UNIVERSITÄT BERN

Institut für Pathologie

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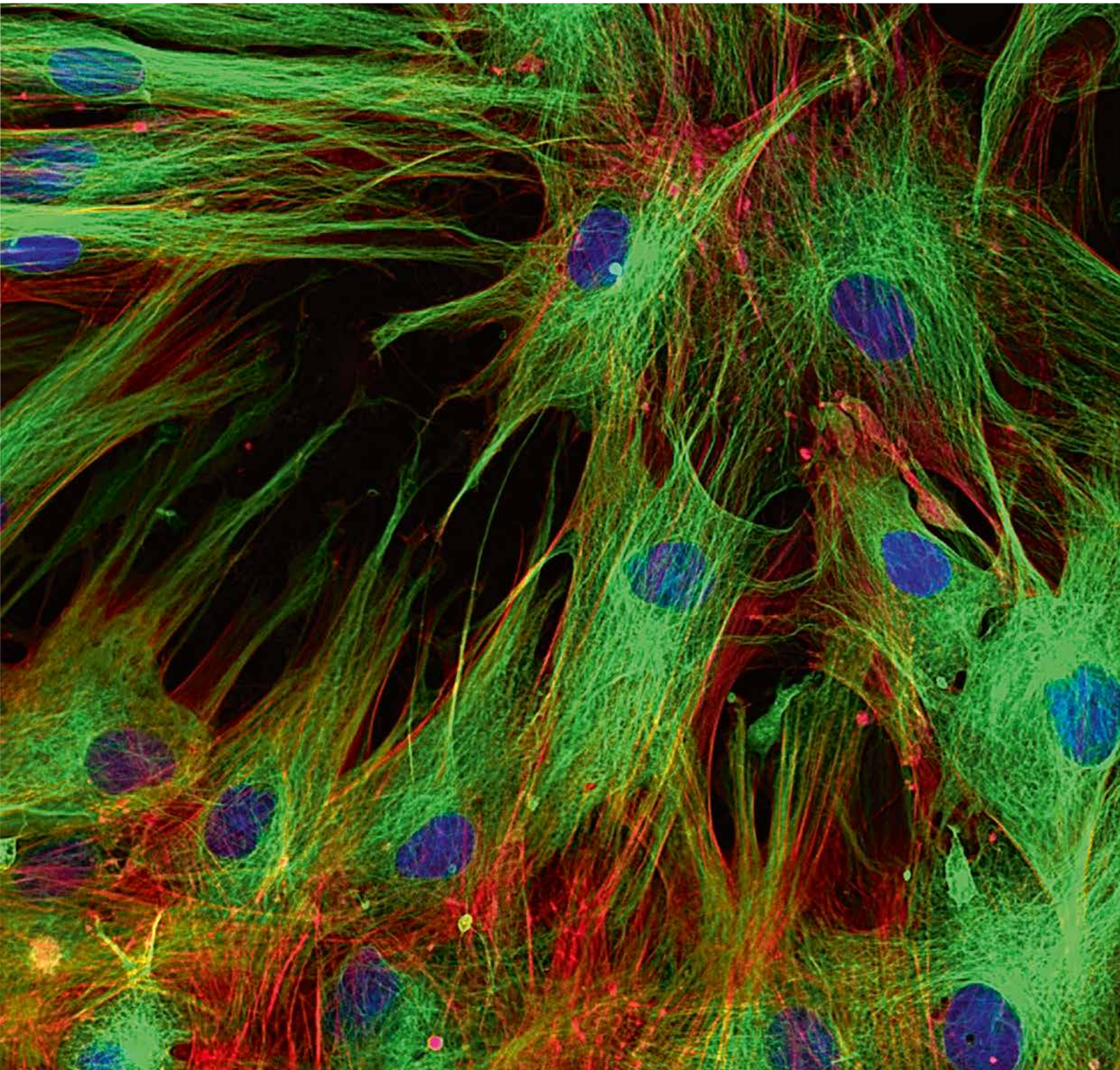
Jahresbericht 2018



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>>> Das Wichtigste in Kürze

Liebe Leserin, lieber Leser

Ich freue mich über Ihr Interesse am Jahresbericht 2018 des Instituts für Pathologie! Auch 2018 konnten wir wichtige Schritte der Weiterentwicklung unseres Institutes abschliessen. Wie Sie «im Fokus» am Ende dieser Ausgabe sehen, haben wir das Akkreditierungs-Audit durch die Schweizerische Akkreditierungsstelle (SAS) erfolgreich bestanden und sind jetzt nach den Normen ISO 17025 und 15189 akkreditiert.

Die Umsetzung **synoptischer Berichte** für maligne Erkrankungen schreitet weiter voran, die wichtigsten malignen Erkrankungen werden strukturiert nach internationalen Vorgaben des ICCR (International Collaboration on Cancer Reporting) oder der CAP (College of American Pathologists) berichtet. Gemeinsam mit allen anderen schweizerischen Pathologie-Instituten arbeiten wir im SNF-geförderten **PathoLINK-Projekt** daran, die Pathologie-Berichte zu standardisieren und alle benötigten Datenpunkte einzeln zu erfassen. Hier konnten wir inzwischen die Machbarkeit nachweisen und hoffen, dass wir dieses System 2019 ausbauen können.

Gemeinsam mit den Insel-Kliniken Humangenetik, der Hämatologie und der Pharmakogenomik läuft das Projekt des **«Clinical Genomics lab»** (CGL). Dieses Labor wird sämtliche molekularen Untersuchungen gemeinsam durchführen, um der Tatsache der laufenden Methodenkonvergenz gerecht zu werden. Wir gehen davon aus, dass in Zukunft immer häufiger Exom- und Genom-Sequenzierungen im klinischen Alltag durchgeführt werden. Das CGL bietet auch die Laborplattform für das neu gegründete Bern Center for Precision Medicine der Universität (BCPM) an. Seit Januar 2019 hat die ehemalige Molekularpathologie als erste Gruppe die neuen Räumlichkeiten beziehen können.

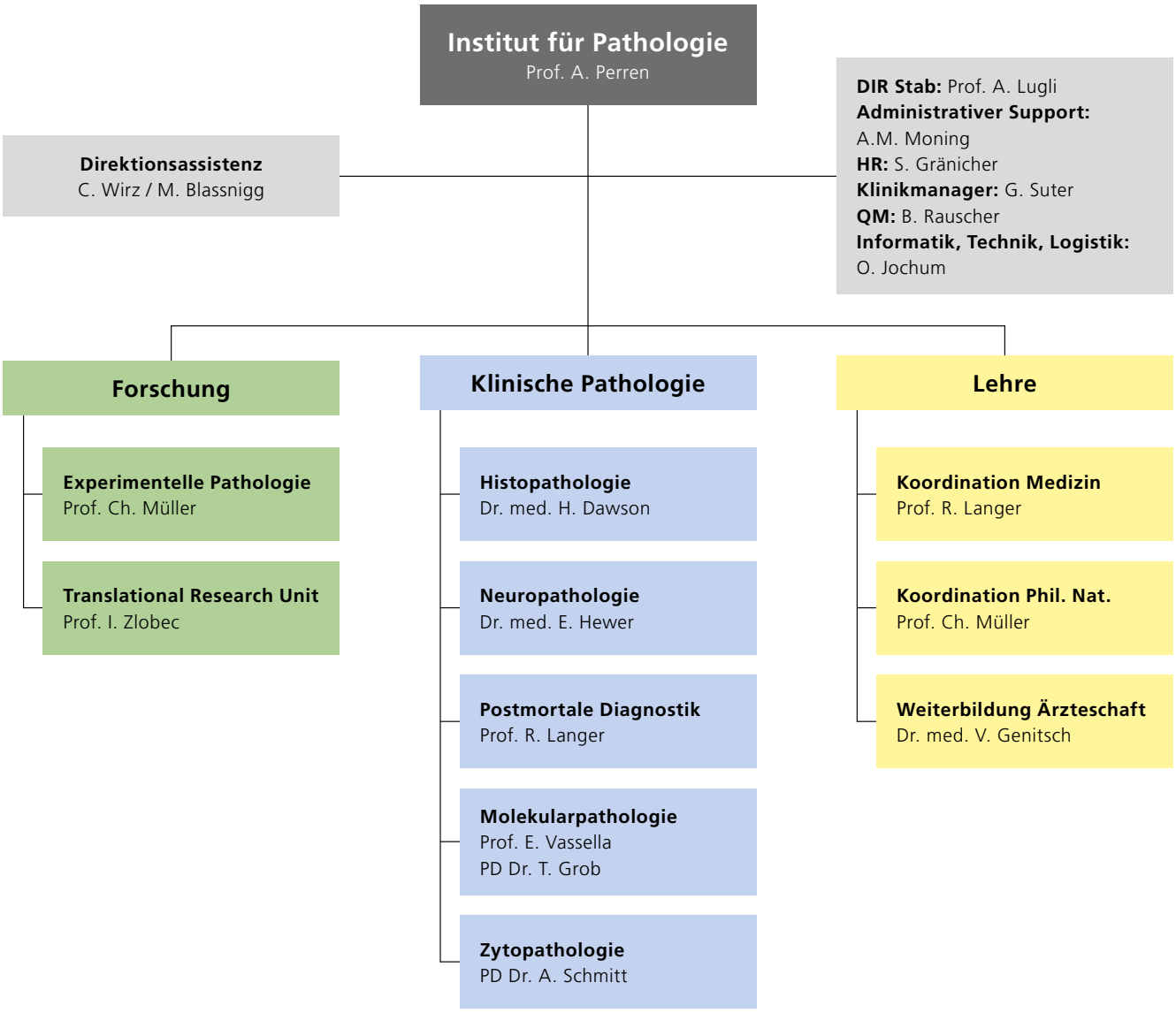
In der Lehre konnten wir die Planung der Vorlesungen mit +100, den zusätzlichen 100 Studierenden der Medizin, welche ab Wintersemester 2019 im 3. Studienjahr mit der Allgemeinen Pathologie beginnen werden, abschliessen. Wir konnten in diesem Rahmen sowohl im Bachelor- als auch im Masterstudiengang die Anzahl Vorlesungen besser den Bedürfnissen der Studierenden anpassen. Wir freuen uns schon auf den Start im Herbst 2019!

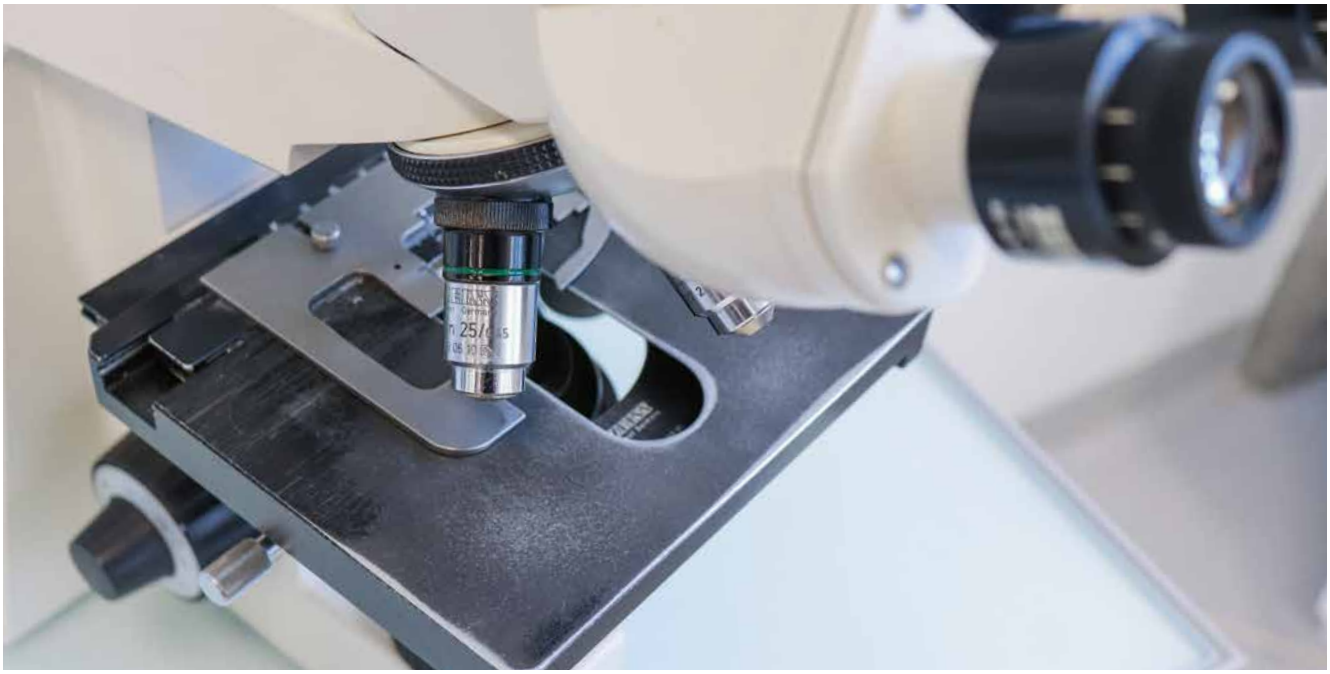
Ich wünsche Ihnen viel Spass bei der Lektüre.

Ihr Aurel Perren, Direktor


Diagnostik
und
Forschung

>>> Organigramm





>>> Dienstleistung

1 Klinische Pathologie

Leiter: Prof. Dr. med. Alessandro Lugli

Im Jahre 2018 lag der Hauptfokus auf die Akkreditierung, welche im März erfolgreich durchgeführt werden konnte. Die im Jahresbericht 2017 definierten Ziele konnten grösstenteils umgesetzt werden. Im Rahmen der stattfindenden Tumorboards wurde die Zusammenarbeit der Fachgruppen der Pathologie mit den Kliniken intensiviert. Die Spracherkennung wurde technisch und logistisch aufgesetzt und wird im Frühjahr 2019 eingeführt. Gemäss unseren organisatorischen Pfeilern «LEAN Management System» und «Projektmanagement» wurde eine Optimierung der Arbeitsprozesse der Klinischen Pathologie und zentralen Dienste durch folgende Restrukturierungsmassnahmen im Hinblick auf das Jahr 2019 vorbereitet: Die Einheiten Administrativer Support (Support Center und Berichtssekretariat), ITL (Informatik, Technik und Logistik), Personalbüro, Klinik- und Qualitätsmanagement bilden neu den Direktionsstab mit dem Ziel, Dienstleistung, Lehre und Forschung optimal zu unterstützen.

Durch die gleichzeitige Inbetriebnahme des Clinical Genomic Lab (CGL) wurde auch die Klinische Pathologie reorganisiert und besteht neu aus den Einheiten Ärzteschaft und Laboratorien, welche auf den Plattformen Histopathologie, Zytopathologie, Immunhistochemie und Postmortaler Diagnostik basieren. Die Ziele für das Jahr 2019 beinhalten die Standardisierung und Festigung der Arbeitsprozesse in den neu definierten Strukturen und die fortlaufende Implementierung digitaler Prozesse im Rahmen der «Digital Pathology» Projekte.

1.1 Ärzteschaft

Die Ärzteschaft ist in 18 Fachgruppen organisiert und besteht aus 19 Fachärztinnen und Fachärzten, welche von 10 Assistierenden unterstützt werden. An den zahlreichen wöchentlichen Tumorboards/Fallbesprechungen innerhalb des Inselspitals und in auswärtigen Spitälern vertritt die Fachärzteschaft die Pathologie in der interdisziplinären Zusammenarbeit mit den Kliniken. Im Rahmen der Mitgliedschaft in den Fachgesellschaften und Arbeitsgruppen auf nationaler und internationaler Ebene wird das Fachwissen durch den Besuch nationaler und internationaler Kongresse auf dem neuesten Stand gehalten. Zusätzlich wird die Forschungsaktivität durch die Translational Research Unit (TRU) und die Experimentelle Pathologie optimal unterstützt.

1.2. Neuropathologie

Im Jahr 2018 untersuchte der Bereich Neuropathologie nahezu 1500 Proben. Wir zählen damit weiterhin zu den diagnostisch aktivsten Neuropathologien in der Schweiz. In Zusammenarbeit mit dem Neuromorphologischen Labor der Neurologischen Klinik des Inselspitals wurden rund 80 Muskelbiopsien untersucht. Im Bereich der Postmortalen Diagnostik führten wir einschliesslich konsiliarischer Untersuchungen im Auftrag des Instituts für Rechtsmedizin rund 80 Hirnsektionen durch. Entsprechend dem Charakter der Neuropathologie als Schnittstelle zwischen den klinischen Neurofächern, der Labordiagnostik und translationaler Forschung war der Fachbereich Neuropathologie auch im Jahr 2018 in zahlreichen Veranstaltungen insbesondere in Zusammenarbeit mit Klinken des Inselspitals engagiert. Darüber hinaus ist das Fach Neuropathologie Teil des Neuroonkologischen Tumorzentrums und einer der Schwerpunkte der Medizinischen Allianz Bern/Basel (MBB).

1.3. Postmortale Diagnostik

Im Jahr 2018 wurden im Institut für Pathologie 134 postmortale Untersuchungen durchgeführt, inclusive neuropathologische und pädopathologische Untersuchungen. 49 davon waren Fälle aus dem Inselspital Bern. Nach dem Abschluss der Implementierung der «Postmortalen Diagnostik» im Vorjahr wurde dieses Konzept erfolgreich weitergeführt. Unsere Erfahrungen konnten zudem im «Virchows Archiv», der Fachzeitschrift der European Society of Pathology publiziert werden (Langer et al. Implementation of modern tools in autopsy practice-the way towards contemporary postmortal diagnostics. Epub 2018 Nov 13).

1.4. Labor Histopathologie und Immunhistochemie

Histopathologie

Im vergangen Jahr lag der Fokus klar bei der Akkreditierung, welche dank guten Vorarbeiten erfolgreich bestanden wurde. Seither werden die Prozesse nach diesen Vorgaben des Qualitätsmanagements ausgeführt. Das Labor Histopathologie wurde bereits nach Lean-Management geführt und die Prozesse nach klaren Richtlinien strukturiert, so dass die Akkreditierung keinen kompletten Kulturwechsel erforderte.

Weiter wurden die im Jahr 2017 eingeführten neuen Organisationsstrukturen weiter vertieft und verfeinert. Auch die Dienstplananpassungen wurden 2018 feinjustiert, so dass der Probenfluss trotz erhöhter Einsendezahl nicht beeinflusst war.

Das Tracking-System, die lückenlose Rückverfolgbarkeit einer Probe, wurde ebenfalls auf alle neuralgischen Punkte im Laborprozess mit Dashboards erweitert. Dies ermöglicht beispielsweise bei der Mikrotomie zu erkennen, wie viele Paraffinblöcke noch zu erwarten sind. Ebenso können die täglichen Fallzahlen der diagnostizierenden Pathologen graphisch dargestellt werden, so dass eine korrekte Verteilung durch das Labor vorgenommen werden kann.

Insgesamt konnte im Vergleich zum Vorjahr die Einsendezahl (Biopsien und Exzisate) von 43607 (2017) auf 45491 (2018) gesteigert werden (4.3%). Die Anzahl Schnellschnitte im Labor und die Einsätze mit unserem Schnellschnittfahrzeug blieb konstant +1.3% (1761 im 2017, 1784 im 2018).

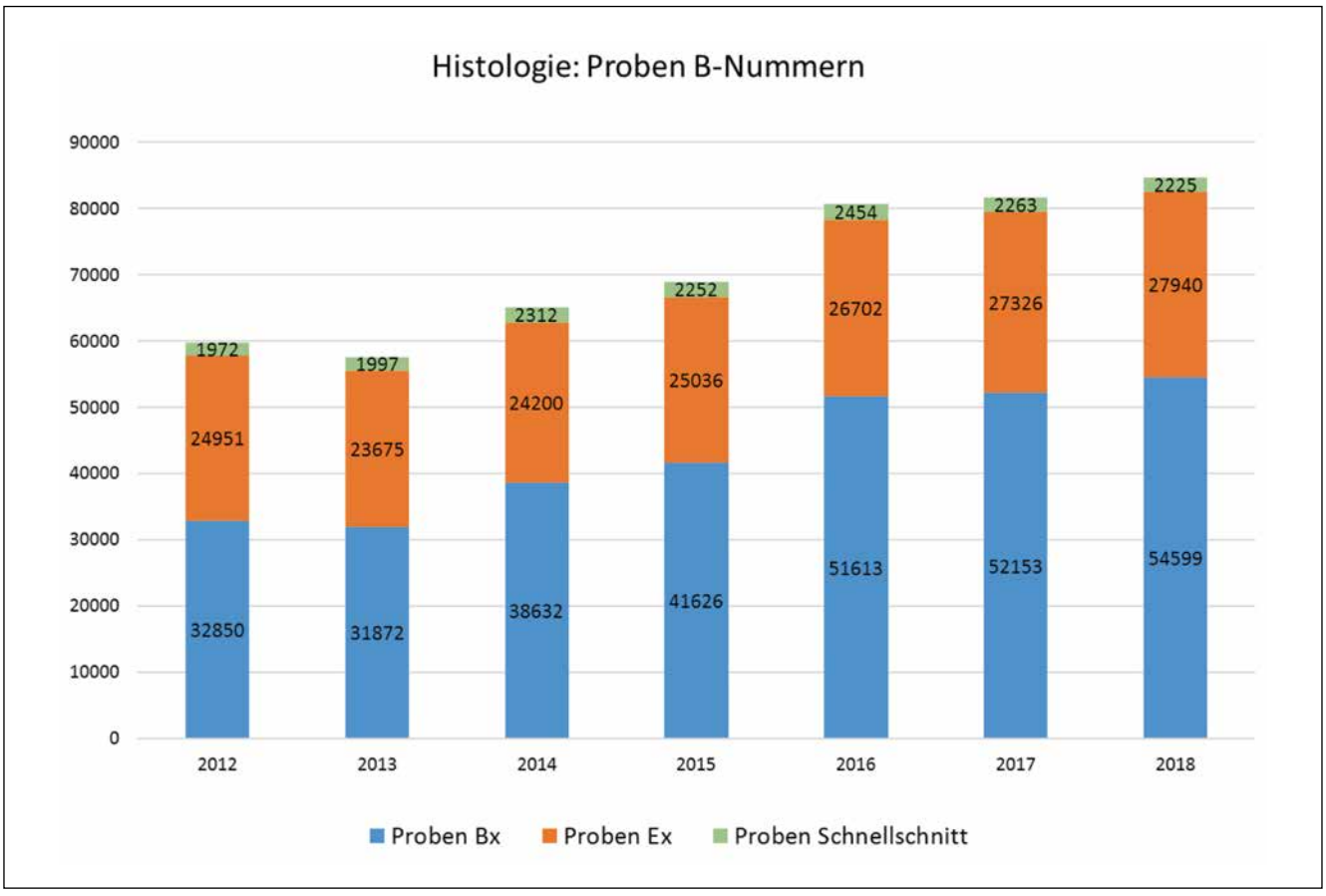
Immunhistochemie
Das Hauptziel 2018 der Abteilung Immunhistochemie war sicherlich die Akkreditierung im Februar 2018, welche dank der optimalen Vorbereitung durch das ganze Team erfolgreich verlaufen ist.

Eine Umstrukturierung in der Leitung, d.h. der Schaffung einer operativen Ebene zur Unterstützung des Teams machte es möglich, die Kernaufgabe des Labors mit hohem Qualitätsstandard weiterzuführen und sich zusammen mit der TRU der Digitalisierung von Schnitten für Tumorboards, Konsilien und Zweitmeinungen zu widmen.

Am Ende des Jahres stehen der Immunhistochemie 276 Primärantikörper für diagnostische Untersuchungen zur Verfügung. Es wurden an 8822 Fällen insgesamt 51'971 diagnostische Färbungen an Paraffinschnitten vorgenommen. Die Anzahl bearbeiteter nativer Nierenbiopsien ist mit 201 Fällen im Jahr 2018 leicht rückläufig.

1.5. Berichtswesen

Per 1. April 2018 wurden in den bis anhin getrennt geführten Bereichen «Befundsekretariat» sowie «Logistik und Support» personelle und strukturelle Veränderungen definiert. Diese Vorbereitungsarbeiten führten strukturell zur Einheit «Administrativen Support», welcher aus dem Befundsekretariat und dem Support Center besteht. Das Ziel ist es, vorhandene Synergien und Ressourcen optimiert einzusetzen und zu nutzen.



2 Molekularpathologie

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

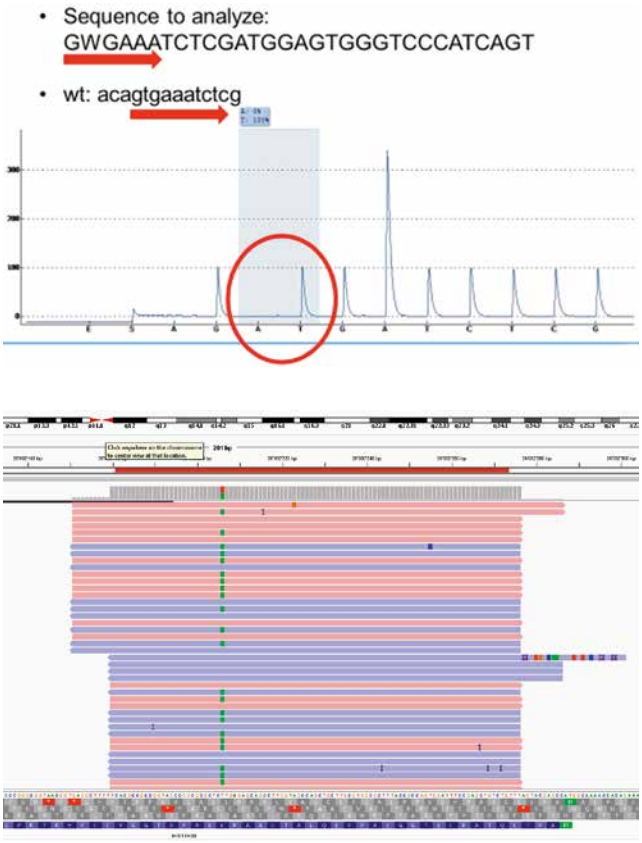
Technischer Leiter: Prof. Dr. pharm. Erik Vassella
Medizinischer Leiter: PD Dr. med. et phil. Tobias Grob

Mitarbeiterinnen Molekularpathologie-Labor
Cornelia Schlup, Laborantin
Nicole Klaus, Laborantin
Brigitte Jossen, Laborantin
Sonja Gempeler, Laborantin
Diana Abele, Laborantin
Regula Tinguely, Laborantin
Maja Neuenschwander, Laborantin

In der Molekularpathologie verwenden wir die Methoden der PCR-Analyse, Sequenzierung (PCR-Labor) und Fluoreszenz *In situ* Hybridisierung (FISH-Labor). Das Molekularpathologie-Labor ist seit dem 29.11.2017 bei der Schweizerischen Akkreditierungsstelle SAS entsprechend der Norm ISO/IEC 17025: 2005, ISO 15189:2012 und SN EN ISO/IEC 17025:2005, SN EN ISO 15189:2013 akkreditiert.

