'000 CHF
- SNF Grant No. 310030_144236 to Aurel Perren (2012–2016), 367'000 CHF
- KFS Grant No. 3360-02-2014 to Aurel Perren (Co-applicant Ilaria Marinoni) (2014–2017), 286'900 CHF
- Tumor Forschung Bern to Ilaria Marinoni (2015–2017), 90'000 CHF

Group of Prof. Inti Zlobec, PhD

Group members:
Stefan Zahnd, MSc, PhD student
Viktor Kölzer, MD

Associated group members
(Gastrointestinal Cancer research group, GIC):
Alessandro Lugli, MD
Lena Sokol, PhD
Heather Dawson, MD
Rupert Langer, MD
Olivia Adams, PhD
Bastian Dislich, MD, PhD
Gregor Rieger, MD

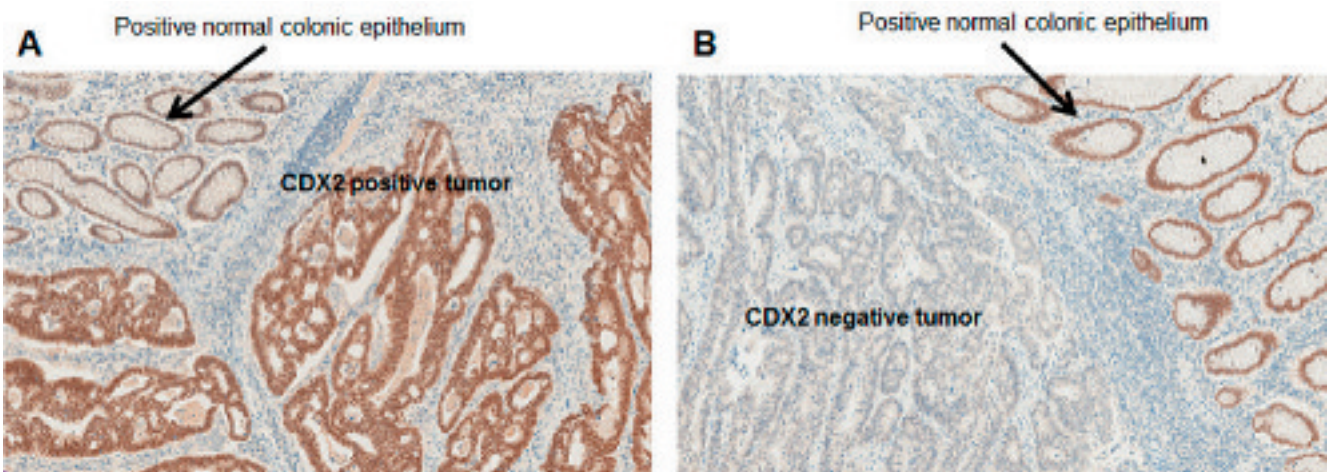
Master cand. med./Dissertation students:
Jacqueline Wyss (2015)
Kristina Seiler (2015)
Sara Meyer (2015)
Elia Fischer (2015)
Karim Hegazy (2014)
David Marx (2014)
Christian Schafroth (2014)
Miriam Flury (2014)
Janina Graule (2014)
Claudia Lädrach (2013)
Katharina Canonica (2012)

Research activities
Under the umbrella of the Gastrointestinal Cancer (GIC) research group, our group takes an interdisciplinary approach to study colorectal cancer, with the goal of understanding transformation, progression and invasion.

Molecular aspects of tumor budding and the tumor microenvironment is a major focus of our research. We are interested in uncovering what makes tumors bud and what genetic or epigenetic influences from various components within the tumor microenvironment may be exerting control on tumor budding. In 2015, we performed the first pyrosequencing and next-generation sequencing analyses on tumor buds and established ISH assays for detection of gene overexpression. We also found evidence of epigenetic control (promoter methylation) of EMT-related genes in the tumor stroma (e.g. TWIST1) that correlate strongly with tumor budding. We intend to continue to profile both the tumor buds and various components of the tumor stroma at DNA, RNA and protein level.

In general, we are interested in the molecular pathogenesis of colorectal cancers and are studying different aspects of the gene CDX2 together with Prof. M. Tschan. During the last years we have identified CDX2 loss not only as an unfavorable prognostic factor linked to tumor progression and dedifferentiation but also as a feature of the serrated pathway characterized by BRAF mutation, high-level CpG Island Methylator Phenotype (CIMP) and microsatellite instability (MSI). We hypothesize that CDX2 promoter methylation is a major regulatory mechanism in these tumors and that hypermethylation coincides with the establishment of high-grade dysplasia in serrated precursor lesions.

Moreover, we are interested in validating new potential therapeutic targets identified by mass spectrometry (PhD work S. Zahnd). We are currently isolating various cell populations from colorectal cancers in order to compare differences in targetable biomarkers between normal tissues and cancer using bioinformatics approaches.



Genetic and epigenetic landscape of CDX2 in colorectal cancer
The homeobox caudal-type 2 gene CDX2 is required for differentiation, proliferation and maintenance of an intestinal cell phenotype. Work by our group has shown that CDX2 protein is markedly reduced in up to 20% of colorectal cancers, which correlates with dedifferentiation, metastatic spread and unfavorable patient outcome. Cell line data confirms that promoter hypermethylation is a likely cause of CDX2 expression loss, since CDX2 expression can be recovered upon treatment with DNA methyltransferase inhibitors (DNMTi). This project aims to study the genetic and epigenetic modifications leading to CDX2 loss that are functionally and clinically relevant.
Figure legend: CDX2 immunohistochemistry.

Our work is supported by numerous internal and external collaborations and by a number of highly motivated students.

Internal collaborations

- Mario Tschan, PhD
- Erik Vassella, PhD
- Philippe Krebs, PhD
- Tilman Rau, MD
- Eva Diamantis, MD
- José Galván, MD
- Irene Centeno, MD

External collaborations

National

- Interdisciplinary research group from Visceral Surgery and Internal Medicine at Inselspital and Spitalnetz Bern (Prof. Daniel Inderbitzin, Dr. Martin D. Berger, Dr. Marion Hädrich, Dr. Lukas Brügger, Dr. Peter Studer, Dr. Beat Schnüriger)
- Prof. Gieri Cathomas, Prof. Robert Rosenberg and Dr. Aino Paasinen (Kantonsspital Baselland, Liestal)
- Prof. Douglas Hanahan (EPFL, Lausanne)
- Dr. Giacomo Puppa (Institute of Pathology, HUG, Genève)
- PD Dr. Manfred Heller and Dr. Sophie Lagache (Proteomics Facility, DKF, Bern)
- Prof. Matthias Hediger (IBMM, Bern)

International

- Dr. Jérôme Galon (INSERM, Paris, France)
- Dr. Ulrich Nitsche (TUM, München, Germany)
- Prof. Ian Tomlinson (University of Oxford, UK)
- Dr. Leanne Li (MIT, Boston, USA)
- Dr. Kristi Baker (University of Edmonton, Alberta, Canada)

Grant support

- Swiss National Science Foundation (2015–2018), Co-PI, 525'000 CHF
- Werner und Hedy Berger Janser Stiftung (2015–2018), 145'620 CHF
- Mach-Gaensslen Foundation (2014–2015), 39'000 CHF
- Johanna Dürmüller-Bol Foundation (2014–2015), 20'000 CHF
- Foundation for clinical & experimental tumor research (2013, extended 2015), 53'226 CHF

2 Akademische Grade

2.1 Akademische Grade intern

Zysset Daniel, PhD
TREM-1 and its role in non-infectious inflammatory conditions
Fakultät: phil. nat. Uni Bern
Betreuer Patho: L. Saurer
Hauptbetreuer: Ch. Müller

von Werdt Diego, Master
Contribution of Regulator of G Protein Signaling Family Members to the Tissue Resident Phenotype of Intestinal Intraepithelial Lymphocytes
Fakultät: phil. nat. Uni Bern
Betreuer Patho: N. Corazza
Hauptbetreuer: Ch. Müller

Sulcova Jitka, PhD
Role of immune cells and environmental influences in a genetic mouse model of chronic skin inflammation
Fakultät: ETH Zürich
Betreuer Patho: Ch. Müller
Hauptbetreuer: S. Werner, ETH Zürich

