UNIVERSITÄT
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Institut für Pathologie

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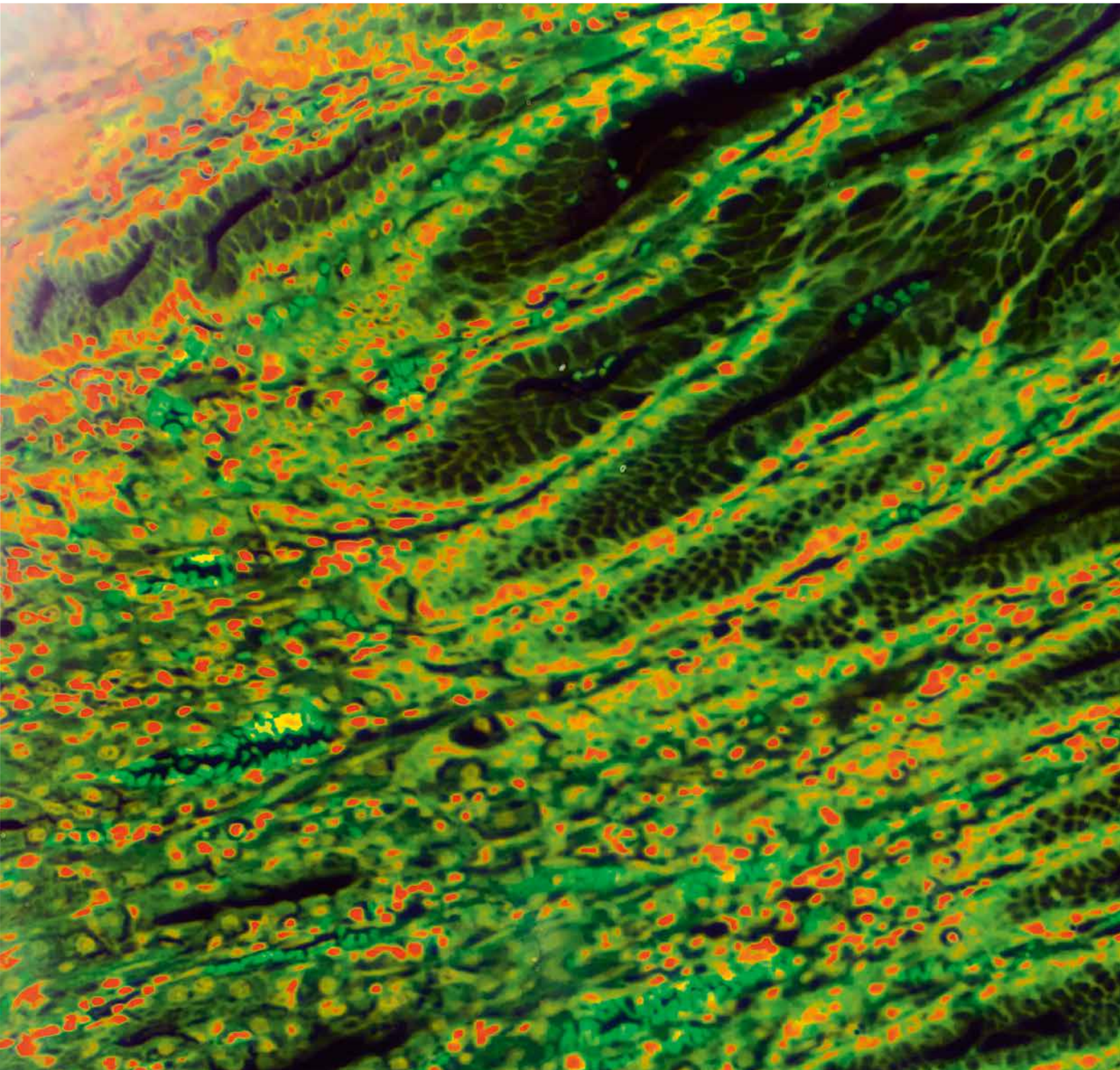
Jahresbericht 2019



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>>> Das Wichtigste in Kürze

Liebe Leserin, lieber Leser

Es freut mich, dass Sie auch dieses Jahr wieder unseren Jahresbericht in Ihren Händen halten.

Was macht eigentlich das Institut für Pathologie? Aus meiner Sicht ist die Antwort einfach: Wir machen Gewebemedizin, nahe bei der Forschung.

In der Dienstleistung arbeiten wir als Teil des Behandlungsteams für Patienten. Wir machen zeitnahe richtige Diagnosen und kommunizieren. Wir decken alle Spezialgebiete mit definierten kompetenten Ansprechpersonen ab, welche ihre nötige Subspezialisierung in kontinuierlicher Zusammenarbeit mit den klinischen Kollegen weiterentwickeln und aufrechterhalten.

In der Lehre vermitteln wir zusätzlich auch Grundmechanismen der Krankheitsentstehung in der Vorklinik. Aufgrund der kontinuierlichen Adaptation der Pathologie-Vorlesungen über die letzten Jahre konnten wir unsere Gesamtstruktur des Lehrkonzeptes verbessern, die durchwegs positiven Rückmeldungen bei der fakultären Lehrevaluation freuen mich besonders. Eine gute Lehre ist zentral, um zukünftige Pathologen und Forschende für das Fach zu motivieren.

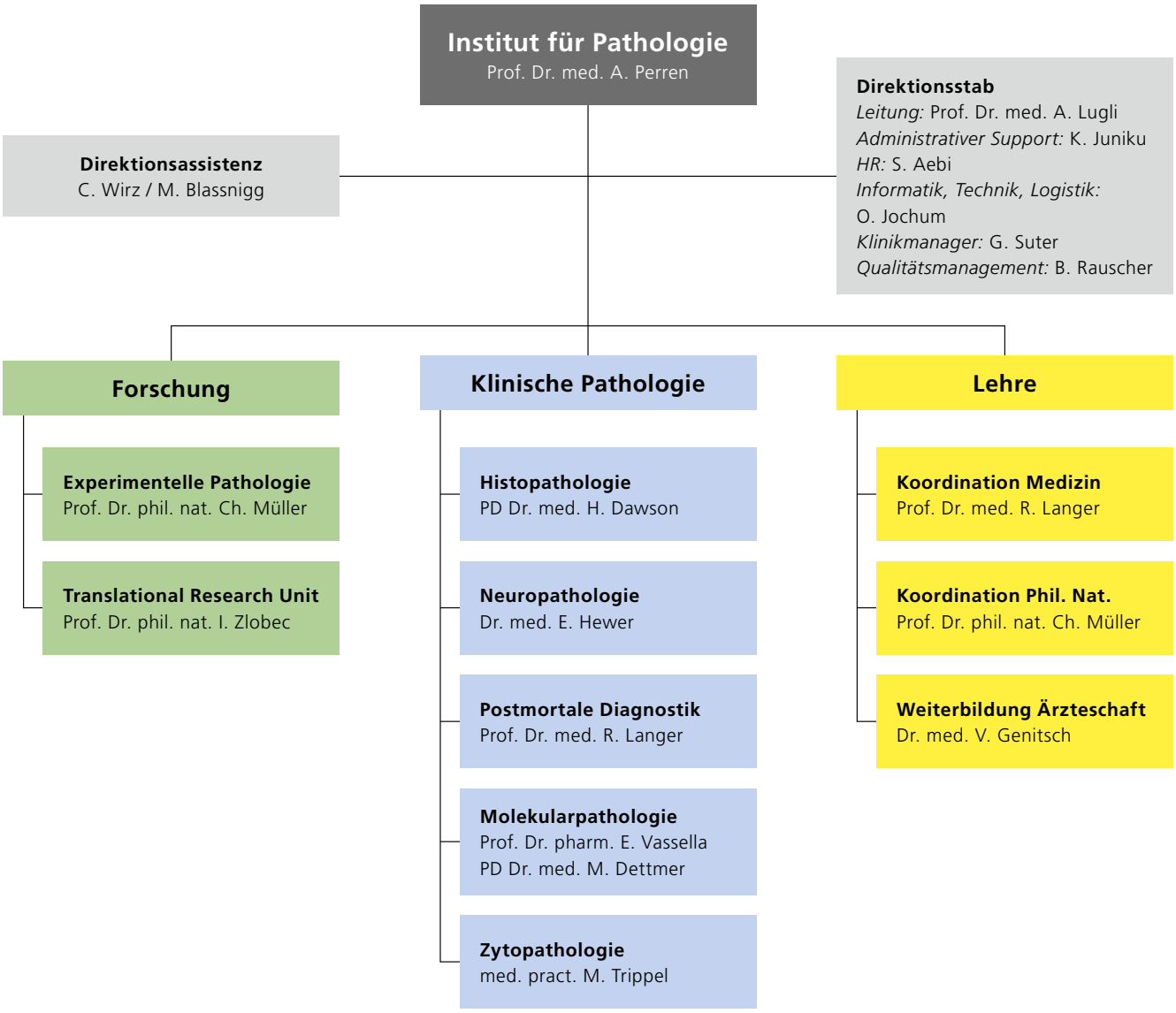
Wie Sie dem Bericht entnehmen können, führen wir im Institut für Pathologie eine breite Palette an Forschungsaktivitäten, einschliesslich experimentellen und translationalen Projekten. Unserer Gewebebank Bern erfüllt die von der Swiss Biobanking Platform geforderten Ansprüche in Qualität. Ein Hauptfokus der Weiterentwicklung des Institutes und Faches liegt auch in der Pathologie in der Digitalisierung: In unserer «Translational Research Unit» wird mit dem Gross-Projekt «Digitale Pathologie» dieser zentrale Wandel in Angriff genommen. Auch in der Pathologie ist das einzig sichere der stetige Wechsel.

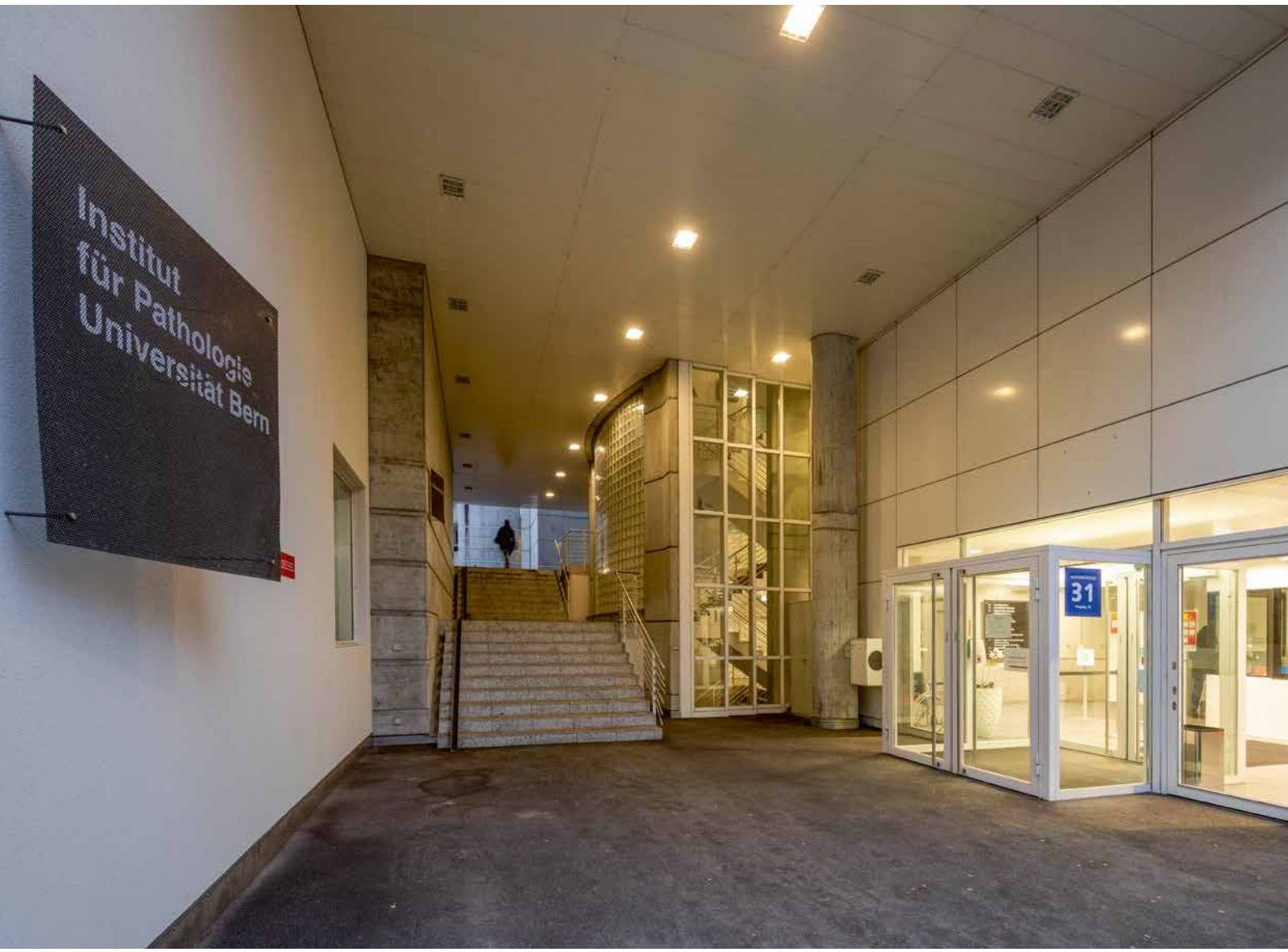
Ich wünsche Ihnen viel Vergnügen bei der Lektüre unseres Berichtes..

Ihr Aurel Perren, Direktor


Diagnostik
und
Forschung

>>> Organigramm




Institut
für Pathologie
Universität Bern
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>>> Dienstleistung

1 Klinische Pathologie

Prof. Dr. med. A. Perren
Stv. Prof. Dr. med. A. Lugli

Im Rahmen der fortlaufenden Arbeitsprozessoptimierung gemäss LEAN Management wurde die Abteilung Klinische Pathologie strukturell weiter optimiert. Seit Januar 2019 ist die Klinische Pathologie in die Hauptgruppen Ärzteschaft und Diagnostische Laboratorien unterteilt, welche die Schwerpunkte der Histopathologie, Neuropathologie, Molekularpathologie, Zytopathologie und Postmortalen Diagnostik abdecken.

1.1 Ärzteschaft

Histopathologie (PD Dr. med. H. Dawson)
Die Ärzteschaft ist in 18 Fachgruppen organisiert und besteht aus 18 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. 2019 konnten wichtige Ziele im Rahmen unserer Vision der Digitalisierung und Automatisierung umgesetzt werden: Die Spracherkennung entlastet zum einen das Berichtsekretariat und erlaubt die sofortige Freigabe der Berichte. Zudem wird die Implementierung der digitalen Pathologie im diagnostischen Alltag fortgeführt mit der Einführung eines Tools zur Unterstützung bei der Auswertung auserwählter Biomarker. Durch die Anschaffung neuer Geräte kann ein Teil der Schnellbeurteilungen und Schnellschnitte von extern beurteilt und innerhalb des Diagnostik-Teams besprochen werden.

Neuropathologie (Dr. med. E. Hewer)
Im Jahr 2019 untersuchten wir mehr als 1500 neurochirurgische und neurologische Proben, davon 380 intraoperative Schnellschnitte. Wir zählen damit weiterhin zu den diagnostisch aktivsten Neuropathologien in der Schweiz. Eine immer grössere Rolle spielt die molekulare Diagnostik von Hirntumoren, zunehmend auch die Genom-weite Methylierungsanalyse, die im Rahmen einer Kooperation mit der Neuropathologie am Universitätsspital Genf erfolgt. In Zusammenarbeit mit dem Neuromorphologischen Labor der Neurologischen Klinik des Inselspitals wurden rund 60 Muskelbiopsien untersucht. Die postmortale Diagnostik einschliesslich konsiliarischer Untersuchungen im Auftrag des Instituts für Rechtsmedizin ergänzt das diagnostische Spektrum. Entsprechend dem Charakter der Neuropathologie als Schnittstelle zwischen den klinischen Neurofächern, der Labordiagnostik und translationaler Forschung war der Fachbereich Neuropathologie auch im Jahr 2019 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).