Das Analysenspektrum des PCR-Labors umfasst den Nachweis von Mutationen, Promoter-Methylierung, Mikrosatelliten-instabilität, B- und T-Zellklonalität sowie den Nachweis spezifischer Erreger. Die Tests haben diagnostische oder prädiktive Implikation und können an Formalin-fixiertem und Paraffin-eingebetteten Gewebe durchgeführt werden. Die Schlüsseltechnologie in der Molekularpathologie ist die «Next-Generation Sequencing» (NGS), welche in den letzten vier Jahren zu einer exponentiellen Zunahme der Aufträge führte. Im letzten Jahr haben insbesondere Auftrage für grosse Genpanels (Oncomine comprehensive gene panel) stark zugenommen. Die NGS erlaubt auch den Nachweis von Fusionstranskripte und wird bei Krebspatienten für den Entscheid einer zielgerichteten Therapie eingesetzt. Die FISH Analyse erlaubt den Nachweis von Translokationen oder Amplifikationen bei unterschiedlichen Tumoren. Im letzten Jahr haben wir insbesondere in die Etablierung eines neuen Genpanels zum Nachweis der Mutationslast investiert. 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.

Pyrosequencing – *BRAF*



Die NGS-Analyse im JGV Browser zeigt eine spezifische Mutation an.

In diesem Jahr wurde Zusammenlegung der vier Labore vorbereitet, welche im Inselspital und der Universität Bern molekulare Diagnostik anbieten: Neben der Molekularen Pathologie sind dies die Speziallabore aus Hämatologie, Genetik und klinischer Chemie. Standort des neuen Labors ist das 6. OG des Instituts für Pathologie, welches durch Umbauarbeiten von Oktober bis Dezember den neuen Bedürfnissen angepasst wurde. Die Gründung des Clinical Genomics Lab (CGL) wurde im Dezember von Universitätsleitung und der Direktion der Insel Gruppe beschlossen. Ab Januar 2019 wird das CGL als eigenständiges Labor des Inselspitals unter der Leitung von Tobias Grob betrieben. Die Kompetenzen der verschiedenen Fachbereiche werden zusammengeführt, um in der neu aufgebauten Einheit das gesamte Spektrum der klinischen molekularen Diagnostik auf höchstem Niveau anzubieten. Das CGL wird zudem ein zentrales Standbein des geplanten Zentrums für Precision Medicine und wird zukünftig als Core Facility für Hochdurchsatzsequenzierung die klinische und translationale Forschung am Standort Bern stärken.

3 Klinische Zytopathologie

Leiterin: PD Dr. med. A. Schmitt Kurrer

«Doing more with less»: das ist die Devise der Zytopathologie und das entspricht den zukünftigen Anforderungen an die Pathologie als Ganzes. Dies spiegelt sich in einer stetig zunehmenden Anzahl zytologischer Proben wider. Im Jahr 2018 untersuchten wir 11623 Proben (+10%) aus der gynäkologischen und 10326 Proben (+4%) aus der extra-gynäkologischen Zytologie. Insgesamt hat im Zeitraum 2013–2018 das Probenvolumen um 33% zugenommen.

Ein Höhepunkt des Jahres war die Ausrichtung der Jahrestagung der Schweizerischen Gesellschaft für Zytologie im Oktober. Es gelang nicht nur, ausgezeichnete Referenten zu gewinnen, sondern auch das Format mit «Tandem Talks» jeweils eines klinischen und eines zytologischen Experten zu Facetten eines Themas wurde vom Publikum sehr positiv aufgenommen.

Die 2016 gegründete interdisziplinären Schilddrüsensprechstunde an der Universitätsklinik für Diabetologie, Endokrinologie, Ernährungsmedizin & Metabolismus (UDEM) des Inselspitals wurde so erfolgreich fortgesetzt, dass nun für 2019 ein Ausbau dieses Angebots vorgesehen ist, um grosse Zahl von Konsultationen bewältigen zu können.

Um auch in Zukunft eine qualitativ hochstehende zytologische Diagnostik anbieten zu können, engagiert sich die Zytologie auch in der Fort- und Weiterbildung von ÄrztInnen und von ZytotechnikerInnen.

4 Fachgruppen des Instituts für Pathologie der Universität Bern

Stand Januar 2018

Dermatopathologie	
H. Dawson	031 632 99 60
Y. Banz	031 632 88 75

Endokrinopathologie	
A. Perren	031 632 32 22
M. Dettmer	031 632 99 69
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
H. Dawson	031 632 99 60
V. Genitsch	031 632 99 22
M. Montani	031 632 32 67
M. Wartenberg	031 632 49 76

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

Herz-, Gefäss- und Rheumapathologie	
Y. Banz	031 632 88 75
V. Genitsch	031 632 99 22
M. Trippel	031 632 32 76

HNO-Pathologie	
M. Dettmer	031 632 99 69
M. Wartenberg	031 632 87 54
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
L. Terracciano	031 632 99 01

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
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
M. Wartenberg	031 632 87 54

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

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

Postmortale Diagnostik	
R. Langer	031 632 32 47
Y. Banz	031 632 88 75
A. Lugli	031 632 99 58
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

Makropathologie	
Y. Banz	031 632 88 75
M. Trippel	031 632 32 76
A. Lugli	031 632 99 58

IHC	
R. Langer	031 632 32 47
S. Berezowska	031 632 49 37
V. Genitsch	031 632 99 22

5 Dienstleistungsstatistik

Klinische Pathologie

Histopathologie	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**
Anzahl Einsendungen	32'710	35'293	37'232	42'422	43'607	**45'491**
Anzahl Lokalisationen	58'795	66'420	70'286	82'069	83'191	**86'253**
Anzahl Einsendungen Schnellschnitte	1'472	1'673	1'647	1'936	1'761	**1'784**
Anzahl Proben Schnellschnitte	1'997	2'307	2'252	2'454	2'264	**2'225**
Autopsie						
Anzahl durchgeführte Autopsien	155	156	152	146	130	**134**
Zytopathologie						
Total Anzahl Einsendungen	14'237	13'788	16'043	16'634	16'995	**17'814**
Anzahl Proben Klinische Zytologie	8'361	8'418	11'582	9'324	9'956	**10'326**
Anzahl Proben Gynäkologische Zytologie	8'054	7'726	9'375	9'869	10'563	**11'623**
Total Anzahl Einsendungen Proben	16'415	16'144	20'957	19'193	20'519	**21'949**
Anzahl Zellblöcke	2'277	2'324	2'748	2'837	3'334	**3'844**
Immunhistochemie						
Anzahl Fälle (Blöcke) Diagnostik (Paraffin)	7'104	8'313	7'843	9'094	7'681	**8'822**
Anzahl Färbungen Immunfluoreszenz (Nierenbiopsien)	2'101	2'280	2'079	2'772	2'464	**2'010**
Anzahl Fälle Immunzytologie am Ausstrich	302	372	197	158	258	**201**
Anzahl Färbungen Immunzytologie am Ausstrich	586	–	240	486	364	**377**
Anzahl Färbungen Diagnostik (Paraffin)	–	52'532	47'944	44'366	47'597	**51'971**
Molekularpathologie						
Anzahl Fälle PCR-basierende Tests	1'420	1'304	1'444	1'624	1'870	**2'020**
Anzahl Fälle Lymphome	214	218	216	221	227	**191**
Anzahl Fälle Methylierungsnachweis	180	128	88	114	174	**136**
Anzahl Fälle Mutationsanalysen (EGFR, kRAS, BRAF, IH1/2 + weitere)	818	902	870	508	251	**225**
Anzahl Fälle NGS-Analysen	–	–	87	247	354	**643**
Anzahl Fälle PAM50 (Nanostring)	–	–	18	48	38	**33**
Anzahl Fälle FISH	287	554	627	744	650	**726**
Anzahl Hybridisierungen FISH	391	683	839	981	715	**974**

Tumorbank

Anzahl Einsendungen Tumorbank	831	894	1'030	1'417	1'879	**1'593**
Anzahl Eingänge TRU	166	465	457	604	602	**738**

>>> 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
Aurel Perren, MD, & Ilaria Marinoni, PhD
Mirjam Schenk, PhD
Mario Tschan, PhD
Erik Vassella, PhD

Translational Research Unit (Core Facility) (TRU)
Research groups supported by TRU
Yara Banz, MD, PhD
Sabina Berezowska, MD
Eva Diamantis-Karamitopoulou, MD
Rupert Langer, MD
Alessandro Lugli, MD
Inti Zlobec, PhD

Organisational aspects

The eight research groups of the **Division Experimental Pathology** pursue their own research projects, primarily supported by extramural funding. Major pieces of equipment are shared among the experimental research groups and, upon an initial training in the approporiate use («support platforms»), can be also accessed by the research personel of the other units of the Institute of Pathology. This allows for an efficient use of the limited financial ressources, but may also foster scientific collaborations among the research staff at the Institute of Pathology.

The core lab of the Translational Research Unit

The Translational Research Unit (TRU) is a research facility providing tissue-based services to internal and external researchers, collaborators in the Department of Biomedical Research (DBMR), Insel hospital, and other university laboratories. Our research platform performs activities for Tissue Bank Bern (TBB) and for the Comparative Pathology Platform of the University of Bern (COMPATH).

1.1 The Division of Experimental Pathology

Head: Christoph Mueller, PhD

Research activities

Thematically the research activities of the currently eight 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, such as the identification of novel biomarkers for disease activity in remitting – relapsing inflammatory disorders and cancer, and the development of novel vaccination strategies against solid tumors.

The Division of Experimental Pathology also hosts the Biobank of the SNSF funded Swiss IBD cohort study (SIBDCS). At the end of 2018 more than 58'000 biosamples (serum, plasma, biopsies, DNA) from 2904 patients with IBD were stored in the biobank and are made available to qualified scientists for research purposes.

Personnell

In 2018 the research group of Prof. Aurel Perren and PD Dr. Ilaria Marinoni became formally affiliated with the Division of Experimental Pathology. At the end of 2018 more than 50 persons were working within these 8 research groups.

Grant Support

In 2018 the total amount of new external funding obtained by the research groups of the Division of Experimental Pathology exceded CHF 3 Mio (for details see: Reports of the individual research groups).

Research infrastructure and collaborations

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, Cell-IQ® continuous live cell imaging and analysis system and a Nanostring® Platform for multiplexed assays for gene expression and mutation analysis, but also on core facilities, provided by the Dept. of Biomedical Research, including the FACS (cytometry) core facility, and the genomics core facility (with access to an Ion Torrent® instrument). 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 Next Generation Sequencing platform of the University of Bern (equipped with an Illumina HiSeq3000, an Illumina MiSeq and, since 2018, with a NovaSeq Sequencing instrument). Several of our research groups also use the central mouse facility, and the germ-free and gnotobiotic mouse facility (Clean Mouse Facility) at the Medical Faculty. In addition to these facilities, through collaborative efforts we also have access to other state-of-the-art facilities, including the metabolomics facilities at the Institute 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), live-cell metabolic assays on a Seahorse XF Analyzer, 3D- cell cultures, but also the entire spectrum of FACS-based techniques in cell sorting and multi-color analysis. Highly sophisticated methodologies are established for the identification of miR's and their target sequences in normal, and diseased tissues, the assessment of autophagy, and several distinct transfection systems, including lentivirus-based transduction systems, and mRNA expression profiling from small numbers of cells and microdissected tissues are available. Furthermore, several of our research groups have a longstanding expertise in isolating and culturing primary cells, such as immune cells, primary AML blast cells, mesenchymal stromal cells, including liver sinusoidal endothelial cells, and epithelial cells from patient material, but also from experimental animals. Experimental protocols for determining the functional capacities of these cell subsets ex vivo and in vitro are established and optimized.

Forschungsgruppe Stefan Freigang (Research group Stefan Freigang).

Group of Stefan Freigang, MD

Johanna Baumgartner, PhD student
Thi Thuy Hang Bui, PhD student
Svenja Ewert, research technician
Olivier Friedli, PhD student
Nadia Oehninger, medical doctorate student
Tiina Partanen, research technician

Summary of research activities

Immune recognition of lipids in inflammation and immunopathology

Lipids represent critical structural components of biological membranes as well as a significant energy source for cellular metabolism, and thus are of fundamental importance for the survival of our organism. In addition, endogenous and environmental lipids may become targets of innate and adaptive immune responses. The immune recognition of microbial and self-lipids is essential for successful anti-infectious immunity, but also contributes to chronic inflammation in metabolic disorders, such as diabetes and cardiovascular disease. Our group investigates the immune recognition of lipids in microbial infections and metabolic dysfunction.

Research Activities

Project 1: Molecular mechanisms of lipid-induced inflammation

Cardiovascular diseases, particularly atherosclerosis-related diseases, remain the leading cause of death worldwide. While first clinical trials demonstrated the beneficial effects of anti-inflammatory therapies in CVD patients, a better understanding of the molecular mechanisms of vascular inflammation will be critical to develop more effective treatment strategies. Recent advances in the field of immunometabolism generated strong interest in delineating metabolic pathways that influence macrophage responses in atherosclerosis. In this project, we study mechanisms of IL-1-driven vascular inflammation that are linked to metabolic perturbation and mitochondrial dysfunction.

Project 2: Immune regulation by oxidized lipids

Exposure of cellular membranes to reactive oxygen species creates a broad range of distinct oxidized phospholipid (OxPL) species that may actively modulate cellular signaling processes and immune responses. We have previously described cyclo-pentenone-containing OxPLs and their isoprostanes as pro-resolving lipid mediators. This project investigates the OxPL-signaling in myeloid cells during atherogenesis and microbial infection using functionalized lipid probes and a novel oxidative stress reporter.

Project 3: Glycolipid-sensing by Natural Killer T cells

Natural killer T (NKT) cells are innate-like T cells with powerful immunoregulatory functions that recognize self and microbial glycolipids presented by CD1d molecules. While the efficacy of NKT cell agonists is currently explored in the immunotherapy of infectious diseases and cancer, the mechanisms that control CD1d antigen presentation and NKT cell activation in vivo still remain incompletely understood. This project cha-

racterizes pathways linking CD1d antigen presentation to lipid metabolism, and aims to define critical effector functions of NKT cells in microbial infections.

Internal Collaborations
- Christoph Mueller, PhD
- Vera Genitsch, MD

External Collaborations
National
- Marc Donath, MD, University of Basel, Switzerland
- Cem Gabay, MD, University of Geneva, Switzerland
- Olivier Guenat, PhD, University of Bern, Switzerland
- Martin Hersberger, PhD, University Children's Hospital Zurich, Switzerland
- Philippe Renaud, PhD, University of Bern, Switzerland

International
- Paul B. Savage, PhD, Brigham Young University, Provo UT, USA

Grant Support
- SNF 310030_152872, S. Freigang, CHF 510'000 (2015–2018)
- Vontobel-Stiftung, S. Freigang, CHF 120'000 (2014–2018)
- UniBE-ID Grant, S. Freigang, CHF 150'000 (2016–2018)
- 3R Research Foundation, S. Freigang (Co-PI), *CHF 138'000 (2016–2018)
- Swiss Lung Liga, S. Freigang (PI), *CHF 162'000 (2017–2019)
- UniBE-ID Grant, S. Freigang (PI), CHF 150'000 (2018–2019)
- UniBE2021 PhD fellowship, J. Baumgartner, CHF 90'000 (2017–2020)

* total amount of funding; funding shared by PI and Co-PI

Administrative duties
- Member of the Expert Commission of the Graduate School for Cellular and Biomedical Sciences of the University of Bern
- Research Retreat of the Institute of Pathology, Kandersteg 2018
- Radiation Safety Officer for the Institute of Pathology

Project 1:
En face preparations of the mouse aorta. The atherosclerotic lesions induced by feeding a high fat diet were revealed by staining with Oil Red O.

Forschungsgruppe Philippe Krebs (Research group Philippe Krebs).

Group of Philippe Krebs, PhD

Ludmila Cardoso Alves, MSc, PhD (until end of 10/2018)
Nick Kirschke, technician (until end of 8/2018)
Thodoris Koutsandreas, guest/exchange PhD student (since 9/2018)
Ioannis Kritikos, BSc, MSc student (until end of 2/2018)
Coline Nydegger (since 15.09.2018)
Regula Stuber Roos, technician, 90%
Lester Thoo Sin Lang, MSc, PhD student
Marie-Hélène Wasmer, MSc, PhD student (until end of 11/2018)
Wen Jie (Jeremy) Yeoh, MSc, PhD student (since 15.11.2018)
Vivian Vu, MSc, PhD student (since 9/2018)

Summary of Research Activities

Chronic inflammation of microbial etiology has been suggested as the underlying cause of several debilitating conditions, particularly in patients afflicted with inflammatory bowel disease (IBD) or certain types of malignancies. Our group uses mouse models and specimens from human patients to study the role of specific genes or molecular pathways for inflammation-triggered immunopathology or tumor development. We aim at a better understanding of the mechanisms underlying these pathways to possibly reveal novel therapeutic targets.

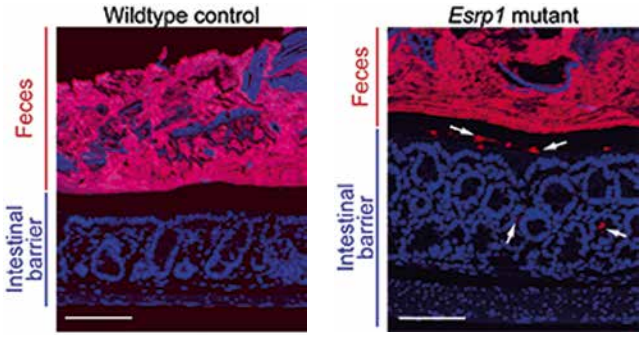
Research Activities

Project 1: Role of cytokine signaling for tumor development

Inflammation is a driver of cancer. We have shown that IL-33 signaling is important for the development of myeloproliferative neoplasms (MPN), a type of blood cancer, and for promoting colorectal cancer (CRC) (Mager et al., J Clin Invest, 2015; Mertz et al., OncoImmunology, 2015). We currently investigate the contribution of IL-33 to MPN progression and to the cellular and molecular mechanisms underlying IL-33-dependent CRC. For these studies, we use patient-derived samples and mouse models.

Project 2: MRNA splicing and epithelial integrity

The intestinal barrier is often disrupted during intestinal diseases, causing gut leakiness. We have recently shown that the protein ESRP1, a regulator of mRNA splicing in epithelial cells, has a critical function to maintain the integrity of the



Project 2: Bacteria (white arrows) penetrate the leaky intestinal barrier of Esrp1 mutant mice.
Scale bars: 100 µm (from Mager et al., eLife, 2017).

intestinal barrier (Mager et al., eLife, 2017). In this project, we further investigate how loss or reduction of ESRP1 leads to intestinal pathogenesis, including 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
- Mario Noti, PhD
- Inti Zlobec, PhD
- Alessandro Lugli, MD
- Yara Banz, MD, PhD

External Collaborations
National
- Alexandre Theocharides, MD, Division of Hematology, University Hospital Zurich, Zurich
- Guido Beldi, MD, Clinics for Visceral Surgery and Medicine, Bern
- Adrian Ochsenbein, MD, Carsten Riether, PhD, Dept. Clinical Res., University of Bern
- Burkhard Ludewig, DVM, Institute of Immunobiology, Cantonal Hospital St.-Gallen
- Esslinger Christoph, PhD, Memo Therapeutics AG, Zürich

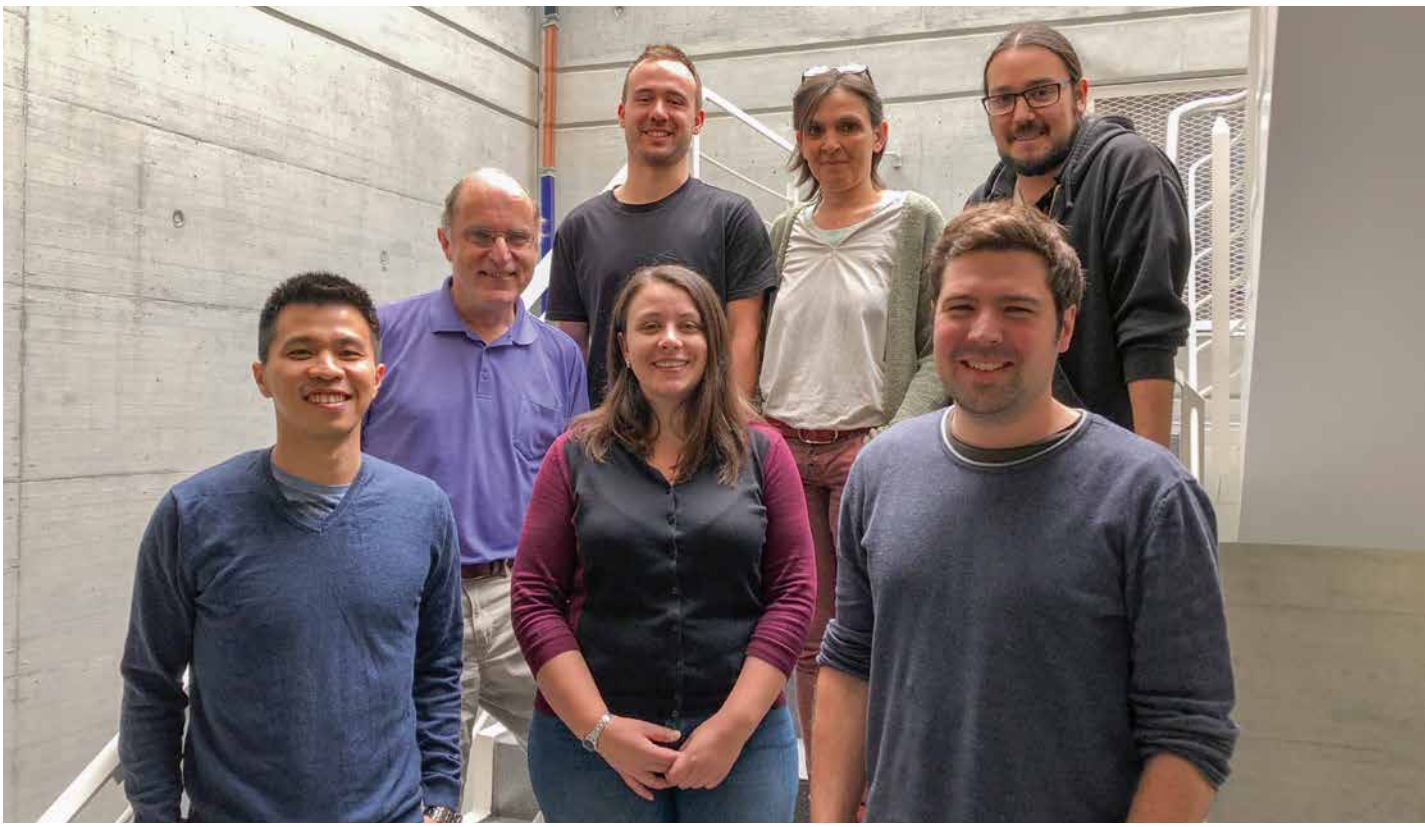
International
- Kathy McCoy, PhD, University of Calgary, Calgary, Canada
- Bruce Beutler, MD, UT Southwestern Medical Center, Dallas, TX, USA
- Astrid Westendorf, PhD, Universitätsklinikum Essen, Essen, Germany

Grant Support
- Marie Curie Career Integration Grants (CIG), Philippe Krebs, EUR 100'000 (2012–)
- Seed money project, Philippe Krebs, CHF 10'000 (2018–2019)
- Lungenliga Bern, Philippe Krebs, CHF 79'554 (2018–2020)
- Lungenliga Schweiz, Philippe Krebs, CHF 79'554 (2018–2020)
- Swiss Cancer Research foundation, Philippe Krebs, CHF 312'500 (2017–2020)
- SNSF 163086, Philippe Krebs, CHF 525'000 (2016–2019)
- Kurt und Senta Herrmann Foundation, Philippe Krebs, CHF 30'000 (2017–2018)
- Fondazione San Salvatore, Philippe Krebs, CHF 120'000 (2016–2018),
- Gertrud-Hagmann-Stiftung, Mager/Krebs, CHF 241'566 (2015–2018)
- Swiss Life/Jubiläumsstiftung, Philippe Krebs, CHF 30'000 (2017–2018)
- Carigest , Philippe Krebs, CHF 130'000 (2018–2020)
- UniBE ID (Interdisciplinary) Grants, Main PI: Philippe Krebs, *CHF 75'000 (2018–2020)
- Commission for Technology and Innovation, Co-PI: Philippe Krebs, **CHF 737'539 (2017–2019)
- EU / Marie Skłodowska-Curie RISE, Co-PI: Philippe Krebs, **€ 904'500 (2018–2022)

* own share

** total amount of funding; funding shared by PI and Co-PI; part for group Krebs is contingent on milestone-based assessment, overall project achievement and number of staff exchanges.