Coutaz Manuel, PhD
The role of Notch receptor signaling in T helper 17 cell differentiation
Fakultät: Universität Lausanne
Betreuer Patho: Ch. Müller
Hauptbetreuer: F. Tacchini-Cottier, Universität Lausanne

Peter Bretscher, PhD
Structural and functional characterization of isolated oxidized phospholipid derivatives
Fakultät: Department of Biology, ETH Zurich
Betreuer Patho: S. Freigang
Hauptbetreuer: Prof. M. Kopf, ETHZ

Loïc Borcard, MSc
Role of basophil-derived factors in the pathogenesis of food allergy
Fakultät: phil. nat. Uni Bern
Hauptbetreuer: M. Noti

Köck Ivonne, MSc
The role of ESRP1-mediated alternative splicing for the integrity of the intestinal epithelial barrier
Fakultät: phil. nat. Uni Bern
Hauptbetreuer: Ph. Krebs / Ch. Müller

Wasmer Marie-Hélène, MSc
Investigation of interleukin-33 signaling in leukemia and colorectal cancer
Fakultät: phil. nat. Uni Bern
Hauptbetreuer: Ph. Krebs / Ch. Müller

Mager Lukas, MD-PhD
Molecular Dissection of Inflammation-induced Immunopathologies
Fakultät: med. Uni Bern
Hauptbetreuer: Ph. Krebs / Ch. Müller

Kwong Chung Cheong Kwet Choy, PhD
Role of antigen-specific antimicrobial CD4+ T cell response in host-microbial mutualism
Fakultät: med. Uni Bern
Betreuer Patho: Ph. Krebs (Mentor)
Hauptbetreuer: Andrew Macpherson / Kathy McCoy

Schärrer Daniel, BMA Master
Fakultät: Medi, Höhere Fachschule Bern
Hauptbetreuer: M. P. Tschan

Auma Emilly, BMA Master
Fakultät: Medi, Höhere Fachschule Bern
Hauptbetreuer: M. P. Tschan

Jutzi Susanne, MD Master
Fakultät: Med. Fak., Uni Bern
Hauptbetreuer: M. P. Tschan

Hardegger Marielle, MD Master
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Hauptbetreuer: M. P. Tschan

Gloor Severin, Dr. med.
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Hauptbetreuer: M. P. Tschan

Messikommer Manuela, Dr. med.
Fakultät: Med. Fak., Uni Bern
Hauptbetreuer: M. P. Tschan

Haimovici Aladin, PhD
Fakultät: GCB, Uni Bern
Hauptbetreuer: M. P. Tschan

Pham Anna, PhD
Fakultät: GCB, Uni Bern
Betreuer Patho: M. P. Tschan (Co-advisor)
Hauptbetreuer: E. Oppliger, Hematology, Inselspital

Haemmig Stephan, PhD
Fakultät: GCB, Uni Bern
Betreuer Patho: M. P. Tschan (Co-advisor)
Hauptbetreuer: E. Vassella

Pastukhov Oleksandr, PhD
Fakultät: GCB, Uni Bern
Betreuer Patho: M. P. Tschan (Mentor)
Hauptbetreuer: A. Huwiler, Institute of Pharmacology

Burda Paul, PhD
Fakultät: GCB, Uni Bern
Betreuer Patho: M. P. Tschan (Mentor)
Hauptbetreuer: V. Heussler, IZB

Roethlisberger Silvan, PhD
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Graule Janina, MD Master
Generation of a tissue microarray of hepatocellular carcinomas (HCC) and collection of baseline clinical characterization of patients
Fakultät: med. Uni Bern
Betreuer Patho: I. Zlobec
Hauptbetreuer: M. Matteo

Helbling Melina, MD Dr. med.
Twist1 and Twist2 promotor methylation and protein expression in tumor stroma influence the epithelial-mesenchymal transition-like tumor budding phenotype in colorectal cancer
Fakultät: med. Uni Bern
Hauptbetreuer: I. Zlobec

Flury Miriam, MD Master
DNA extraction from tumor buds in colorectal cancer
Fakultät: med. Uni Bern
Hauptbetreuer: I. Zlobec

Schmid Petra, MD Master
Charakterisierung von Tumor-Buddingzellen im Pankreaskarzinom und Identifizierung eines «Budding-Förderungs»-Profils
Fakultät: med. Uni Bern
Betreuer Patho: I. Zlobec
Hauptbetreuer: E. Diamantis

Elsa Sartori, Master
Zusammenstellung eines Patienten- und Gewebekollektivs für die Untersuchung von Heat-shock-Proteinen und ErbB-Rezeptoren in Glioblastomen
Fakultät: med. Uni Bern
Betreuer Patho: S. Berezowska
Hauptbetreuer: S. Berezowska (Leitung: I. Zlobec)

Serena Galli, Dr. med.
D47 protein expression in acute myeloid leukemia: a tissue-microarray-based analysis
Fakultät: med. Uni Bern
Hauptbetreuer: Y. Banz

Jens Brönnimann, Dr. med. cand.
Role of SADS in epithelial mesenchymal transition in pancreatic cancer
Fakultät: Medizinische Fakultät
Hauptbetreuer: E. Diamantis

Petra Schmid, Dr. med. cand.
Frequency and prognostic impact of putative stem cell markers in pancreatic ductal adenocarcinoma
Fakultät: Medizinische Fakultät
Hauptbetreuer: E. Diamantis

Stefan Haemmig, PhD
The role of microRNAs in the regulation of chemoresistance in glioblastomas
Fakultät: phil. nat. Uni Bern
Hauptbetreuer: E. Vassella

Stephanie Langsch, PhD
miR-29b is a mediator of KRAS-induced NF-kB activation in non-small cell lung cancer
Fakultät: phil. nat. Uni Bern
Hauptbetreuer: E. Vassella

Nicole Wirth, MSc
Chemoresistance in glioblastomas: the role of microRNAs
Fakultät: phil. nat. Uni Bern
Hauptbetreuer: E. Vassella

Philipp Odermatt, PhD
Spinal muscular atrophy: the contribution of microRNAs and the development of a somatic gene therapy by SMN2 spicing correction
Fakultät: phil. nat. Uni Bern
Betreuer Patho: E. Vassella
Hauptbetreuer: Prof. D. Schümperli, Institute of Cell Biology

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3.3 Übrige Publikationen

- Faderl M, Noti M, Corazza N, Mueller C
  Keeping bugs in check: The mucus layer as a critical component in maintaining intestinal homeostasis.
  IUBMB LIFE, 67(4): 275-85, IF 3.143, MR 0.606
- Hewer E, Dettmer MS, Vajtai I
  Oligoastrocytoma: Who's afraid of the … Liger?
  HISTOPATHOLOGY, : n/a-, IF 3.453, MR 0.8
- Hirzel C, Nueesch S, Wendland T, Langer R
  Necrotizing herpes-simplex virus tonsillitis mimicking peritonsillar abscess.
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- Kollár A, Hewer E, Kellner-Weldon F, Ochsenbein A
  Complete pain relief after bevacizumab in a patient with neurofibromatosis type 2.
  ACTA ONCOL, 54(2): 280-8, IF 2.997, MR 0.53
- Yang SH
  Sigmund Freud and Moritz Kaposi: A Resurfaced Collision.
  AM J DERMATOPATH, 37(10): 805-7, IF 1.387, MR 0.459

4 Vorträge

Banz Yara
- 13.11.15, IL-33 signaling contributes to the pathogenesis of myeloproliferative neoplasms, SGPath Jahrestagung, Basel
- 20.01.15, Melanomas in dogs and humans, Compath Seminar, Bern

Berezowska Sabina
- 12.01.15, Lungenkarzinome: Up-to-date zu Molekularpathologie und molekularer Diagnostik. Fortbildung der Thoraxchirurgie/ Pneumologie, Department of Thoracic surgery and Department of Pulmonology, Inselspital Bern
- 14.04.2015, Influenza, COMPATH Seminar, Bern
- 11.05.15, Lungentumore: WHO Klassifikation 2015 – was ist neu. Fortbildung der Thoraxchirurgie/Pneumologie, Department of Thoracic surgery and Department of Pulmonology, Inselspital Bern
- 21.–23.08.2015, Histopathology pearls. SYNS, Seminar
- 03.09.15, Working on the tissue-Pathology, IHC, TMA, COMPATH. First Symposium of the DCR Research Cluster Lung Development Regeneration and Disease, Bern
- 19.11.15, Der Weg zur Diagnose aus Sicht des Pathologen. 2. Fortbildungskurs Bern HRCT – Interstitielle Lungenerkrankungen. Institut für Radiologie, Bern