Postmortale Diagnostik (Prof. Dr. med. R. Langer)
Im Jahr 2019 wurden im Institut für Pathologie 105 Postmortale Untersuchungen durchgeführt, inclusive neuropathologische und pädopathologische Untersuchungen. 40 davon waren Verstorbene aus dem Inselspital Bern. Nachdem Abschluss der Implementierung der «Postmortalen Diagnostik» im Vorjahr wurde dieses Konzept erfolgreich weitergeführt. Unsere Erfahrungen bezüglich postmortaler Lungendiagnostik wurden bei der Jahrestagung der Deutschen Gesellschaft für Pathologie im Rahmen eines Vortrags präsentiert, die Erfahrungen der Umsetzung des Gesamtkonzeptes wurden im «Virchows Archiv», der Fachzeitschrift der European Society of Pathology, publiziert (Langer et al. Implementation of modern tools in autopsy practice – the way towards contemporary postmortal diagnostics, Virchows Arch. 2019 Feb;474(2):149-158. doi: 10.1007/s00428-018-2482-2.).

Zytopathologie (Med. Pract. M. Trippel)
Die Zytologie ist als minimal-invasive und gleichzeitig maximal effiziente und kostengünstige Methode zukunftsweisend. Im Jahr 2019 untersuchten wir insgesamt 21'787 Proben mit 10'789 Proben aus der extra-gynäkologischen Zytologie und 10’998 Proben aus der gynäkologischen Zytologie.
Die schon seit längerem bestehende interdisziplinäre Schilddrüsensprechstunde an der Universitätsklinik für Diabetologie, Endokrinologie, Ernährungsmedizin & Metabolismus (UDEM) wurde im Jahr 2019 aufgrund der grossen Anzahl der Konsultationen erfolgreich ausgebaut.
Die gynäkologischen zytologisch-histologischen Korrelationstreffen mit den Klinikern der Dysplasiesprechstunde, bei denen schwierige Befunde zusammen mit den Klinikern besprochen werden, viel auf ein reges Interesse und wird aktuell in einem dreimonatigen Turnus abgehalten.

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.

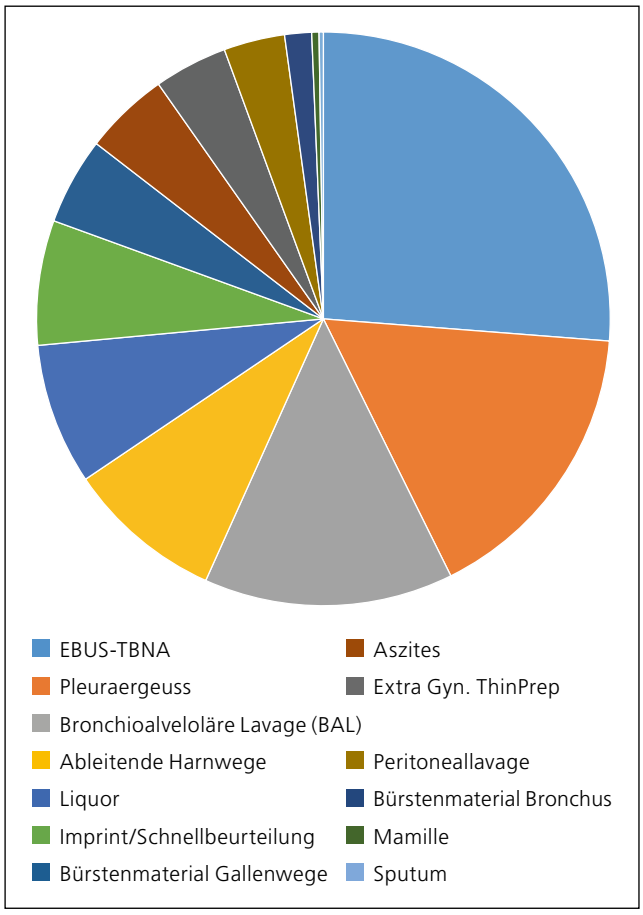
1.2. Labor

Histopathologie (M. Bänziger)
Das Überwachungsaudit duch die Akkreditierungsstelle SAS wurde mit nur wenigen Nichtkonformitäten sehr positiv abgeschlossen. Die Überarbeitung der Hilfsmittel erforderte viel Arbeit, da Prozessanpassungen vorgenommen werden mussten. Die internen Qualitätskontrollen für die Färbungen und die Mikrotomie wurden optimiert, so dass ein genauer Verlauf der Qualität sichergestellt werden kann. So können Trends frühzeitig erkennt und die dazugehörigen Massnahmen ergriffen werden.
Dank weiterer Optimierungen im gesamten Laborprozess konnte die erneut gestiegene Probenanzahl der Biopsien (11%) gut bearbeitet werden. Für die Exzisate resultierte ein Rückgang von 3% und die Schnellschnitt-Fälle stiegen um 4% an, wobei jedoch die Anzahl der Schnellschnittfahrzeugeinsätze gegenüber dem Vorjahr leicht rückgängig war.
Auf Grund der gestiegenen Probenanzahl bei den Biopsien, erhöhte sich die Zahl der HE-Färbungen um 6%.
Seit dem Jahr 2015 verzeichnen wir insgesamt 45% mehr Biopsien, bei den Exzisat- und Schnellschnittfällen kam es zu einem leichten Rückgang resp. zu stabilen Probenanzahlen.

Immunhistochemie (T. Waldburger)
Das Jahr 2019 war für die Abteilung Immunhistochemie ein Jahr der Konsolidierung. Zum einen hat sich die Führungsstruktur gefestigt, die Einführung der Dienstleistung in der Klinischen Pathologie, die Digitalisierung von Schnitten für Tumorboards, Konsilien und Zweitmeinungen wurde rege genutzt und ist zu einem festen Bestandteil im Routinebetrieb des Labors geworden. Eine neue Herausforderung stellte die Digitalisierung für die Entwicklung der Bildanalyse dar, welche sich in Zusammenarbeit mit der TRU als sehr spannend erwiesen und auf den Workflow im Labor einen recht grossen Einfluss genommen hat. Die diesbezügliche Weiterentwicklung wird uns weiterhin beschäftigen und den technischen Fortschritt im Labor nicht nur unterstreichen, sondern auch vorantreiben.
Im Jahr 2019 wurden an 11616 Fällen insgesamt 59249 immunhistochemische Färbungen an Paraffinschnitten vorgenommen. Die Anzahl bearbeiteter nativer Nierenbiopsien hat mit 256 Fällen gegenüber dem Vorjahr leicht zugenommen.
Insgesamt stieg die Anzahl der Färbungen gegenüber dem Vorjahr um 14%, was vor allem auf eine Zunahme der Einsendungen zurückzuführen war.
Es standen 276 Primärantikörper für diagnostische Untersuchungen zur Verfügung.

Zytopathologie (C. Baumann)
Universitäre Institute, Kantonsspitäler und Privatlabors der ganzen Schweiz führen zytologische Untersuchungen durch. Ein Grossteil bilden die gynäkologischen Vorsorgeuntersuchungen. Die Anzahl der extragynäkologischen Untersuchungen steigt jedoch stetig. Auch die Art des eingesendeten Materials ist auch im Wandel, gab es früher z.B. häufiger Feinnadelpunktionen der Mamma oder der Leber, werden jetzt häufiger Feinnadelpunktionen der Bauchspeicheldrüse, der Speicheldrüsen und der Schilddrüse eingesandt. Die Möglichkeiten der zytologischen Verarbeitung ist auch im Wandel, ein Beispiel ist die Herstellung der Zellblöcke, dadurch können wir den Material zusätzliche Daten entnehmen, sei es durch ergänzende immunzytochemische oder molekularpathologische Untersuchungen. Diese ergänzenden Untersuchungen sind aus der heutigen Diagnostik gar nicht mehr wegzudenken und führen den Kliniker zur korrekten Therapie des betroffenen Patienten.

Die Zytologie sieht sich als Routinedienstleistungsbetrieb in dem durch kontinuierliche Verbesserungen nicht nur die Qualität gesteigert und die zeitliche Verarbeitung optimiert wurde, sondern auch mit grossen Engagement in die Ausbildung und Weiterbildung In Zytodiagnostik investiert wurde.



Material (Proben) extragynäkologischen Zytologie 2019.

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

Prof. Dr. pharm. Erik Vassella, Fachverantwortlicher molekulare Pathologie

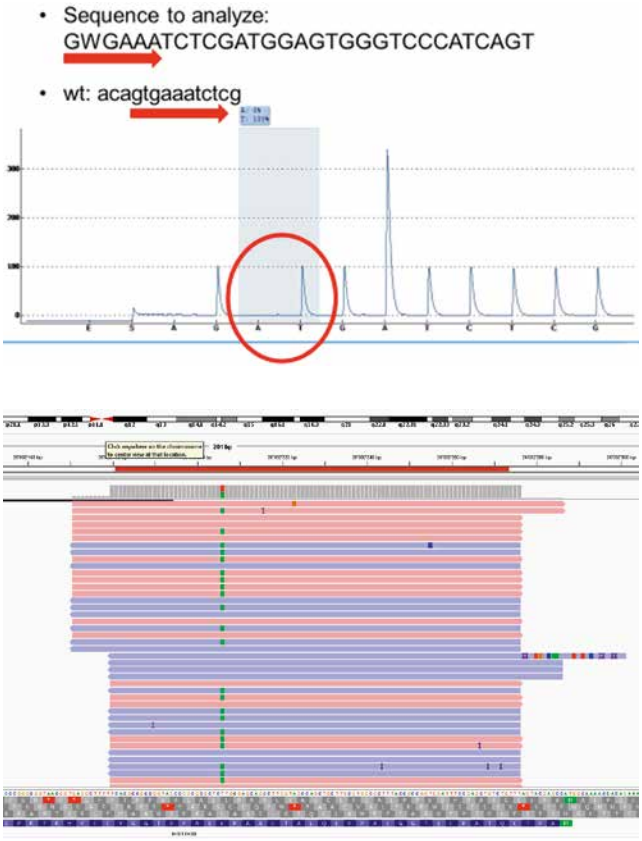
Am 1. Januar 2019 wurde das Clinical Genomics Lab des Inselspital Bern als Zusammenschluss der molekularen Diagnostik der Bereiche Humangenetik, Hämatologie, Molekularpathologie und der klinischen Chemie unter der Leitung von PD Dr. med. et phil. Tobias Grob gegründet. Das interdisziplinäre Labor deckt das gesamte Spektrum der Diagnostik aus den verschiedenen Fachbereichen ab. Gleichzeitig dient das Clinical Genomics Lab als Core Facility für Hochdurchsatzsequenzierung für die klinische Forschung und dient als zentrales Standbein für das Zentrum für Precision Medicine. Durch die Nutzung von Synergien und die interdisziplinäre Zusammenarbeit werden Leistungen für die Patientenversorgung und die Forschung auf hohem Niveau ermöglicht.

Die Dienstleistung der Molekularpathologie im Clinical Genomics Lab ist eine Zusammenarbeit des Inselspital Berns und des Instituts für Pathologie. Die in diesem Fachbereich verwendeten Methoden umfassen insbesondere Hochdurchsatz-Sequenzierung, Sanger-Sequenzierung, Pyrosequenzierung, PCR-Analysen und Fluoreszenz In situ Hybridisierung. Mit diesem breiten Methodenspektrum werden prädiktive Biomarker als Therapieentscheid beim Adenokarzinom der Lunge (inklusiv EGFR T790M Liquid Biopsy), kolorektalem Karzinom, malignen Melanom, GIST, Ovarialkarzinom und Gliom abgedeckt. Zur Bestimmung Therapie-relevanter Biomarker wird insbesondere das Oncomine Comprehensive Cancer Panel v3, welches auch relevante NTRK-, ALK, ROS- und RET Fusionen abdeckt, verwendet. Weitere Analysen umfassen die Bestimmung der Tumor-Mutationslast (mutational burden), Genotypisierung der Blasenmole, Risikostratifizierung Mammakarzinom, Abklärung Mikrosatelliteninstabilität, B- und T-Zellklonalität, Diagnostik von Pankreaszysten sowie Nachweis spezifischer Erreger. Die Tests können an Formalin-fixiertem und Paraffin-eingebetteten Gewebe durchgeführt werden. Die molekulardiagnostischen Befunde werden am molekularen Tumorboard besprochen.

Gegenüber dem letzten Jahr hat sich die Zahl der mittels Hochdurchsatz-Sequenzierung durchgeführten Analysen nahezu verdoppelt (+96%). Kleinere Gen-Panels wurden weitgehend durch das Oncomine Comprehensive Cancer Panel (+246%) ersetzt. In diesem Jahr wurde zudem in die Entwicklung neuer diagnostischer Tests (TSO 500 mittels Illumina Technologie) sowie Etablierung eines gemeinsam betriebenen Laborinformationssystems investiert. Aufgrund der Überführung der molekularen Diagnostik vom Institut für Pathologie in das CGL ist die Akkreditierung für diesen Bereich aktuell sistiert.

Der Fachbereich Molekularpathologie dient zudem 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.

3 Fachgruppen des Instituts für Pathologie der Universität Bern

Stand Dezember 2019

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

Endokrinopathologie	
A. Perren	031 632 32 23
M. Dettmer	031 632 99 69
S. Berezowska	031 632 49 37

Gastrointestinalpathologie	
A. Lugli	031 632 99 58
R. Langer	031 632 32 47
A. Blank	031 632 99 01
H. Dawson	031 632 99 60
B. Dislich	031 632 71 90
M. Montani	031 632 32 67

Mamma- und Gynäkopathologie (Kernteam)	
T. Rau	031 632 87 56
M. Trippel	031 632 32 76
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
E. Hewer	031 632 99 51
Ch. Neppl	031 632 52 03

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

HNO-/Ophtalmopathologie	
M. Dettmer	031 632 99 69
M. Wartenberg	031 632 49 76
E. Hewer	031 632 99 51
T. Rau	031 632 87 56

Leber- und Pankreaspathologie	
A. Perren	031 632 32 23
A. Blank	031 632 99 01
M. Montani	031 632 32 67
M. Wartenberg	031 632 49 76
T. Rau	031 632 87 56
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
Ch. Neppl	031 632 52 03

Nephropathologie	
V. Genitsch	031 632 99 22
R. Langer	031 632 32 47
M. Montani	031 632 32 67

Neuropathologie	
E. Hewer	031 632 99 51
S. Berezowska	031 632 49 37
M. Wartenberg	031 632 49 76

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

Uropathologie	
V. Genitsch	031 632 99 22
M. Montani	031 632 32 67
M. Dettmer	031 632 99 69
B. Dislich	031 632 71 90

Weichteil- und Knochenpathologie	
R. Langer	031 632 32 47
H. Dawson	031 632 99 60
B. Dislich	031 632 71 90

Postmortale Diagnostik und Makropathologie	
R. Langer	031 632 32 47
A. Blank	031 632 99 01
Y. Banz	031 632 88 75
C. Neppl	031 632 52 03
T. Rau	031 632 87 56
M. Trippel	031 632 32 76
E. Hewer	031 632 99 51

Zytologie	
M. Trippel	031 632 32 76
E. Hewer	031 632 99 51
Y. Banz	031 632 88 75
C. Neppl	031 632 52 03

Molekularpathologie	
E. Vassella	031 632 99 43
T. Grob	031 632 82 37
H. Dawson	031 632 99 60
M. Dettmer	031 632 99 69

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

5 Dienstleistungsstatistik

Klinische Pathologie

Histopathologie	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**
Anzahl Einsendungen	35'293	37'232	42'422	43'607	45'491	**48'601**
Anzahl Lokalisationen	66'420	70'286	82'069	83'191	86'253	**93'835**
Anzahl Einsendungen Schnellschnitte	1'673	1'648	1'936	1'761	1'784	**1'831**
Anzahl Proben Schnellschnitte	2'307	2'252	2'454	2'264	2'225	**2'313**

Autopsie						
Anzahl durchgeführte Autopsien	156	152	146	130	134	**106**

Zytopathologie						
Total Anzahl Einsendungen	13'788	16'043	16'634	16'995	17'814	**17'576**
Anzahl Proben Klinische Zytologie	8'418	11'582	9'324	9'956	10'326	**10'789**
Anzahl Proben Gynäkologische Zytologie	7'726	9'375	9'869	10'563	11'623	**10'998**
Total Anzahl Einsendungen Proben	16'144	20'957	19'193	20'519	21'949	**21'787**
Anzahl Zellblöcke	2'324	2'748	2'837	3'334	3'844	**4'011**

Immunhistochemie						
Anzahl Fälle (Blöcke) Diagnostik (Paraffin)	8'313	7'843	9'094	7'681	8'822	**11'616**
Anzahl Färbungen Immunfluoreszenz (Nierenbiopsien)	2'280	2'079	2'772	2'464	2'010	**2'486**
Anzahl Fälle Immunzytologie am Ausstrich	372	197	158	258	201	**246**
Anzahl Färbungen Immunzytologie am Ausstrich	–	240	486	364	377	**353**
Anzahl Färbungen Diagnostik (Paraffin)	52'532	47'944	44'366	47'597	51'971	**59'249**

Tumorbank

Anzahl Einsendungen Tumorbank	894	1'030	1'417	1'879	1'593	**1'823**
Anzahl Eingänge TRU	465	457	604	602	738	**850**

>>> Forschung/Research

1 Research at the Institute of Pathology

Research groups Experimental Pathology
Stefan Freigang, MD
Philippe Krebs, PhD
Christoph Mueller, PhD
Aurel Perren, MD, PhD & Ilaria Marinoni, PhD
Mirjam Schenk, PhD
Mario Tschan, PhD
Erik Vassella, PhD

Translational Research Unit (Core Facility) (TRU)
Research groups supported by TRU
Sabina Berezowska, MD
Rupert Langer, MD
Alessandro Lugli, MD
Inti Zlobec, PhD

Organisational aspects

The seven 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 core facility specializing in tissue-based techniques. Our portfolio of services includes histology, tissue visualisation, digital slide scanning, and next-generation Tissue Microarray construction. TRU also provides support for Tissue Bank Bern and collaborates with researchers from the University, DBMR and Inselspital, as well as other researchers in Switzerland and abroad.