Administrative duties
- Member of the Expert Commission of the Graduate School for Cellular and Biomedical Sciences of the University of Bern
- Biosafety Officer for the Institute of Pathology
- Member of the in-house Steering Committee «Digital Pathology»
- Panel member of the Scientific Evaluation Committee French National Cancer Institute (INCa), 2018 Call



Forschungsgruppe Christoph Mueller (Research group Christoph Mueller).

Group of Christoph Mueller, PhD

Pablo Banicles, MSc, technician, 90% (since 2/2018)
Nadia Corazza, PhD, staff scientist/co-PI, 60%
Kwong Chung Cheong Kwet Choy, PhD, post-doc
Silvia Rihs, technician, 90% (till 3/2018)
Alexandra Suter, technician, 60% (SIBDCS biobank)
Diego von Werdt, PhD student
Daniel Zysset, PhD, post-doc

Summary of Research Activities

Immune surveillance in tissues

Our research focuses on the complex immunoregulatory mechanisms operative in the intestine during homeostatic conditions, and on potential predispositions for the development of chronic inflammatory conditions, notably, in patients with inflammatory bowel diseases (IBD).

Current research topics include:

– Molecular and cellular events that are operative during induction and resolution of chronic intestinal inflammation
– Functional plasticity of tissue-resident T cells and the regulation of their resident life style in barrier tissues
– The contribution of distinct monocyte/macrophage subsets in the induction of chronic inflammatory disorders such as IBD or atherosclerosis, but also in the immunosurveillance of tumors.

Research Activities

Project 1: Changes in local immune cell subsets during in onset vs. remission of inflammatory bowel diseases

Understanding the mechanisms that drive remission induction and maintenance in the intestine is critical for a rational treatment of patients with inflammatory bowel diseases. We have recently established a reversible, relapsing-remitting mouse model of colitis with reproducible onset of colitis and induced remission (Brasseit et al., Mucosal Immunol 2016). In this model we will monitor the composition of the intestinal microbiota during relapsing – remitting colitis and define its consequences on the metabolic profile in the feces and the host. Furthermore, we investigate how these changes influence the host immune response and vice versa. An ultimate goal is to identify strategies to specifically extend the remission period, or even prevent further relapses of the disease.

Projekt 2: TREM-1 as an amplifier of inflammation in immunosurveillance and immunopathologies

TREM-1 (Triggering Receptor Expressed on Myeloid Cells-1) is an activating innate immune receptor on neutrophils and subsets of monocytes / macrophages. We previously described a critical pathogenic role for TREM-1 in acute inflammation, and also during chronic inflammation such as in inflammatory bowel diseases (Schenk et al., J Immunol 2005, J Clin Invest 2007). We further generated a Trem1-/- mouse (Weber et al.

PLoS Pathog 2014) and investigated the consequences of TREM-1-activation on the pathogenesis of atherosclerosis (Zysset et al., Nat Comms 2016) and on the development of colitis-associated colorectal carcinoma (Saurer and Zysset et al., Sci Rep 2017). Current research interests include the involvement of TREM-1 in neurological disorders and in infections with intracellular pathogens.

Project 3: Functional plasticity and retention of tissue-resident TRM cells in the intestinal mucosa
Our group has a longstanding interest in the functions of intestinal T cells which comprise a heterogenous population of conventional and unconventional T cells. Some intestinal T cell subsets represent the prototypical example of tissue-resident T cells due to their resident location at a barrier site, their abundance, and their limited capacity to recirculate. Currently, we mainly focus on the regulation of intestinal resident T cells in protective immunity during infectious diseases (e.g. infection with Listeria monocytogenes), but also on their contribution to the development of chronic inflammatory disorders. In particular, we investigate the molecular mechanisms that regulate their tissue-resident phenotype, notably, their retention in the intestinal mucosa, and assess how functional activities of this T cell subset may contribute to protective immunity versus inflammatory or even immunopathological conditions.

Internal Collaborations
- Stefan Freigang, MD
- Vera Genitsch, MD
- Philippe Krebs, PhD
- Mario Noti, PhD
- Mirjam Schenk PhD

External Collaborations
National
- Andrew Macpherson, MD, Department of Clinical Research, University of Bern
- Uwe Sauer, PhD, Institute of Molecular Systems Biology, ETH Zurich
- Daniela Finke, MD, Department of Biomedicine, University of Basel
- Gerhard Rogler, MD PhD, Division of Gastroenterology & Hepatology, University Hospital Zurich
- Markus Britschgi, PhD, Roche Pharma Research & Early Development, F. Hoffmann-La Roche Ltd., Basel

International
- Katrin Andreasson, MD, Neurology and Neurosciences, Stanford University Medical Center, USA
- Phil A. Beachy, PhD, Stanford University Medical Center, USA
- John Kehrl, NIAID, Bethesda, MD, USA
- Bärbel Stecher, PhD, Max von Pettenkofer Institute of Hygiene and Medical Microbiology, Ludwig-Maximilians-University of Munich, Germany

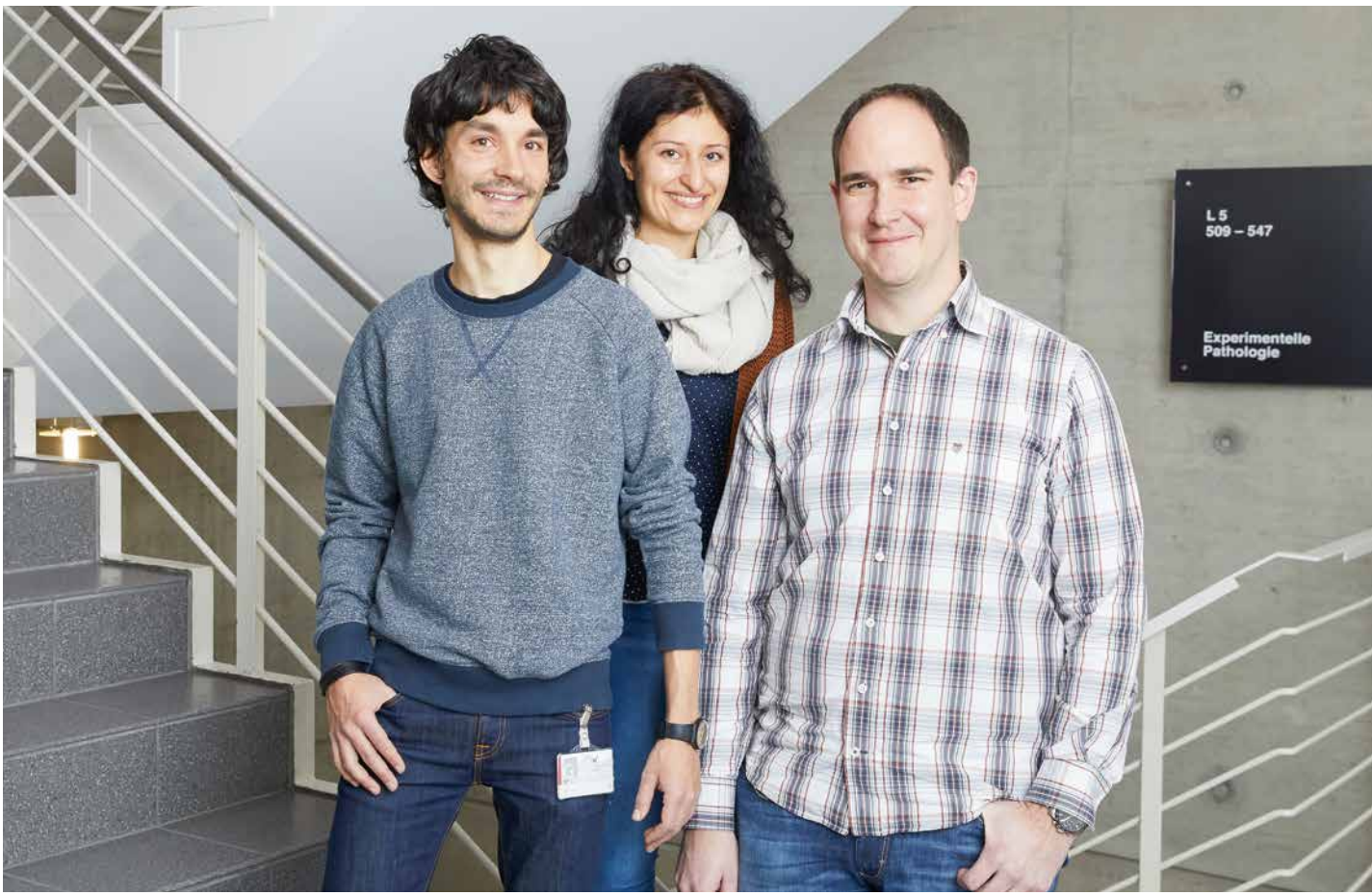
Grant Support

- SNF 310030_170084, Christoph Mueller, CHF 525'000 (2016–2019)
- SNF 33CS30_148422, (SIBDCS; Co-PI), CHF 200'000* (2016–2018)
- SNF 33CS30_177523, (SIBDCS; Co-PI), CHF 304'500* (2018–2020)
- Monique Dornonville de la Cour Stiftung (to Daniel Zysset), CHF 52'387 (2018–2019)

(* own share)

Administrative Duties
Christoph Mueller
- Chair, Program Board «Certificate of Advanced Studies in Research Management» (CAS «Forschungsmanagement»), University of Bern
- Member, Scientific Board, Swiss IBD Cohort Study (SIBDCS)
- Member, Executive Board, Swiss IBD Cohort Study (SIBDCS)
- Head, Biobank, Swiss IBD Cohort Study (SIBDCS)
- Member, Evaluation Committee Lutz-Zwillenberg Prize (University of Bern)
- Member, Evaluation Committee, SNSF, ambizione and PRIMA program
- Stiftungsrat, Stiftung für klinisch-experimentelle Tumorforschung Bern (since 12/2018; Chair)
- Member Task Force Experimental Animal Center, Med Faculty
- Member Kuratorium Clean Mouse Facility, University of Bern
- Member, Research Committee, Medical Faculty
- Member of Faculty Committees (e.g. habilitation, professorship)

Nadia Corazza
- Member «Gleichstellungskommission», Medical Faculty, University of Bern



Forschungsgruppe Mario Noti (Research group Mario Noti, Maryam Hussain, Lukas Bäriswyl).

Group of Mario Noti, PhD

Maryam Hussain, MSc, PhD student

Short Summary

Employing models of allergic inflammation, microbial colonization and/or manipulation, current research focuses on how mammalian host genetics and signals derived from commensal microbial communities influence innate and adaptive immune responses at multiple barriers surfaces. In another line of research we study whether targeting age-related changes in innate immune cell function can alter immunological, metabolic, physical and/or cognitive signatures of aging.

Research Activities

Project 1: Aging – a reversible biological process?

For many people, extended lifetime goes along with poor general health associated with common inflammatory, neurodegenerative and metabolic disorders ultimately leading to a progressive decline in organ function and death. Therefore, elucidating the complex pathways controlling the rate of aging is of significant clinical importance in order to improve health and maintaining wellbeing throughout the life-course. In a series of new studies, we are currently investigating how changes in plasma factors associated with aging alter immune cell function at different tissue sites and whether targeted manipulation of such age-related changes have a beneficial effect on the aging organism.

Project 2: Basophils – what role play basophils in the initiation of type 2 immune responses

As the public health and economic burden of food allergies continues to grow, there is an urgent need to develop new intervention strategies to prevent and treat this disease. While the effector functions mediating food allergies are well described, little is known how food allergic responses are initiated. In recent studies, we demonstrated that cutaneous sensitization to food allergens is associated with the infiltration of thymic stromal lymphopoietin (TSLP)-elicited basophils that promote Th2 polarization and the development of food allergies. Employing in vitro and in vivo model systems, current research is investigating what basophil intrinsic factors promote the pathogenesis of IgE-mediated food allergies.

Project 3: Microbiota – do changes in the gut microbiota promote allergic inflammation?
Recent studies have highlighted that the trillions of bacteria hosting our bodies are not just hitchhikers, but actively communicate and contribute to the maturation of the host's immune system. Alterations in dietary habits, improved sanitary installations and limited exposure to infections associated with a Western lifestyle significantly impact the diversity of the microbiota. Perturbations in this sophisticated host-microbial interaction may cause uncontrolled immune responses fostering the development of allergic inflammation. Employing axenic, gnotobiotic and humanized microbiota models we investigate whether changes in the gut microbiome associated with a Western lifestyle promote allergic inflammation.

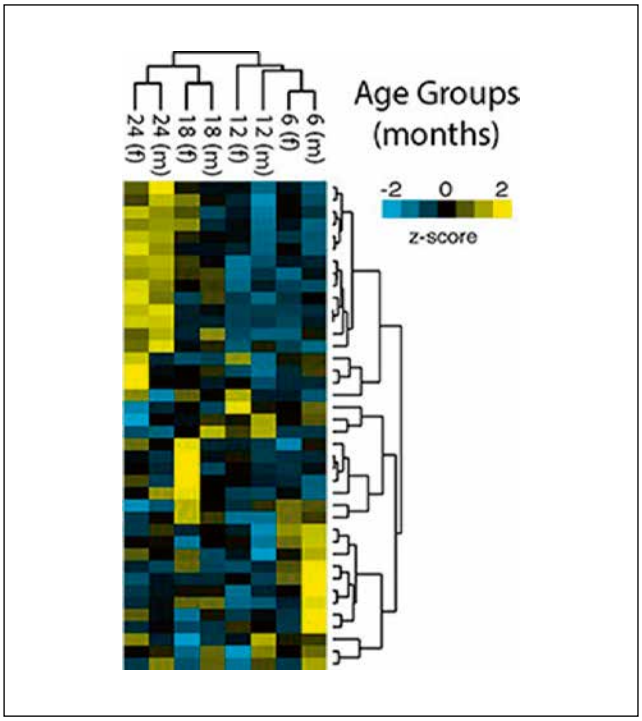
Internal Collaborations
- Christoph Müller, PhD
- Nadia Corazza, PhD
- Philippe Krebs, PhD

External Collaborations
National
- Alexander Eggel, PhD, Institute of Rheumatology and Immunology, University of Bern
- Carsten Riether, PhD, DBMR, University of Bern
- Johan Auwerx, PhD, EPFL Lausanne
- Philipp Engel, PhD, University of Lausanne
- Jan Niess, MD, PhD, Unisversity of Basel

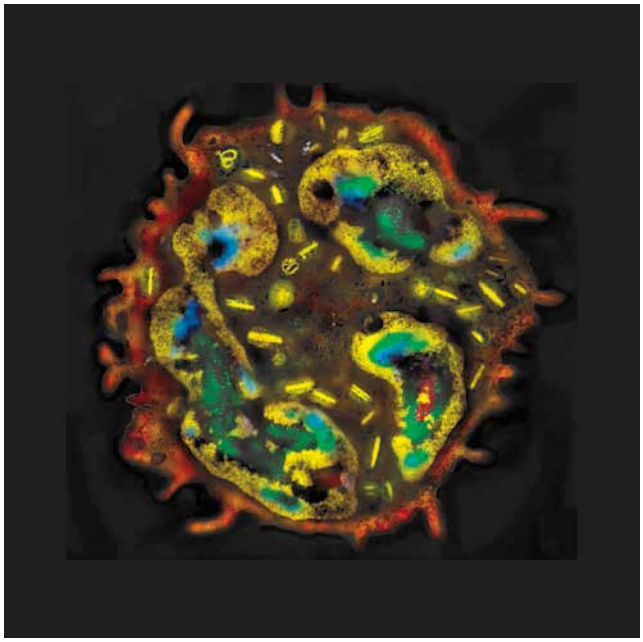
International
- David Artis, PhD, Weill Cornell University, USA
- Jonathan Spergel, MD, PhD, Childrens Hospital of Philadelphia, USA
- Brian S. Kim, MD, PhD Washington University, USA
- Thomas Brunner, PhD, Universität Konstanz, Germany

Grant Support
- Fondation ACTERIA, Mario Noti, EUR 150'000 (2018–2020)
- Novartis FreeNovation, Mario Noti, CHF 180'000 (2016–2018)

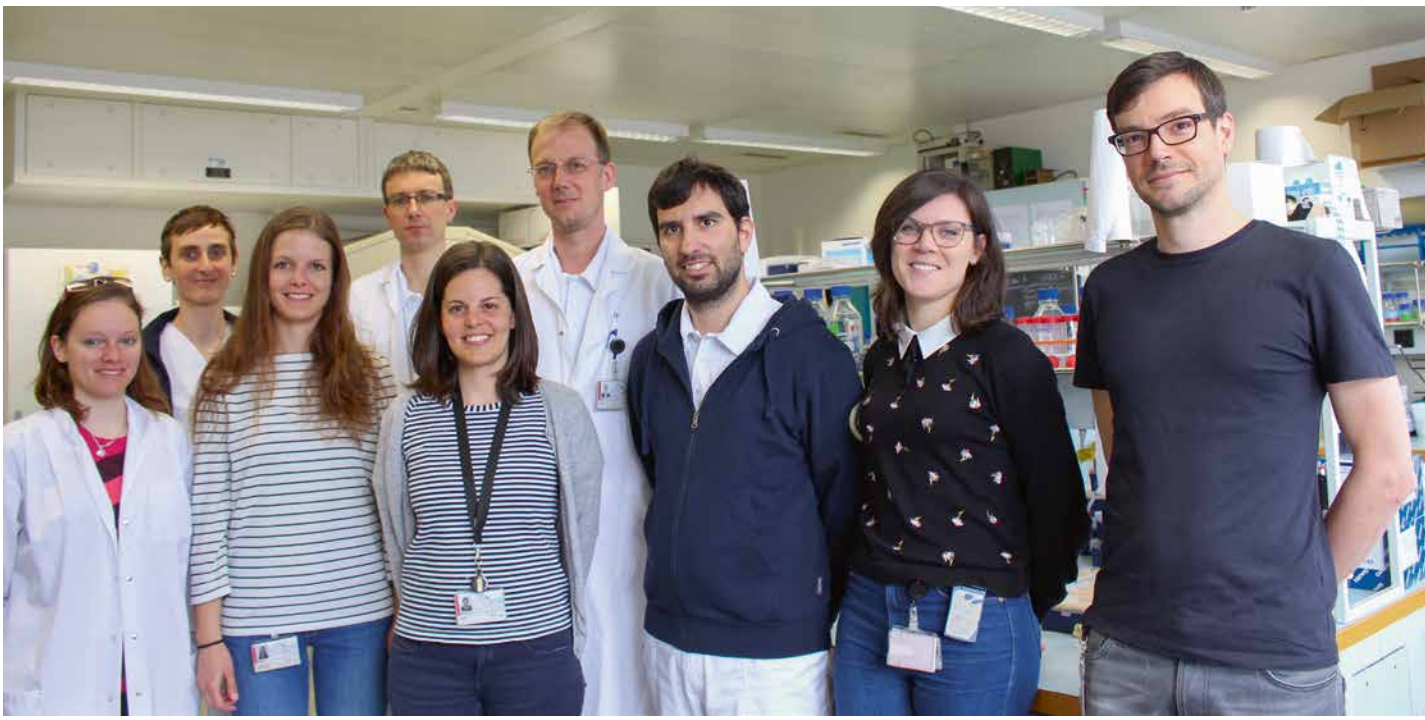
Administrative duties
- Secretary EAACI Task Force, Animal Models
- Organizer T2I Meeting Bern
- COST Working Group Member ImPARAS



Project 1: Age-related changes of immune factors in the plasma proteome of mice.



Project 2: Computer-enhanced electron microscopic image of a TSLP-elicited mouse basophil.



Forschungsgruppe Aurel Perren.

Group of Aurel Perren, MD

Ilaria Marinoni, PhD, Co-PI, 80%
Matthias Dettmer, MD Attending Pathologist
Annunziata Di Domenico, MSc, PhD-student
Simon April, MSc, PhD student
Renaud Maire, MSc, Technician, 90%
Charalampos Saganas, MD, Resident
Avanee Ketkar, BSc master Student (Bio)
Michelle Buri, BSc master Student (BMS)
Nicolas Munz, BSc master student (Bio)
Janine Straub, Cand. Med.

Short Summary

familial pancreatic neuroendocrine tumors (PanNETs). PanNETs are highly heterogeneous and the mechanisms leading to tumor development are still elusive. We focus on the understanding of the molecular events leading to PanNET formation and progression as well as on the investigation of the mechanisms mediating therapy resistance and tumor aggressiveness. We integrate molecular biological (in vitro and in vivo) and clinical (human tissue based ex vivo) research approaches.

Research Activities

Project 1: Dissection of the role of DAXX and ATRX in PanNETs

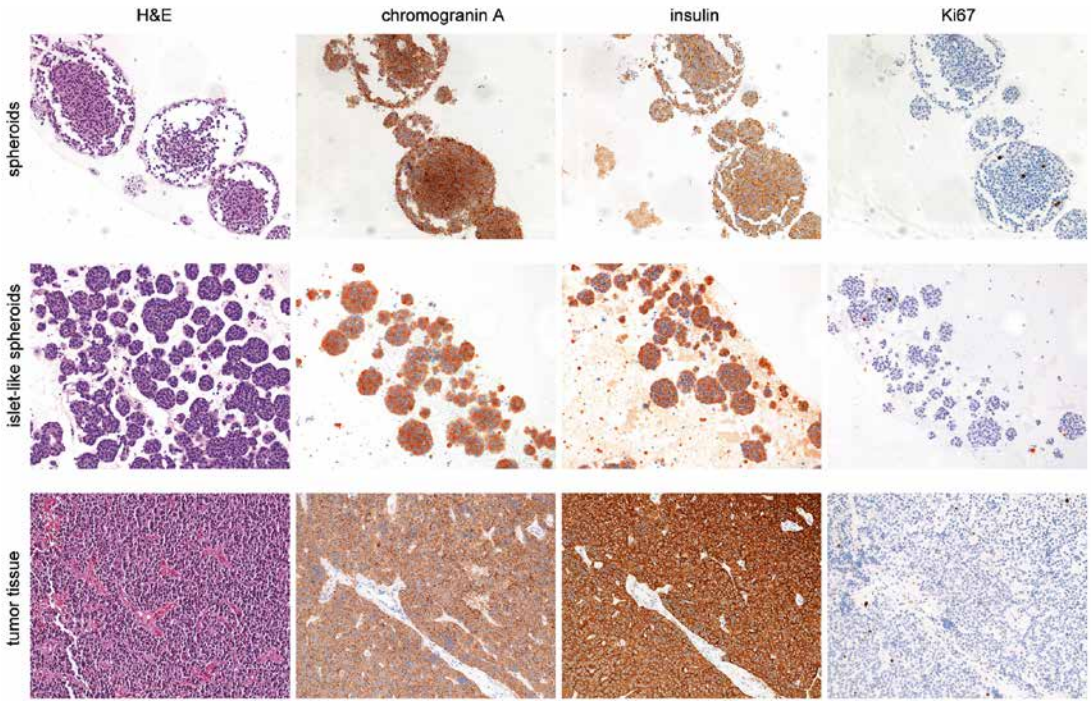
Almost, half of Pancreatic Neuro-endocrine Tumors (PanNETs) show loss of expression of DAXX or ATRX. We could show that DAXX/ATRX loss correlates with an increased risk of metastasis. DAXX and ATRX negative tumors show chromosomal instability and ALT (Alternative Lengthening Telomeres) activation, a mechanism for telomeres length maintenance. We focus on unraveling the mechanism underlying this new cancer-associated pathway using in vivo mouse model, in vitro cell culture and ex-vivo human patient tissues. We specifically focus on the role of epigenetic changes occurring in DAXX/ATRX negative PanNETs.

Project 2: Precision medicine approach for PanNET

No therapy prediction based on specific molecular profiles is possible for PanNET, yet. We recently established an organoid culture model of PanNETs which resembles original tumor tissues and which can be treated with drugs. We are currently assessing the possibility of exploiting PanNET organoids to predict patient therapy response and to identify new epigenetic drugs. Also, we aim at identifying specific molecular profiles through high throughput sequencing of DNA, DNA methylation- and gene expression analysis to predict therapy response in vitro and on the patients.

Project 3: Tall cell variant of papillary thyroid carcinoma (PTC)

It is known that this variant of PTC is associated with an adverse outcome. These tumors respond less often to the standard treatment with radioiodine. However, the reason for this on a molecular level remains elusive. It's also not known, what defines a so-called «tall cell», the hallmark of this histopathological PTC subtype on a molecular level. These are important clinical questions that we are currently trying to answer.



Projekt 2:
3D Primärzellkultur von PanNET (Mitte und rechts) behalten Eigenschaften des Tumors (links).