Diamantis Eva
- 06.09.15, Indications for a strategic role of the stromal cells in the tumour progression of pancreatic cancer, European Congress of Pathology, Belgrade

Freigang Stefan
- 24.02.15, Mitochondrial control of vascular inflammation, Zurich Center for Integrative Human Physiology (ZIHP), Zurich
- 18.03.15, Immune regulation by oxidized phospholipids, World Immune Regulation Meeting (WIRM IX), Davos
- 01.04.15, Fatty acids in the induction and resolution of inflammation, Endocrinology Seminar, University Hospital Basel, Basel
- 21.04.15, Ein neuer Mechanismus der vaskulären Entzündung in der Arteriosklerose, Meeting of the Swiss Heart Foundation, Zurich
- 12.06.15, A novel pathway of vascular inflammation in atherosclerosis, Jahrestagung der Schweizerischen Gesellschaft Kardiologie (SGK) Zurich, Zurich
- 27.11.15, Innate immune recognition of lipids in vascular inflammation, Department of Immunology, University of Geneva, Geneva
- 03.12.15, Fatty acids as pro- and anti-inflammatory mediators in metabolic disease, Cardiovascular and Metabolism Symposium, University of Lausanne, Lausanne

Jin Jing
- 22.05.15, PU.1-regulated ATG16L2 functions in AML differentiation and autophagy, Swiss Society of Hematology, Basel

Krebs Philippe
- 22.01.15, SLC15A4 – a link between lysosomal transport and innate immune receptor function, Institute of Biochemistry and Molecular Medicine, University of Bern, Bern
- 23.02.15, Inflammation, microbes and cancer – Models of immunopathology, Institute of Cell Biology, University of Bern, Bern
- 14.04.15, Cytokines and regulation of myeloproliferative neoplasms, Department of Biomedicine, University of Basel, Basel
- 05.05.15, The IL-33/ST2 pathway contributes to intestinal tumorigenesis in humans and mice, Institute of Immunobiology, Kantonalspital St-Gallen, St. Gallen
- 11.08.15, SLC15A4 – a link between lysosomal transport and innate immune receptor function, Meeting on BioMedical Transporters, Lugano
- 09.11.15, Role of IL-33 signaling for tumorigenesis, Theodor Kocher Institute, University of Bern, Bern
- 17.12.15, mRNA splicing and epithelial integrity, Clinics for Visceral Surgery and Medicine, University of Bern, Bern

Langer Rupert
- 05.06.15, Regression grading after neoadjuvant chemo (rad)/ targeted therapy in the primary tumour and the lymph nodes – which system to use?, 11th International Gastric Cancer Congress Sao Paulo, Brazil June 04–06
- 30.06.15, Tumor regression grading of gastrointestinal carcinomas after neoadjuvant treatment, University of Michigan, Ann Arbor
- 30.06.15, Mesenchymal Lesions of the GI tract, University of Michigan, Ann Arbor
- 03.11.15, Tumor regression grading of gastrointestinal carcinomas after neoadjuvant treatment, University of Geneva, Institute of Pathology

Lugli Alessandro
- 22.03.15, Tumor budding in pre-operative biopsies and resections, Rodger Haggitt Symposium, USCAP, Boston, USA
- 23.03.15, The role of next generation tissue microarray (ngTMA) in biomarker research, 3D-Histtech Symposium, USCAP, Boston, USA
- 06.09.15, Host-related factors in the tumour microenvironment of colorectal cancer : the immunoscore, ESP Annual Meeting, Belgrad, Serbien
- 08.10.15, The prognostic role of the tumor microenvironment in colorectal cancer: Clinicopathological aspects of tumor budding and the immunoscore, Continuing Medical Education Rounds, Institut für Pathologie, Calgary, Kanada
- 06.11.15, Tumor Pathology : the past, the present, the future, Sakura Meeting, Malaga, Spanien
- 23.11.15, The tumor microenvironment in colorectal cancer, Visiopharm Meeting, Kopenhagen, Dänemark
- 24.11.15, LEAN Management System in Clinical Pathology, Internal education rounds, Institut für Pathologie, Kopenhagen, Dänemark

Müller Christoph
- 12.03.2015, Chair, Annual Meeting Swiss Society of Allergology and Immunology 2015
- 25.–27.02.2015, Chair, Wolfsberg Immunology PhD Student Meeting 2015, Wolfsberg
- 19.06.2015, Key note speaker, Mainz D. Annual Meeting of DACED
- 20.10.2015, Research seminaire, Stanford University Medical Center, Department of Neurology and Neurosciences, Stanford USA

Noti Mario
- 25.03.15, Basophils make food hard to swallow, Bern Immunology club (BIC), Institut für Pharmakologie, Bern
- 03.09.15, Innate immune cells in food allergy, imPARAS Food Allergy Meeting, Universidas Madrid, Madrid

Parts Julia
- 22.05.15, Inhibition of the glycolytic enzyme PKM2 allows neutrophil differentiation of ATRA-resistant APL cells, Swiss Society of Hematology, Basel

Perren Aurel
- 27.01.15, One year of the HRA: opportunities and Challenges for the future, BAG-Symposium, Bern
- 11.03.15, How useful is Ki67- should the G1-G3 values be changed?, ENETS Barcelona, Barcelona
- 12.03.15, NEC and MANEC, ENETS Barcelona, Barcelona
- 09.04.15, Pathologie von NET: Derzeitige Standards und neue Trends, Post-ENETS Congress News & Current Standards, Zürich
- 07.05.15, Schilddrüsenpathologie, Symposium Schilddrüsen-zentrum, Zürich
- 21.05.15, How to optimize outcome in patients with GEP-NET (Diagnosis and Prognosis), Scientific Symposium Brüssel, Brüssel
- 02.07.15, The approach for rare NETs: appendix and rectal (Tandem Talk), ESMO 17th Word Congress Gastrointestinal Cancer, Barcelona
- 27.08.15, Lean Management in Pathology, ETH Lausanne, Lausanne
- 08.09.15, Hereditary neuroendocrine tumours in the gastroentero-pancreatic system, 27th European Congress ESP, Belgrad
- 05.10.15, Lean , Präsentation Lean, Biel Spitalzentrum
- 23.10.15, Intestinal NET, NEC and MANEC, 6th Belgian Week of Pathology, Ghent, Beligen
- 23.11.15, Pulmonary NET, the pathological view, Swiss Advisiory Board Meeting, Bern
- 03.12.15, DAXX, ATRX, mechanisms of chromatin remodeling, functions and roles, possible implications in NET (diagnostic, treatment?) also with some «simple» informations for «non-specialized clinicians», The National Congress of GTE, Paris

Rau Tilman
- 10.03.2015, Biobanking 3.0 – what are our expectations?, Tuesday research seminar, Bern
- 28.05.2015, Immunoscore in colorectal cancer: Feasibility aspects to integrate digital pathology for a better healthcare of colorectal cancer patients, DGP, Frankfurt a.M.
- 01.10.2015, Text mining pathology reports for Biobanking: Strenths, limits and perspectives, ESBB congress, London
- 31.10.2015, Identifying Lynch-syndrom patients. The impact of MMR protein detection in endometrial cancer, SGPath, Gyn-Fachgruppen-Meeting, Zürich
- 12.11.2015, Molecularpathological events along the «serrated route» to colorectal cancer, Medical faculty talk, Erlangen
- 03.12.2015, The Immunoscore in colorectal cancer highlights the importance of digital scoring systems in surgical pathology, Melanoma-Bridge, Naples
- 17.12.2015, Mammakarzinom-Subtypen. lokale Erfahrung mit PAM50. Personalisierte Medizin in der Gynäko-onkologie: Fort-schritt oder falsches Versprechen, Brustzentrum Inselspital, Bern