1.1 The Division of Experimental Pathology

Head: Christoph Mueller, PhD

Research activities

Thematically the research activities of the currently seven 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 in 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 2019 more than 60'000 biosamples (serum, plasma, biopsies, DNA) from approx. 3000 patients with IBD were stored in the biobank and are made available to qualified scientists for research purposes.

Personnell

At the end of February 2019 Dr. Mario Noti, junior research group leader, left the Institute to accept a new position in industry. We wish him all the best and are grateful for all the important contributions he and his team made. At the end of 2019 more than 50 persons were working in the Division of Experimental Pathology.

Grant Support

In 2019 the total amount of new external funding obtained by the research groups of the Division of Experimental Pathology more than CHF 2.1 Mio (for details see: Reports of the individual research groups).

Research infrastructure and collaborations

The research activities at the Institute of Pathology are well integrated on a national and international level. In our experimental work we can both 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 state-of-the-art genomics core facility. 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 granted. 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 an illumina NovaSeq 6000). Several of our research groups also use the central mouse facility (CAF), and the germ-free and gnotobiotic mouse facility (Clean Mouse Facility) at the Medical Faculty.

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 microRNAs 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 (e.g. NanoString®analysis, scRNA sequencing). 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.

Jean-Claude Reubi, MD (Prof. Dr. med. em.)

Professor Jean-Claude Reubi, MD, formally retired in 2012, but still continued in 2019 his most successful publication activities in the field of peptide receptor imaging and therapy.

Forschungsgruppe Stefan Freigang (Research group Stefan Freigang).

Group of Stefan Freigang, MD

Johanna Baumgartner, PhD student
Thi Thuy Hang Bui, PhD student
Olivier Friedli, PhD student (until 28.03.2019)
Nadia Oehninger, medical doctorate student

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 diseases.

Research Activities

Project 1: Molecular mechanisms of lipid induced inflammation

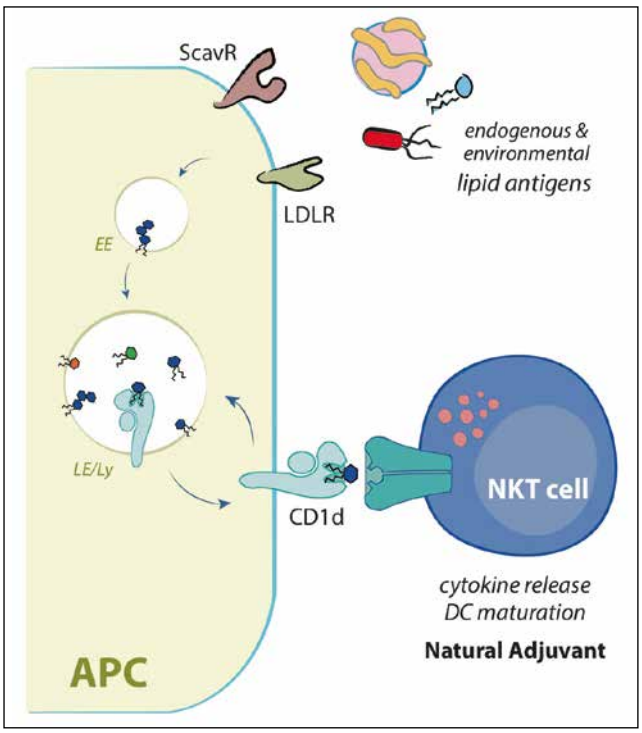
Cardiovascular diseases, particularly atherosclerosis-related diseases, remain the leading cause of death worldwide. While first clinical trials demonstrated the beneficial effects of anti-inflammatory therapies in CVD patients, a better understanding of the molecular mechanisms of vascular inflammation 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. The efficacy of NKT cell agonists is explored in the immunotherapy of infectious diseases and cancer; however, the mechanisms that control CD1d antigen presentation and NKT cell activation in vivo still remain incompletely understood. This project characterizes pathways linking CD1d antigen presentation to lipid metabolism, and aims to define critical effector functions of NKT cells in microbial infections.



Glycolipid-sensing by Natural Killer T cells.

Internal Collaborations

- Christoph Mueller, PhD
- Vera Genitsch, MD

External Collaborations

National

- Cem Gabay, MD, University of Geneva, Switzerland
- Olivier Guenat, PhD, University of Bern, Switzerland
- Georgia Konstantinidou, PhD, University of Bern, Switzerland
- Adrian Ochsenbein, MD, University of Bern, Switzerland
- Philippe Renaud, PhD, University of Bern, Switzerland

International

- Hozumi Motohashi, PhD, Tohoku University, Sendai, Japan
- Paul B. Savage, PhD, Brigham Young University, Provo UT, USA

Grant Support

- UniBE-ID Grant, S. Freigang, 2016–2019, CHF 150'000
- Swiss Lung Liga, S. Freigang (PI), 2017–2020, *CHF 162'000
- UniBE-ID Grant, S. Freigang (PI), 2018–2020, CHF 150'000
- UniBE2021 PhD fellowship, J. Baumgartner, 2017–2021, CHF 90'000

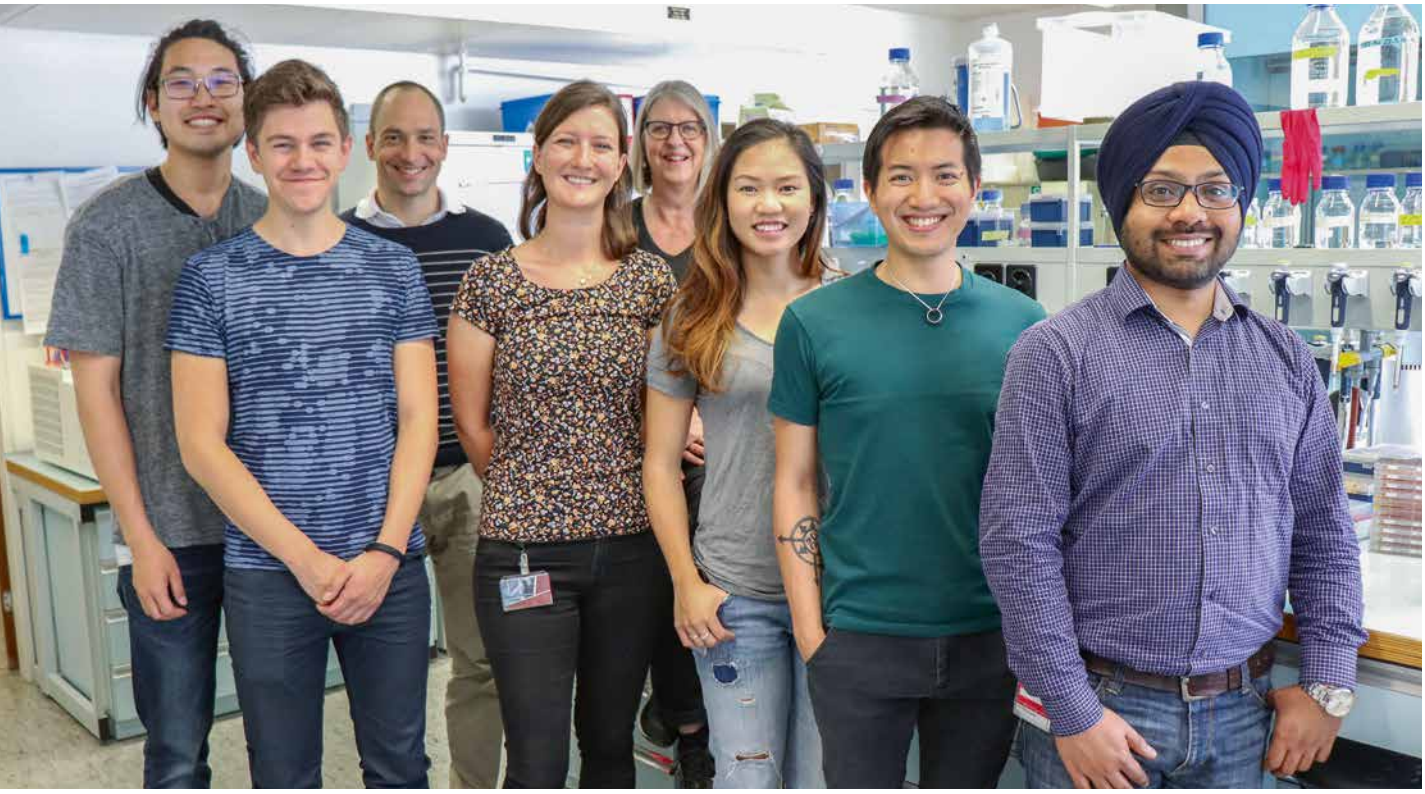
** total amount of funding; funding shared by PI and Co-PI*

Completed PhD thesis

- PhD: Olivier Friedli (Supervisor: Stefan Freigang) «Impact of mitochondrial uncoupling protein 2 on the generation and functionality of distinct T lymphocyte subsets»
- PhD: Elisa Roesti (Supervisor: Martin Bachmann, Mentor: Stefan Freigang) «New therapeutic approaches against Type two Diabetes mellitus using virus-like particles»

Administrative duties

- Member of the Expert Commission of the Graduate School for Cellular and Biomedical Sciences of the University of Bern
- Radiation Safety Officer for the Institute of Pathology



Forschungsgruppe Philippe Krebs (Research group Philippe Krebs).

Group of Philippe Krebs, PhD

Patrick van Delden, MSc student
(from 14.02.2019 to 31.08.2019)
Kristýna Hlavačková, MSc, technician (since 29.04.2019)
Thodoris Koutsandreas, guest/exchange PhD student
(until 28.02.2019)
Coline Nydegger, technician, 90%
Regula Stuber Roos, technician, 90% (until 30.06.2019)
Lester Thoo Sin Lang, MSc, PhD student
Wen Jie (Jeremy) Yeoh, MSc, PhD student
Vivian Vu, MSc, PhD student

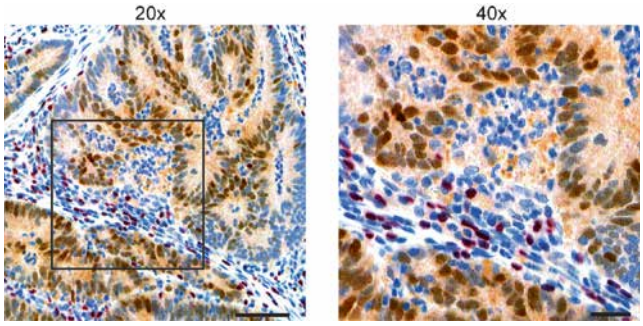
Summary of Research Activities

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.

Keywords:
- Cross-talk innate / adaptive immunity
- Role of inflammation for cancer development
- Immunopathology

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, J Clin Invest, 2015; Mertz, OncoImmunology, 2015; Pastille, Mucosal Immunol, 2019). We currently investigate the contribution of IL-33 to MPN progression and to the cellular and molecular mechanisms underlying CRC. For these studies, we use patient-derived samples and mouse models.



Accumulation of IL-33-responsive FOXP3+ regulatory T cells during colorectal cancer. Immunohistochemistry of human colorectal cancer tissue showing FOXP3-expressing lymphocytes (red) in the vicinity of IL-33-positive transformed intestinal epithelial cells (brown). Image magnification is indicated. Scale bars: 100 and 50 µm, respectively. Pastille & Wasmer et al., Mucosal Immunol. 2019 Jul;12(4):990-1003.

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 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; Cardoso Alves, EMBO Reports, 2019) 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
- Karl Lang, MD, Universitätsklinikum Essen, Essen, Germany
- Kathy McCoy, PhD, University of Calgary, Calgary, Canada
- Rebekka Schneider-Kramann, MD, Erasmus MC Cancer Center, Rotterdam, The Netherlands
- Astrid Westendorf, PhD, Universitätsklinikum Essen, Essen, Germany