Internal Collaborations

- Mario Tschan, PhD
- Philippe Krebs, PhD
- Erik Vassella, PhD

External Collaborations

National

- Prof. H. Moch, USZ (PathoLINK)
- Prof. M. Rubin, DBMR (SOCIP)
- Prof. Martin Walter, Dept. Of nuclear medicine, University of Geneva
- Prof. Roche-Philippe Charles, Institut für Biochemie, University of Bern
- Prof. Massimo Bongiovanni, Institut universitaire de pathologie, CHUV, Lausanne

International

- Dr. Chrissie Thirlwell, Department of Cancer Biology, Clinical Lecturer Medical Oncology University College London, United Kingdom
- Prof. Marja Jäättelä, Head of Research Cell Death and Metabolism, Danish Cancer Society Research Center Copenhagen, Denmark
- Prof. Anne Couvelard and Dr. Jérôm Cros, Department of Pathology, Hospital Beaujon, Clichy, France
- Prof. Marianne Pavel, Friedrich-Alexander-University of Erlangen-Nürnberg
- Prof. Massimo Falconi, Surgery Departement, San Raffaele, Milan, Italy
- Dr. Christopher Heaphy, John Hopkins University School of Medicine, US

Grant Support

- Tumor Forschung Bern (Ilaria Marinoni), CHF 90'000 (2015–2018)
- SNF Marie Heim-Vögtlin (Ilaria Marinoni), CHF 206'000 (2016–2018)
- Desirée and Niels Yde Foundation (Ilaria Marinoni), CHF 54'000 (2016–2019)
- Wilhelm Sander Stiftung (Ilaria Marinoni), CHF 210'000 (2018–2019)
- KLS-4227-08-2017 (Aurel Perren PI, and Ilaria Marinoni co-PI), CHF 360'000 (2018–2022)
- Bernische Krebsliga (Ilaria Marinoni), CHF 40'000 (2018–2019)
- Berner Krebsliga (Matthias Dettmer), CHF 70'000 (2017–2022)

Administrative Duties

Aurel Perren

- Präsidium fakultäre Kommission, Strukturkommission Genetik
- Leiter Ressourcenausschuss medizinische Fakultät
- Mitglied Fakultätsausschuss
- Mitglied Fakultäre Strategie- und Beförderungskommission
- Mitglied Direktorium CCC Inselspital
- Co-Pi und Vize-Präsident Swiss Biobanking Platform (SBP)
- Vorstandsmitlglied Krebsliga Bern, Ressortleiter Forschung
- Executive Comitee -Mitglied, Europäische Neuroendocrine Tumor Society
- Leiter Krebsregister Bern
- Stiftungsrat NICER
- Mitglied Forschungskommission SKL
- Mitglied Senat SAMW

Ilaria Marinoni

- Member of the MIC (Microscope Imaging Center) commission of the University of Bern

Group of Mirjam Schenk, PhD

Thomas Gruber, PhD student
Hassan Sadozai, PhD
Mirela Kremenovich, PhD
Nives Rombini, Master student
Lukas Bäriswyl, Technician (50%)

Short Summary

The incidence of cancer is steadily rising and presents a major public health problem in many parts of the world. A key player in preventing and controlling malignant disease is the immune system. Unfortunately, in many cancer patients anti-tumor immunity is diminished. This malfunction can be caused by improper maturation of dendritic cells (DC), which thus cannot prime and activate cells of the adaptive immune system, in particular CD8+ T lymphocytes. Cytotoxic CD8+ T lymphocytes (CTL) are essential for killing tumor cells. Using tumor-immunotherapy we aim to enhance the function of the immune system to battle cancer. Specifically, our research group aims to investigate mechanisms to induce DC that can cross-present tumor specific antigens and induce an effective anti-tumor CTL response.

Research Activities

Project 1: Dendritic cells and their co-stimulatory properties for cytotoxic T cells in melanoma

The activation of an effective adaptive anti-tumor response relies mainly on presentation of tumor antigens and stimulation by DC. Despite extensive research, the phenotypes and functions of tumor-infiltrating DC (TIDC) remain largely elusive and cross-presentation of tumor antigen is not well understood. We are elucidating the phenotypes and functions of TIDC and how to manipulate them both in vitro and in vivo to induce a tumor- specific CTL response in melanoma. Thereby, we aim to identify ways to reprogram TIDC to present tumor antigens and activate an adaptive immune response against melanoma.

Project 2: Generation of potent cross-presenting dendritic cells (DC) for tumour immunotherapy

Only specific subsets of DC are able to present tumor antigens to CD8+ T cells in a process called cross-presentation. We aim to elucidate the mechanism(s) of cross-presentation and how this process can be manipulated in melanoma. Therefore, we are establishing models to test human monocyte derived DC as well as mouse bone marrow derived DC (BM-DC) for their ability to cross-present antigen. The knowledge of how cross-presentation is regulated in vitro may allow us to manipulate this process in vivo. Treated BM-derived DC will be tested in adoptive transfer experiments as prophylactic and therapeutic treatment for established melanoma. Together, these data should identify ways to promote frequency and enhance function of cross-presenting DC and to contribute to anti-tumor response.

Internal Collaborations

- Evanthia Karamitopoulou Diamantis, MD

External Collaborations

National

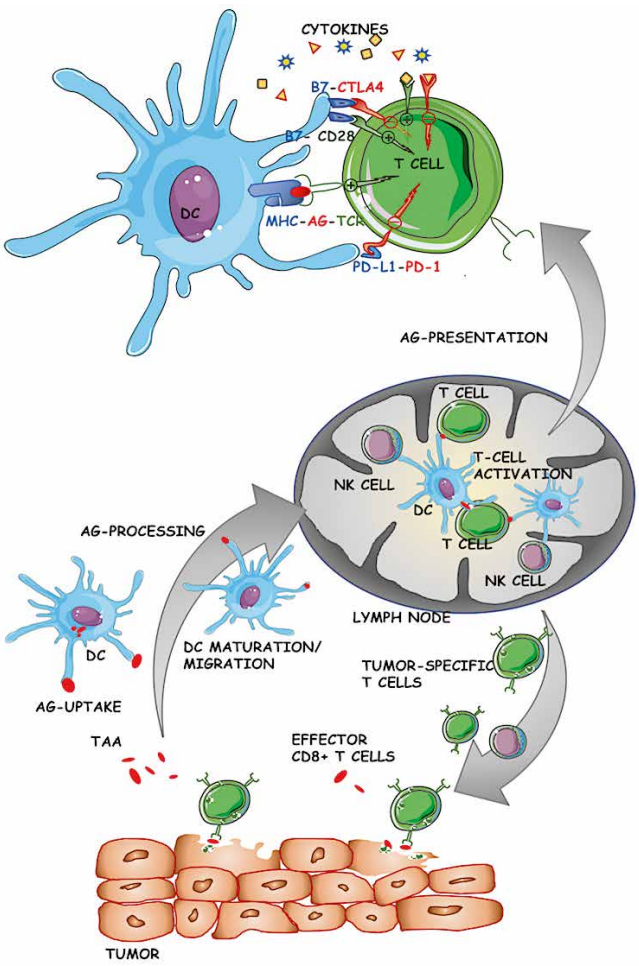
- Li Tang, PhD, Istitute of Bioengineering, Institute of Materials Science and Engineering EPFL, Lausanne
- Michel Gilliet, MD, Department of Dermatology, CHUV Lausanne
- Robert Hunger, MD, Department of Dermatology, Inselspital, University of Bern

International

- Robert Modlin, MD, David Geffen School of Medicine, Dermatology, UCLA, USA

Grant Support

- Stiftung experimentelle Biomedizin, CHF 763'000 (2016–2019)
- Werner Hedy Berger-Janser, CHF 110'000 (2016–2018)
- Klinisch Experimentelle Tumorforschung, CHF 150'000 (2016–2019)
- Helmut Horten, CHF 180'000 (2017–2020)
- SNF, CHF 566'109 (2018–2022)



Research group Mario P. Tschan.

Group of Mario P. Tschan, PhD

Magali Humbert, PhD postdoc
Vera Imboden, Master student (BMS)
(Co-supervision, PD Dr. M. Schaller)
Félice Janser, PhD student (Co-supervision, Prof. R. Langer)
Sophie Milesi, Master student (BIO) (until October, 31st)
Irene Mungure, Master student (BIO) (start September 17th)
Nicolas Niklaus, PhD student
Sarah Parejo, MSc, 80% (until November 30th)
Proiti Poddar, Master student (BIO) (start September 17th)
Sreoshee Rafiq, PhD student (Supervisor, Dr. M. Humbert)
(start March 1st)
Anna Schläfli (-Bill), PhD postdoc, 70%)
Kristina Seiler, MD-PhD student (start January 1st)
Deborah Shan, technician, 80%
Igor Tokarchuk, MD-PhD student
Kristin Uth, PhD student (Co-Supervision Prof. I. Zlobec)

Short Summary

My research team investigates molecular mechanisms in the pathogenesis of acute myeloid leukemias (AML) and in therapy resistances of this disease. Currently, we are focusing on the role of autophagy and the transcription factor PU.1 in this diesease. Additional research projects led by Magali Humbert (AML) and Anna Schläfli (Breast cancer) address the function of the autophagy recycling pathway in the resistance of hematological and solid cancers to chemotherapeutic agents and targeted therapies. All these pre-clinical studies in targeted, personalized cancer therapy are conducted in close collaboration with clinical pathologists and the Translational Research Unit.

Research Activities

Project 1: Function of chaperone-mediated autophagy in myeloid leukemia therapy

While classification of the heterogeneous blood cancer, acute myeloid leukemia (AML) improved significantly, scarce progress has been made in terms of treatment. Relapse and therapy failures remain high due to chemotherapy-resistant leukemic cells (CRLC). Our preliminary data link increased chaperone-mediated autophagy (CMA) to resistance mechanisms in differentiation therapy and an immature developmental stage of AML blasts. Therefore, we are aiming at understanding the role of CMA in the biology of AML cells and CRLC including the interaction with the microenvironment.

Project 2: Understanding the role of autophagy in retinoic acid threapy of breast cancer

Epithelial-to-mesenchymal transition (EMT) plays a key role in therapy-resistance and metastasis formation. In the present study, we therefore aim at reversing the EMT phenotype of breast cancer cells using differentiation-based therapy based on all-trans retinoic acid (ATRA). Cellular differentiation is often associated with upregulation of autophagy.

Autophagy is a lysosomal degradation and recycling system and may supports cellular differentiation by removing superfluous organelles, keeping energy levels or by regulating signalling by selective removal of proteins. Therefore, we study autophagy functions during therapy-induced MET and how modulation of autophagy can support differentiation-based therapy. Furthermore, we investigate how cancer associated fibroblasts influence cancer autophagy and therapy efficiency.

Project 3: Identification and analysis of PU.1 cell death pathways
The ETS-transcription factor PU.1 is needed throughout hematopoietic differentiation particularly by orchestrating terminal differentiation of macrophages and neutrophils. Importantly, low PU.1 expression can lead to the transformation of myeloid progenitor cells to acute myeloid leukemia (AML) blast cells. We found a new tumor suppressor function for PU.1 by supporting TNF-related apoptosis-inducing ligand (TRAIL)-mediated apoptosis in AML cells. Currently, we are investigating how PU.1 regulates alternative splicing of anti-apoptotic genes and how this affects AML therapy responses.

Internal Collaborations
- Rupert Langer, MD
- Inti Zlobec, PhD
- Sabina Berezowska, MD
- Tilman Rau, MD
- Yara Banz, MD-PhD

External Collaborations
National
- Thomas Kaufmann, PhD, Institute of Pharmacology, University of Bern
- Deborah Stroka, PhD, Dpt. of Clinical Research, University of Bern
- Urban Novak, MD, Medical Oncology, University of Bern
- Jörn Dengjel, PhD, Dpt. of Biology, University of Fribourg
- Carsten Riether, PhD, DBMR, University of Bern

International
- Bruce E. Torbett, PhD, TSRI, La Jolla, CA, USA
- Tassula Proikas-Cezanne, PhD, Dpt. of Molecular Biology, University of Tuebingen, Germany
- Enrico Garattini, MD, Istituto di Ricerche Farmacologiche Mario Negri, Milano, Italy
- Thomas Brunner, PhD, Dpt. of Biology, University of Konstanz, Germany
- Jean-Emmanuel Sarry, PhD, Centre de Recherches en Cancérologie de Toulouse – CRCT, Toulouse, France

Grant Support

- SNSF_31003A_173219, Mario Tschan, CHF 693'600 (2017–2021)
- SNSF MD-PhD 03/17, Kristina Seiler, Mario Tschan, CHF 180'000 (2018–2020)
- UniBE international 2021, I.Tokarchuk, Mario Tschan, CHF 90'000 (2018–2020)
- BKL, Magali Humbert, CHF 85'000 (2017–2018)
- UniBE Initiator Grants, Magali Humbert, CHF 16'500 (2017–2018)
- KFS, KFS-3409-02-2014, Mario Tschan, CHF 390'000 (2014–2018)
- Werner und Hedy Berger-Janser Stiftung, Anna (Schläfli) Bill, CHF 77'000 (2018–2019)
- COST Action: CA15138, Short Term Scientific Mission (STSM), Mario Tschan, EUR 2500 (2018)
- Stiftung Für Klinisch-Experimentelle Tumorforschung, Magali Humbert, CHF 20'000 (2018)
- UniBE Forschungsstiftung, 45/2018, Mario Tschan, CHF 9600 (2018)
- Claudia von Schilling Foundation for Breast Cancer Research, R. Langer, Co-PI Mario Tschan, *CHF 30'000 (2018)
- SNSF31003A_166578, Inti Zlobec, Co-PI Mario Tschan, *CHF 305'000 (2016–2019)
- Werner und Hedy Berger-Janser, UniBE ID Grant, T. Ochsenreiter, Co-PI Mario Tschan, *CHF 105'000 (2018–2019)
- Partenariat Hubert Curien/Germaine de Staël Funding, J.E. Sarry, Co-PI Mario Tschan, *CHF 9000 (2019–2020)

* total amount of funding; funding shared by PI and Co-PI

Adinistrative duties
- Management committee member and co-chair working group 4 of the COST action TRANSAUTOPHAGY
- Member of the Interfacultary PhD Committee, Graduate School for Cellular, Biomedical Sciences (GCB)
- Chair Expert Committees Cell Biology of GCB.
- Member of the steering board of the Master study program Biomedical Sciences at the Medical Faculty and organizer of the teaching block tumor biology for this program
- Member of the «Vereinigung der Dozentinnen und Dozenten der Medizinischen Fakultät Bern» representing the interests of the lecturers at the Medical Faculty meetings
- Member of the Expert Committee for Biomedical Analysts, «Zentrum für medizinische Bildung, Höhere Fachschule»
- Associate Professor Committee Prof. J.K Rössler, Co-referent; «Nachfolgekommission ISTB, Vertreter VDM»
- Grant reviewing for The Netherlands Organisation for Scientific Research (NWO), The Swiss National Science Foundation, and the Foundation for Polish Science

Group of Erik Vassella, Dr. pharm.

Elham Kashani, PhD student (from April 1, 2018)
Jaison Phour, technician
Senija Selimovic-Hamza, assistant Bioinformatician and Data Coordinator (from September 17, 2018))
Carmen Trefny, Master student (BIO) (from October 1, 2018)
Catia Coito, (Medi) (from November 26, 2018)

Short summary

microRNAs are short regulatory RNAs at the post-transcriptional level that are implicated in a wide variety of basic biological processes as well as in cancer. My research team is aiming at identifying microRNAs that are implicated in resistance to chemo- and targeted therapy of non-small cell lung cancer and gliomas. Our results suggest that antagomirs that block the expression of endogenous microRNAs could be used in adjuvant cancer therapy.

Research Activities

Project 1: Screening for micrornas conferring temozolomide resistance in glioblastoma cell lines

We follow an unbiased approach for the identification of microRNAs that are most efficient at conferring resistance to the alkylating agent temozolomide in glioblastoma cells, which are the most common and most aggressive primary malignant brain tumour. To this end, glioblastoma cell lines were screened with a lentiviral microRNA library and selected for temozolomide resistance. Resistent clones were identified by next generation sequencing. We are currently investigating the molecular mechanism of temozolomide resistance elicited by these miRNAs.

Project 2: Chemoresistance mechanisms in glioblastomas

Glioblastoma is the most common and among the most aggressive primary malignant brain tumour in adults. This tumour is incurable due to its highly infiltrative growth and its intrinsic resistance to radiochemotherapy. DNA repair mechanisms play an important role in the development of resistance, but the underlying molecular mechanisms are largely unknown. We follow a translational approach for the identification of secondary mutations as well as alterations in gene expression profile, and will assess clinical-pathological characteristics of recurrent glioblastomas, which have developed resistance to radio-chemotherapy. In future, this approach may help for the development of new personalized medicine. This project is currently supported by the Swiss National Science Foundation.

Internal Collaborations

- Ekkehard Hewer
- Sabina Berezowska
- Mario Tschan
- Eva Diamantis
- Rupert Langer

External Collaborations

National

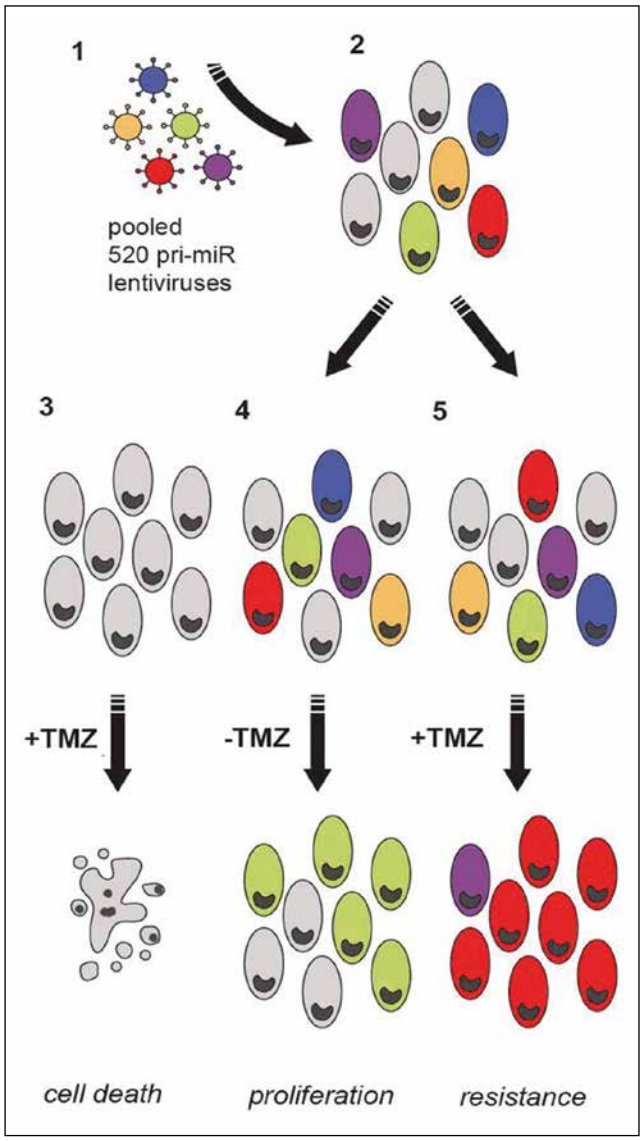
- Markus Lüdi, MD, Anästhesiologie, Inselspital
- Peng Ren-Wang, PhD, and Thomas Marti, PhD, Universitätsklinik für Thoraxchirurgie
- Michael Reinert, MD, Ospedale Regionale di Lugano, Lugano

International

- Stephan Schäfer, MD, Universitätsspital Köln, Köln

Grant Support

- SNF (31003A_175656), CHF 408'509 (2018–2022)
- SAKK 75/08 Rupert Langer (PI), Erik Vassella (Co-PI), CHF 130'000 (2018)



Screening for microRNAs conferring temozolomide resistance in glioblastoma cell lines.

1.2 Translational Research Unit (TRU)

Head: Inti Zlobec, PhD

Technical and Scientific Staff:
Carmen Cardozo
Dr. Irene Centeno
Micha Eichmann (20%)
Dr. José A. Galván
Patricia Ney (50%)
Stefan Reinhard (80%)
Sandrine Ruppen
Dr. Magdalena Skowronska

Overview

The Translational Research Unit (TRU) is a core facility of the Institute of Pathology, University of Bern. Our aim is to share our expertise with and provide services in tissue-based methods for internal co-workers, researchers from the University and Insel Hospital as well as external groups from Switzerland and abroad. Our main areas of interest are in tissue biobanking, histology, tissue microarraying, tissue visualisation, digital pathology and image analysis. TRU has 147 clients and has handled 738 requests this year stemming from 139 different projects (excluding tissue biobank projects). Collaborative projects with external research groups comprise 20%. Of note, approximately 9% of all requests are related to animal tissues, 70% human tissues and 19% involve clinical studies and SAKK trials. In contrast to previous years, only 6% of the services performed in TRU were sponsored directly by the Institute of Pathology. The overwhelming majority of TRU services were covered by third-party funding.

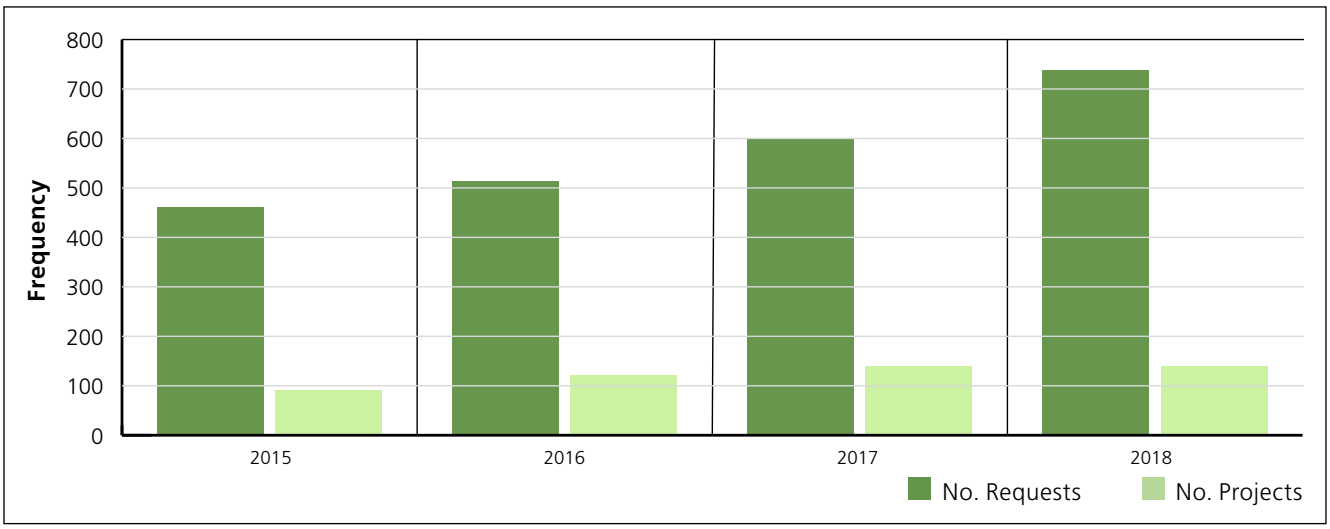
Histology

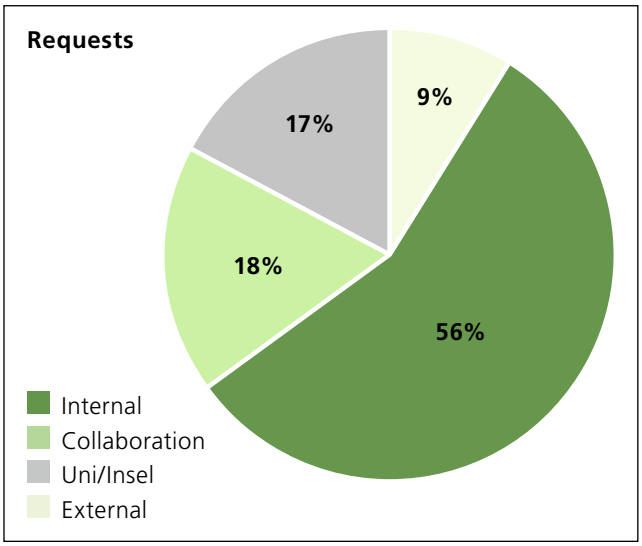
Histology techniques are the basis of all the work in TRU and our lab personalizes each research project. Sections are cut for many purposes: laser capture microdissection, DNA/RNA extraction, immunohistochemistry and other special downstream techniques (e.g. MALDI). This year, we have re-embedded 1637 blocks, and cut thousands of slides for H&E or special stains (n=2476), immunohistochemistry, TUNEL or ISH (n=6161), empty sections (n=2200) or slides requiring special DNAse/RNAse-free conditions (n=443).

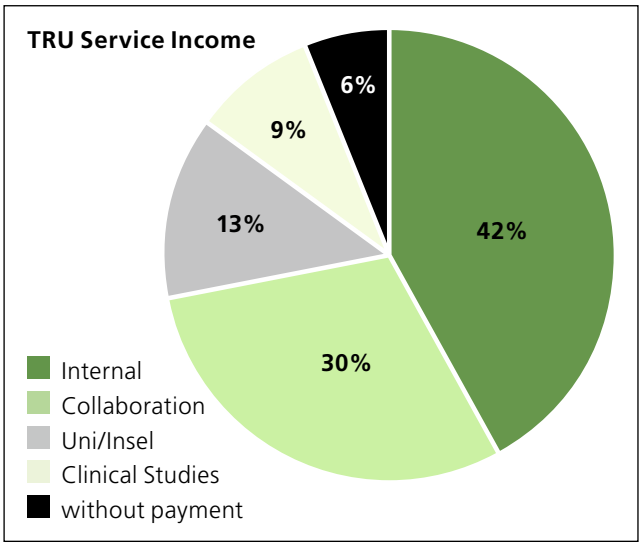
Tissue Visualisation

Each year a large number of antibodies is established in TRU. This year again, 58 different markers were newly set up not only for human tissues or cell lines but also for animal models (mouse, rat, monkey, horse and pig tissue) in collaboration with the comparative pathology platform, COMPATH (collaboration with the Institute for Animal Pathology).