Reubi Jean Claude
- 13.01.15, Plenary lecture: «Peptide membrane receptors as targets in cancer», 3rd Theranostics World Congress on Gallium 68 and PRRT, The Society of Nuclear Medicine and Molecular Imaging (SNMMI) and Johns Hopkins University, Baltimore, USA
- 22.09.15, Invited lecture: «Peptide membrane receptors as targets in cancer», Ipsen Biopharma Ltd, Paris, France
- 21.11.15, Invited lecture: «Regulatory peptide receptors as targets for tumor diagnosis and therapy», 4th annual meeting of the GDR3545: GPCRs, from physiology to drugs, INSERM, Toulouse, France

Schläfli Anna M.
- 28.07.15, RA-mediated autophagy in breast cancer, 11th Summer School, Bönigen

Schmitt Anja
- 23.04.15, FNP: Wie wird`s gemacht und wie ist die Auswertung, Hands On-Kurs SGUM, Sektion ORL, Inselspital Bern
- 23.04.15, FNP Schilddrüse, Abendkurs SGUM, Sektion ORL, Inselspital Bern
- 04.12.15, Hypoxia and Microvessels in Pancreatic Neuroendocrine Tumours – Chicken or Egg?, Labmeeting ARTORG Center, Bern
- 10.12.15, FNP Schilddrüse und Bethesda-Klassifikation, Fortbildung HNO, Inselspital Bern

Schmitt Anja, Mottini Matthias
- 18.12.15, Pathologische Munschleimhaut, was nun? – Von der Erkennung zur Diagnose, Weiterbildung «Rund um's Gesicht», Bellevue Palace Bern

Tschan Mario P.
- 03.10.15, Retinoic Acid (RA)-Mediated Autophagy in Acute Myeloid Leukemia and Breast Cancer Treatment, Invited speaker, Seminar Series, The Beatson Institute, Glasgow
- 19.09.15, Regulation and function of autophagy in retinoic acid mediated therapy of myeloid leukemia and breast cancer, Plenary Speaker: 69° CONGRESSO NAZIONALE Società Italiana di Anatomia e Istologia, University of Ferrara, Ferrara
- 01.12.15, Autophagy, Invited speaker, Autophagy Seminar, University of Konstanz, Konstanz

Vassella Erik
- 12.11.15, Molecular profiling of lung adenosquamous carcinoma: hybrid or genuine type?, Annual Meeting Swiss Society of Pathology, Basel, Switzerland

Wartenberg Martin
- 06.09.15, PTEN aberrations in different tissue compartments of pancreatic cancer are associated with adverse features and worse prognosis., European Congress of Pathology, Belgrade
- 06.09.15, SMAD proteins in pancreatic cancer: A two sided story, European Congress of Pathology, Belgrade

Zlobec Inti
- 18.–22.4.2015, Making the most of your tissue microarrays: the ngTMA for translational (and reverse translational) research, Philadelphia, PA, USA
- 03.–04.12.2015, Application of digital pathology to the construction of high-quality tissue microarrays for biomarker research: the next-generation Tissue Microarray (ngTMA) approach, London, UK

5 Drittmittel

Berezowska Sabina
- Bernische Krebsliga, 02.01.15–31.12.16, CHF 30'000, Nebengesuchsteller: Tschan M. P., Pathologie

Bouchardy Christine
- Swiss National Science Foundation, Co-PI, 01.03.15–28.02.18, CHF 525'000, Nebengesuchsteller: Pierre Chapuis, Giaccomo Puppa, Inti Zlobec

Corazza Nadia
- Novartis, 01.03.12–31.12.50, CHF 60'000.00, Nebengesuchsteller: Ch. Müller, Pathologie

Diamantis Eva
- Bernische Krebsliga, 12.03.13–30.03.16, CHF 70'000

Dislich Bastian
- Bernische Krebsliga, 04.09.15–31.12.16, CHF 60'000, Nebengesuchsteller: R. Langer und M.P. Tschan, Pathologie

Freigang Stefan
- Olga Mayenfisch Stiftung, 01.04.14–31.03.15, CHF 50'000
- Vontobel-Stiftung, 01.10.14–30.09.17, CHF 120'000
- UniBern Forschungsstiftung, 01.06.14–31.05.17, CHF 15'000
- Fondation Johanna Dürrmüller-Bol, 25.08.14–24.08.50, CHF 26'993
- UniBern ID Grant, 01.12.15–30.04.18, CHF 149'517
- SNF, 01.01.15–31.12.17, CHF 510'890
- Nationalfonds R'equip , 01.12.14–30.11.15, CHF 240'876

Guenat Olivier, ATORG
- 3R Research Stiftung, 01.11.15–31.10.16, CHF 138'192, Nebengesuchsteller: St. Freigang, Pathologie

Krebs Philippe
- Marie Curie Career Integration Grants, 01.01.14–31.12.17, CHF 100'000
- Stiftung für klinisch-experimentelle Tumorforschung, 01.05.14–31.12.15, CHF 80'000 Nebengesuchsteller: Y. Banz, Pathologie
- Fondation Johanna Dürrmüller-Bol, 01.02.15–31.01.16, CHF 20'000, Nebengesuchsteller: L. Mager, Pathologie
- Krebsliga Schweiz, 01.12.15–31.11.2016, CHF 124'350
- Olga Mayenfisch Stiftung, 01.10.15–30.09.16, CHF 23'000
- SNF, 01.09.12–31.12.15, CHF 377'366

Langer Rupert
- Cancer Research Switzerland, 31.04.16, CHF 287'000, Nebengesuchsteller: M. Tschan, Pathologie
- Krebsliga Schweiz, 01.09.13–31.12.15, CHF 236'000, Nebengesuchsteller: Tschan M. P., Pathologie
- Krebsliga Schweiz, 22.12.2015–21.12.17, CHF 214'000, Nebengesuchsteller: Tschan M. P., Pathologie

Lugli Alessandro
- Krebsforschung Schweiz, Bern, 01.01.14–31.03.16, CHF 233'700, Nebengesuchsteller: V. Kölzer, Pathologie

MacPherson Andrew, Bern
- SNF (Sinergia), 01.01.15–31.12.17, Total: CHF 2'253291, Nebengesuchsteller: Ch. Müller, Pathologie, CHF 456'531

Mager Lukas
- Gertrud-Hagmann-Stiftung, 01.10.15–30.09.17, CHF 241'566

Marinoni Ilaria
- Stiftung klin.exp.Tumorforschung, 01.06.15–31.05.18, CHF 83'000

Müller Christoph
- SNF, 01.11.11–31.10.16, CHF 623'000.00

Noti Mario
- Novartis Foundation, 01.08.15, CHF 60'000
- Olga Mayenfisch, 01.09.15, CHF 25'000
- Project Pool Mittelbau, 01.08.15–01.08.16, CHF 3'000
- SNF (Ambizione), 01.10.14–30.09.17, CHF 599'156

Perren Aurel
- Krebsforschung Schweiz, 01.08.14–31.08.17, CHF 286'900

Perren Aurel, Marinoni Ilaria
- SNF DAXX, 01.10.12–30.09.15, CHF 367'573
- SNF DAXX, 01.05.15–31.03.16, CHF 27'818

Rogler Gerhard, Uni Zürich
- SNF (SIBDCS), 01.07.14–31.03.16, Total: CHF 7'494'383, Nebengesuchsteller: Ch. Müller, Pathologie, CHF 257'000

Saurer Leslie
- Bernische Krebsliga, 01.10.13–30.09.15, CHF 45'000.00, Nebengesuchsteller: Ph. Krebs, Pathologie
- Novartis, 01.01.14–30.04.16, CHF 60'000.00,

Schäfer Stephan, Vassella Erik
- Bernische Krebsliga, 01.04.14–31.07.15, CHF 70'000

Schmitt Anja
- Bernische Krebsliga, 01.10.12–31.12.15, CHF 76'000

Sokol Lena
- Bernische Krebsliga, 01.06.15–31.05.16, CHF 60'000, Nebegesuchsteller: V. Kölzer, Pathologie