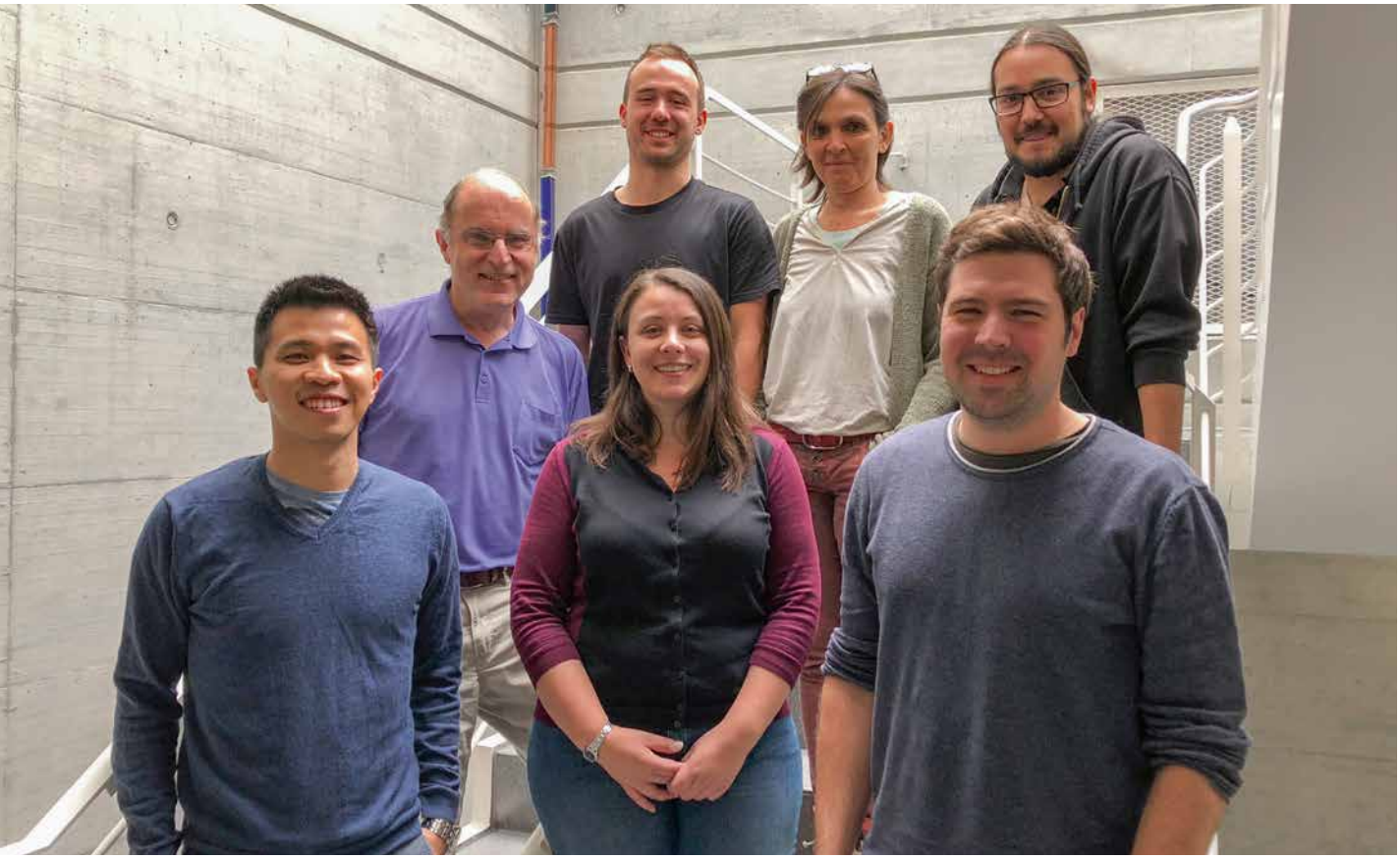
Grant Support
- Seed money project, Philippe Krebs, 2018–2019, CHF 10'000
- Lungenliga Bern, Philippe Krebs, 2018–2020, CHF 79'554
- Lungenliga Schweiz, Philippe Krebs, 2018–2020, CHF 79'554
- Swiss Cancer Research foundation, KFS-4162-02-2017-R, Philippe Krebs, 2017–020, CHF 312'500
- SNSF 314730_163086, Philippe Krebs, 2016–2019, CHF 525'000
- UniBE ID (Interdisciplinary) Grants Main, PI: Philippe Krebs, 2018–2020, *CHF 75'000
- EU / Marie Skłodowska-Curie RISE, Co-PI: Philippe Krebs, 2018–2022, **€ 904'500
- Helmut Horten Stiftung, Philippe Krebs, 2019–2021, CHF 130'000

** 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.*

Media
- 19.11.2019: Media Relations University of Bern: «A new pathway to "reprogram" killer cells» (https://www.unibe.ch/news/media_news/media_relations_e/media_releases/2019/medienmitteilungen_2019/a_new_pathway_to_reprogram_killer_cells/index_eng.html); outreach article based on the publication from Cardoso Alves et al, EMBO Rep. 2020 Jan 7;21(1):e48789.
- 19.11.2019: GENTECHNIK/296: Neuer Weg entdeckt, um Killerzellen «umzuprogrammieren» (idw) Schattenblick
- 19.11.2019: Neuer Weg zur Umprogrammierung von Killerzellen entdeckt, APA Zukunftwissen
- 19.11.2019: A new pathway to «reprogram» killer cells, bionity.com
- 19.11.2019: Mit programmierten Killerzellen gegen Krebs, Der Bund Online
- 19.11.2019: Forscher programmieren Killerzellen um, Wiener Zeitung
- 19.11.2019: Neuer Weg entdeckt, um Killerzellen «umzuprogrammieren», GIT-Labor
- 19.11.2019: Neuer Weg entdeckt, um Killerzellen «umzuprogrammieren», infoticker.ch
- 19.11.2019: Researchers discover new pathway to 'reprogram' killer cells, news-medical.net
- 20.11.2019: Steuerung von Killerzellen, 20 Minuten – Bern
- 20.11.2019: A New Pathway To «Reprogram» Killer Cells, Technology Networks
- 20.11.2019: A new pathway to 'reprogram' killer cells, medicalxpress.com
- 20.11.2019: Forschung: Killerzellen umprogrammieren, schweizerbauer.ch
- 20.11.2019: A new pathway to 'reprogram' killer cells, sciencedaily.com
- 21.11.2019: A new pathway to «reprogram» killer cells, Bioportfolio

Completed BSc, MSc, and PhD thesis
- MSc: Patrick van Delden (Supervisor: Philippe Krebs & Lester Thoo) «The role of ESRP1 in Epithelial to Mesenchymal Transition in Intestinal Epithelial Cells»
- MD/PhD: Michel Ernest Jean-Pierre Dosch (Supervisor: Guido Beldi; Co-advisor: Philippe Krebs) «ATP release mechanisms modulating inflammatory responses»
- PhD: Veronika Lysenko, University of Zurich (Supervisor: Alexandre Theocharides; external reviewer: Philippe Krebs) «Modeling Myeloproliferative Neoplasms to Elucidate the Disease Pathogenesis and to Understand Immune Responses»
- PhD: Karl-Leonhard von Meyenn (Supervisor: Christoph Schlapbach; mentor: Philippe Krebs) «PPARγ modulates IL-9 expression in TH2 cells by regulating glucose metabolism»
- PhD: Sandra Stephanie Ring, University of Zurich (Supervisor: Lukas Flatz; external reviewer: Philippe Krebs) «LCMV-Based Vectors in Melanoma Therapy – Induction and Maintenance of Efficient T Cell Responses»

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 Steering Committee «Digital Pathology»



Forschungsgruppe Christoph Mueller (Research group Christoph Mueller).

Group of Christoph Mueller, PhD

Pablo Banicles, MSc, technician, 80%
Nadia Corazza, PhD, staff scientist/co-PI, 60%
Cheong Kwet Choy Kwong Chung, PhD, post-doc (till Nov 2019)
Nadja Schüpbach, MSc student (med) (Apr–Aug 2019)
Alexandra Suter, technician, 60% (SIBDCS biobank)
Diego von Werdt, PhD student
Daniel Zysset, PhD, post-doc
(Jan–Aug 100 %, Oct–Dec 40%)

Summary of Research Activities

Immune surveillance in tissues

Our group has a longstanding interest in the complex immunoregulatory mechanisms that are operative in the intestinal mucosa during homeostatic conditions and the potential predispositions or events which can lead to disruption of tissue homeostasis during inflammatory conditions as in the case of inflammatory bowel diseases (Crohn's disease, Ulcerative colitis). In recent years, the importance of the intestinal microflora in shaping the education of the local immune system, but also the reciprocal effects of local immune responses on the composition of the intestinal microflora have become increasingly acknowledged. Thus, we aim to link the molecular and cellular characterization of distinct immune cell subsets in the intestinal mucosa and their phenotypical and functional alterations during intestinal inflammation with concurrent analyses of the intestinal microflora and any associated metabolic changes. Since microbial-driven immune responses can predispose for development of tumors or even cardiovascular diseases, we have recently extended our research to other chronic inflammatory disorders (e.g. colorectal tumors and atherosclerosis). While we often use experimental mouse models to test our hypotheses, whenever possible, we validate these experimental findings using state-of-the-art technologies with patient materials, mostly archived tissue samples or biosamples obtained from the SIBDCS biobank (Head: Christoph Mueller).

Specific research interests

The research interests of our group are currently focused on:

- The molecular and cellular events that are operative during induction and resolution of chronic intestinal inflammation
- The functional plasticity of tissue-resident T cell subsets, notably in the intestinal mucosa
- The contribution of distinct monocyte / macrophage subsets in immunosurveillance of tumors but also in the induction of chronic inflammatory disorders such as inflammatory bowel diseases or atherosclerosis.

Research Activities

Project 1: Changes in local immune cells during onset vs. remission vs. relapse of colitis

Understanding the mechanisms that drive remission induction and maintenance is key 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 intestinal inflammation, induced remission and spontaneous relapse of the disease (Brasseit et al., Mucosal Immunol 2016). In this model we 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 and on the functions exerted by

distinct CD4 T cell clones during induction of colitis, remission and relapse of the disease (using scRNASeq). An ultimate goal is to identify strategies to specifically extend the remission period, or even prevent a further relapse of disease.

Projekt 2: TREM-1 as an amplifier of inflammation of inflammation in immuno-surveillance and immunopathologies
TREM-1 (Triggering Receptor Expressed on Myeloid Cells-1) is an activating innate immune receptor on neutrophils and monocytes/macrophages. We previously described a critical pathogenic role for TREM-1 not only in acute, but also in chronic inflammation, notably, in inflammatory bowel diseases (Schenk et al., J Immunol 2005, J Clin Invest 2007). We generated a Trem1-/- mouse (Weber et al. PLoS Pathog 2014) to determine the critical Trem1 mediated effects in 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, such as stroke (Liu et al., Nat Immunol 2019), neurodegenerative disorders, and in infections with intracellular pathogens.

Project 3: Functional plasticity and retention of tissue-resident memory T cells in the intestinal mucosa
Understanding the functions and their regulation in intestinal T cell subsets is one of our long-standing goals. Some of these intestinal T cell subsets represent the prototypical example of tissue-resident T cells due to their resident location at a barrier site and their limited capacity to recirculate. Currently, we investigate the regulation of intestinal resident T cells in protective immunity during infectious diseases (e.g. infection with Listeria monocytogenes), but also their contribution to the development of chronic inflammatory disorders. In particular, we investigate the molecular mechanisms that regulate their tissue-resident phenotype, and assess how distinct functional activities of this T cell subset may contribute to protective immunity versus inflammatory conditions.

Internal Collaborations
- Stefan Freigang, MD
- Vera Genitsch, MD
- Mirjam Schenk PhD

External Collaborations
National
- Andrew Macpherson, MD, Department of Clinical Research, University of Bern
- 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
- Jens V. Stein, PhD, Department of Medicine, University of Fribourg

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
- Klaas van Gisbergen, Sanquin Research & Amsterdam University, NL

Grant Support
- SNF 310030_170084, Christoph Mueller, 2016–2019, CHF 525'000
- SNF 314730_189277, Christoph Mueller , 2019–2022, CHF 516'667
- SNF 33CS30_177523 (SIBDCS; Co-PI), 2018–2020, *CHF 304'500
- Monique Dornonville de la Cour Stiftung (to Daniel Zysset), 2018–2020, CHF 52'387

** own share*

Completed BSc, MSc, PhD and MD thesis
- MSc (med) Nadja Schüpbach
  (Supervisor: Prof. Christoph Müller)
  «Immunological memory of the innate immune system: influence of repeated exposure of intestinal bacteria on human monocytes»
- PhD (University of Geneva) Ilke Cadosh
  (Christoph Müller, External Advisor)
  «The role of BTN2A2 in Immune Regulation of B Cells»

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 program
- Chair, Stiftung für klinisch-experimentelle Tumorforschung Bern
- Member, Experimental Animal Center (EAC) – Committee (University of Bern)
- Member, Research Committee, Medical Faculty
- Member of several faculty committees (appointments)

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

Forschungsgruppe Aurel Perren.

Group of Aurel Perren, MD

Ilaria Marinoni, PhD, Co-PI
Matthias Dettmer, MD Attending Pathologist
Martin Wartenberg MD, Attending Pathologist
Annunziata Di Domenico, MSc, PhD-student
Simon April, MSc, PhD student
Renaud Maire, MSc, Technician
Bräutigam Konstantin, MD, Resident
Nicolas Munz, BSc master student (Bio)
Michelle Buri BSc master student (BMS)
Magdalena Skowronska, PhD
Umara Rafiqi, MSc, PhD student
Janine Straub, Cand. Med.

Summary of Research Activities

The research focus of our group is the study of endocrine tumors; notably sporadic and 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 /ATRX in PanNET
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 as well as different epigenetic signatures. We specifically focus on the role of epigenetic changes occurring in DAXX/ATRX negative PanNETs and their involvement in tumor progression.

Project 2: Precision medicine approach for PanNet treatment
No therapy prediction based on specific molecular profile is possible for PanNET, yet. We recently established organoid culture of PanNETs which resemble original tumor tissue features and that 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: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 therapeutic approach.

Project 4: 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.

Internal Collaborations
- Mario Tschan, PhD
- Philippe Krebs, PhD
- Erik Vassella, PhD
- Inti Zlobec, PhD
- Irene Centeno, PhD
- José Galvàn, PhD

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

International
- Dr. Chrissie Thirlwell, Department of Cancer Biology, Clinical Lecturer Medical Oncology University College London, United Kingdom
- Prof. Anne Couvelard and Dr. Jérôm Cros, Department of Pathology, Hospital Beaujon, Clichy, France
- Prof. Massimo Falconi, Surgery Departement, San Raffaele, Milan, Italy
- Prof. Halfdan Sorbeye, Oncology, Bergen

Grant Support
- SNF, 310030-188639 / 1, Aurel Perren, 2019–2023, CHF 632'000
- Uniscientia Stiftung, Aurel Perren, 2019–2021, CHF 135'000
- Desirée and Niels Yde Foundation, Ilaria Marinoni, 2016–2019, CHF 51'000
- KLS-4227-08-2017, Aurel Perren PI and Ilaria Marinoni co-PI, 2018–2022, CHF 360'000
- ENETS CoE Synergy Grant, Ilaria Marinoni, 2019–2021, Euro 69'700
- Wilhelm Sander Stiftung, Ilaria Marinoni, 2018–2019, CHF 210'000
- Berner Krebsliga, Ilaria Marinoni, 2019–2020, CHF 40'000
- Berner Krebsliga, Matthias Dettmer, 2017–2022, CHF 70'000

Honors/Awards
Mitglied Leopoldina, Nationale Akademie der Wissenschaften

Completed BSc, MSc, PhD and MD thesis
- Michelle Buri, MSc, Biomedical Science «Targeting Epigenetic modification In Pancreatic Neuroendocrine tumors»

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 Committee -Mitglied, Europäische Neuroendocrine Tumor Society
- Leiter Krebsregister Bern
- Stiftungsrat NICER
- Mitglied Forschungskommission SKL
- Mitglied Senat SAMW

Ilaria Marinoni
- Member of MIC Comission University of Bern
- Member of ENETS NEXT generation committee of the European Neuroendocrine Tumor Society
- Member of European Neuroendocrine Excellence academy

Group of Mirjam Schenk, PhD

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

Summary of Research Activities

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 tumor 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, Institute 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
- Delphine Lee, MD, Division of Dermatology, Department of Medicine Harbor-UCLA Medical Center, Los Angeles Biomedical Research Institute

Grant Support

- Stiftung experimentelle Biomedizin, 2016–2019, CHF 763'000
- Stiftung experimentelle Biomedizin, 2019–2021, CHF 520'000
- Klinisch Experimentelle Tumorforschung, 2016–2019, CHF 150'000
- Helmut Horten, 2017–2020, CHF 180'000
- SNF 320030_176083, 2018–2022, CHF 566'109
- Wilhelm Sander Stiftung, 2019–2020, Euro 49'700

Honors/Awards

17.09.2019: Venia Docendi für das Fach Experimentelle Immunologie, Universität Bern, Medizinische Fakltät

Research group Mario P. Tschan.

Group of Mario P. Tschan, PhD

Fabienne Anderegg, BMA-Praktikantin (since November 25th)
Magali Humbert, PhD postdoc
Vera Imboden, Master student (BMS)
(Co-supervision, PD Dr. M. Schaller, until February 2019)
Félice Janser, PhD student (Co-supervision, Prof. R. Langer, until August 2019)
Filip Manevski, Master student (BIO) (since February 18th)
Irene Mungure, Master student (BIO)
Nicolas Niklaus, PhD student
Proiti Poddar, Master student (BIO) (until September 30th)
Sreoshee Rafiq, PhD student (Supervisor, Dr. M. Humbert)
Anna Schläfli (-Bill), PhD postdoc, 70%
Robin Schweri, Master student (BIO) (since February 1st)
Kristina Seiler, MD-PhD student
Deborah Shan, technician, 80%
Igor Tokarchuk, MD-PhD student
Kristin Uth, PhD student (Co-Supervision Prof. I. Zlobec) (until August 31st)

Summary of Research Activities

My research team investigates molecular mechanisms involved in the pathogenesis of acute myeloid leukemias (AML). Currently, we are deciphering the function of autophagy and the transcription factor PU.1 in this disease. 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.