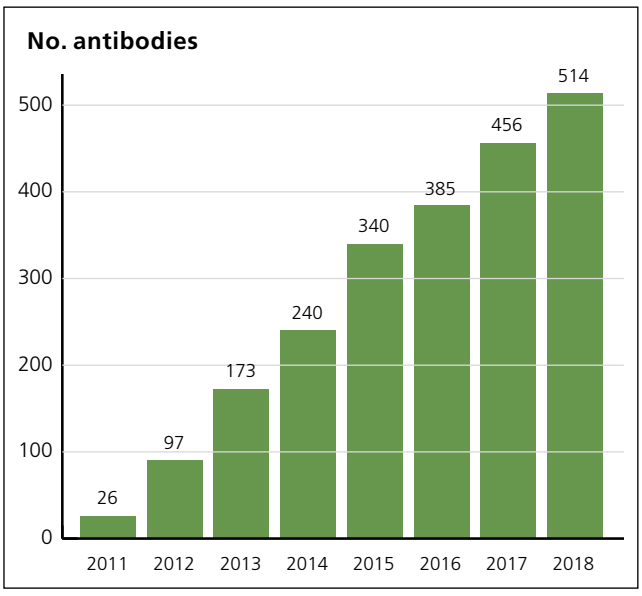
In 2018, 190 different antibodies were used for various research projects. We routinely perform mRNA in situ hybridisation (ISH) using automated immunostainers and can now additionally offer TUNEL assays for human and mouse. New this year, we have included the cell chambers for immunocytochemistry detection (ICC/IF) and new ISH probes for zebrafish, mouse retina, mouse prostate. Immunostaining of routinely used diagnostic biomarkers is performed in collaboration with the Immunohistochemistry Lab of the Clinical Pathology Division.

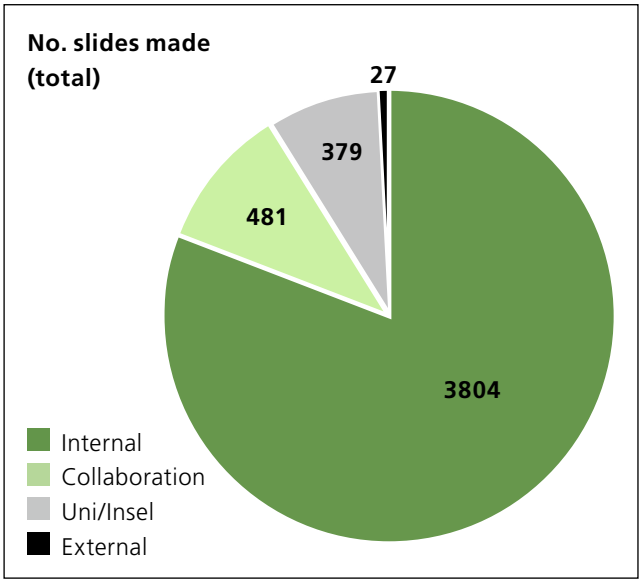

800
700
600
500
400
300
200
100
0
Frequency
2015
2016
2017
2018
No. Requests
No. Projects

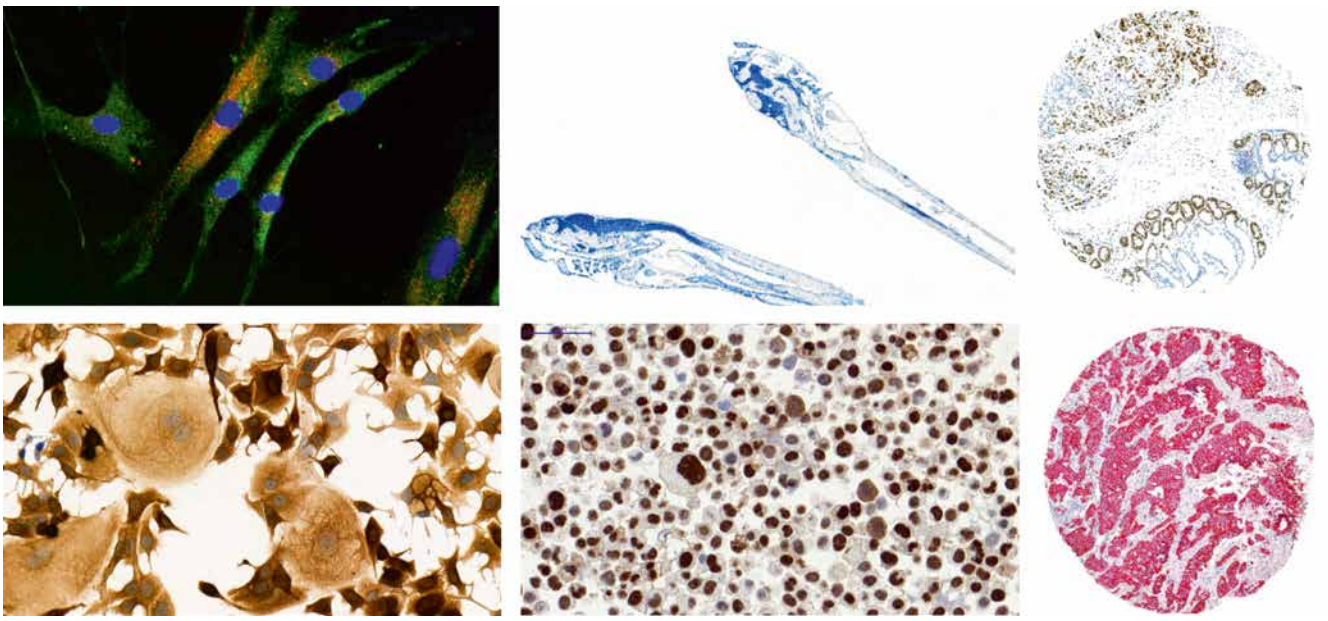

Requests
9%
17%
18%
56%
Internal
Collaboration
Uni/Insel
External


TRU Service Income
6%
9%
13%
42%
30%
Internal
Collaboration
Uni/Insel
Clinical Studies
without payment

Overview


No. antibodies
514
456
385
340
240
173
97
26
500
400
300
200
100
0
2011
2012
2013
2014
2015
2016
2017
2018


No. slides made (total)
27
379
481
3804
Internal
Collaboration
Uni/Insel
External



Upper: LC3b/p62-IF in cell chamber; MyoD-ISH in Zebrafish; KI67-DAB chromogen-IHC in TMA, Lower: Vimentin-ICC in cell chamber; CDX2-DAB chromogen-IHC in cell block and PanCK-AP chromogen in TMA

Digital Pathology

Modern pathology goes hand-in-hand with digitisation. TRU has been working on digital pathology on different fronts.

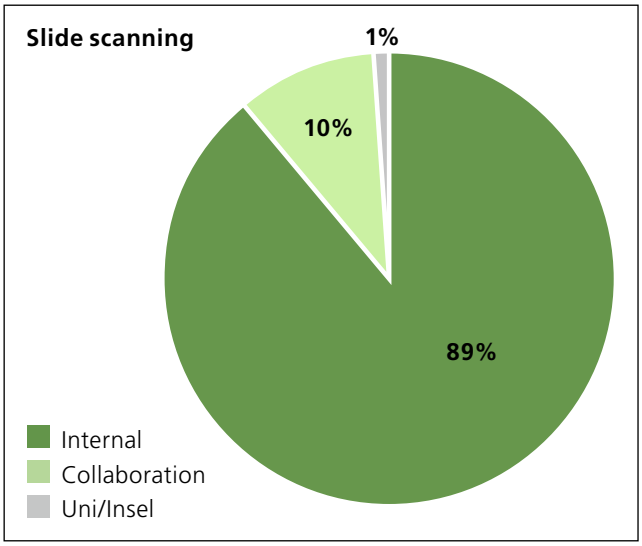
1. Slide scanning

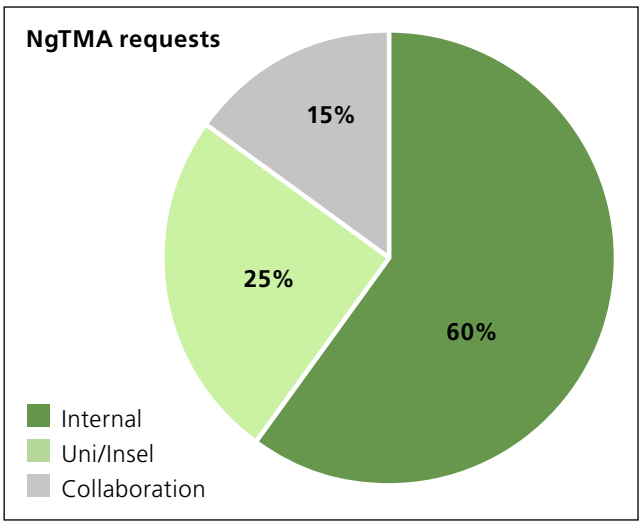
The requests for slide scanning in TRU are either for publication, education or research purposes. Over the last year, 7455 slides were scanned, mainly for internal researchers. Downstream work includes histomorphological evaluation of tissue slides after H&E staining, immunohistochemistry, or other stains/ hybridisation using manual or digital image analysis solutions and for further use in tissue microarray construction.

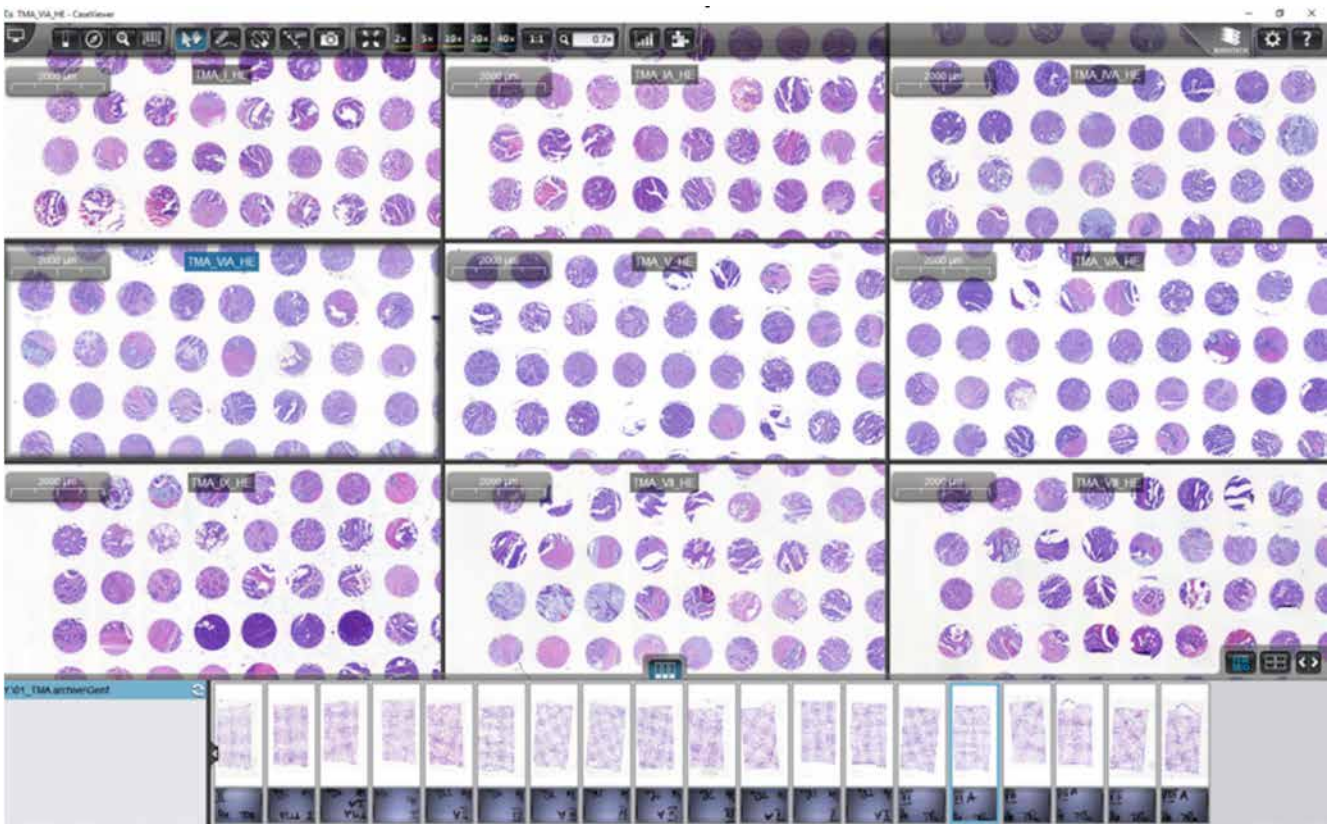
Our slides are saved locally on a NAS with 100 TB of storage, and on an external Case Center accessible via the web. More than 100 users have access to Case Center for slide viewing, sharing and annotation-creation. This platform is also being used for diagnostic slide sharing by the medical doctors of the Clinical Pathology laboratory. The success of our digital pathology platform is also owed to the strong collaboration with our informatics team. Led by Mr. Oliver Jochum, the IT department at the Institute of Pathology is fundamental to most aspects of TRU's daily business.

2. Next-generation Tissue Microarrays (ngTMA®)

The ngTMA platform has made huge strides over the last years to increase its performance and meet the requests by researchers. Again this year, TRU has received 30 different requests for ngTMAs, which translates into 69 ngTMA blocks using 2495 donor tissues. The largest on-going TRU project is a collaboration with the Cancer Registry of Geneva and the University Hospital of Geneva: we are compiling approxima-

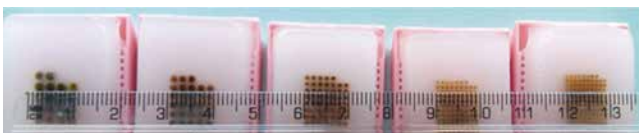






tely 6'000 patients into 60 different ngTMAs. Sixty percent of requests for ngTMAs this year stem from the Institute of Pathology, whereas 25% are tasked by the Insel Hospital or University of Bern and 15% are collaborations between researchers and our Institute.

The interest in ngTMA construction and the need for more personalized TMAs is constantly on the rise. For example, we have requests not only for TMAs using human tissues, but also cell lines, and animal tissues such as monkey. This year, in collaboration with the lab of Dr. Gary Nolan and colleagues from Stanford (C. Schürch and coworkers), TRU has generated specialized TMAs to help with the establishment of CODEX technology (see TMA image below).



In addition to these, we have generated ngTMAs from neurological samples, lung tissues, endocrine tumors, cancers of the upper gastrointestinal tract, sarcomas, liver specimens, pancreas and colorectal cancers. Extra punches for downstream molecular analysis are also taken, using the same technology (this year: 538 punches).

We use Case Center to upload the digital images, thus giving access to external collaborators and clients. This permits them to annotate whole slides for ngTMA construction and also to have access to their arrays once constructed.

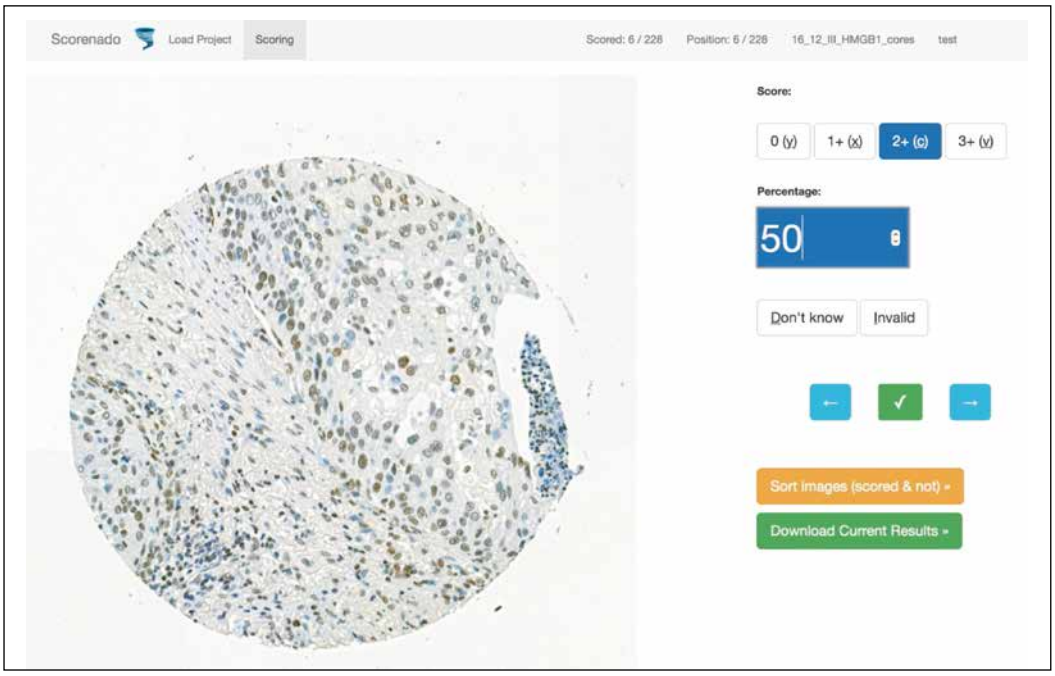
3. Digital image analysis
a. Scorenado
TRU started developing Scorenado, an efficient and user-friendly visual assessment tool for scoring TMA slide spots and other sets of images in a blinded and randomized manner. Since its test launch, a total of 29 Scorenado projects, including 368 slide scans, were set up for research conducted in-house, at Insel, and at other institutes in Switzerland and abroad.

Overall, 88'293 TMA spot images or whole-tissue slide crop images have been scored with Scorenado. Project types included scoring different IHC markers, estimating percentages of tumor positivity, counting tumor buds, and image classifications in colon, lung, breast, pancreas, and endometrium tissue. Over the course of this test period, a substantial amount of feedback has been collected in order to improve Scorenado for its official release scheduled for 2019. At the 14th European Congress on Digital Pathology in Helsinki, Scorenado was presented for the first time at an international congress.

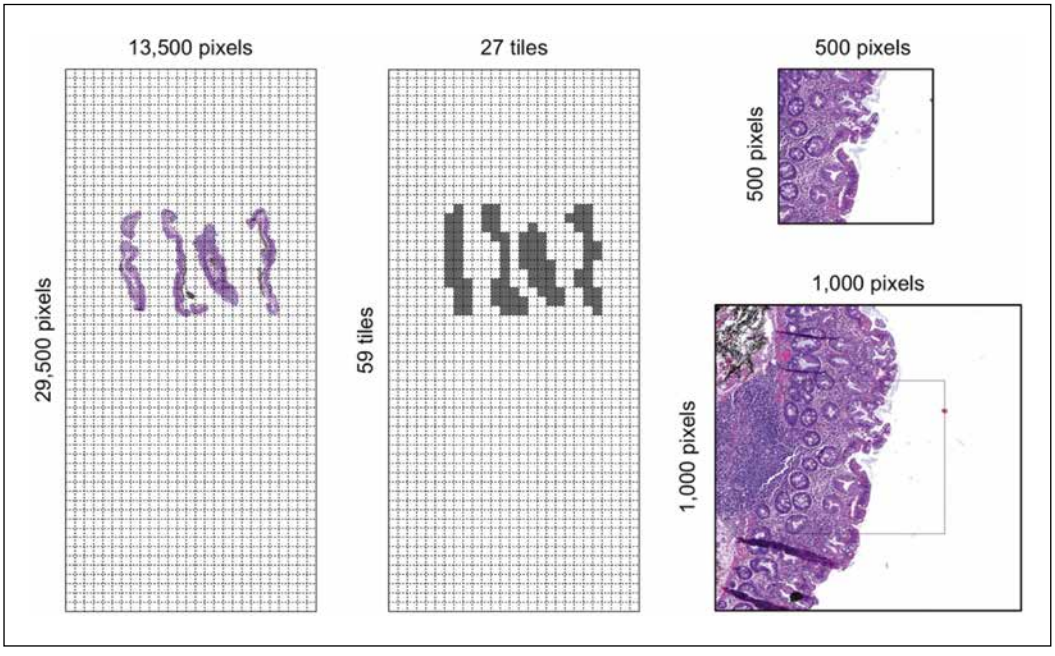
b. Analysis
TRU has performed digital image analysis with QuPath for 3 research projects and has provided training in QuPath for 10 projects. In addition, a collection of scripts facilitating image analysis in QuPath and TMA data handling was created.

TRU has further built its collaboration with the ARTORG center of the University of Bern and trained artificial neural networks on their GPU clusters for different image classification tasks concerning colorectal polyps. For this purpose, a massive dataset of colon tissue image tiles was created and a subset labeled in collaboration with pathologists.

4. ngTMA® and digital pathology speaking engagements
ngTMA and the work of TRU has been represented at numerous national and international events including the 5th Digital Pathology and AI Congress in London, the European Congress of Pathology in Bilbao, the European Congress of Digital and Integrative Pathology (ECDP) in Helsinki and the Swiss Clinical Trial Group (SAKK)Semi-Annual.



A screenshot of Scorenado's customized user interface.



Polyp tissue tile image extraction: Tile grid overlay on slide image (left), tissue detection (middle), extracted tissue tile images with and without context margin (right).

Tissue Bank Bern (TBB)

Director: Prof. Aurel Perren

Manager and co-manager:
Prof. Inti Zlobec and PD. Dr. med. Tilman Rau

Operative functions and project management:
Dr. Irene Centeno and Dr. Magdalena Skowronska

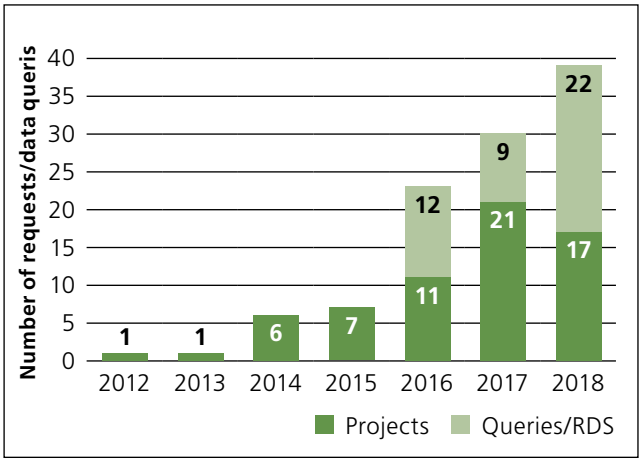
Additional members:
technical and medical staff of TRU and
Clinical Pathology Division

The TBB works together with the Clinical Pathology Laboratory at the Institute of Pathology to ensure collection of high-quality tissue samples in an ethico-legal manner. TBB services are, since October 2016, being performed by the Translational Research Unit (TRU) thus, personnel and resources are shared.

1. Projects by TBB 2018

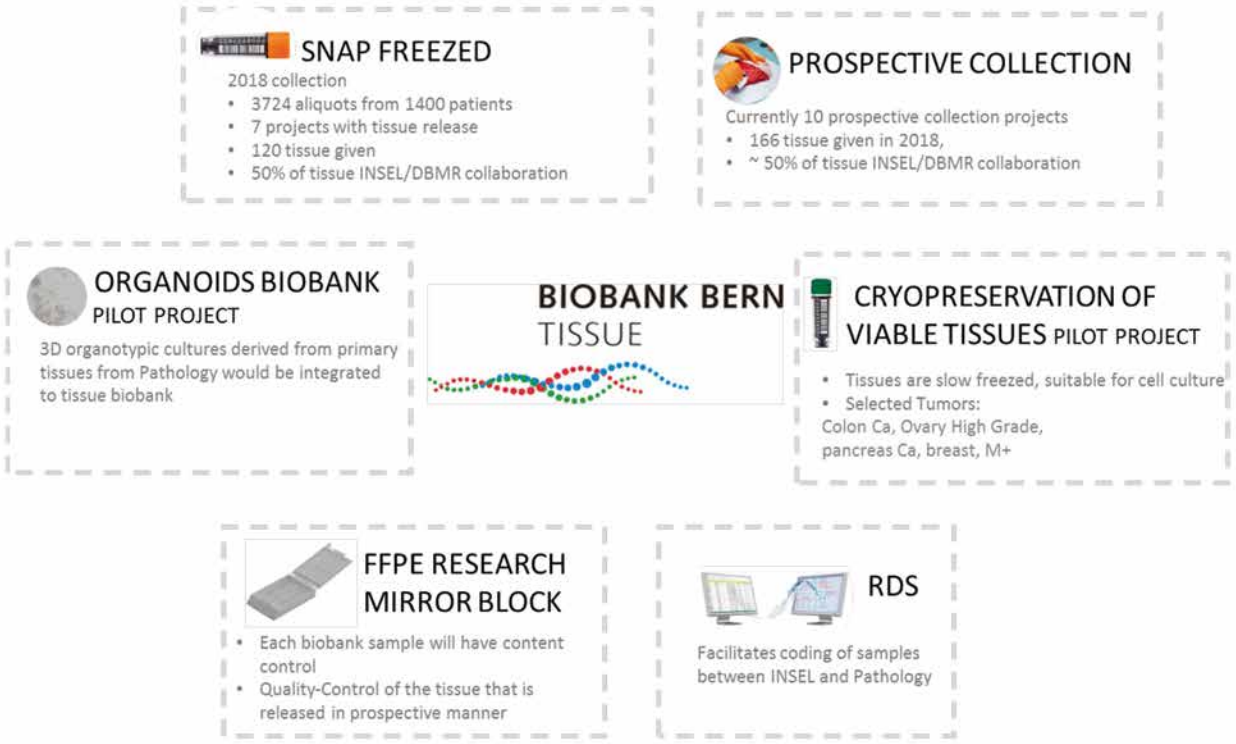
The number of TBB projects continues to rise. In year 2018, aside from providing the scientist with frozen and native material, we work on processes to satisfy the growing interest of the «live» tissue. In 2019, we plan to introduce slow freezing as an alternative cryopreservation method for selected tumours, in order to preserve live cells in frozen tissue. Additionally we will include FFPE Research mirror blocks, which would serve as a histopathological control for each given tissue. In 2018, TBB introduced the Research Data Support team (RDS) that performs tissue queries and helps researchers link data to tissue internally and externally (Inselspital, Cancer Registry). Details of these aspects of TBB 2018 are summarized in the Figure below.