Tschan Mario P.
- Cancer Research Switzerland, 08.01.14–31.07.17, CHF 369'700
- Diverse kleinere Forschungskredite, CHF 90'000
- Berger-Janser Stiftung, 01.01.15–31.12.16, CHF 30'000
- Stiftung für klinisch-experimentelle Tumorforschung, 01.05.15–30.04.17, CHF 81'000
- SNF , 01.01.13–30/6/16, CHF 390'000

Vassella Erik
- Schweiz. Krebsforschung, 01.04.12–31.12.15, CHF 204'400
- SNF, 01.04.12–31.03.15, CHF 290'066, Nebengesuchsteller: Istvan Vajtai, Pathologie Länggasse

Zlobec Inti
- Mach-Gaensslen Foundation, 2014–2015, CHF 39'000
- Johanna Dürmüller-Bol Foundation, 2014–2015, CHF 20'000
- Berger-Janser Stiftung, 2015–2018, CHF 145'620
- Tumorforschung Bern, 2014–2016, CHF 53'226
- Stiftung für klin exp Tumorforschung Bern, 2013–2015, CHF 53'226, Nebengesuchsteller: E. Vassella, Pathologie

6 Preise, Ernennungen, Auszeichnungen

Eva Diamantis
- 06.09.15: Tiniakos ward for best contribution in Digestive Diseases Pathology
  European Congress of Pathology, Belgrade

Stefan Freigang
- 05.02.15: Pfizer Forschungspreis
  Jährliche Preisverleihung, Stiftung Pfizer Forschungspreis, Zürich
  siehe www.pfizerforschungspreis.ch
- 21.04.15: Forschungspreis der Schweizerischen Herzstiftung
  Jährliche Preisverleihung, Schweizerische Herzstiftung, Bern
  siehe www.swissheart.ch/index.php?id=2634
- 31.03.15: Top-5-Finalist, ETH Spark Award 2015
  Jährliche Preisverleihung, ETH Zurich, Zürich
  siehe www.ethz.ch/de/wirtschaft-gesellschaft/erfindungen-patente-lizenzen/spark-award/spark-award-2015.html
- 06.01.15: Universität Bern, Umhabilitation an die Universtät Bern

Jing Jin
- 10.–12. September 2015: Das Autophagie-Gen ATG16L2 ist ein neues transkriptionelles Zielgen des hämatopoietischen Transkriptionsfaktors PU.1 in der Differenzierung von akuten myeloischen Leukämien
  Scholarship AML ESH, International Conference on acute myeloid leukemia «Molecular and translational»: advances in biology and treatment, Budapest, Ungarn

Koelzer Viktor
- 2015: Stowell-Orbison Award, United Stated and Canadian Academy of Pathology (USCAP), Boston

Mario Noti
- 12.03.15: Preis für bestes Poster in Allergologie
  Jahresversammlung SGAI, Basel

Julia Parts
- 10.–12. September 2015: Eine neue Funktion des Glykolyse-Genes PKM2 in der Resistenz zu Retinsäure während der akuten myeloischen Leukämie-Differenzierung
  Scholarship AML ESH, International Conference on acute myeloid leukemia «Molecular and translational»: advances in biology and treatment, Budapest, Ungarn

Inti Zlobec
- 24.–28.10.2015: Travel Grant
  UEGW 2015, United European Gastroenterology Week), Barcelona
- 17.–23.3.2015: Stowell Orbison Award
  United States and Canadian Academy of Pathology (USCAP) 2015, Boston, Preis an Dr. Viktor Kölzer

2015: Stowell-Orbison Award.

Scholarship AML ESH, International Conference on acute myeloid leukemia «Molecular and translational»: advances in biology and treatment, Budapest, Ungarn.

>>> Studentische Lehre

Der Einsatz der Pathologie besteht in Vorlesungen und Kursen für die Studenten der Humanmedizin, der Zahnmedizin, des Studienganges Biomedical Sciences und der Zellbiologie (Cell Biology), wo verschiedenste Vorlesungen, Kurse und Praktika über Histologie, Allgemeine und Spezielle Pathologie, Molekularpathologie und Tumorpathologie von Mitgliedern des Instituts für Pathologie organisiert und angeboten werden. Zudem sind Mitglieder des Instituts aktiv in der Ausbildung von PhD-Studenten der Graduate School for Cellular and Biomedical Science involviert. Die Lehrveranstaltungen werden von Mitarbeitern sowohl der klinischen als auch der experimentellen Pathologie gehalten, wobei je nach Thema und Schwerpunkt des Studienganges bzw. der Veranstaltung Ärzte oder Naturwissenschaftler als Dozenten fungieren.

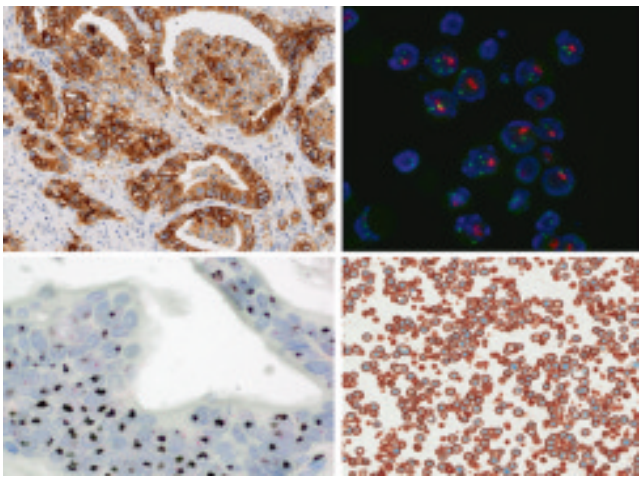
Im Studiengang Humanmedizin begleitet das Fach Pathologie die Studierenden während ihrer gesamten klinischen Ausbildung vom 3. bis zum 6. Studienjahr. In dieser Zeit erhalten sie in Vorlesungen, Makroskopie- und Mikroskopiekursen sowie wöchentlichen Falldemonstrationen einen mehrjährigen strukturierten Unterricht, der die Kenntnisse und das Verständnis für Mechanismen, Zusammenhänge und Morphologie von Erkrankungen vermittelt. In den Kursen werden hierbei makroskopische Präparate aus unserer umfassenden Sammlung zum «Begreifen» der morphologischen Veränderungen als Lehrmittel eingesetzt. Der komplementäre «digitale Histologie-Schnittkasten» erlaubt es den Studierenden, die histologischen Schnittpräparate virtuell zu mikroskopieren, die dann später im Histologiekurs zusammen mit den jeweiligen Fachdozenten besprochen werden.

Die Grundlagen der Allgemeinen Pathologie lernen die Studierenden im 3. Studienjahr (Einführungskurs 1). Dies geschieht zum einen eingebettet in interdisziplinäre Vorlesungsveranstaltungen, die spezielle Themenblöcke behandeln, zum anderen im Fachpraktikum Pathologie, wo unterstützt durch die Histologie die Grundmechanismen der Pathologie und der entsprechenden wesentlichen morphologischen Veränderungen behandelt werden. Daneben ist die Pathologie auch an zahlreichen PBL-Tutoriaten des 1. bis 3. Studienjahrs beteiligt. In einem Vertiefungsseminar «Pathologie» haben die Studierenden zudem die Gelegenheit, das Tätigkeitsbild des Pathologen hautnah im Rahmen von Führungen durch das Institut kennenzulernen.

Im 4. Studienjahr (Einführungskurs 2) und im 5. Studienjahr (Schlusskurs 1) wird das erlangte Wissen auf die spezielle, organbezogene Pathologie angewendet. Hierbei wird ein systematisches Curriculum durchlaufen, das alle Organsysteme und ihre wichtigsten Erkrankungen abdeckt. Es besteht aus theoretischen Vorlesungen und praktischen Kursen, in denen die Studierenden sich mittels Makroskopie und Mikroskopie vertiefende Kenntnisse aktiv erarbeiten. Ergänzend finden wöchentliche Autopsiedemonstrationen statt, in denen anhand aktueller Fallbeispiele die aktive Erarbeitung pathophysiologischer Zusammenhänge und Sequenzen verschiedenster Krankheiten im Vordergrund steht.

Im 6. Studienjahr ist die Pathologie im Schlusskurs 2 als fachübergreifende Disziplin an mehreren interdisziplinären Vorlesungen beteiligt und behandelt auch eigene Schwerpunkte, wie die «Klinisch Pathologische Konferenz», die fest im Stundenplan verankert ist.