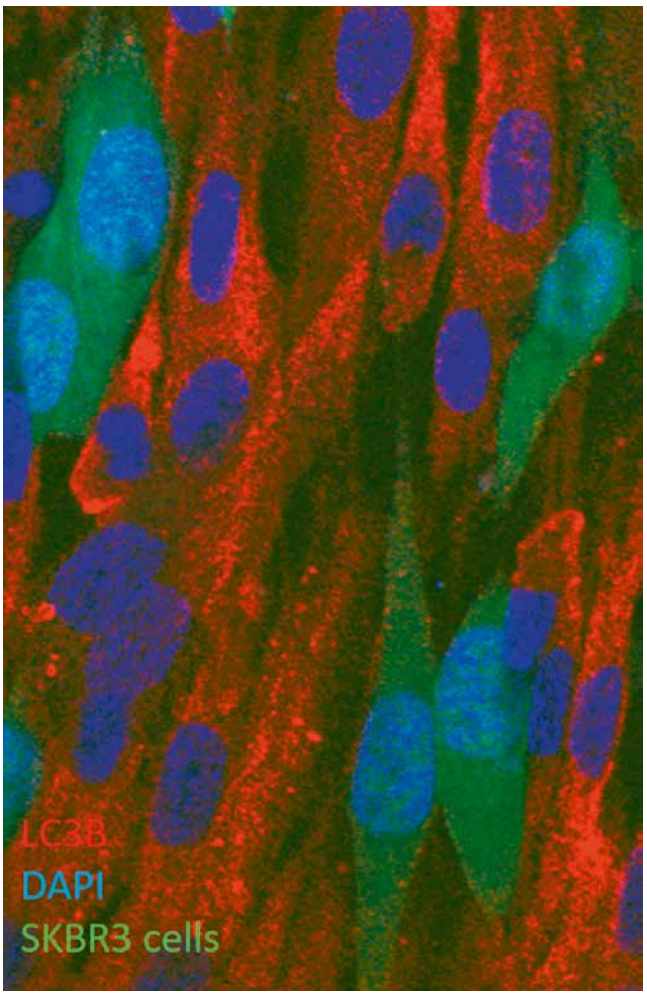
Research Activities

Project 1: Functionof chaperone mediated autophagy in myeloid leukemia

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 therapy 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



Cancer-associated fibroblasts co-cultured with SKBR3 breast cancer cells (green). Staining: autophagy marker LC3B (red).

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 signaling 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
- Jean-Emmanuel Sarry, PhD, Centre de Recherches en Cancérologie de Toulouse - CRCT, Toulouse, France
- Sylviane Muller, PhD, CNRS UMR7242 Biotechnology and Cell Signaling, University of Strasbourg, France

Grant Support
- SNSF_31003A_173219, Mario Tschan, 2017–2021, CHF 693'600
- SNSF MD-PhD 03/17, Kristina Seiler, Mario Tschan, 2018–2020, CHF 180'000
- UniBE international 2021, I.Tokarchuk, Mario Tschan, 2018–2020, CHF 90'000
- Bernische Krebsliga, Magali Humbert, 2017–2021, CHF 85'000
- Werner und Hedy Berger-Janser Stiftung, Anna (Schläfli) Bill, 2018–2019, CHF 77'000
- Stiftung Für Klinisch-Experimentelle Tumorforschung, Magali Humbert, 2018–2019, CHF 20'000
- SNSF31003A_166578, Inti Zlobec, Co-PI Mario Tschan, 2016–2019, *CHF 305'040
- UniBE ID Grant, T. Ochsenreiter, Co-PI Mario Tschan, 2018–2019, *CHF 105'000
- Partenariat Hubert Curien/Germaine de Staël Funding, J.E. Sarry, Co-PI Mario Tschan, 2019–2020, *CHF 9'000

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

Completed BSc, MSc, and PhD thesis
- MSc: Proiti Poddar (Supervisor: Mario P. Tschan) «Splice factor gene modification in AML: Impact on cellular differentiation and apoptosis during ATRA therapy»
- MD thesis: Susanne Jutzi (Supervisor: Mario P. Tschan) «What is the role of autophagy in response to ALK inhibition in lung cancer?»

- PhD: Félice A. Janser
  (Co-Supervisors: Mario P. Tschan, Rupert Langer)
  «The role of macro- and chaperone mediated autophagy in therapeutic response and resistance formation to HER2 targeted treatment»
- PhD: Livia Niklaus
  (Supervisor: Volker Heussler; Mentor: Mario P. Tschan)
  «Host cell autophagic and lysosomal defence mechanisms against the Plasmodium liver stage and parasite evasion mechanisms»
- PhD: Dorota Dudka
  (Supervisor: Michaela Medova; Mentor: Mario P. Tschan)
  «Unraveling the molecular response to dose-rate and delivery time of ionising radiation in 2D vs 3D cell culture»
- PhD: Lionel Rohner
  (Supervisor: Michaela Fux; Mentor: Mario P. Tschan)
  «Influence of the activation status of human basophils on apoptosis»
- PhD: Morten Luhr
  (Supervisor: Nikolai Engedal; First Opponent, External Expert: Mario P. Tschan), University of Oslo, Norway
  «The unfolded protein response and the ATG8 protein family in autophagy»

Administrative 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 the GCB Graduate School
- 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
- Organization Translational Cancer Research course 2019
- Member of the «Vereinigung der Dozentinnen und Dozenten der Medizinischen Fakultät Bern» representing the interests of UniBE lecturers at the Medical Faculty meetings
- Member of the Expert Committee for Biomedical Analysts, «Zentrum für medizinische Bildung, Höhere Fachschule»
- LS2 section autophagy, current president.
- Grant reviewing for «L' institut national de la santé et de la recherche médicale (INSERM)» and the Polish National Science Center
- Jury member Johanna Dürmüller-Bol DBMR Research Award 2019
- Guest editor: Cells, Special Issue «Chaperone-Mediated Autophagy» (https://www.mdpi.com/journal/cells/special_issues/Chaperone_mediated_autophagy, and Biology, Special Issue "Autophagy in Cancer" (https://www.mdpi.com/journal/biology/special_issues/Autophagy_in_Cancer)

Group of Erik Vassella, Dr. pharm.

Catia Coito, BMA-Praktikantin (Medi)
Bushra Fakher, Master student (BIO)
(from September 16, 2019)
Elham Kashani, PhD student
Jaison Phour, technician
Senija Selimovic-Hamza, assistant Bioinformatician and Data Coordinator
Carmen Trefny, Master student (BIO)

Summary of Research Activities

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 temozolmide 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
- Ilaria Marinoni und Aurel Perren
- Rupert Langer

External Collaborations

National

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

Grant Support

- SNF (31003A_175656), 2018–2022, CHF 408'509
- SAKK 75/08 Rupert Langer (PI), Erik Vassella (Co-PI), 2018–2020, CHF 132’640

1.2 Translational Research Unit (TRU)

Head: Inti Zlobec, PhD

Administration: Caroline Hammer

Technical and Scientific Staff:
Carmen Cardozo
Dr. Irene Centeno
Loredana Daminescu (from October)
Dr. José A. Galván
Patricia Ney (until October)
Stefan Reinhard
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.

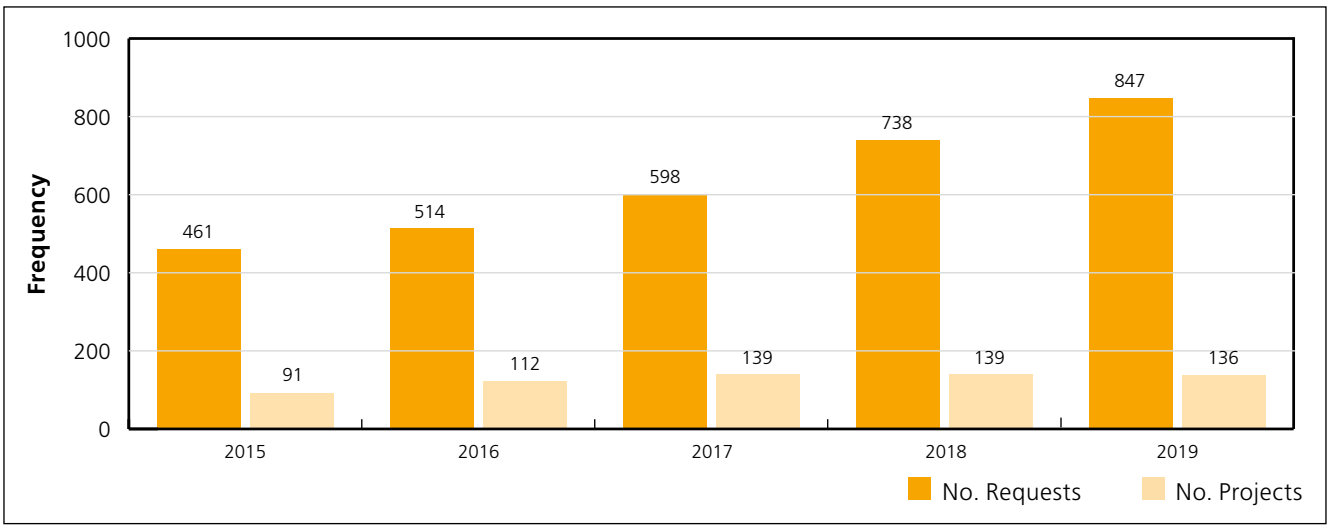
TRU has facilitated research in 2019 from 169 projects and has handled 847 requests (excluding Tissue Biobanking, see TBB). Collaborative projects with external research groups comprise 23% of the projects in TRU.

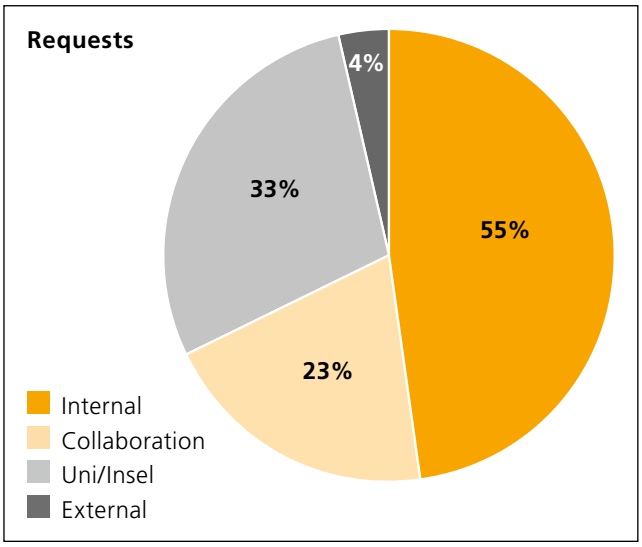
Distribution of requests

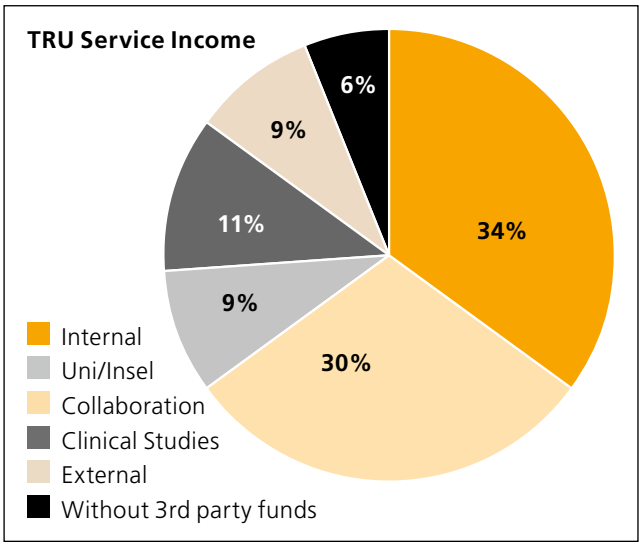
Approximately 8% of all projects in TRU derive from animal tissue use, 24% from clinical studies (including requests from SAKK), while the remaining are human tissue-related requests. Sources of income vary: 94% of all of TRU's services in 2019 were funded by third party money, while the remaining 6% were sponsored by the Institute of Pathology. This institutional funding aims to cover start-up projects for our pathologists and researchers.

Histology

Our lab has expertise in histological techniques and tries to personalize each research project. Sections are cut for many purposes: laser capture microdissection, DNA/RNA extraction, immunohistochemistry and other special downstream techniques (e.g. MALDI). Histology is the basis of all the work performed in TRU. This year, we have re-embedded 2662 (2018 n=1637) blocks, and cut thousands of slides for H&E or special stains (n=3189; 2018 n=2476 slides), immunohistochemistry, TUNEL or ISH (n=4936; 2018 n=6161), empty cuts 3887 and slides requiring special DNAse/RNAse-free conditions (n=166; 2018 n=443).





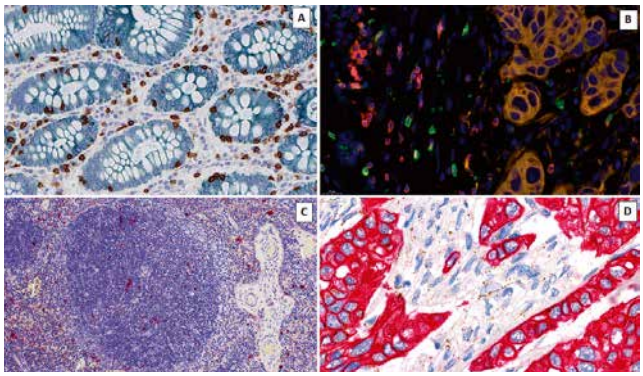


Overview

Tissue Visualisation

The TRU has expertise in tissue visualisation methods, including assays for immunohistochemistry mRNA in situ hybridisation, immunofluorescence, TUNEL and combinations of these. This year highlights the introduction of multiplex 4-colour OPAL, which has been used to study the tumor microenvironment (PanCK, CD8, CD3 and DAPI). More than 5000 slides have been stained this year, including approximately 10% on animal tissues. Tissue Microarray slides play an important role in our daily routine.

Again this year, a large number of antibodies has been established for human and animal tissue samples (n=74). This brings the TRU catalogue of antibodies to nearly 600. Approximately 30% of all our staining requests are performed as part of collaborations with researchers from the University, Insel Hospital or abroad.



A) Double immunohistochemistry
(PanCytokeratin – green and CD8 – brown) in colon tissue
B) Multiplex Immunofluorescence
(Pancytokeratin – orange; CD3 – red and CD8 – green in tumor microenvironment)
C) TUNEL staining on spleen tissue
D) Double in situ hybridization / immunohistochemistry
(Vimentin – brown and Pancytokeratin – red)

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 processed for diverse purposes such as publication, education, or other research purposes. Additionally, we have specific scanning profiles for digital analysis that require an extra quality standard.

Over the last year, 11'448 slides were scanned, mainly for internal researchers (48%) and collaborators from the University and Inselspital (52%). 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.