In 2018 we received 39 requests for tissue and or data. We have provided scientists with 120 frozen tissues, all with pathological tumour content control and 166 tissue were handed out in prospective manner. These numbers are summarized in the following graph, showing requests for tissue and data.



2. Towards the best quality of service

The delivery of optimal quality tissues to the researchers is one of the main aims of TBB. In order to achieve this objective, we have systems that allow us to trace samples and associated data automatically. The collection and storage of the TBB samples are included under the Institute of Pathology accreditation by the Swiss Accreditation Service (SAS) according to ISO 17025:2005 and ISO 15189:2013 since 21.08.2018.



Vita Label certificate from the Swiss Biobanking Platform.

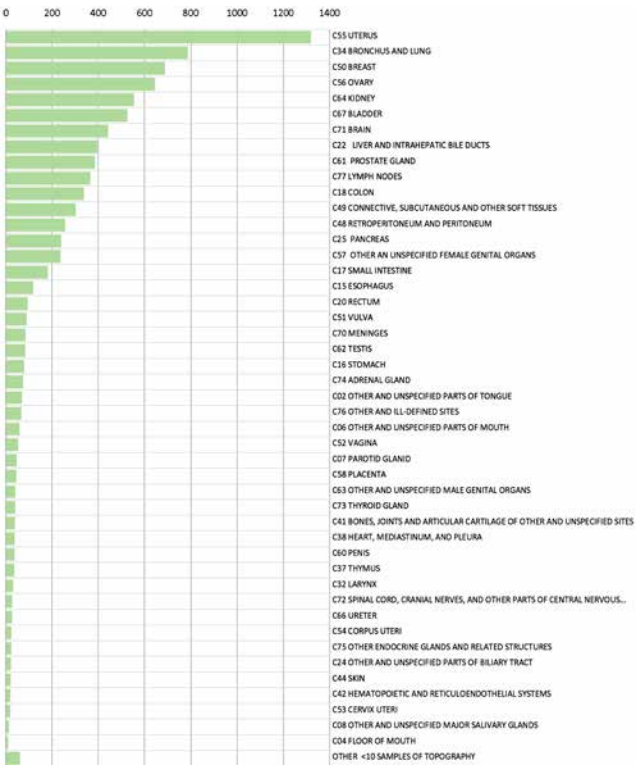
To ensure a reliable and accurate information about the sample quality we have a detailed pre-analytical data set including time points for all the critical activities and the sample storage temperature is continuously registered. Additionally, every tissue given for a project undergoes an exit quality control in which an H&E staining is done and reviewed by an expert pathologist. During this year, we have worked on new SOPs and documentation towards the new ISO 20387:2018 that is leading to an improvement in the quality of the service.

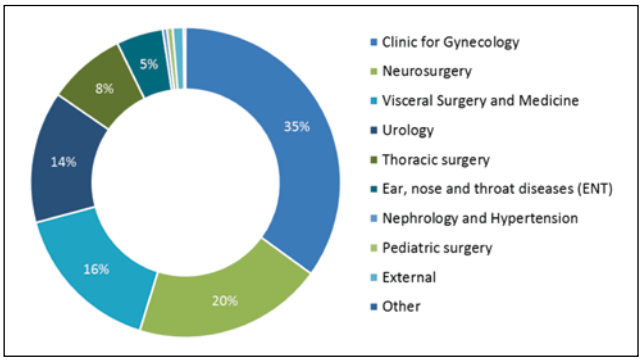
The ethical and legal aspects are also a key part of the functioning of the biobank. TBB works according to the Human Research Act (Humanforschungsgesetz, HFG). This year, we received the Vita Label certificate from the Swiss Biobanking Platform as evidence of our compliance with its legal and ethical standards.

3. TBB institutional collection statistics

TBB markedly expanded its tissue collection reaching a total collection of more than 11'000 different samples stored in more than 42'000 tubes. For most of our samples Topography and Morphology has been assigned according to ICD-O codes (INTERNATIONAL CLASSIFICATION OF DISEASES FOR ONCOLOGY). In the graph below, the distribution of samples in our TBB collection based on ICD-O topography codes can be appreciated.

This year different clinics continue their important contribution to the biobank. With 1664 samples, the distribution by clinic can be found in the chart below, with the largest amount of samples deriving from the Frauenklinik (Gynecology), followed by the clinics of Neurosurgery, Visceral Surgery and Urology as well as Thoracic Surgery.





4. Fit-for-purpose TBB collections

Special projects «fit-for-purpose» are also developed upon request. This year TBB has implemented a procedure to snap freeze samples immediately after resection in the operating theatres, reaching therefore cold ischemia times of less than 1 minute, which makes the realization of metabolic studies possible and assures an optimal conservation of the sample.

Surgery personnel trained by TBB staff will freeze the sample in the operating room. All the required material for processing the sample is delivered before the surgery in the TBB snap freezing box and the frozen sample is sent to Pathology on dry ice through the pneumatic post. An H&E section is made in the Clinical Pathology laboratory to confirm the tumor percentage and quality at arrival. After this quality check, the sample is delivered to the TBB staff to prepare the tissue for molecular analysis.

5. TBB networks

The TBB continues this year to collaborate closely with the Liquid Biobank at the Insel Hospital as well as with the newly established Insel Data Coordination Lab (IDCL). TBB works together with the Swiss Biobanking Platform (SBP) to help standardize and harmonize biobanking procedures across Switzerland with the final aim of being able to search and exchange samples between the different University Hospitals.

Our project «PathoLink» is on-going. This Swiss National Science Foundation funded project aims to deliver standardized tissue-related data (by means of synoptic reporting and coding, as well as minimal datasets for pre-analytical variables and tissue handling) across each of five major tumor entities to a central biobank repository managed by the SBP.

6. Collaborators

Excellence in biobanking is a multi-institutional and cross-departmental goal. To that end, we have numerous collaborators that need to be acknowledged. The clinics that continue to send samples for biobanking are invaluable as are the medical doctors and the technical staff of the Clinical Pathology Lab at the Institute of Pathology. Support from the IT department is of upmost importance to ensure high quality documentation and our LEAN officer ensures that workflows continue to be optimal, despite numerous improvmenets.

In particular, for support in cryopreservation of samples, we would like to thank:

- Dr. med. Martin Wartenberg, Institute of Pathology
- Dr. Ilaria Marinoni, PhD Institute of Pathology
- PD Dr. phil. Marianna Kruithof-de Julio, Urology Department, Inselspital
- PhD candidate Chantal Bachmann from Prof. Adrian Ochsenbein group, Tumor Immunology, DBMR, Inselspital

Group of Sabina Berezowska, MD

Christina Neppl, MD, Resident
Tereza Losmanová, MD, Resident
Manuel Keller, MD student
Alexandra Kündig, MD student
Yasin Irmak, MD student
Philipp Zens, MD student
Corina Bello, MD student
Annina Rahel Leuenberger, MD student
Jana Brühlmann, MD student
Martina Ninck, MD student

Short Summary

The main ongoing research projects include the morphological and molecular characterization of lung cancer and its metastases, in particular brain metastases. In a subset of projects we focus on immunooncology including PD-L1 expression. Furthermore, we investigate the role of autophagy in tissue, e.g. after neoadjuvant treatment and in resistance mechanisms to targeted therapies, whereby we are particularly interested in non-small cell lung cancer with ALK-inversion. We design our projects with a translational approach in an inter-disciplinary setting. Furthermore, we participate in various basic research projects in conjunction with our collaboration partners.

Research Activities

Project 1: Autophagy in lung cancer

Lung cancer remains the leading cause of cancer death worldwide. Modulation of autophagy – the stress response and homeostasis mechanism in normal and neoplastic cells – may be one way to interfere with resistance mechanisms, tumor cell adaptation and viability. Therefore, we investigate the role of autophagy – a druggable mechanism – in lung cancer, using functional cell culture based and tissue-based analyses.

Project 2:Immunooncological Markes in lung cancer

Lung cancer is amenable to immunotherapeutic approaches. Several PD-1 and PD-L1 immune checkpoint inhibitors have already been approved for the treatment of patients with advanced NSCLC or are in advanced clinical studies. PD-L1 expression and tumor infiltrating lymphocytes are in the focus of many investigators. Mostly primary tumors are studied. We are currently interested in brain metastases and post-therapeutical modification.

Internal Collaborations

- Mario Tschan, PhD
- Erik Vassella, PhD
- Philippe Krebs, PhD
- Rupert Langer, MD
- Ekkehard Hewer, MD

External Collaborations

National

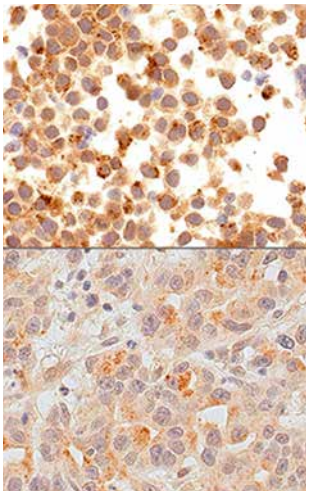
- Lukas Bubendorf, MD and Spasenija Savic-Prince, MD, Institute of Pathology, University Hospital Basel
- Thoracic surgery research group DKF, Bern (Ralph A. Schmid, MD, Thomas M. Marti, PhD, Sean Hall, PhD, Ren-Wang Peng, PhD) http://www.thoraxchirurgie.insel.ch/
- Urspeter Knecht, MD, Universitätsklinik für Diagnostische und Interventionelle Neuroradiologie, Inselspital Bern
- Christian Fung, MD, Universitätsklinik für Neurochirurgie, Inselspital Bern

International

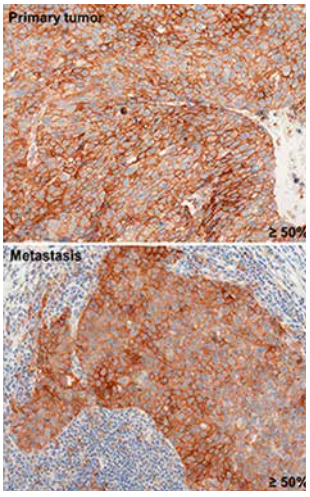
- Michaela Aichler, PhD, and Axel K. Walch, MD, Abt. Analytische Pathologie, Helmholtz Zentrum München, Germany

Grant Support

- Hedy Berger-Janser Stiftung, PI Sabina Berezowska, CHF 80'000, (2018)
- Fondation Johanna Dürmüller-Bol, PI Sabina Berezowska, CHF 9500 (2017–2018)
- Stiftung zur Krebsbekämpfung, PI Sabina Berezowska, CHF 20'000 (2018)



Project 1:
Dot-like LC3B expression in in-vitro cells (upper picture) and lung tissue (lower picture), represents autophagosomes.



Project 2:
Membranous expression of PD-L1 in the primary lung tumor and the brain metastasis.

Group of Eva Diamantis-Karamitopoulou, MD

Eva Diamantis-Karamitopoulou, MD
Martin Wartenberg, MD
Silvia Cibin, MD, Resident
Jon Brugger, MD (Resident)
Jens Brönnimann, Medical Student (MD-Thesis)

Short Summary

The main interest of the group is the study of the tumor microenvironment (TME) of the ductal pancreatic adenocarcinoma (PDAC). Since specific immune constellations may render the TME more or less amenable to cancer cell invasion, understanding the interaction between tumor- and immune cells will increase our knowledge of the diverse mechanisms of immune evasion employed by PDAC. Integration of molecular, morphologic and immunophenotypic findings, may lead to the identification of valuable clues for the development of strategies for targeted approach to the use of immunotherapy and/or other combinatorial treatments to augment immunity in the TME of PDAC.

Research Activities

Project 1: Integrated genomic and immunophenotypic classification of pancreatic cancer

By integrating immune cell background, molecular and histomorphologic data, we describe three distinct, clinically/biologically relevant pancreatic ductal adenocarcinoma (PDAC) subtypes: «immune escape», «immune rich» and «immune exhausted». These largely correspond to previously described molecular PDAC subtypes, thus providing a recognizable morphologic substrate integrating host immune response patterns with tumor-associated factors, including molecular features and biologic behavior of the tumors. This will enable the translation of molecular findings into clinically relevant information and may provide a basis for a more successful and individualized therape

Project 2: Identification of TME-Signatures of clinical subgroups of PDAC-patients

In this project we explore whether different PDAC survival groups, including long-rem, mid-term and short-term survivors, display subgroup-specific signatures regarding genomic and microenvironmental landscapes that influence tumor progression and therapy responses. The identification of unique microenvironmental characteristics and significant differences in subgroup-specific signatures and cytokine profiles would support the use of signature-tailored, individualized therapeutic approaches for PDAC-patients.

Internal Collaborations

- Aurel Perren, MD
- Erik Vassella, PhD
- Inti Zlobec, PhD
- Mirjam Schenk, PhD
- Hassan Sadozai, PhD

External Collaborations

National

- Beat Gloor, MD, Department of Visceral Surgery, Insel University Hospital, Bern
- Mathias Worni, MD, Department of Visceral Surgery, Insel University Hospital, Bern
- Luigi Terracciano, MD, Institute of Pathology, University of Basel
- Christine Sempoux, MD, Institute of Pathology, University of Lausanne
- Douglas Hanahan, PhD, Swiss Federal Institute of Technology Lausanne (EPFL)

International

- Prof. D. Tiniakos, Department of Pathology, Aretaieion University Hospital, University of Athens
- Prof. I. Esposito, Institute of Pathology, Heinrich-Heine-University and University Hospital of Duesseldorf

Grant Support

- Stiftung für klinisch-experimentelle, Eva Diamantis, CHF 60'000 (2016–2018)
- Tumorforschung Celgene, Eva Diamantis, CHF 100'000 (2018–2020)

Administrative duties

Eva Diamantis

- Coordination of Pathology Training Program, Institute of Pathology, University of Bern
- Coordination of the weekly research seminars, Institute of Pathology, University of Bern
- Member of the «Weiter- und Fortbildungskommission» of the Swiss Society of Pathology
- Fachdelegierte der SGPath in der Weiterbildungsstättenkommission (WBSK)

Group of Rupert Langer, MD

Bastian Dislich, MD, PhD
Ariane Janser, PhD Student (Co-supervision Mario Tschan)
José Galvàn, PhD (20%)

Master students / dissertation candidates:
Nicola Blaser, Julia Wiprechtiger, Matea Sunic,
Lisa Alfare, Sandra Reschke, Mafalda Trippel, Ronan Gabriel,
Andreas Schmid, Claudia Jaccard, Short Summary

Short Summary

The focus of the working group are tumors of the upper gastrointestinal tract, in particular of carcinomas of the esophagus. We investigate different morphological and molecular pathological characteristics in correlation with biological and clinical factors, response to therapy (e.g., neoadjuvant chemotherapy or targeted therapy), and patient prognosis. In addition to tissue-based analyzes that include histomorphological and immunohistochemical studies, functional studies on cell lines in 2D and 3D culture models are also part of our research activity.

Research Activities

Project 1: Mechanisms of response to chemo- and targeted therapy in esophageal carcinomas

Esophageal carcinomas show a high rate of resistance to chemotherapy, but also to targeted therapies (such as Her2 or EGFR directed therapies). We are investigating molecular characteristics that may predict the response to such therapies, or mechanisms that may explain this resistance. In this context, we focus on the cellular mechanism of autophagy, which can ensure survival under stress in both normal and neoplastic cells. On the other hand, tumors may also show intrinsic molecular aberrations associated with response to particular forms of therapy. Here we investigate case collections of neoadjuvant treated tumors using comprehensive moleculargenetic methods.

Project 2: The role of cancer associated fibroblasts in the therapeutic response

Several studies indicate that Cancer Associated Fibroblasts (CAFs) promote cancer progression and chemoresistance through multiple growth factors and signaling pathways, which are potential targets for anticancer therapies. We investigate the role of CAFs in Esophageal Adenocarcinomas and Esophageal Squamous Cell Carcinoma with a special focus on therapy response and tumor regression after neoadjuvant chemo- or radiochemotherapy. Visualization of CAFs is performed by immunohistochemical detection of proteins such as COL11A1, CD90 and SPARC. Scores are determined in primary resected tumors in comparison to tumors after neoadjuvant treatment. Since the tumor stroma has been recently considered also as potential therapeutic target, our results may also serve as base for the development of future cancer therapy.

Project 3: Tumor Immunology of gastric adenocarcinoms

Immune checkpoint inhibitors represent a promising therapeutic approach in the setting of locally advanced and metastasized gastric adenocarcinomas. Selection of patients that are likely to respond to therapy is crucial, as not all tumors will demonstrate a significant response to immunotherapy. In order to identify predictive features in those tumors, this project focusses on the immunological landscape and its dynamic during tumorigenesis and tumor progression. The main focus is the analysis of PD-L1 expression and the characterization of the immune cell infiltrate in primary tumors, as well as lymph node and distant metastases. Tissue will be analyzed using conventional histomorphological and immunohistochemical techniques and digital image analysis Our aim is to identify predictive tumoral features and gain more insight into the role of the immunsystem during tumor progression.

Internal Collaborations

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

External Collaborations

National

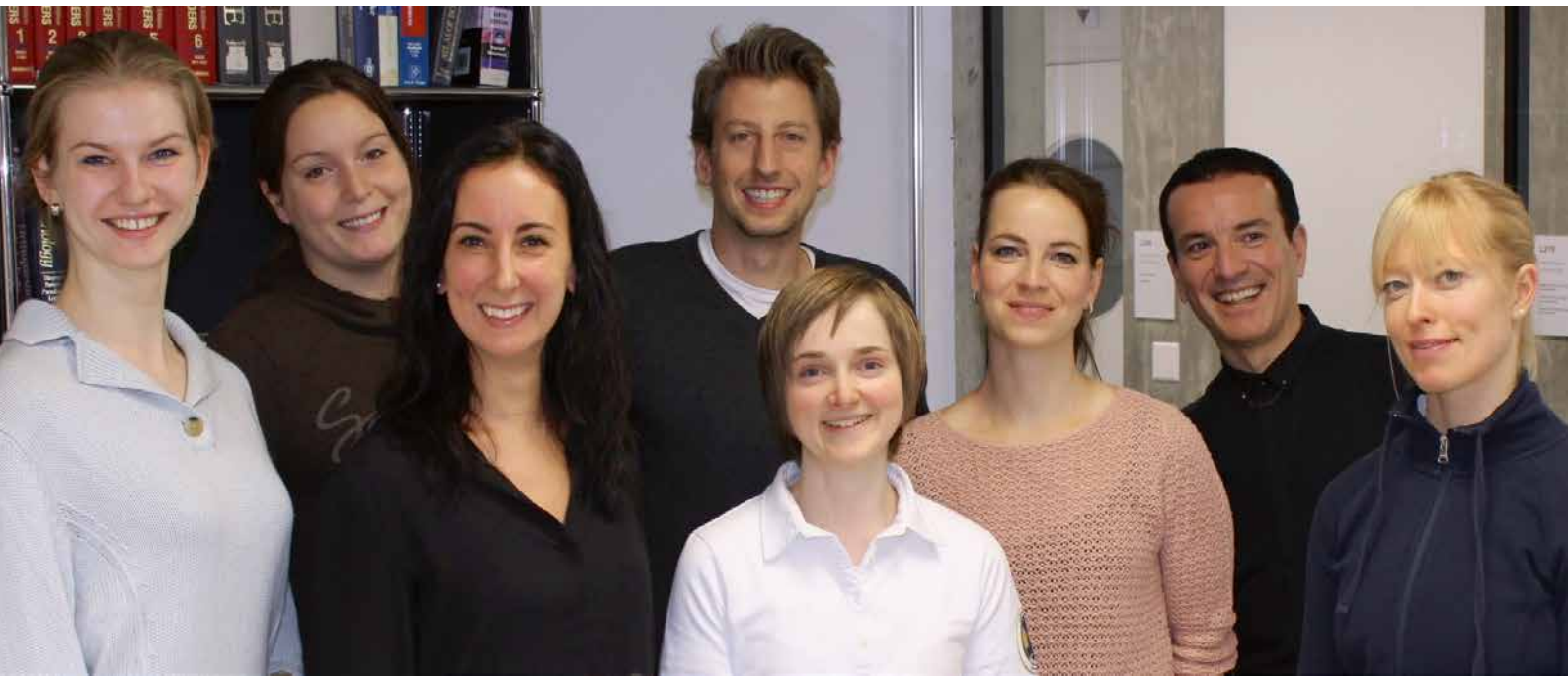
- Prof. C.A. Seiler and Dr. Dino Kroell, Department of Surgery, Inselspital

International

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

Grant Support

- Schweizerische Krebsliga KFS-3700-08-2015, Rupert Langer (PI), Mario Tschan (Co-I), *CHF 214'000 (2016–2018)
- SAKK 75/08, Rupert Langer (PI), Erik Vassella (Co-PI), CHF 130'000 (2018)
- Krebsstiftung Schweiz, Rupert Langer and José Gàlvan, CHF 15'000 (2017–2018)
- Hans-Altschüler-Stiftung, Rupert Langer and José Gàlvan, CHF 9700 (2018)
- Claudia von Schilling Stiftung, Rupert Langer, CHF 30'000 (2018)



Team Translational Research Unit (TRU).

Group of Inti Zlobec, PhD, and Alessandro Lugli, MD

Alessandro Lugli, MD, Vice Chair
Inti Zlobec, PhD, Head of TRU
Annika Blank, MD, staff pathologist
Heather Dawson, MD, staff pathologist
Kristin Uth-Gottardi, MSc, PhD student
Stefan Zahnd, MSc, PhD student

MD Thesis and Dissertation students:
Melanie Bächli
Sandra Burren, MD
Lucine Christe, MD
Elia Fischer, MD
Christian Lambert
David Marx, MD;
Sara Nada Meyer, MD
Luca Noti
Katharina Reche
Lynn Richmond, MD
Carla Schenker, MD
Julia Unternaehrer

Short Summary

Our research focuses on histopathological, translational and molecular aspects of colorectal cancers. We are particularly interested in the diagnostic and biological aspects of tumor budding and their microenvironment, the molecular classification of colorectal cancers, the identification or validation of biomarkers and their implementation into clinical routine.

Research Activities

Project 1: The epigentic landscape of CDX2

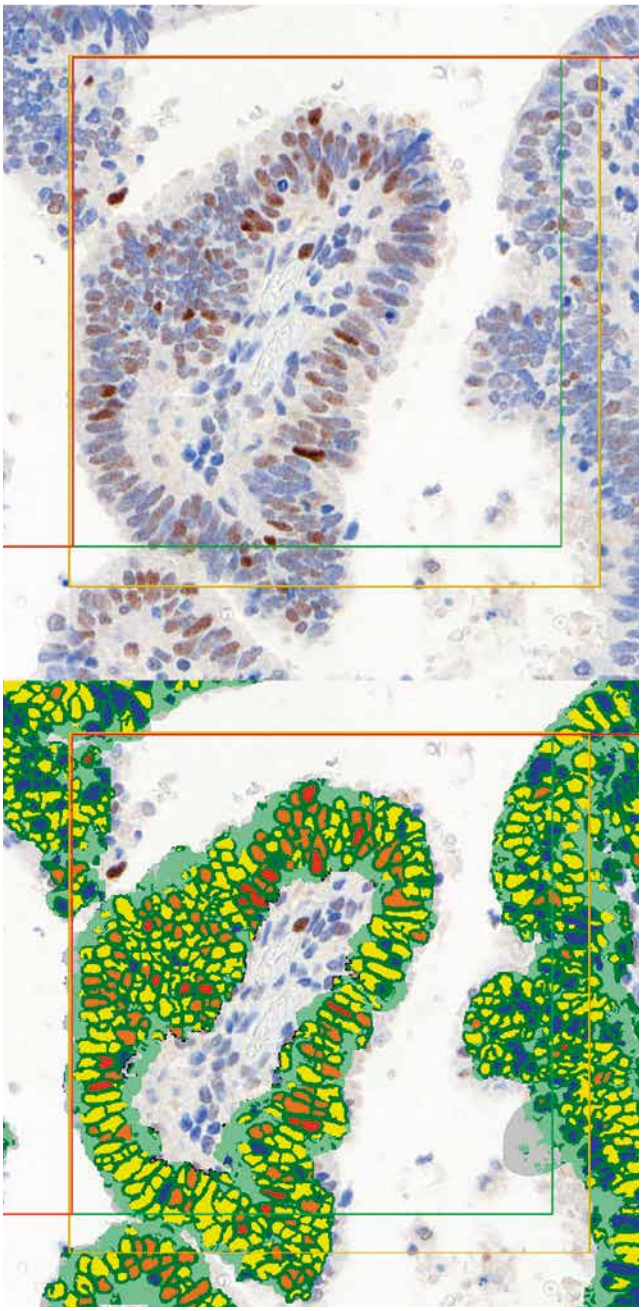
Up to 20% of colorectal cancers have decreased expression or complete loss of CDX2 protein. CDX2 loss is associated with microsatellite instability, high-level CpG island methylation and BRAF mutation, features consistent with the serrated pathway. Our functional studies show that hypermethylation of the CDX2 promoter is a major reason for this loss and can be recovered with DNMTi treatment. Together with the group of Prof. M. Tschan, we investigate genetic and epigenetic modifications of CDX2 using CRISPR/Cas9 technology.