Zuletzt gibt es für Studierende, die ihre Kenntnisse im Fach Pathologie vertiefen wollen oder sich für eine spätere Fachausbildung in diesem Fach interessieren, die Möglichkeit eines 1- bis 2-monatigen Einsatz im Rahmen des Wahlstudienjahrs. Hier durchlaufen die Wahlstudierenden ein strukturiertes Curriculum, im Rahmen dessen alle Tätigkeitsgebiete der Pathologie, wie die Autopsie, die makroskopische und die histologische Diagnostik und die Zytologie, aber auch die Molekularpathologie, kennengelernt werden können. Ebenso wird unser Institut bei den Studierenden als sehr guter Ort angesehen, um im Rahmen einer Masterarbeit einen ersten Kontakt mit wissenschaftlichen Arbeiten zu erhalten und auch später wird die Möglichkeit wahrgenommen, solche Arbeiten zum Beispiel in einer späteren Dissertation fortzusetzen.



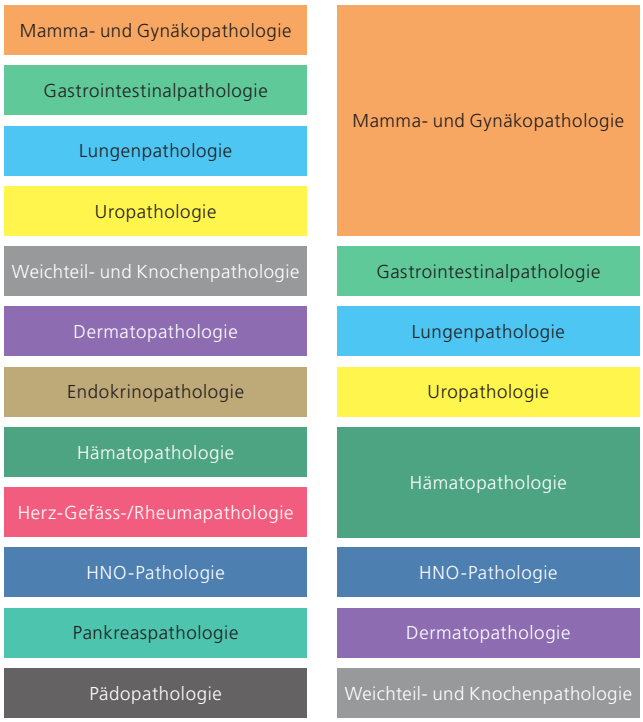
Verschiedene Methoden zur Bestimmung von HER2 an Adenokarzinomen des Ösophagus: Tumorgewebe (links) mittels Immunhistochemie und Silber-In-situ-Hybridisierung; Tumorzelllinien (rechts) mittels Fluoreszenz-In-situ-Hybridisierung und Immunhistochemie.

>>> Weiterbildung

Ärztliche Weiterbildung im 21. Jahrhundert soll nicht nur den Nachwuchs für den Fachbereich garantieren, sondern Perspektiven schaffen, die zukunftsweisend sind und eine neue Wendung nehmen, um dem Strukturwandel und dem jährlich steigenden Spezialisierungsdrang Rechnung zu tragen. Zusätzlich soll sie modern, attraktiv und motivierend, gleichzeitig aber auch bedarfsgerecht sein und die notwendigen Kompetenzen ökonomisch vermitteln. Strategisches Ziel unseres Pathologie-Weiterbildungsprogramms ist, herausragende Diagnostiker, Forscher, und führende Pathologen in dieser sich entwickelnden Spezialität auszubilden.

Unser Weiterbildungsprogramm stellt die klinisch orientierte Funktion der Pathologie in den Vordergrund und entspricht den wachsenden fachlichen Anforderungen. Es verfügt über **definierte Abschnitte (Module),** welche durch das Mitbestimmen durch die Assistenzärzte selbst, unterschiedlich gestaltet werden können, sodass keine starre, aber eine klare, zeitlich und inhaltlich flexible Struktur entsteht, welche den unterschiedlichen Bedürfnissen und Fähigkeiten der Assistenzärzte entspricht.

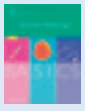
Das Modul 1 ermöglicht einen Einblick in die Pathologie, vermittelt das Basiswissen und ist sowohl als Einstieg für Fachanwärter direkt nach dem Staatsexamen (Erstjahr-Pathologieassistenten) als auch für Assistenzärzte mit anderen Fachrichtungen, welche ein Jahr Pathologie als Fremdjahr absolvieren möchten, geeignet. Die Dauer des Moduls 1 beträgt maximal 12 Monate und kann je nach Erfahrung und Lernkapazität verkürzt werden. Die Reihenfolge innerhalb des Moduls ist nicht vorgegeben, so kann z.B. der Themenblock 1B oder 1C vor 1A absolviert werden.



Weiterbildungsmodule.

Das Modul 2 stellt den Hauptkorpus der spezifischen Pathologie-Ausbildung dar, dauert maximal 36 Monate und kann ebenfalls je nach Erfahrung und Lernkapazität verkürzt werden. Die Reihenfolge, der Inhalt und die Schwerpunkte können und sollen flexibel gestaltet werden. Die Absolvierung der Themenblöcke setzt das Erfüllen der Mindestanforderungen der FMH voraus.

Modul 1



- **1A: Autopsie 1**
- **1B: Zuschnitt 1**
- **1C: Histo 1**
- **Mini-CEX**
- **DOPS**

6–12 Monate

Modul 2

- **2A: Histo 2**
- **2B: Schnellschnitte**
- **2C: Zuschnitt 2**
- **2D: Autopsie 2**
- **Mini-CEX**
- **DOPS**

24–36 Monate

Modul 3

- **3A: Zytologie**
- **3B: Niere, Leber, Neuro, Sarkome**
- **Tumorboards**

6 Monate

Modul 4

- **4A: Mol Path**

6 Monate

- **4B: Forschung**
- **TRU**
- **ExPath**

6 Monate

Modul 2 mit flexiblen Untereinheiten.

Das Modul 3 verkörpert die Ausbildung im Bereich Zytologie und gibt den Assistenzärzten die Möglichkeit, einen Einblick in die Diagnostik von hoch spezialisierten Gebieten, wie die Nieren- und Leberbiopsien, zu gewinnen. Selbstständige Vorbereitung und Präsentation von klinisch pathologischen Konferenzen und Tumorboards sind ebenfalls Inhalt dieses Moduls.

Es wird empfohlen, dass die Anmeldung für die Facharzt-Prüfung erst nach Absolvierung aller Themenblöcke der Module 1 und 2 sowie des Themenblocks A des Moduls 3 erfolgt.

Das Modul 4A ermöglicht einen Einblick in die modernen diagnostischen Methoden der Molekularpathologie, die für die Patienten therapierelevant sind.

Themenblock 4B des Moduls 4 ist fakultativ, gibt den Assistenzärzten die Möglichkeit, sich näher mit modernen Forschungsmethoden auseinanderzusetzen und an existierenden Forschungsprogrammen der Translational Research Unit und/oder der experimentellen Pathologie teilzunehmen.

Die Reihenfolge zwischen den verschiedenen Modulen und deren Untereinheiten ist mit wenigen Ausnahmen nicht vorgegeben und kann zeitlich und inhaltlich individuell je nach Bedürfnis der Assistenzärzte unterschiedlich gestaltet werden.

Zusätzlich sind in das Weiterbildungsprogramm Zwischenevaluationen (Arbeitsplatz-basierte Assessments) als Etappenkontrollen integriert. Evaluationsmethoden wie Mini-CEX und DOPS werden als essenzieller Bestandteil der Weiterbildung und strukturiertes Rückmeldungsinstrument betrachtet. Aus der Zwischenbilanz erfolgt eine neue Zielvereinbarung.