2. Next-generation Tissue Microarrays (ngTMA®)

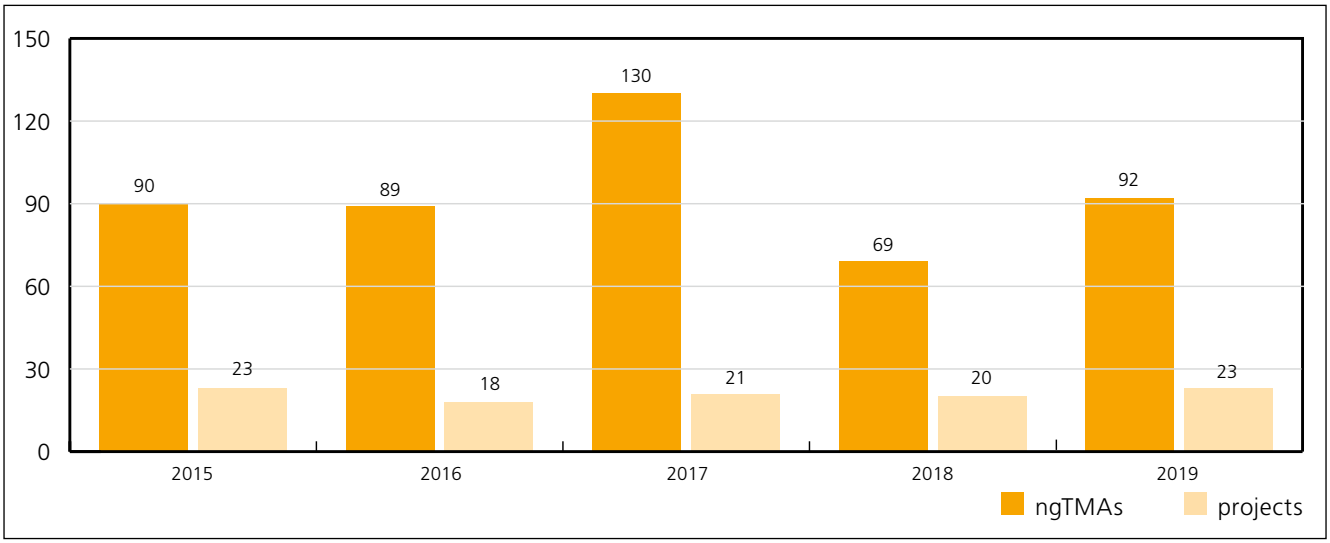
Our ngTMA core facility has evolved into an internationally-recognized platform for the construction of high-quality tissue microarrays. By incorporating digital pathology and a downstream data-handling pipeline, ngTMA supports histopathology-based and computationally-driven AI research.

The diagram below shows the progression of ngTMA construction over the last 5-years. We have observed a change in ngTMA trends. Originally used as a screening tool for different biomarkers, ngTMA is now employed for development of new methodologies, mainly multiplexed immunofluorescence (e.g. OPAL, CODEX) and for assessment of intratumoral heterogeneity.

Since TRU has consistently scanned each ngTMA slide after H&E or immunostaining, a massive digital archive of more than 1'000'000 spot images and several thousand whole slide images from an array of tissue types has been generated with links back to clinicopathological data. These images can now be used to train AI algorithms for prediction of clinical outcomes, molecular subtypes or other endpoints.

Example of a colorectal cancer ngTMA slide stained with H&E.

Since it's inception in 2012, TRU has created more than 650 ngTMA blocks, totaling more than 110'000 punches in recipient blocks and 20'000 punches for tubes, and hence downstream molecular analysis. The number of donor blocks involved totals more than 16'000. The content of these donor blocks includes a large number of upper and lower gastrointestinal cancers, lung cancers, neurological tumors and endo-



Number of ngTMA projects (i.e. requests) and number of blocks made over the last 5-years.

crine (including neuroendocrine) cancers, but also sarcomas, pancreas cancers, gynecological tumors and urological specimens.

In addition to our numerous internal project partners, the number of external collaborators grows more each year. We are proud to include the University of Stanford, University of California, Cancer Barts Institute, University of Amsterdam and Karolinska Institutet among our international partners. On a national level, we continue our collaborations with the EPFL Lausanne, University of Basel, University or Geneva, Inselspital and the Department for Biomedical Research (DBMR) of the University of Bern.

3. Data management

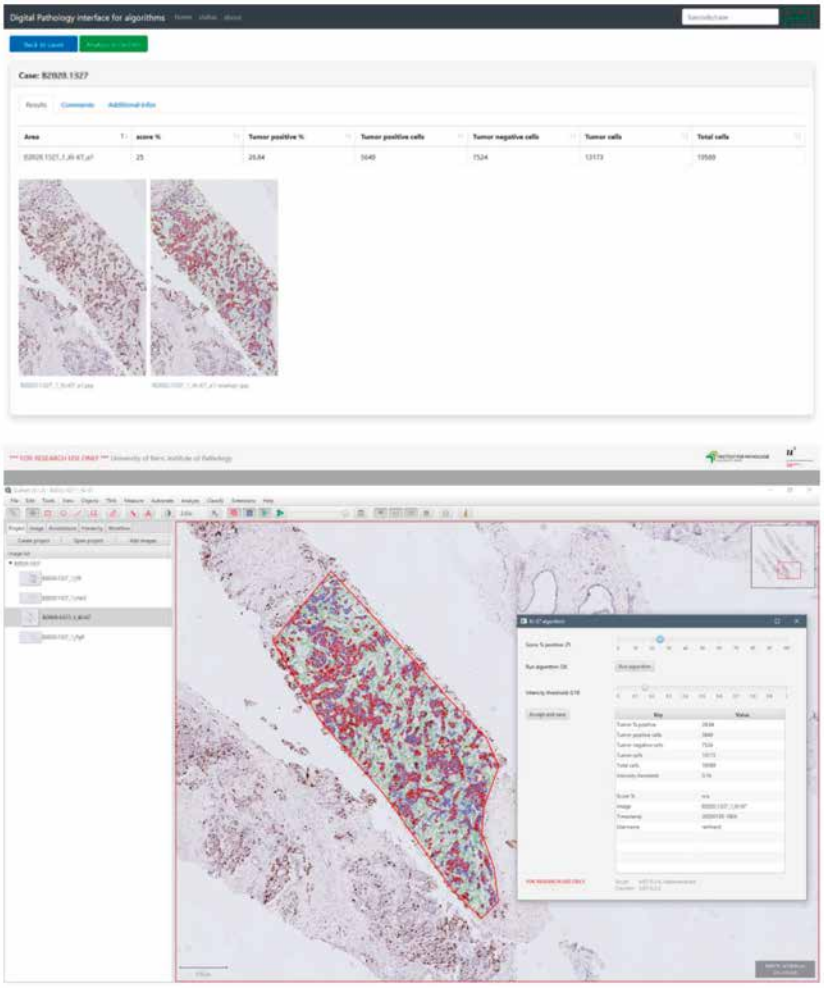
Digitisation, data management and data sharing are topics of substantial importance for TRU. As such, major efforts were undertaken for the development of a Human Research Act (HFG2014) compliant research database together with the company Telemis for integration of not only clinicopathological and outcome data for patients and tissue samples but also for whole slide images, and most importantly ngTMA images and related data. So far, clinical data from 1939 patients, 73 TMAs corresponding to 13068 spots and 2430 whole slide images comprising five different patient cohorts were processed and imported. An important task for data import is in the preparatory phase of data cleaning, as such TRU helps support researchers in data preparation and are on the way to consolidate another 10 research cohorts. Enhancement of the database will continue in 2020.

4. Digital image analysis

a. Analysis

TRU has developed an open source workflow to analyze Ki-67 breast cancer cases in diagnostic routine; this includes the management of the data from the scanner to the actual result. A web-app provides an overview of the status of the cases and a self-developed and in collaboration with five MDs in-house trained algorithm performs the analysis. Since its recent launch, 40 cases have so far been examined for research purposes to optimize the algorithm.

TRU has provided training in image analysis using the free, open-source tool QuPath for nine different projects. In addition, a collection of scripts facilitating image analysis in QuPath and TMA data handling was established.

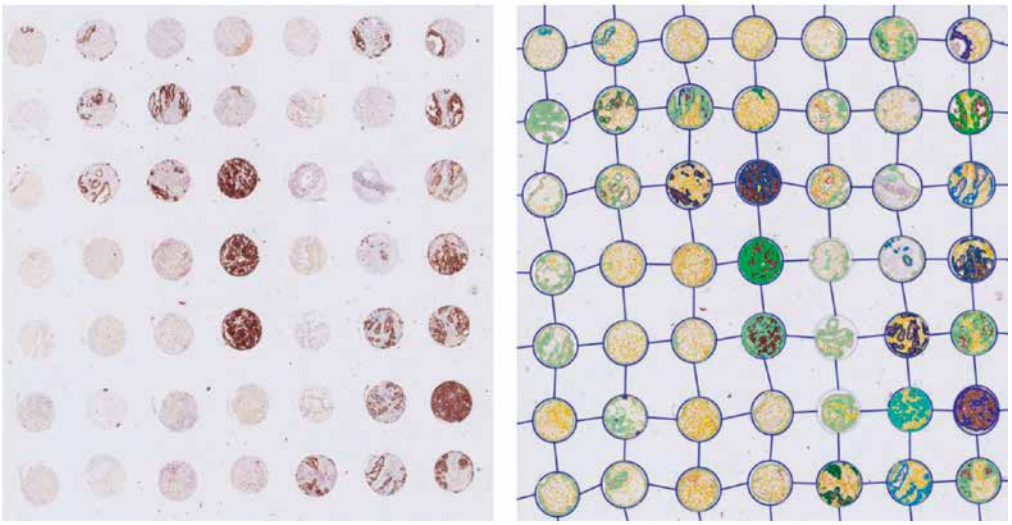


Ki-67 diagnostic workflow with interface to select and open case (top) and Qupath algorithm in progress (bottom).

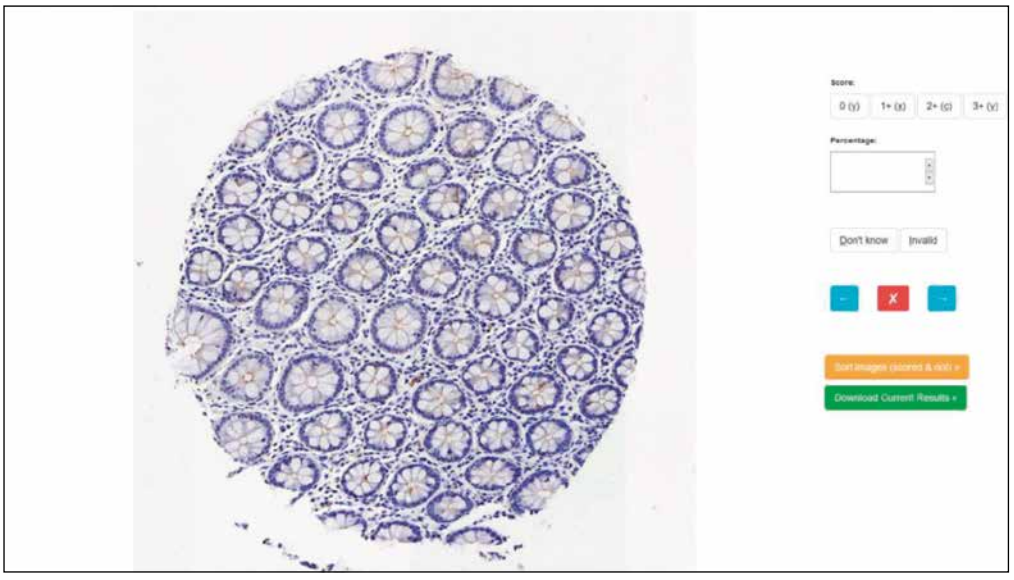
b. Scorenado

TRU has created 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, which will continue to be developed. Since its test launch, a total of 43 Scorenado projects, including 553 slide scans, were set up for research conducted in-house, at Insel Hospital, and at other institutes in Switzerland and abroad.

Overall, 136'578 TMA spot images or whole-tissue slide crop images have been scored with Scorenado. Project types included scoring different immunohistochemistry markers, estimating percentages of tumor positivity, counting tumor buds, and image classifications in colon, lung, breast, pancreas, and endometrium tissue.



QuPath project immune cell detection and calculation distance to tumor within spots.



Scorenado scoring on pNR2B_Y1472 stain.

Tissue Bank Bern (TBB)

Director: Prof. Aurel Perren

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

The TBB works together with the Clinical Pathology Division at the Institute of Pathology to ensure the collection and distribution of high-quality human tissue samples conform to the Human Research Act, 2014. TBB services are, since October 2016, being performed by the Translational Research Unit (TRU) thus, personnel and resources are shared.

Workflow

The requirements to use samples from our tissue collection include the description of the project, the type and characteristics of the requested tissue and essential information regarding the ethical approval. The request process is simple and does not mean additional bureaucracy for the researcher. Our committee of experts in scientific and ethical research will evaluate each request and provide advice, if needed. The estimated timelines and processes are displayed in the picture below.

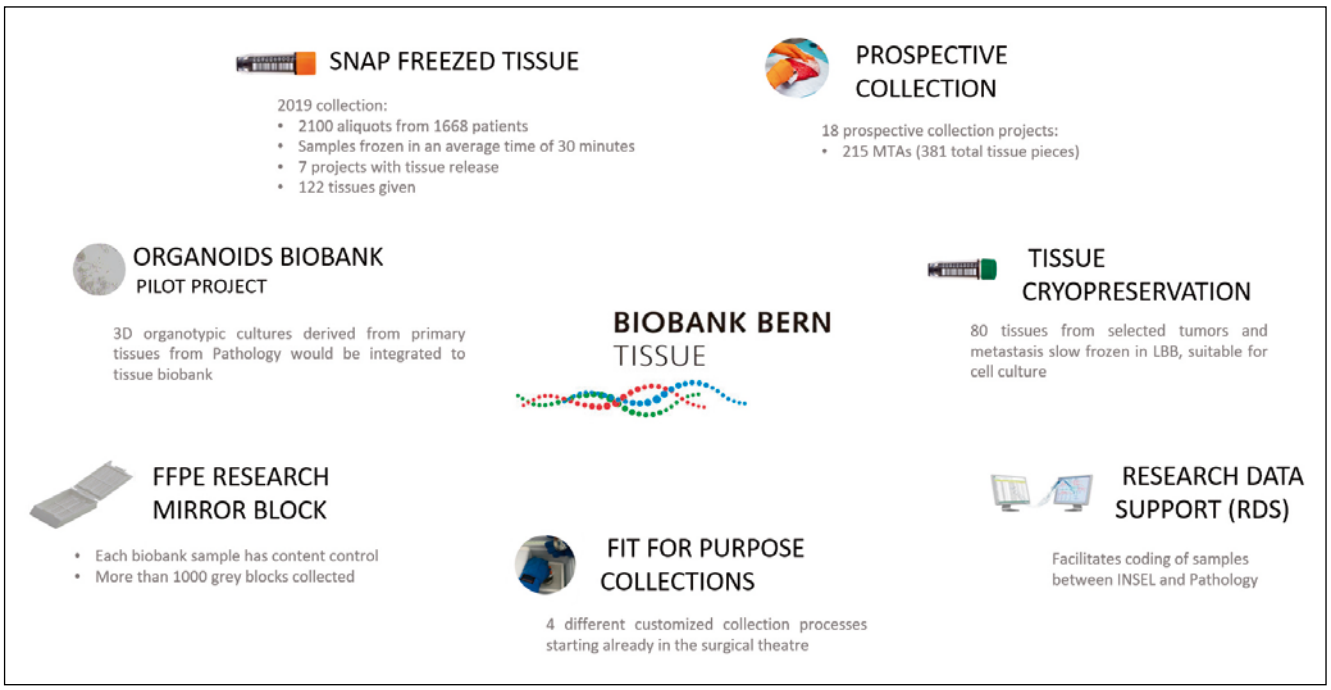
TBB activities

In 2019, aside from providing the scientist with frozen and native material, we have increased the portfolio of customized collections, implying strong multi-institutional and cross-departmental collaboration. Additionally, we work on processes to satisfy the growing interest in «live» tissue. In order to preserve live cells in frozen tissue, we have introduced slow freezing processes as an alternative cryopreservation method for selected tumours. These on-going and novel aspects of TBB 2019 are summarized in the Figure.