Project 2: Tumor budding in colorectal cancer

Tumor buds are linked to aggressive tumor behaviour and poor prognosis. One of our objectives is to standardize the assessment and reporting of tumor budding in routine diagnostics. This was the main incentive for our group to initiate and organize the first International Tumor Budding Consensus Conference (ITBCC) which took place in 2016. The proceedings of the ITBCC were published in the journal 'Modern Pathology' in 2017 and have since been integrated in reporting protocols of major societies such as the College of American Pathologists. One of our ongoing projects is to validate the ITBCC recommendations on large colorectal cancer cohorts, also in collaboration with the International Budding Consortium (IBC). Other aspects of our research are focused on further characterization of tumor buds in primary colorectal cancer and colorectal liver metastases within the tumor microenvironment. Our ultimate goal is to find targets that can be used against tumor buds in a therapeutic setting.

Project 3: Development of NGTMA Pipelines

We investigate the role of machine and deep learning in addressing clinically relevant research questions, predominantly in gynecological and colorectal cancers. Together with PD Dr. Tilman Rau, the TRU and the digital pathology team, pipelines for handling data from next-generation Tissue Microarray (ngTMA®) construction to assessment of immunostaining and integration of scores with clinical, histopathological and other research data for statistical analysis are performed by the group. We create and implement tools for quality control and optimization of digital workflows and apply these tools as a basis for our clinically oriented biomarker studies.



Project 3: Example of p53 in an endometrial cancer within an ngTMA experiment.

Internal Collaborations

- Mario Tschan, PhD
- Erik Vassella, PhD
- Tilman Rau, MD
- Philippe Krebs, PhD
- Rupert Langer, MD
- Eva Diamantis, MD

External collaboration

National

- Lukas Brügger, Beat Schnüriger, Peter Studer Drs. and members of the Departments of Oncology and Visceral Surgery, Inselspital, Bern, Switzerland
- Raphael Sznitman, Prof. (Ophtalmic Technology Laboratory, ARTORG, University of Bern, Switzerland)
- Luigi Terracciano, Prof. (Institute of Pathology, University Hospital Basel, Switzerland)
- Gieri Cathomas, Prof. (Institute of Pathology, Kantonsspital Liestal, Switzerland)

International

- Louis Vermeulen, Prof. and Anne Trinh, Dr. (University of Amsterdam, Netherlands)
- Iris Nagtegaal, Prof. (University of Radboud, Nijmegen, Netherlands) and members of the International Tumor Budding Consensus Conference (ITBCC) and Budding Consortium

Grant support

- Personalized Health and Related Technologies, J.P. Thiran, I. Zlobec, CHF 182'918 (2018–2020)
- Swiss National Science Foundation, D. Stroka-Keough, I.Zlobec, CHF 759'800 (2018–)
- Rising Tide Foundation, I.Zlobec, J.P. Thiran, CHF 293'800 (2018–2021)
- Swiss Cancer League, I.Zlobec, J.P. Thiran, CHF 361'270 (2018–2021)
- Dutch Cancer Society (Consortia grant), Prof. Iris Nagtegaal, I.Zlobec, A. Lugli, Consortia, EUR 100'000 (2017–2020)
- Swiss Cancer League, Prof. M. Hediger, I.Zlobec, CHF 50'000 (2017–2020)
- Swiss National Science Foundation, I.Zlobec, M. Tschan, CHF 305'040 (2016–2019)
- Swiss National Science Foundation, S. Benhamou, I.Zlobec, CHF 191'117 (2015–2018)
- Swiss Cancer League, A. Lugli, H. Dawson, CHF 139'450 (2017–2019)

2 Akademische Grade

Olivier Blanchard, PhD
The Role of Sphingosine-1-Phosphate in Renal Proximal Tubular Epithelial Cell Inflammation and Fibrosis

Xenia Ficht, PhD
Mechanisms underlying tissue-resident memory T cell surveillance of non-lymphoid tissues

Claire Micossé, PhD
IL-4- and TGF-β-induced PPAR-γ promotes the IL-9-expressing subpopulation of TH2 cells

Nadia Oehninger, MSc
The regulation of the inflammatory response by oxidized lipids

Raviprasadh Rajasekaran, PhD
Influence of HINT-2 on Mitochondrial Protein Acetylation: Mechanism and Significance

Ioannis Kritikos, MSc
The differential role of IL-33 in colorectal cancer development

Marie-Hélène Wasmer, PhD
The role of IL-33/ST2 signaling in tumorigenesis and immunopathology

Catherine Mooser, PhD
A novel gnotobiotic mouse model as a tool to study dietary effects on the microbiota, the host, and their interplay

Egle Radice, PhD
Functional expression of the scavenger ACKR3 on B Lymphocytes of Secondary Lymphoid Organs

Marcel Sorribas Olivera, PhD
Intestinal mucus and vascular barrier in liver cirrhosis: entry site for bacterial translocation independent from portal hypertension and lymphatic route

Martin F. Faderl, PhD
Host-microbial interactions during steady state and intestinal inflammation in a gnotobiotic mouse model of remitting-relapsing colitis

Andreas Gutersohn, MD
The chemokines CCL11, CCL20, CCL21, and CCL24 are preferentially expressed in polarized human secondary lymphoid follicles

Maryam Hussain, PhD
Role and Regulation of the Microbiota and Innate Immune Cells in the Pathogenesis of Food Allergies

Janine Straub, M Med
Organisation und Aktualisierung des Berner PanNET-Kollektives

Fabrizio Motta, BSc
Epigenetic treatment in pancreatic murine NET cells

Avanee Ketkar, MSc
Targeting epigenetic changes in Pancreatic Neuroendocrine tumors

Sophie Milesi, MSc
Cancer-associated fibroblasts and their role in autophagy modulation and therapy resistance in breast cancer

Limei Wang, PhD
Distinct mesenchymal and epithelial lineages in human lung and diverse settings of lung diseaseas

Rahel Wacker, PhD
The host cell cytosolic immune response during Plasmodium berghei liver stage follows a noncanonical autophagy pathway

Elias Bührer, PhD
Extrinsic and intrinsic regulation of cancer stem cells

Manuel Keller, MD
Adverse prognostic value of PD-L1 expression in primary resected squamous cell carcinomas of the lung and paired mediastinal lymph node metastases

Corina Bello, Mmed
Komplettierung der klinisch-pathologischen Charakteristika und Überlebensdaten eines Kollektivs neoadjuvant behandelter Lungenkarzinome und einer Kontrollgruppe primär resezierter Tumore

Jens Brönnimann, Dr. med
Role of SMADs in epithelial mesenchymal transition in pancreatic cancer

S. Cibin, Dr. med
Integrative immunophenotypic and genetic analysis of pancreatic cancer reveals distinct immunophenotypes with prognostic/predictive significance

Ronan Gabriel, Dr. med
Assessment of coronary artery stenosis in routine autopsy practice

Simon Nobs, Dr. med
Erweiterung und Verbesserung des interaktiven MorphoMed Histopathologiekurses durch Annotationen, Begleittexte und Verlinkung von Bildern makroskopischer Präparate

Laura Noser, Dr. med
Application of the 8th edition of the AJCC yTNM staging system shows improved prognostication in a single center cohort of esophageal carcinomas

Mariana Bustamante Eduardo, PhD
A comparison of molecular signatures for breast cancer and analysis of the role of the progesterone receptor in breast cancer cells

Janina Graule, MD
CDX2 in colorectal cancer is an independent prognostic factor and regulated by promoter methylation and histone deacetylation in tumors of the serrated pathway

Claudia Lädrach, MD
Immunophenotypic profile of tumor buds in breast cancer

3 Publikationen

Artikel in Fachzeitschrift

- Adams OJ, Janser AF, Dislich B, Berezowska SA, Humbert M, Seiler CA, Kröll D, Slotta-Huspenina J, Feith M, Ott K, Tschan M, Langer R
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  NAT REV CANCER, 18(4): 203-4

4 Vorträge

Stefan Freigang
- 23.05.18: Unravelling protective signaling pathways in acute lung injury using a novel lung-on-chip technology
  Annual Meeting of the Swiss Society of Pneumonology, talk
- 29.07.18: Immune recognition of lipids in inflammation and immunopathology
  International Summer School 2018, talk

Olivier Friedli (Group Stefan Freigang)
- 30.08.18: Mitochondrial uncoupling in the regulation of T lymphocyte function
  Annual Meeting of the Swiss Society of Allergology and Immunology, poster

Philippe Krebs
- 16.01.18: Determine the role of death receptor and death ligand signaling in sculpting NK cell functions
  DISCOVER (consortium) Meeting, Dublin, Ireland, seminar
- 15.02.18: Transcriptional and post-transcriptional regulation of immunopathology
  Hebrew University of Jerusalem, Jerusalem, Israel, seminar
- 15.03.18: Transcriptional and post-transcriptional regulation of immunopathology
  IRIBHM, Université Libre de Bruxelles (ULB), Belgium, seminar
- 19.04.18: IL-33/ST2 signaling in cancer und immunopathology
  Institute of Immunobiology, Kantonsspital St.Gallen, seminar
- 09.05.18: The ESRP1-GPR137 axis contributes to intestinal pathogenesis
  ZHAW, Wädenswil, seminar
- 27.06.18: The role of IL-33 signaling for the pathogenesis of myeloproliferative neoplasms
  Swiss Oncology & Hematology Congress (SOHC), Zurich, conference
- 24.08.18: Establishment of a tumor tissue bank containing infectious samples
  SBNet meeting, Lugano, conference
- 15.10.18: Determine the role of death receptor and death ligand signaling in sculpting NK cell functions
  DISCOVER (consortium) Meeting, Athens, Greece, seminar
- 06.12.18: Role of IL-33/ST2 signaling for myeloproliferative neoplasms
  University Hospital Bern, Switzerland, seminar

Christoph Müller
- 30.06.18: Shaping of immunity by the microbiota
  Annual Meeting Swiss Society of Allergology and Immunology (Interlaken) 2018 (Chair)
- 27.09.18: Commensals, pathobionts and pathogens: lessons learnt from a gnotobiotic mouse model of colitis
  International Conference on Oral Mucosal Immunity and Microbiome (Crete, GR) / Invited speaker

Mairo Noti
- 24.05.18: The aging gut microbiome
  Free Novation Symposium, Novartis Institutes for Biomedical Research, Basel, Switzerland. Invited Seminar
- 18.04.18: Type-2 immune cells in allergic inflammation and beyond
  RIA Lunch meeting, invited Seminar, Bern, Switzerland
- 18.02.18: Food allergies and the microbiome
  Nestlé Research Center, Epalinges, Switzerland

Aurel Perren
- 01.01.18: Lean management in Pathology
  SydPath St. Vincent Pathology, Sydney, Australia
- 09.09.18: Chair: best poster session
  European Congress of Pathlogy, Bilbao, Spain
- 11.09.18: Grade 3 GEP neuroendocrine neoplasms: from pathology to the clinic and back
  ENETS an Endocrine PathologyWG Joint Symposium, Bilbao, Spain
- 16.09.18: Recent Advances in Pathology of Gstroentero-pancreatic Neuroendocrine Tumors
  2018 Bejiing International Symposium on Gastroentero-pancreatic Neuroendocrine Tumors, Beijing, China
- 02.11.18: Der Pathologe im Zentrum der neuroendokrinen Tumore
  28. Berner Chirurgie Symposium, Inselspital, Bern
- 29.11.18: Standardised Reporting in NET: Pathology
  ENETS Advisory Board Meeting, Palma de Mallorca
- 13.12.18: Keynote Lecture: Pathology – what's new, what's hot
  Surger-I-nnsbruck 2018, Innsbruck, Germany

Ilaria Marinoni
- 22.09.18: Organoide: Neue Zielproteine und innovative Ansätze
  5th Interdisciplinary Symposium: Neuroendocrine Neoplasia Berlin, Germany

Matthias Dettmer
- 04.10.18: Bekanntes und neues von Schilddrüsenkarzinomen: Pathology meets surgery
  Fortbildung «Chirurgie Update», Triemlispital Zürich, Germany

Mario P. Tschan
- 12–13.02.2018: Chair: Novel Regulatory Mechanisms in Autophagy and Apoptosis
  Life Sciences Switzerland (LS2) Annual Meeting, Lausanne
- 28.08.18: Autophagy in Breast Cancer Therapy and Migration
  Basel Breast Consortium, invited talk
- 12.09.18: Concepts and Methods in Cell Death and Autophagy, Crosstalk in Academic and Pharamceutical Biomedical Research
  LS2 Satellite Symposium Bern, Co-Organizer and Symposium Chair

Magali Humbert (Group Mario Tschan)
- 13.09.18: Elucidating the Non-Catalytic Function of Fatty Acid Synthase and its Autophagy-Dependent Degradation in Acute Myelocytic Leukemia Differentiation Therapy
  10th Swiss Apoptosis Meeting, Bern

Anna Schläfli (Group Mario Tschan)
- 19.10.18: Ceritinib induces autophagy-dependent proteolysis in EML4-ALK positive lung cancer cells – Is it LC3B independent autophagy?
  8th Annual CFATG «Club Francophone de l'AuTophaGie

Sabina Berezowska
- 03.02.18: Chair und Vortrag: PD-L1 Testung
  Wintertagung der AG Thoraxpathologie DGP, Zürich
- 28.06.18: Gemeinsam zur Diagnose – praktisches ILD Board
  «Lungentag» der Universitätsklinik für Pneumologie mit Unterstützung des BIHAM
- 30.06.18: Diagnostik interstitieller Lungenerkrankungen im multidisziplinären Team
  IAP-Ganztagstutorial, Bonn
- 14.09.18: Update on the WHO brain tumor classification: an integrative approach
  10. Swiss Young Neurosurgeons Symposium «Neuro-Oncology», Vevey

- 19.10.18: ILD-Diagnostics – radiological and pathological correlations
  Belgian Days of Pathology, Brussels
- 01.11.18: Pathology classification & TNM staging
  (Certificate of Advanced Studies in Lung Cancer Programme, University of Zurich (UZH) in co-operation with the European School of Oncology (ESO) – e-learning platform)
- 19.11.18: Autophagie und assoziierte Erkrankungen in der Lunge
  Department of Thoracic surgery and Department of Pulmonology, Inselspital Bern

Eva Diamantis-Karamitopoulou

- 06.04.18: The impact of tumor microenvironment on phenotype and prognosis of pancreatic cancer
  Freitagskolloquium des Instituts für Pathologie & Molekular-pathologie am Universitätsspital Zürich
- 09.09.18: Chair, Symposium: What's new in Pancreatic Cancer
  30th European Congress of Pathology, Bilbao, Spain
- 09.09.18: Pancreatic cancer and its microenvironment
  30th European Congress of Pathology, Bilbao, Spain
- 11.09.18: Chair: Poster Session Digestive Diseases Pathology: Liver and Pancreas
  30th European Congress of Pathology, Bilbao, Spain
- 12.09.18: Pancreatic cancer: what is hot
  30th European Congress of Pathology, Bilbao, Spain

Alessandro Lugli

- 2.2.–3.2.2018: Colorectal cancer subtyping
  SAMO GI Tumors, Luzern
- 19.06.18: Session: Early Colorectal Cancer – Bowel Cancer Screening
  Maastricht Pathology Days, Maastricht
- 18.07.18: L'Autopsie de Napoléon
  Interne Fortbildung, Spitalzentrum Biel
- 23.08.18: Update in Pathology of inflammatory bowel disease
  SAGIP Meeting, Bern
- 1.11.–3.11.2018, Tumor Budding in colorectal cancer
  Pathology Congress, Bucharest
- 03.12.18: Tumor Budding in colorectal cancer
  Interne Fortbildung, Pathologie Basel
- 19.12.18: Tumor Budding in colorectal cancer
  Interne Fortbildung, Radioonkologie, Inselspital Bern

Inti Zlobec

- 07.12.18: The next-generation of tissue microarray challenges: data integration into digital workflows
  5th Digital pathology and AI congress: Europe, London, UK
- 28.11.18: Digital pathology in Translational Research
  Current topics in Pharmacology and Theranostics, Department of Pharmacology, UniBern
- 23.11.18: Digital pathology: the Bern experience
  SAKK Semi-Annual Meeting, Zurich, Switzerland
- 09.09.18: Digital pathology in Translational Research
  European Congress of Pathology, Bilbao, Spain
- 15.03.18: CDX2- an unfinished story
  Basic-Clinical-Translational Meeting, Insel Hospital, Bern

Heather Dawson

- 13.01.18: Tumor Budding 2.0 – Aktuelle Möglichkeiten und Perspektiven
  Bamberger Morphologietage
- 30.05.18: Lean-Management und Leadership in der klinischen Pathologie im Zeitalter der Digitalisierung und Automatisierung
  Lean Healthcare Symposium, Rüschlikon

5 Drittmittel

Stefan Freigang
- SNF 310030_152872 (2015–2018), CHF 510'000
- Vontobel-Stiftung (2014–2018), CHF 120'000
- UniBE-ID Grant (2016–2018), CHF 150'000

Stefan Freigang (Co-PI)
- 3R Research Foundation (2016–2018), *CHF 138'000

Stefan Freigang (PI)
- Swiss Lung Liga (2017–2019), *CHF 162'000
- UniBE-ID Grant (2018–2019), CHF 150'000

J. Baumgartner
- UniBE2021 PhD fellowship (2017–2020), CHF 90'000

Philippe Krebs
- Marie Curie Career Integration Grants (CIG) (2012–), € 100'000
- Seed money project (2018–2019), CHF 10'000
- Lungenliga Bern (2018–2020), CHF 79'554
- Lungenliga Schweiz (2018–2020), CHF 79'554
- Swiss Cancer Research foundation (2017–2020), CHF 312'500
- SNSF163086 (2016–2019), CHF 525'000
- Kurt und Senta Herrmann Foundation (2017–2018), CHF 30'000
- Fondazione San Salvatore (2016–2018), CHF 120'000
- Swiss Life / Jubiläumsstiftung (2017–2018), CHF 30'000
- Carigest (2018–2020), CHF 130'000

Main PI: Philippe Krebs
- UniBE ID (Interdisciplinary) Grants (2018–2020), *CHF 75'000

Co-PI: Philippe Krebs
- Commission for Technology and Innovation (2017–2019), CHF 163'416
- EU / Marie Skłodowska-Curie RISE (2018–2022), € 67'500

Mager, Krebs
- Gertrud-Hagmann-Stiftung (2015–2018), CHF 241'566

Christoph Mueller
- SNF 310030_170084 (2016–2019), CHF 525'000
- SNF 33CS30_148422 (SIBDCS, Co-PI) (2016-2018), CHF 200'000 *
- SNF 33CS30_177523 8 (SIBDCS Co-PI) (2018–2020), CHF 304'500 *

Christoph Müller, Daniel Zysset
- Monique Dornonville de la Cour Stiftung (2018–2019), CHF 52'387

Mario Noti
- Fondation ACTERIA (2018–2020), EUR 150'000
- Novartis FreeNovation (2016–2018), CHF 180'000

Ilaria Marinoni
- Tumor Forschung Bern (2015–2018), CHF 90'000
- SNF Marie Heim-Vögtlin (2016–2018), CHF 206'000
- Desirée and Niels Yde Foundation (2016–2019), CHF 54'000
- Wilhelm Sander Stiftung (2018–2019), CHF 210'000
- Bernische Krebsliga (2018–2022), CHF 40'000

Aurel Perren, Ilaria Marinoni
- KLS-4227-08-2017 (Aurel Perren PI and Ilaria Marinoni co-PI) (2018–2019), CHF 360'000

Matthias Dettmer
- Berner Krebsliga (2017–2022), CHF 70'000

Mirjam Schenk
- Stiftung experimentelle Biomedizin (2016–2019), CHF 763'000
- Werner Hedy Berger-Janser (2016–2018), CHF 110'000
- Klinisch Experimentelle Tumorforschung (2016–2019), CHF 150'000
- Helmut Horten (2017–2020), CHF 180'000
- SNF (2018–2022), CHF 566'109

Mario Tschan
- SNSF_31003A_173219 (2017–2021), CHF 693'600
- SNSF MD-PhD 03/17, Kristina Seiler (2018–2020), CHF 180'000
- UniBE international 2021, I.Tokarchuk (2018–2020), CHF 90'000

Magali Humbert
- BKL (2017–2018), CHF 85'000
- UniBE Initiator Grants (2017–2018), CHF 16'500
- Stiftung Für Klinisch-Experimentelle Tumorforschung (2018), CHF 20'000

Mario Tschan
- KFS, KFS-3409-02-2014 (2014–2018), CHF 390'000
- COST Action: CA15138, Short Term Scientific Mission (STSM) (2018), EUR 2'500
- UniBE Forschungsstiftung, 45/2018, Claudia von Schilling Foundation (2018), CHF 9'600

Co-PI Mario Tschan
- Werner und Hedy Berger-Janser, UniBE ID Grant, T. Ochsenreiter (2018–2019), *CHF 105'000
- Partenariat Hubert Curien/Germaine de Staël Funding, J.E. Sarry (2019–2020), *CHF 9'000

Anna (Schläfli) Bill
- Werner und Hedy Berger-Janser Stiftung (2018–2019), CHF 77'000

Erik Vassella
- SNF (31003A_175656) (2018–2022), CHF 408'509

PI Sabina Berezowska
- Hedy Berger-Janser Stiftung (2018), CHF 80'000
- Fondation Johanna Dürmüller-Bol (2017–2018), CHF 9'500
- Stiftung zur Krebsbekämpfung (2018), CHF 20'000

Eva Diamantis
- Stiftung für klinisch-experimentelle Tumorforschung (2016–2018), CHF 60'000
- Celgene (2018–2020), CHF 100'000

Rupert Langer (PI), Mario Tschan (Co-I)
- Schweizerische Krebsliga KFS-3700-08-2015 (2016–2018), *CHF 214'000

Rupert Langer (PI), Erik Vassella (Co-PI)
- SAKK 75/08, Rupert Langer (PI), Erik Vassella (Co-PI) (2018), *CHF 130'000

Rupert Langer and José Galván
- Krebsstiftung Schweiz (2017–2018), CHF 15'000
- Hans-Altschüler-Stiftung (2018), CHF 9'700

PI Rupert Langer, Co-PI M. Tschan
- Claudia von Schilling Stiftung, CHF 30'000

PI D. Stroka-Keough, Co-PI I.Zlobec
- Swiss National Science Foundation, 316030_183501/1 (2018), CHF 50'653

PI J.P. Thiran, Co-PI I. Zlobec
- Personalized Health and Related Technologies, PHRT-327 (2018–2020), CHF 182'918

PI I. Zlobec, Co-PI J.P. Thiran
- Rising Tide Foundation, CR-18-800 (2018–2021), CHF 293'800
- Swiss Cancer League, KFS-4427-02-2018 (2018–2021), CHF 361'270

PI Prof. Iris Nagtegaal, Co-PI I. Zlobec, A. Lugli
- Dutch Cancer Society (Consortia grant) (2017–2020), CHF 100'000

PI Prof. M. Hediger, Co-PI I. Zlobec
- Swiss Cancer League, KFS-3966-08-2016 (2017–2020), CHF 50'000

PI I. Zlobec, Co-PI M. Tschan
- Swiss National Science Foundation, 31003A_166578 (2016–2019), CHF 305'040

PI S. Benhamou , Co-PI I. Zlobec
- Swiss National Science Foundation, 320030_163342 (2015–2018), CHF 191'117

PI A. Lugli, Co-PI H. Dawson
- Swiss Cancer League, KFS 4108-02-2017 (2017–2019), CHF 139'450

6 Preise, Ernennungen, Auszeichnungen

Annunziata Di Domenico
7.–9.03.2018: First prize for best Oral Basic Science Abstract European Neuro-Endocrine Tumor Society 14th Annual Conference, Barcelona, Spain

Ulrich Baumgartner
01.12.2018: Lutz-Zwillenberg Prize
Dies academicus, Universität Bern

Yara Banz
01.12.2018: Teacher of the Year
Dies academicus, Universität Bern

Heather Dawson
30.05.2018: Lean Healthcare Award 2018
Lean Healthcare Symposium 2018

Ulrich Baumgartner sowie Manon Karin Schweinfurth, Dr. Lutz-Zwillenberg-Preis.

Rektor Christian Leumann und Yara Banz Wälti, Teacher of the Year.

Lean Healthcare Award 2018.

>>> 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, Allgemeinen und Speziellen 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 Sciences (GCB) 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.

Studiengang Humanmedizin und Zahnmedizin
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 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, histologische Schnittpräparate virtuell zu mikroskopieren, und diese anhand von bereits eingearbeiteten Annotationen für die spätere Besprechung im Histologiekurs vorzubereiten.

Die Grundlagen der Allgemeinen Pathologie lernen die Studierenden im letzten Jahr des Bachelor-Teils des Medizinstudiums im 3. Studienjahr (Einführungskurs 1). Dieses geschieht eingebettet in interdisziplinäre Vorlesungsveranstaltungen, die spezielle Themenblöcke behandeln, zum anderen im Fachpraktikum Pathologie, wo unterstützt durch die Histologie die Grundmechanismen der Pathologie und 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 Masterstudiengang, hier zunächst im 4. Studienjahr (Einführungskurs 2) und im 5. Studienjahr (Schlusskurs 1) wird das erlangte Wissen auf die spezielle organbezogenen 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 wöchentlichen Autopsiedemonstrationen statt, in denen anhand aktueller Fallbeispiele die aktive Erarbeitung pathophysiologischer Zusammenhänge und Sequenzen verschiedenster Krankheiten im Vordergrund steht. Zudem wird unser Institut bei den Studierenden als sehr guter Ort angesehen, um im Rahmen einer Masterarbeit ersten Kontakt mit wissenschaftlichen Arbeiten zu erhalten, und auch später wird die Möglichkeit angenommen, dieses in einer folgenden Dissertation fortzusetzen.