Mini-CEXs werden zweimal jährlich durchgeführt. Dabei wird der Assistenzarzt bei der mikroskopischen Fallabgabe, unter Beachtung folgender spezieller Punkte, beobachtet:

Arbeitsplatz-basiertes Assessment

Fokus		**Mini-CEX** Problemstellung: Mikroskopische Fall-Beurteilung	Was war gut	Was kann verbessert werden	Gemeinsam formulierte Lernziele
	Vorbereitung des Falles: – Alle Schnitte und Spezialfärbungen gut angeschaut? – Vorbefunde kontrolliert? – Makro gelesen und evtl. korrigiert?				
	Klinische Urteilsfähigkeit: – Beste Evidenz gefunden und kritisch bewertet? – Evidenz auf den Patienten gemäss klinischen Angaben anwendbar? – Evidenz in eine passende Diagnose bzw. DD umgesetzt? – Kommentar?				
	Spezielle Punkte: – TNM vollständig (Parallelbefunde einbezogen)? – Abstände kontrolliert? (falls passend) – IHC oder Spezialfärbung nötig? Wenn ja, welche? (angemessen?) – Zweitbericht nötig?				
	Organisation / Effizienz				
	Professionelles Verhalten				
	Gesamteindruck				

Datum der Durchführung:

Weiterbildner/in: Ärztin/Arzt in Weiterbildung:

Unterschrift: Unterschrift:

Mini-CEX-Formular.

DOPS (ebenfalls zweimal jährlich) wird bei der makroskopischen Präparatverarbeitung eingesetzt. Dabei werden die praktischen Fertigkeiten des Assistenzarztes direkt beobachtet. Es folgt die Erteilung eines relevanten Feedbacks.

Arbeitsplatz-basiertes Assessment

Fokus		**DOPS** Problemstellung: Makro-Zuschnitt	Was war gut	Was kann verbessert werden	Gemeinsam formulierte Lernziele
	Vorbereitung: – Makrobuch gelesen?				
	Technische Fertigkeit und Geschick: – Zuschnitt effizient? – Beste Evidenz gefunden? – Alle relevanten Befunde erkannt und eingebettet? – Deutlich und effizient diktiert? –Makro-Foto? – Laborlegende (wo was entnommen wurde, Spezielles)?				
	Klinische Urteilsfähigkeit: – Makroskopische Diagnose (Differentialdiagnose) – Klinische Angaben mitberücksichtigt?				
	Sicherheit				
	Organisation / Effizienz				
	Professionelles Verhalten				
	Gesamteindruck				

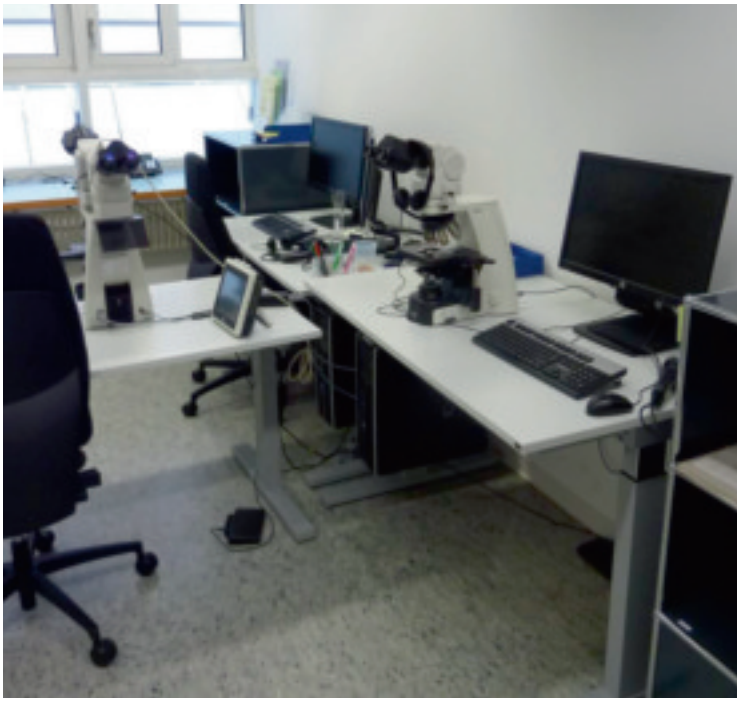
Datum der Durchführung:

Weiterbildner/in: Ärztin/Arzt in Weiterbildung:

Unterschrift: Unterschrift:

DOPS-Formular.

Im Institut für Pathologie der Universität Bern wird die Assistentenweiterbildung in der Routine-Diagnostik («sign-out»), in für diesen Zweck und für die bessere Dienstleistung speziell ausgestatteten «sign-out rooms» durchgeführt. Diese erlauben die ungestörte Durchführung der Routine-Diagnostik unter optimalen Bedingungen. Zudem verstärken sie das «Team-Gefühl» zwischen Facharzt und Assistenzarzt, erhöhen die Motivation, dienen einer schnelleren und besseren Dienstleistung und bieten täglich reichlich Gelegenheit für Teaching und Evaluation.



Einrichtung eines Diagnostikraums.

>>> Fortbildung

Dienstagsseminare 2015

	Titel	Referent/-in
13.01.	COMPATH: one medicine, one pathology, one platform	Dr. Alessandra Piersigilli Institute of Animal Pathology
20.01.	Naturally occurring melanomas in dogs as models for human melanoma	Comparative pathology (Joint Seminar with Vetsuisse) Bongiovanni Laura, Banz Yara
27.01.	News in digital pathology	Dr. Carol Geppert Pathology Institute, Universitätsklinikum Erlangen
03.02.	Rectal Cancer from the Surgery's Point of View	Dr. med. Lukas Brügger Chirurgie Inselspital
10.02.	The Cdx2 homeobox gene: from intestinal homeostasis to alternative splicing	Prof. Jean-Noël Freund INSERM Institut Strassburg
24.02.	The role of TREM-1 in the pathogenesis of atherosclerosis	Dr. D. Zysset Institut für Pathologie, Bern
03.03.	Virus-induced susceptibility to superinfections	Dr. Andreas Bergthaler Research Center for Molecular Medicine of the Austrian Academy of Sciences, Vienna, Austria
10.03.	Biobanking 3.0 – what are our expectations?	Dr. med. T. Rau
17.03.	Probevorträge USCAP	intern
24.03.	Inflammation in metabolic disease and atherothrombosis – from JNK to sirtuins	Prof. Dr. med. Christian M. Matter Universitätsspital Zürich, Klinik für Kardiologie
31.03.	Functions of metabolic reprogramming in disease	Dr. Dimitrios Anastasiou MRC National Institute for Medical Research, The Ridgeway Mill Hill, London, UK
07.04.	miRNA-mediated control of autophagy in Crizotinib-treated ALK-positive Anaplastic Large Cell Lymphoma	Dr. Sylvie Giuriato Research Group Leader, Cancer Research Center of Toulouse (CRCT)
14.04.	Morphologic aspects of Aspergillosis in birds, comparisons with human infections	Comparative pathology (Joint Seminar with Vetsuisse) Regenscheit Nadine, Berezowska Sabina
21.04.	Targeting Tumor Initiating Cells in Lung Cancer	Thomas Marti, PhD, Group Leader Forschungsabteilung Thoraxchirurgie
28.04.	Molecular and histopathological basis for individualized therapy in patients with gastro-oesophageal cancer	Prof. Dr. Heike Grabsch Department of Pathology, Maastricht University Medical Center
05.05.	Islet inflammation in type 2 diabetes: from physiology to pathology	Professor Marc Donath Endocrinology, Diabetes and Metabolism & Dept of Biomedicine, Uni Basel
12.05.	Vascular molecules in inflammation and leukocyte migration	Professor Beat Imhof Department of Pathology and Immunology, University of Geneva
19.05.	CNS tumors: Pathogenesis and new concepts of molecular classification	Prof. Sebastian Brandner UCL Institute of Neurology, The National Hospital For Neurology and Neurosurgery, London