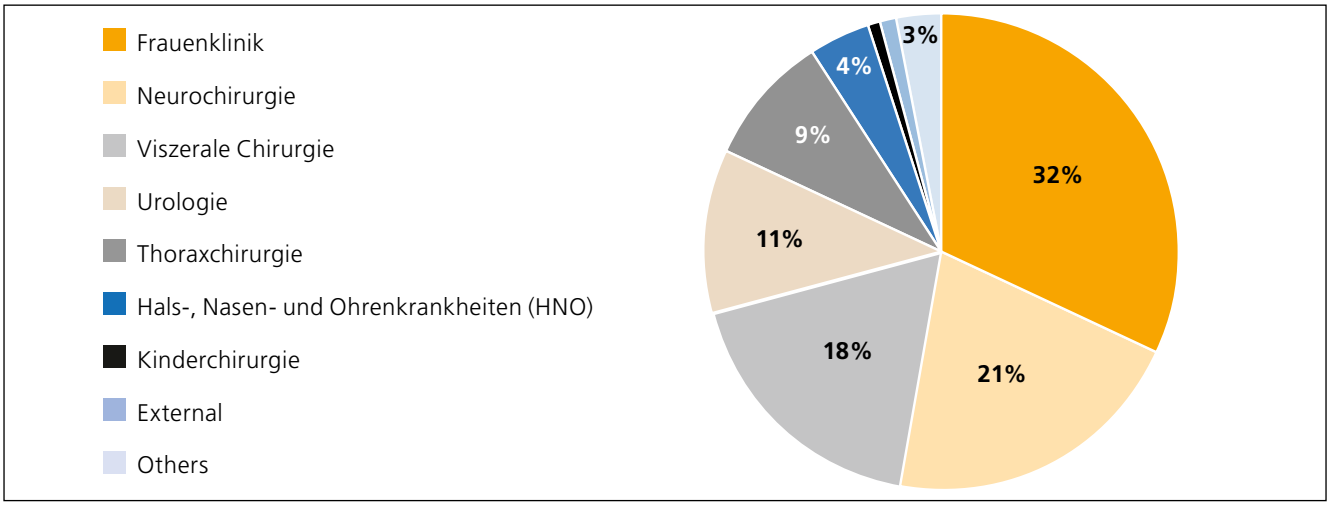
TBB institutional collection statistics

TBB markedly expanded its tissue collection reaching a total of more than 11'000 different samples stored in more than 42'000 tubes. This year different clinics continue their important contribution to the biobank. With 2100 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.

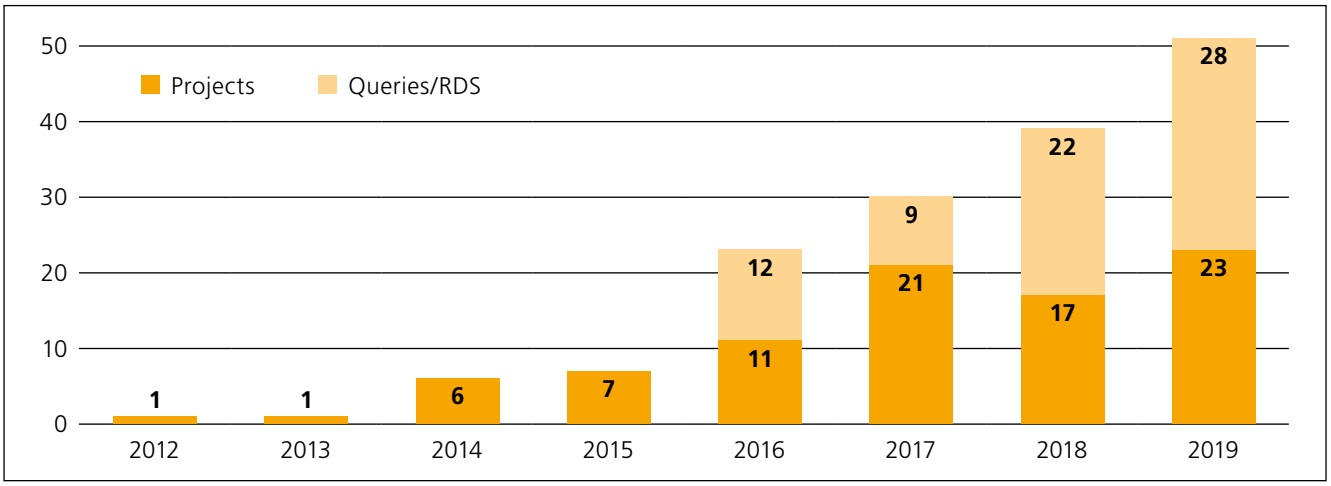
REQUEST FORM	TBB ORDER PREOCESSING	SAMPLE DELIVERY
Project description Request sample Request of data Provide ethics approval	Technical acceptance Query Clinical acceptance Consent proofing	Exit control MTA contact Material transfer to researcher
1–8 weeks	2–3 weeks	1–2 weeks



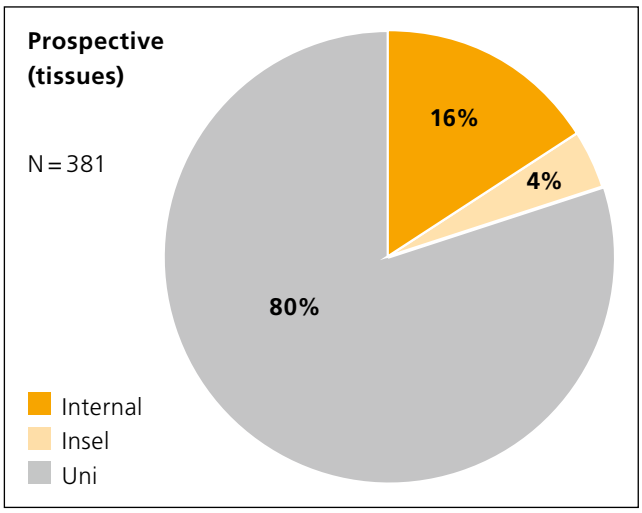
Different activities performed by TBB in 2019.

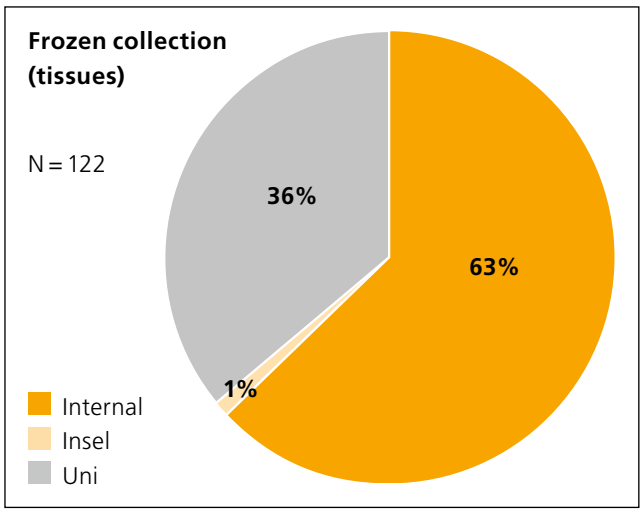


Distribution of incoming tissue specimens for biobanking.



Number of TBB requests for tissues/data showing growth of usage over the last years.





Summary of tissue usage by internal, Insel Hospital or University of Bern (incl. DBMR) researchers for prospective projects and retrospective (frozen collection) in 2019.

Projects by tissue bank Bern 2019

The number of TBB projects continues to rise. In 2019, we received 51 requests for tissue and/or data.

Usage of tissue samples

We have provided scientists with 122 frozen tissues, all with pathological tumour content control. Additionally, 381 tissues were given in a prospective manner.

Towards the best quality of service

The delivery of optimal quality tissues to researchers is one of the main aims of TBB. In this regard, TBB has been strongly focused on the standardization of the multiple biobanking processes together with the Swiss Biobanking Platform (SBP), including collection, transport, processing, storage and distribution of the sample as well as personnel and equipment management. The improvements in these areas have led us to the achievement of the SBP Norma label in July 2019.

Strong quality monitoring systems are essential for the development and maintenance of the highest service quality and guarantee a continual improvement; in this field, we have accomplished the SBP standards, acknowledged by the acquisition of the SBP Optima label in December 2019.


CERTIFICATE

We, Swiss Biobanking Platform, confirm the labelling of

Tissue Biobank Bern (TBB)

University of Bern

SCOPE OF THE NORMA LABEL

COLLECTION, TRANSPORT, RECEPTION, PROCESSING, STORAGE AND DISTRIBUTION OF BIOLOGICAL RESOURCES

The Norma Label demonstrates compliance with the Good Biobanking Practices; in particular, OECD Best practice guidelines for biological resource centres (2007), ISBER Best Practices (2018) and IARC Common minimum technical standards (2017). It follows established standards, including the ISO 20387:2018 - General requirements for biobanking.

The compliance check is based on the answers provided in the Biobank 3QAN and the on-site-evaluation performed by SBP Team on 2019-02-05

RESPONSIBLE PERSON(S): Aurel Perren, Inti Zlobec

LABELLING DATE: 2019-07-15

CERTIFICATE NUMBER: UB_1907_BB_02

NORMA GOVERNANCE PROCESS

JOSEPHINE ULDRY, SBP Evaluator

CHRISTINE CURRAT, PhD, SBP Executive Director


CERTIFICATE

We, Swiss Biobanking Platform, confirm the labelling of

TISSUE BIOBANK BERN

UNIVERSITY OF BERN

SCOPE OF THE OPTIMA LABEL

IMPLEMENTATION OF QUALITY ASSURANCE MEASURES

The Optima Label demonstrates compliance with the Good Biobanking Practices; in particular, OECD Best practice guidelines for biological resource centres (2009), ISBER Best Practices (2018) and IARC Common minimum technical standards (2017). It follows established standards, including the ISO 20387:2018 - General requirements for biobanking.

The compliance review is based on the answers provided in the Biobank 3QAN and the evaluation performed by SBP Team on 2019/11/04

RESPONSIBLE PERSON(S): Prof. Aurel Perren, Prof. Inti Zlobec

LABELLING DATE: 2019/12/16

CERTIFICATE NUMBER: UB_1911_BB_01

OPTIMA GOVERNANCE PROCESS

JOSEPHINE ULDRY, SBP Evaluator

CHRISTINE CURRAT, PhD, SBP Executive Director

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.

Altogether, in 2019 we have worked on new standard operational procedures and documentation towards the new ISO 20387:2018, which is one of our overall goals for the near future.

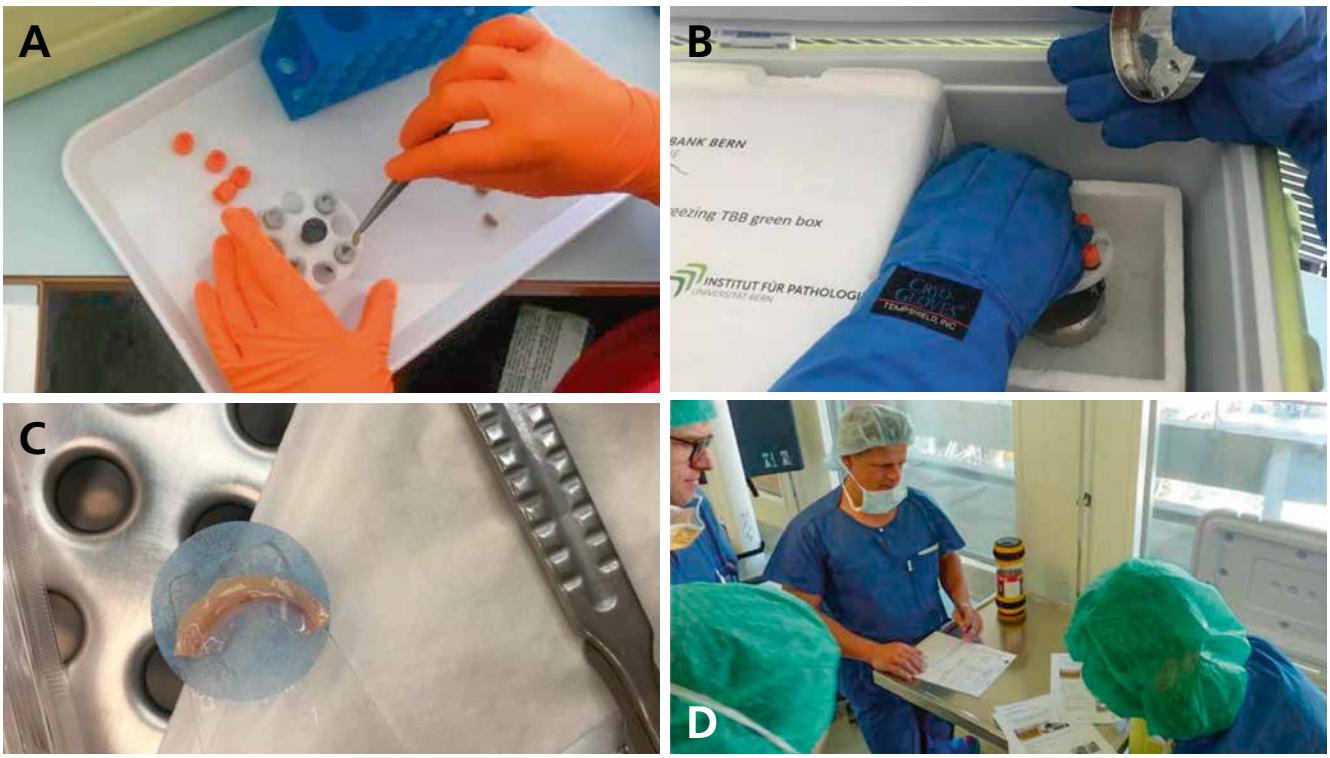
The ethical and legal aspects are also a key part of the functioning of the biobank. TBB adheres to the Human Research Act (Humanforschungsgesetz, HFG) as evidenced by the SBP Vita Label certificate achieved already in 2018.

Fit-for-purpose TBB collections

Our commitment towards satisfying the requirements of the researcher is demonstrated in our enhanced procedures for customized collections. Our advanced process optimization is the result of strong simultaneous collaboration of TBB, clinics and researchers. This year we have developed four customized collection processes starting already in the surgical theatre, where the personnel was trained by TBB staff. The clinics mainly involved in this type of projects are Heart and Vascular, Ophthalmology, Paediatrics and Head and Neck Surgery Clinics at the Inselspital.

Partnerships

Excellence in biobanking is a multi-institutional and cross-departmental goal. We work in close collaboration with the Clinical Pathology division for sample acquisition; with the Insel Data Coordination Lab (IDCL) for general consent status and treatment related data management; with Liquid Biobank Bern for collaborative projects liquid-tissue and harmonisation of processes; with Krebsregister for follow-up data



A and B: Collection procedure of peripheral artery disease tissue samples in the surgical theatre.
C: Leftover donor cornea tissue collection in the Ophthalmology Clinic.
D: Surgery personel from the Head and Neck Surgery Clinic being trained for project based customized sample collecction.

on cancer patients and with the Swiss Biobanking Platform for quality monitoring and process standardization.

The clinics that continue to send samples for biobanking and participating actively in the implementation of «fit for purpose» collections are invaluable as are the medical doctors and 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 and LEAN processes.

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The TBB has been referenced in numerous articles this year:

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Group of Sabina Berezowska, MD

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

Summary of Research Activities

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: Molecular and immunooncological markers in lung cancer

Lung cancer is amenable to targeted therapy and 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.

Project 3: Budding in lung cancer

There is no internationally accepted consensus on grading squamous cell carcinomas of the lung. We are evaluating the concept of budding as a prognostic marker.

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

- Axel K. Walch, MD, Abt. Analytische Pathologie, Helmholtz Zentrum München, Germany

Grant Support

- Swiss Cancer League (2019–2022), PI Sabina Berezowska, CHF 365'500
- Stiftung zur Krebsbekämpfung (2018–2019), PI Sabina Berezowska, CHF 20'000

Honors/Awards

- Prize for the best project by a medical student to Philipp Zens, Day of BioMedical Research 2019, Department for BioMedical Research (DBMR), Bern, Switzerland, 13.11.2019
- Selected for participation in the 2019–2020 IASLC Academy (Berezowska)
- 3rd Poster Award to Tereza Losmanová, 12th Joint Meeting of the pathological Society and the British Division of the IAP, Harrowgate, Great Britain, 02.–04.07.2019

Group of Rupert Langer, MD

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

Master Students / Dissertation Candidates
Nicola Blaser
Julia Wiprechtiger
Matea Sunic
Sandra Reschke
Mafalda Trippel
Andreas Schmid
Claudia Jaccard
Marek Osecky
Anja Hohl

Summary of Research Activities

The focus of the working group are tumors of the upper gastrointestinal tract, in particular of carcinomas of the esophagus. We investigate different morphological, immunological 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, as well as comprehensive molecular and digital imaging analysis, 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 currently focus on molecular genetic profiling of pre-therapeutic biopsy tissue of well characterized cases collections (including clinical trials) using next generation sequencing in order to identify alterations or pathways that are linked with tumor regression after neoadjuvant treatment.