Vorlesungen	Kurse	Fakultativ
Studiengang Humanmedizin, 3. Jahr		
Allgemeine Pathologie innerhalb von Themenblöcken	Fachpraktikum	Vertiefungsseminar
	PBL (Problembasiertes Lernen)	
Studiengang Humanmedizin, 4. und 5. Jahr		
Spezielle Pathologie	Makrokurs (4. Jahr)	Masterarbeit
	Histologiekurs (4./5. Jahr)	
Vorlesungen	Autopsiedemo (4./5. Jahr)	
Studiengang Humanmedizin, 6. Jahr		
		Wahlpraktikum

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

Im 6. Studienjahr können Studierende, die ihre Kenntnisse im Fach Pathologie vertiefen wollen, oder sich für eine spätere Fachausbildung in diesem Fach interessieren, im Rahmen des «Wahlstudienjahrs» 1–2 Monate auf der Pathologie verbringen. Hier durchlaufen sie ein strukturiertes Curriculum, im Rahmen dessen alle Tätigkeitsgebiete der Pathologie, wie die Autopsie, die makroskopische und histologische Diagnostik und die Zytologie, aber auch die Molekularpathologie kennengelernt werden können.

Für die Studierenden der Zahnmedizin gibt es im 3. Jahr eine Vorlesungsreihe «Pathologie», in der sowohl die Allgemeine Pathologie, als auch die spezielle Pathologie einzelner wichtiger Organsysteme abgebildet ist. Im 5. Jahr werden spezielle orale Pathologien in weiteren Vorlesungen behandelt.

Studiengang Zahnmedizin Vorlesungen	
3. Jahr	**5. Jahr**
Allgemeine und Spezielle Pathologie	Spezielle Pathologie des Mund- und HNO-Bereichs

Studiengänge der Philosophisch-Naturwissenschaftliche Fakultät

Die Mitarbeitenden der Experimentellen Pathologie sind ausserdem an der Ausbildung der Studierenden der philosophisch-naturwissenschaftlichen Fakultät (phil. nat.) beteiligt. Diese Lehrveranstaltungen werden in einem Modulformat angeboten, so dass Studierende verschiedener Fächer gleiche Vorlesungsreihen besuchen.

1. Seminarreihen

- Journal Club
  (Gruppen des Instituts für Pathologie, monatlich)
- Joint Immunology Group Meeting
  (Institut für Pathologie, monatlich)
- Joint Immunology Group Meeting
  (Gruppen der Universität Bern, monatlich)
- Bern Immunology Club
  (Vorträge externer Seminargäste, monatlich)
- DKF Research Conference (monatlich)

2. Vorlesungsreihen im Fachgebiet Pathologie

Im Rahmen der phil. nat. Fakultät der UniBE werden von Dozierenden des Instituts folgende Vorlesungsreihen im Modulformat angeboten und koordiniert:

2.1. General Pathology and Histology

Coordinator: Philippe Krebs

Affiliation of lecturers: Institute of Pathology und Institute of Anatomy, UniBE
Target students: BSc, MSc and PhD students in Cell Biology and Biomedical Sciences.

General overview of the course:

Cellular mechanisms of pathology
Histology of normal tissue
Molecular mechanisms of pathology
Pathology of specific organ systems: – theoretical classes – practical classes

2.2. Selected Topics in Molecular Pathology

Coordinator: Erik Vassella

Affiliation of lecturers: Institute of Pathology, UniBe, DKF/Inselspital, Institute of Pathology, UniBas
Target students: BSc, MSc and PhD students in Cell Biology or Biomedical Sciences.

General overview of the course:

Methods and animal models of pathology
Molecular mechanisms of pathology
Tumor biology and molecular oncology
Molecular diagnostics

2.3. Cellular and Molecular Immunology

Coordinator: Christoph Müller

Affiliation of lecturers: Institute of Pathology, DKF/Inselspital, Vetsuisse-Fakultät
Target students: BSc, MSc and PhD students in Cell Biology or Biomedical Sciences.

Methods and animal models in immunology research
Specific immune cell subsets in health and disease
Molecular mechanisms of inflammation
Molecular aspects of vaccine development

3. Weitere Lehrveranstaltungen

Dozierende der Experimentellen Pathologie unterrichten zudem in Lehrmodulen, die von anderen Instituten koordiniert werden, wie dem «Practical Course in Immunology» des Instituts für Zellbiologie (phil. nat. Fakultät), in Seminarveranstaltungen im Gebiet Tumorpathologie, in der Vorlesungsreihe «Blut und Abwehr» im 2. Studienjahr Medizin und dem dazu gehörenden Lerngruppenunterricht (PBL). Weiterhin sind Dozierende des Instituts im Rahmen von 3–4–wöchigen experimentellen Praktika an der Ausbildung von Studierenden der Studienrichtungen «Cell Biology» (UniBE) und im Studiengang «Biomedical Sciences» beteiligt, der durch die Universitäten Fribourg und Bern angeboten wird.

Der Abschlussvortrag der Masterarbeit findet im Rahmen eines halbjährlich stattfindenden Masterarbeits-Symposium statt. Hier werden neu begonnene Projekte kurz präsentiert und diskutiert, und die Ergebnisse von abgeschlossenen Masterarbeiten vorgestellt.

>>> Weiterbildung

Das Institut für Pathologie der Universität Bern ist eine nach SIWF zertifizierte Weiterbildungsstätte und bietet die Schwerpunktitel Zytopathologie und Molekularpathologie sowie den FMH-Weiterbildungstitel Neuropathologie an.

Das Institut für Pathologie konnte auch 2018 zwischen 8–10 Plätze für die Weiterbildung zum Facharzt Pathologie besetzen und zwei jungen Kolleginnen zu erfolgreichen Abschlüssen verhelfen. Das Format der internen Weiterbildung hat sich bewährt und beinhaltet nach wie vor eine strukturierte Besprechung histopathologischer und zytologischer Fälle im Rahmen des all-morgendlichen Teachings, ergänzt durch Themen-spezifische Vorträge bzw. Journal Clubs wie auch ein Teaching im Bereich Makropathologie / postmortale Diagnostik welches durch ein entsprechendes Fachteam geleitet wird.

Regelmässige Bewertungen und Standortbestimmungen finden in Form von zweimal jährlich durchgeführten Zwischenevaluationen statt (Arbeitsplatz-basierte Assessments). Dabei wird das Alltagswissen in der mikroskopischen Fallabgabe als auch in der Verarbeitung makroskopischer Präparate geprüft. Ein Tutoren-System soll allen jungen Kolleginnen und Kollegen die Möglichkeit geben, einerseits regelmässige Feedbacks im Arbeitsalltag zu bekommen, andererseits – falls gewünscht – einen Einblick in ein Forschungsprojekt zu bekommen und hier eine strukturierte Begleitung zu erhalten.

Den Assistierenden wird auch die Möglichkeit geboten, an den wöchentlichen Tumorboards und regelmässig stattfindenden klinisch-pathologischen Konferenzen teilzunehmen. Spezifische Fachthemen, welche zu Teil detailliertes Spezialwissen beinhalten, werden einmal monatlich im Rahmen eines «Abendteachings» durch die Fachärzteschaft unter Berücksichtigung der Wünsche der Auszubildenden besprochen.

Interne Weiterbildungsveranstaltungen

Weiterbildung	**Zeitraum**	**Ziel**
Montag		
Assistenten-Fälle	08:35–09:00	Übung Fallpräsentation. Interessante Fälle der Vorwoche werden demonstriert und kurz das Wesentliche erwähnt
Makro-Visite	13:00–13:15	Makroskopische Beurteilung von Operationspräparaten, praktisches Vorgehen
Dienstag		
Vortrag oder Journal Club	08:35–09:00	Vermittlung von theoretischem Wissen Präsentation einer wissenschaftlichen Arbeit
Makro-Visite	13:00–13:15	Makroskopische Beurteilung von Operationspräparaten, praktisches Vorgehen
Mittwoch		
Schnitte des Tages	08:35–09:00	Inhaltliche Vorbereitung zu didaktischen Fällen aus einem Gebiet der täglichen Diagnostik
Makro-Visite	13:00–13:15	Makroskopische Beurteilung von Operationspräparaten, praktisches Vorgehen
Bern Teaching Round in Pathology	1x Monat 17:00–18:30	Vertiefung in grösseren diagnostischen Themenblöcken (separates Programm)
Donnerstag		
PMD-Teaching	08:35–09:00	Makroskopische Beurteilung von wichtigen Autopsie-Befunden
Makro-Visite	13:00–13:15	Makroskopische Beurteilung von Operationspräparaten, praktisches Vorgehen
Seminar	17:15–18:00	Gast-Vorträge zu wissenschaftlichen Themen
Freitag		
Schnitte des Tages	08:35–09:00	Inhaltliche Vorbereitung zu didaktischen Fällen aus einem Gebiet der täglichen Diagnostik
Makro-Visite		Makroskopische Beurteilung von Operationspräparaten, praktisches Vorgehen

>>> Fortbildung

Auf Grund der zunehmenden Spezialisierung im Fachgebiet der Pathologie, erachten wir es als äusserst wichtig, sowohl im Bereich der Zytopathologie als auch der Molekularpathologie fortlaufend jungen Kolleginnen und Kollegen die Möglichkeit anzubieten, eines dieser beiden Spezialgebiete im Rahmen einer Schwerpunkt-Ausbildung erlernen zu können.

Zytopathologie
Zusätzlich zur 6-Monats Rotationsstelle für in Weiterbildung sich befindende Assistierende, bilden wir auch fortlaufend Kolleginnen und Kollegen aus, die den Schwerpunktitel Zytopathologie erwerben. Dies führte im Jahr 2018 zu einem erfolgreichen Abschluss und weiterer Ergänzung des Zytopathologie Teams.

Molekularpathologie
Trotz eines intensiven Jahres mit Vorbereitungen für die Inbetriebnahme des neu gegründeten Clinical Genomics Lab (CGL), konnte auch 2018 eine Stelle für den Schwerpunkt Molekularpathologie besetzt werden.

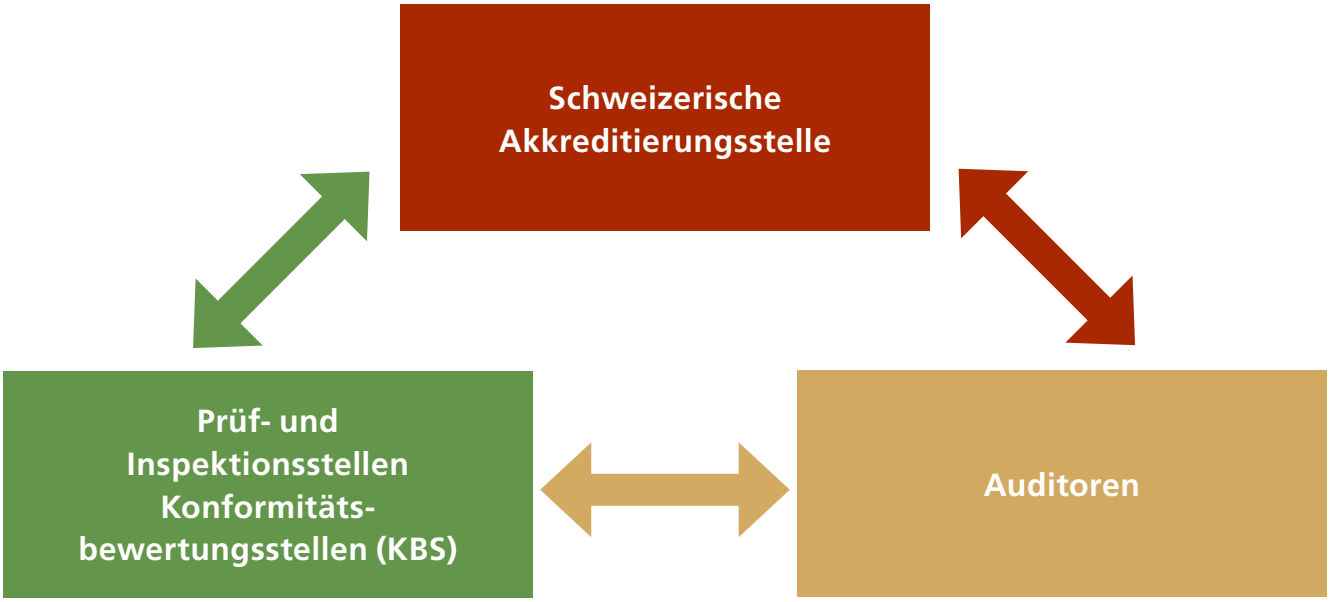
Donnerstagsseminare 2018
Wie auch in den Vorjahren konnten wir 2018 ein attraktives und vielseitiges Angebot an Vorträgen im Rahmen der wöchentlichen Fortbildungen anbieten.

Donnerstagsseminare 2018

Datum	Titel	Referent/-in
11.01.	Interplay between gut microbiota and immune contexture in human colorectal cancer	Prof. Giandomenica Iezzi Department of Biomedicine, University Hospital Basel, Switzerland
15.01.	Anterior Mediastinal Lesions. Diagnostic Challenges and Recent Developments	Prof. Anja Roden Mayo Clinic Rochester
18.01.	Diagnostic and Molecular Challenges in Endometrial Cancer	Joseph Carlson Karolinska Institutet, Stockholm
01.03.	Lipid Metabolic Regulation of lung and pancreatic adenocarcinomas	SNF Prof. Dr, G. Konstantinidou Translational Cancer Therapeutics, Institute of Pharmacology, University of Bern
08.03.	The tuft cell–ILC2 circuit in intestinal physiology	Dr. Christoph Schneider, Postdoctoral Fellow Department of Medicine, University of California, USA
15.03.	Immune Reconstitution in Pediatric Hematopoietic Stem Cell Transplant Recipients	Dr. med. Dr. phil nat. Mathias Hauri-Hohl Leiter Forschung Stammzelltransplantation, Universitäts-Kinderspital Zürich
29.03.	BRCA1/BRCA2 mutations in ovarian cancers	Dr. S.I. Labidi-Galy University of Geneva
04.04.	Mitochondrial metabolic flexibility in drug resistance of acute myeloid leukemia	Jean-Emmanuel Sarry Team Leader & Principal Investigator in Hemato-Oncology, Centre de Recherches en Cancérologie de Toulouse – CRCT
12.04.	Clinical Dynamics Form© – Silver Bullet for Increasing Medical Reporting Complexity	Nikola Cihoric, MD Radio-Onkologie, Inselspital Bern
26.04.	Characterize the hematopoietic niche in the vertebrate embryo to better expand HSCs ex vivo.	Julien Bertrand, Ph.D., Assistant Professor Department of Pathology and Immunology, School of Medicine – CMU, Geneva
03.05.	2.–4. May 2018, Research Retreat	Institute of Pathology University of Bern

Datum	Titel	Referent/-in
31.05.	The tumor microenvironment: a physical barrier protecting tumor cells	Erik Henke, PhD, Research Group Leader Institute for Anatomy and Cell Biology II, University of Würzburg
07.06.	What's New about Fibrolamellar Carcinoma and Why it Matters	Rondell P. Graham MBBS Gastrointestinal/Liver Pathology/Molecular Pathology, Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester
12.06.	Dissecting cellular niches and neighborhoods by CODEX hyper-parameter tissue imaging	Christian M. Schürch, MD, PhD, Postdoctoral Fellow Department of Microbiology & Immunology, Baxter Laboratories for Stem Cell Biology, Stanford University
14.06.	Identifying Machinery and Cargo of Selective Autophagy	Prof. Dr. Christian Behrends W2-Professor for «Systems Biology of Neuro-degenerative Diseases» Medical Faculty, Ludwig-Maximilians-Universität München
06.09.	Slide Seminar Pancreatobiliary Neoplasms	Prof. Volkan Adsay Director of Anatomic Pathology, Medical College of Wisconsin, USA
06.09.	High-grade gastroenteropancreatic neoplasms	Prof. Halfdan Sorbye Department of Oncology, Haukeland University Hospital, Bergen, Norway
11.10.	Genomic landscape of Pancreatic Neuroendocrine Tumors	Dr. V. Corbo University of Verona
18.10.	Pancreatic cancer following neoadjuvant therapy: characterisation and mapping of phenotypic intratumour heterogeneity	Prof. Caroline Verbeke, MD, PhD, FRCPath Dept of Pathology, Institute of Clinical Medicine, University of Oslo
25.10.	Robotic Telecytology	Prof. Oscar Lin, MD. PhD Chief Cytology Service, Memorial Sloan Kettering Cancer Center, USA
01.11.	Biologic Function of IL-1 Cytokine inhibitors in Inflammation	Professor Cem Gabay Division of Rheumatology, Department of Internal Medicine Specialties, Geneva University Hospital, Switzerland
06.11.	From Hematoxylin & Eosin to Highly Multiplexed Single-Cell Tissue Proteomics	PD Dr med Ch. Schürch, Postdoctoral Fellow Department of Microbiology & Immunology, Baxter Laboratories for Stem Cell Biology, Stanford University
08.11.	Jahrestagung SGPath, 8–10 November 2018, Lugano	
15.11.	Rapid Whole Genome Sequencing for Critically Ill Infants: a Coming Standard of Care to Improve Outcomes	Lauge Farnaes MD PhD Assistant Medical Director Rady Children's Institute for Genomic Medicine University of California, San Diego – School of Medicine
13.12.	Quantification in digital pathology, use cases from brightfield to fluorescence scans	Prof. Teijo Pellinen Univeristy of Helsinki
20.12.	Harnessing the potential of the microbiota and immune system for the treatment of colorectal cancer	Dr. Lukas Mager, Postdoctoral Fellow University of Calgary, Canada

>>> Im Fokus: Akkreditierung



Akteure im Kontext der Akkreditierung von Konformitätsbewertungsstellen.

Wenn Sie an den Prozess der Akkreditierung denken, was fällt Ihnen spontan dazu ein? Formalismus, Bürokratie, Aufwand, Nutzen, Audit, Qualität, Akkreditierungsverfahren, Mitarbeiterkompetenz, Kosten und möglicherweise vieles mehr. Wenn die Akkreditierung vor 20 Jahren noch ein Label für Fortschritt und Innovation war, ist sie heute explizierter Teil des Qualitätsmanagements.
Nach Abschluss unserer LEAN-Reorganisation haben wir uns der externen Kontrolle durch die schweizerische Akkreditierungsstelle (SAS) gestellt, nicht um einem gegenwärtigen Modetrend zu folgen, sondern aus der Überzeugung heraus, dass es uns als Institut für Pathologie wesentliche Vorteile bringt. Vor diesem Hintergrund wurde nach mehrmonatiger Vorbereitungszeit im Jahr 2016 das Projekt «STS-Akkreditierung der Bereiche Molekularpathologie, Histopathologie, Zytopathologie, Immunhistochemie und der Postmortalen Diagnostik» lanciert.

Wir haben uns für eine Akkreditierung nach *«ISO 15189 – Medizinische Laboratorien, Anforderungen an die Qualität und Kompetenz»* und nach der Schweizerischen Norm, *«ISO 17025 – Anforderungen an die Kompetenz von Prüflaboratorien und Kalibrierlaboratorien»* entschieden. Die Akkreditierung beinhaltet eine Wertung des End-Produkts, unserer Diagnose, und ist kein starres Gebilde, sondern wird gepflegt, weiterentwickelt und auch überwacht. Sie hilft uns, die Qualität der geleisteten Arbeit stetig zu verbessern und um die Sicherheit der Diagnostik an Patientengewebe zu gewährleisten.

Akkreditierung in Zusammenspiel mit LEAN management

Die Abläufe im IFP werden auch weiterhin mit Werkzeugen des LEAN-management weiterentwickelt, und jetzt durchgehend nach den obigen Normen definiert und dokumentiert. Interne und externe Rückmeldungen über das Q-System werden im Wochenrhythmus monitorisiert und wo sinnvoll angepasst. Wir sind stolz, seit dem Begutachtungs-Audit im August 2018 durch die Schweizerische Akkreditierungsstelle nach beiden Normen akkreditiert.

Ein herzliches Dankeschön an die Mitarbeitenden und Qualitätsverantwortlichen, die die über 2000 notwendigen Dokumente erstellt haben.

Was wird besser?

Sie als Kunde werden die Effekte der Akkreditierung kurzfristig nicht bemerken. Die Akkreditierung gibt Ihnen jedoch Sicherheit, dass unsere Prozesse standardisiert und in hoher Qualität durchgeführt werden und von externer Stelle genauestens kontrolliert werden.

Wir wollen uns weiterhin überall verbessern: Akkreditierung ist keine einmalige und kosmetische Bestätigung eines Prozesses, sondern ein hochwertiges Instrument der Erfolgssicherung und der Nachhaltigkeit, und wir freuen uns über Rückmeldungen von Ihnen.

Schweizerische Eidgenossenschaft
Confédération suisse
Confederazione Svizzera
Confederaziun svizra

Eidgenössisches Departement für Wirtschaft, Bildung und Forschung WBF
Staatssekretariat für Wirtschaft SECO
Schweizerische Akkreditierungsstelle SAS

Gestützt auf die Akkreditierungs- und Bezeichnungsverordnung vom 17. Juni 1996 und die Stellungnahme der Eidgenössischen Akkreditierungskommission erteilt die Schweizerische Akkreditierungsstelle (SAS) dem

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die Akkreditierung als

Dauer der Akkreditierung:
29.11.2017 bis 28.11.2022
(1. Akkreditierung: 29.11.2017)

Prüflaboratorium für pathologische Diagnostik

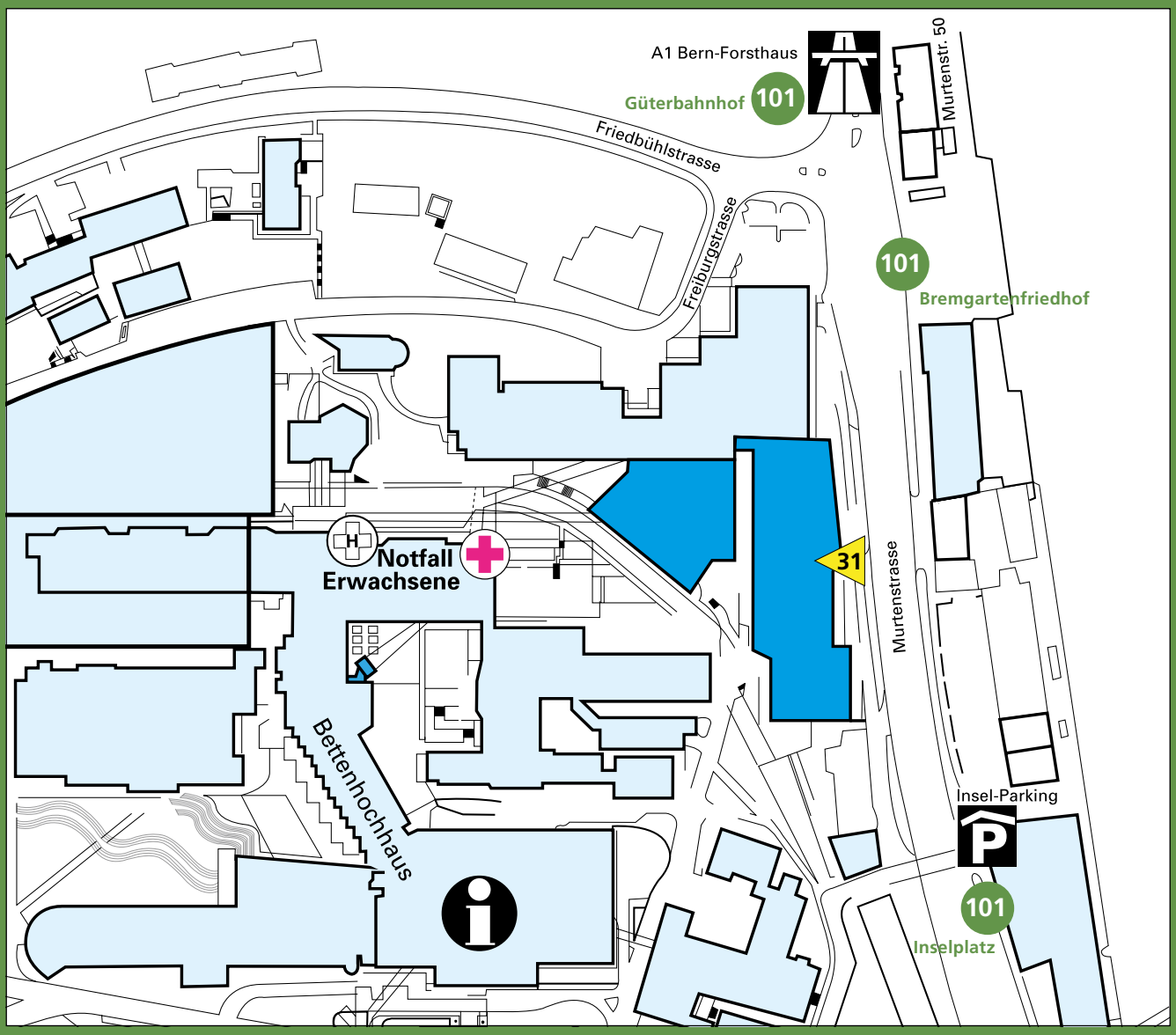
Internationale Norm: ISO/IEC 17025:2005, ISO 15189:2012
Schweizer Norm: SN EN ISO/IEC 17025:2005, SN EN ISO 15189:2013

3003 Bern, 01.03.2019
Schweizerische Akkreditierungsstelle SAS

Leiter der SAS
Konrad Flück

Die SAS ist Mitglied der multilateralen Abkommen der European co-operation for Accreditation (EA) für die Bereiche Prüfen, Kalibrieren, Inspizieren und Zertifizieren von Managementsystemen, Zertifizieren von Personen und Zertifizieren von Produkten, Prozessen und Dienstleistungen, des International Accreditation Forum (IAF) für die Bereiche Zertifizieren von Managementsystemen und Zertifizieren von Produkten, Prozessen und Dienstleistungen und der International Laboratory Accreditation Cooperation (ILAC) für die Bereiche Prüfen und Kalibrieren.

>>> Situationsplan



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