	Titel	**Referent/-in**
26.05.	Involvement of RANK signaling in the development of non-small cell lung cancer	Prof. Meylan Etienne EPFL, School of Life Sciences, ISREC Institute, Lausanne
02.06.–18.08.	Semesterferien	
25.08.	Probevorträge ECP	intern
01.09.	Barrett Esophagus: the gastroenterologist's point of view	Prof. Radu Tutuian Gastroenterologie, Tiefenauspital
21.09.	GI cancer sequencing inside and outside the 100,000 Genomes Project	Prof. Ian Tomlinson Molecular and Population Genetics, Wellcome Trust for Human Genetics, Oxford
08.09.	Epigenetics in neuroendocrine tumors (ausgefallen)	Prof. Chrissie Thirlwell Kings College, London
22.09.	Clinical Data Warehouse als Bestandteil einer nachhaltigen Forschungsinfrastruktur	Dr. med. Thomas Ganslandt Leiter Abteilung IT für Forschung & Management, Universitätsklinikum Erlangen
29.09.	Angiogenesis and vascular differentiation in NETs	Prof. Jean-Yves Scoazec Institut Gustave Roussy, France
06.10.	Immunoregulatory function of a putative new microRNA encoded by small nucleolar RNA 104	Dr. med. Stefan Kuchen Oberarzt und Laborleiter Department für Rheumatologie, Immunologie und Allergologie, Inselspital
13.10.	Mouse model of endocrine pancreatic cancer	Comparative pathology (Joint Seminar with Vet Suisse) Piersigilli Alessandra, Perren Aurel
20.10.	FAQs on the Whipple Resection	Prof. Beat Gloor Viszeralchirurgie, Inselspital
23.10.	The interpretation of mismatch repair gene mutations in Lynch syndrome	Dr. Ian M. Frayling, MA MB BChir PhD FRCPath FEBLM University Hospital of Wales, Cardiff
03.11.	Probevorträge SGPath	intern
10.11.	Tumor host interaction, tumor progression and therapy	Prof. C. Rüegg University of Freiburg (CH)
24.11.	The influence of tissue oxygenation and interstitial salt deposition on macrophage-driven antimicrobial defense	Prof. Dr. Jonathan Jantsch Institute for Medical Microbiology and Hygiene, Franz-Josef-Strauss-Allee 11, D-93053 Regensburg
01.12.	Organs-on-chip technologies: hopes and challenges	Olivier T. Guenat, PhD, Assistant Prof. Lung Regeneration Technologies Lab, ARTORG Center, University of Bern
08.12.	Die nicht abheilende Pneumonie	Dr. Michael Grob Pneumologie, Spitalzentrum Biel
15.12.	Research in Progress	Gruppe Prof. M. Tschan
22.12.–29.12.	Semesterferien	

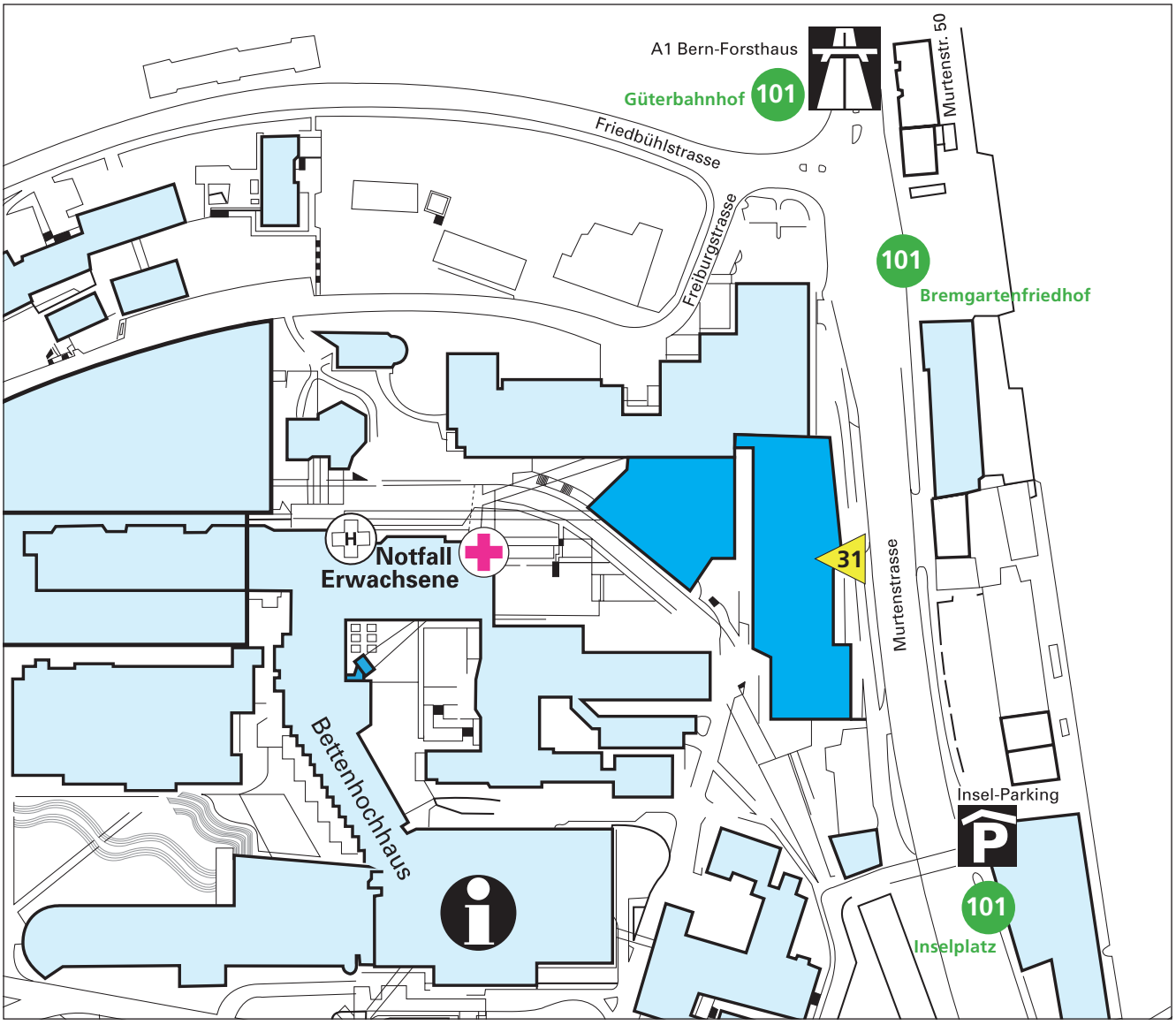
>>> Im Fokus: Schnellschnittfahrzeug

Eine rasche und sichere Diagnose steht bei den Kunden an oberster Stelle. Gerade bei den intraoperativen Schnellschnitten spielt der Faktor Zeit eine grosse Rolle; hier muss ein eingespieltes Team aus Ärzteschaft und Laborpersonal Arbeit auf höchstem Niveau verrichten. Interne Schnellschnitte werden per Kurier oder Rohrpost in die Klinische Pathologie gesendet. Von diesem Zeitpunkt an dauert es bei internen Schnellschnitten zirka 20 Minuten, bis die Diagnose dem Operationsteam mitgeteilt und somit das weitere operative Prozedere festgelegt werden kann.

Was passiert aber mit den Spitälern, welche nicht mit einem eigenen Institut für Pathologie ausgestattet sind?
Die Proben werden jeweils entweder per Kurier oder Taxi in ein naheliegendes pathologisches Institut eingesandt. Dies hat einen hohen Zeitverlust zur Folge und es dauert dementsprechend länger, bis das entscheidende Telefonat an das Operationsteam erfolgen kann. Will diese Klinik dennoch nicht auf ein rasches Resultat verzichten, muss ein entsprechender Raum eingerichtet werden. Dies wiederum steht mit finanziellem und personellem Mehraufwand in Verbindung, wobei in den meisten Fällen die Kosten-Nutzen-Rechnung suboptimal ist.

An unserem Institut wurde dieses Thema durch ein Projektteam aufgegriffen und die Lösung eines Schnellschnittfahrzeuges, eines mobilen Labors, erarbeitet. Das Resultat ist ein komplett ausgerüstetes und den Sicherheitsstandards entsprechendes Schnellschnittlabor auf vier Rädern. Der Einsatzort ist flexibel, die einzige Voraussetzung seitens der Klinik ist ein Stromanschluss. Qualifiziertes Fachpersonal steht aus dem bestehenden Mitarbeiterkontingent zur Verfügung, sodass die Implementierung sehr erfolgreich verlaufen ist und das Fahrzeug in regelmässigem Einsatz steht. Im Jahr 2015 wurden ab August 23 Einsätze für die Spitäler Solothurn und Burgdorf durchgeführt.

>>> Situationsplan



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