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 gastroesopageal adenocarcinomas

Immune checkpoint inhibitors represent a promising therapeutic approach in the setting of locally advanced and metastasized gastro-esophageal 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, RNA profiling by comprehensive next generation sequencing methods 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

- Dr. Dino Kroell, Department of Surgery, Inselspital and Charité, Berlin
- Dr. Martin Berger, Department of Medical Oncology, Inselspital

International

- Dr. J. Slotta-Huspenina, Institute of Pathology, Technische Universität München, Germany
- Prof. A. Walch, Institute of Pathology, Helmholtz-Zentrum Neuherberg, Germany
- Prof. H. Grabsch, institute of Pathology, University of Maastricht, Netherpands

Grant Support

- SAKK 75/08, Rupert Langer (PI), Erik Vassella (Co-PI), 2018–2020, CHF 130'000
- Krebsstiftung Schweiz (2017–2019), CHF 15'000
- Hans-Altschüler-Stiftung, Rupert Langer and José Gàlvan, 2018–2019, CHF 9'700

- Claudia von Schilling Stiftung, Rupert Langer, 2018–2019, CHF 30'000
- Stiftung für Klinisch-Experimentelle Tumorforschung Bern, Bastian Dislich, 2019–2020, CHF 120'000

Completed Doctoral thesis (PhD)

- Ariane Félice Bill-Janser
  « The role of macro- and chaperone mediated autophagy in therapeutic response and resistance formation to HER2 targeted treatment»

Administrative duties

Rupert Langer

- Coordinator Lehre Humamedizin
- President of the Section Pathology of the Schweizerische Arbeitsgruppe für Klinische Krebsforschung (SAKK)
- Vice-President of the Arbeitsgruppe Gastroenteropathologie der Deutschen Gesellschaft für Pathologie

The Colorectal Cancer Research Group (Zlobec/Lugli).

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

Alessandro Lugli, MD
Inti Zlobec, PhD
Annika Blank, MD
Heather Dawson, MD
Huu Giao Nguyen, Post-doc
Amjad Khan, PhD student
Kristin Uth-Gottardi, PhD student
Linda Studer, PhD student (50%) shared Uni Fribourg (A. Fischer)
Christian Abbet, PhD student shared EPFL (JP Thiran)

Master or dissertation students (MSc or Medicine)
Melanie Bächli (MMed)
Usina Begré (MMed)
Sandra Burren, MD
Elia Fischer, MD
Esther Niemack (MMed)
Luca Noti (MMed)
Sophie Lechner (MMed)
Tim Ogi (MSc)
Katharina Reche, MD
Lynn Richmond, MD
Jannis Wallau (MSc)
Sven Wallau (MSc)

Summary of research activities

Our research focuses on diagnostic, molecular and biological aspects of colorectal cancers, especially on the clinical impact of tumor budding and various components of the tumor microenvironment. We use computational approaches, including deep learning to address clinical problems, with the future aim of validation and routine implementation.

Research Activities

Project 1: The role of CDX2 in colorectal cancer

Up to 20% of colorectal cancers have decreased expression of CDX2 protein, associated with aggressive tumor features and worse patient outcome. Our work shows that CDX2 expression is affected by epigenetic changes (hypermethylation, histone deacetylation). CRISPR-Cas9 knock-outs of CDX2 in vitro are associated with reduced proflieration, increased migration and colony formation as well as other features of Epithelial-Mesenchymal Transition (EMT) (Project Kristin Uth-Gottardi). These aspects are remininiscent of so-called «tumor budding». In this collaborative project with Prof. Mario Tschan, we continue to explore the impact of epigenetic aberrations on CDX2 and the role of CDX2 in EMT and tumor budding.

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 procee-

dings 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: The histopathology image as a new biomarker
We use machine learning applied to histopathology images to address clinically relevant problems. On the one hand, we are establishing a method for lymph node segmentation and metastasis detection in colorectal cancer. Aim is a validated screening tool for potential routine integration (Project of Amjad Khan). On the other hand, using our massive archive of more than 15'000 H&E images from next-generation Tissue Microarrays (ngTMA), we are performing genotype-phenotype correlations for the prediction of microsatellite instability, and consequently the development of deep learning algorithms for specific histopathological features (e.g. cancer) (Project of Giao Nguyen). We use graphs and geometric deep learning on images from early CRCs to understand tumor budding and the interaction with CD8+ lymphocytes (Project Linda Studer) and are extracting elements from the TME for prediction of prognosis (Project Christian Abbet).

Internal Collaborations
- Mario Tschan, PhD
- Tilman Rau, MD
- Philippe Krebs, PhD
- Rupert Langer, MD

External collaboration
National
- Prof. Andreas Fischer, UniFribourg and HESO
- Prof. Jean-Philippe Thiran, EPFL
- Lukas Brügger, Beat Schnüriger, Peter Studer Drs. and members of the Departments of Oncology and Visceral Surgery, Inselspital, Bern, Switzerland
- Luigi Terracciano, Prof. (Institute of Pathology, University Hospital Basel, Switzerland)
- Gieri Cathomas, Prof. (Institute of Pathology, Kantonsspital Liestal, Switzerland)

International
- Prof. Michael Hahne, University of Montpellier
- Prof. Iris Nagtegaal (University of Radboud, Nijmegen, Netherlands) and members of the International Tumor Budding Consensus Conference (ITBCC) and Budding Consortium

Grant support
- Rising Tide Foundation, CCR-18-130, H. Dawson, A. Fischer, 2019–2022, CHF 108'984
- Personalized Health and Related Technologies, PHRT-327, J.P. Thiran, I. Zlobec, 2018–2020, CHF 182'918
- Swiss National Science Foundation, 316030_183501/1, D. Stroka-Keough, I.Zlobec, 2018–, CHF 759'800 CHF
- Rising Tide Foundation, CR-18-800, I. Zlobec, J.P. Thiran, 2018–2021CHF 293'800
- Swiss Cancer League, KFS-4427-02-2018, I.Zlobec, J.P. Thiran, 2018–2021, CHF 361'270
- Dutch Cancer Society (Consortia grant), 10602, Prof. Iris Nagtegaal, I. Zlobec, A. Lugli, Consortia, 2017–2020, CHF 100'000
- Swiss Cancer League, KFS-3966-08-2016 , Prof. M. Hediger, I. Zlobec, 2017–2020, CHF 50'000
- Swiss National Science Foundation, 31003A_166578, I. Zlobec, M. Tschan, 2016–2019, CHF 305'040
- Swiss National Science Foundation, 320030_163342, S. Benhamou, I. Zlobec, 2015–2018, CHF 191'117
- Swiss Cancer League, KFS 4108-02-2017 , A. Lugli, H. Dawson, 2017–2019, CHF 139'450

Completed MD Thesis/Dissertations
- Lucine Christe, MD
  «Tumour Budding/T-cell infiltrates in Colorectal Cancer: Proposal of a Novel Combined Score»
- 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»
- Sara Nada Meyer, MD:
  «Co-expression of cytokeratin and vimentin in colorectal cancer highlights a subset of tumor buds and an atypical cancer-associated stroma»
- Carla Schenker, MD
  «Evaluation of Tumor Budding in Primary Colorectal Cancer and Corresponding Liver Metastases Based on H&E and Pancytokeratin Staining»
- Julia Unternaehrer
  «Current opinion, status and future development of digital pathology in Switzerland»

2 Akademische Grade

Prof. Dr. Viktor Kölzer
wurde auf den 1. April 2019 zum Assistenzprofessor für Computergestützte Bildanalyse in der Pathologie der Universität Zürich ernannt

Mirjam Schenk
Venia Docendi für das Fach Experimentelle Immunologie, Universität Bern

Frau Heather Dawson
Venia Docendi für das Fach Pathologie, Universität Bern

Dosch Michel Ernest Jean-Pierre, MD/PhD
ATP release mechanisms modulating inflammatory responses

Bill-Janser Félice A., PhD
The role of macro- and chaperone mediated autophagy in therapeutic response and resistance formation to HER2 targeted treatment

Cadosh Ilke, PhD
The role of BTN2A2 in Immune Regulation of B Cells

Dudka Dorota, PhD
Unraveling the molecular response to dose-rate and delivery time of ionising radiation in 2D vs 3D cell culture

Friedli Oliver, PhD
Impact of mitochondrial uncoupling protein 2 on the generation and functionality of distinct T lymphocyte subsets

Luhr Morten, PhD
The unfolded protein response and the ATG8 protein family in autophagy

Lysenko Veronika, PhD
Modeling Myeloproliferative Neoplasms to Elucidate the Disease Pathogenesis and to Understand Immune Responses

Niklaus Livia, PhD
Host cell autophagic and lysosomal defence mechanisms against the Plasmodium liver stage and parasite evasion mechanisms

Ring Sandra Stephanie, PhD
LCMV-Based Vectors in Melanoma Therapy – Induction and Maintenance of Efficient T Cell Responses

Roesti Elisa, PhD
New therapeutic approaches against Type two Diabetes mellitus using virus-like particles

Rohner Lionel, PhD
Influence of the activation status of human basophils on apoptosis

von Meyenn Karl-Leonhard, PhD
PPARg modulates IL-9 expression in TH2 cells by regulating glucose metabolism

Burren Sandra, MD
The role of RHAMM in colorectal liver metastases

Christe Lucine, MD
Tumour Budding/T-cell infiltrates in Colorectal Cancer: Proposal of a Novel Combined Score

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

Jutzi Susanne, MD
What is the role of autophagy in response to ALK inhibition in lung cancer?

Meyer Sara Nada, MD
Co-expression of cytokeratin and vimentin in colorectal cancer highlights a subset of tumor buds and an atypical cancer-associated stroma

Schenker Carla, MD
Evaluation of Tumor Budding in Primary Colorectal Cancer and Corresponding Liver Metastases Based on H&E and Pancytokeratin Staining

Unternährer Julia, MD
Current opinion, status and future development of digital pathology in Switzerland

van Delden Patrick, MSc
The role of ESRP1 in Epithelial to Mesenchymal Transition in Intestinal Epithelial Cells

Buri Michele, MSc Biomedical Science
Targeting Epigenetic modification In Pancreatic Neuroendocrine tumors

Schüpbach Nadja, MSc
Immunological memory of the innate immune system: influence of repeated exposure of intestinal bacteria on human monocyte

Poddar Proiti, MSc
Splice factor gene modification in AML: Impact on cellular differentiation and apoptosis during ATRA therapy

Publikationen

Originalarbeiten In-House

- Berezowska S, Pöllinger A, Ulmer F, Trippel M
  Respiratory Failure due to Rapidly Progressive Metastatic Lung Calcifications after Heart Transplantation in a Six-Year-Old Girl.
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  AIP-mutated acromegaly resistant to first-generation somatostatin analogs: long-term control with pasireotide LAR in two patients.
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  Multidisciplinary approach for risk-oriented treatment of low-risk papillary thyroid cancer in Switzerland.
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4 Vorträge

Philippe Krebs
- 09.–11.01.2019: Session: «Microbiota and systemic organ diseases» 2nd Young Scientists Meeting in Bern, Switzerland, Session, chair
- 21.03.19: Strategies to block death ligand-induced tumor immune tolerance DISCOVER (consortium) Meeting, Galway, Ireland, Seminar
- 26.03.19: T cell regulation during infection and in the tumor environment Institute of Experimental Immunology University of Zurich, Seminar
- 10.05.19: Molecular regulation of lymphoid cells type 2 in lung disease SGP Meeting (Swiss Society of Pneumology), Montreux, Switzerland, Conference
- 28.06.19: Non-apoptotic TRAIL function modulates NK cell activity during viral infection Villa Vigoni Cell Death Meeting, Loveno di Menaggio, Conference
- 15.10.19: Determine the role of death receptor and death ligand signaling in sculpting NK cell functions DISCOVER (consortium) Meeting, Izmir, Turkey, Seminar
- 25.10.19: Cytokine-dependent immunoregulation in cancer and pathology Erasmus MC Cancer Center, Rotterdam, The Netherlands, Seminar
- 29.10.19: The IL-33/ST2 pathway shapes the regulatory T cell phenotype to promote intestinal cancer University of Lausanne / Ludwig Institute for Cancer Research, Lausanne, Seminar
- 27.11.19: Mechanotransduction and immunity – feel the touch Bern Immunology Club (BIC), University of Bern, Bern, Seminar

Philippe Krebs / Lester Thoo
- 09.–11.01.2019: Alternative splicing modulates intestinal homeostasis & pathology 2nd Young Scientists Meeting in Bern, Switzerland, Invited talk

Christoph Müller
- 13.–15.03.2019: Wolfsberg Immunology PhD Student Meeting 2019, Thun, Chair

Aurel Perren
- 14.02.19: Advances in primary NET cell culture Scientific exchange meeting Hamburg,Universitätsklinikum Hamburg Eppendorf, Germany, Invited talk
- 22.02.19: Zystische Pankreasläsionen und klinische Aspekte Schnittseminar endokrine Organe, IAP, Bonn, Germany
- 07.03.19: New WHO Classification – Important News 16th Annual ENETS Conference for the Diagnosis and Treatment of Neuroendcrine Tumor Disease, Barcelona, Spain, Invited talk
- 28.03.19: Klassifikation, Epidemiologie und Pathologie von Neuroendokrinen Tumoren NET Fortbildung Basel, Switzerland, Invited talk
- 04.04.19: Update in the GEP-NENs Histo-pathological Diagnosis National Workshop on Neuroendocrine Tumor Histo-pathological Diagnosis, Jerusalem, Israel, Invited talk
- 06.05.19: The genetics of NET: towards a molecular classification 5th edition of the WORKSHOP «NIKE – Neuroendocrine Tumors, Innovation in Knowledge and Education», Napoli, Italy, Invited talk
- 10.05.19: Introducing Synoptic reporting, the Bern experience PathoLink Symposium, Zürich, Germany, Invited talk
- 15.06.19: 3D primary cell culture: A new pre-clinical model for pancreatic neuroendocrine tumors (PanNETs) DGP 103. Jahrestagung, Frankfurt, Germany, Invited talk
- 05.07.19: Classifying Neuroendocrine Tumors and Neuroendocrine Carcinomas ESMO, 21st World Congress on Gastrointestinal Cancer, Barcelona, Spain, Invited talk
- 10.09.19: The new WHO classification of digestive neuroendocrine neoplasms (NEN) and beyond Symposium Endocrine Pathology, 31st European Congress of Pathology, Nice, France, Chair
- 12.09.19: Synoptic reporting, the Bern experience Swiss Health, Bern, Kursaal, Switzerland, Invited talk
- 23.10.19: Updates of pathological classification of NET UEG Week, Barcelona, Spain, Invited talk

Ilaria Marinoni
- 04.11.19: Preclinical models as a tool to personalized treatment 5th Quality innovation in Pancreatic disorder, San Raffaele, Milano, Invited talk

Matthias Dettmer
- 13.–15.06.2019: Poorly differentiated thyroid carcinoma – an underdiagnosed entity 103. Jahrestagung der Deutschen Gesellschaft für Pathologie, Frankfurt / Main, Invited talk

Mirjam Schenk
- 07.02.19: Role of IL-32 in Cancer Immunity Symposium Stiftung Experimentelle Biomedizin, University Hospital Zürich, Invited talk
- 10.04.19: IL32: a treatment to convert tumors from «cold» to «hot» RIA – Immunology lunch meeting, Universitätsklinik RIA Bern, Invited talk
- 24.04.19: Current topics in Pharmacology and Theranostics PKI, Pharmakologie Bern, Invited talk
- 18.12.19: The role of macrophages and dendritic cells:From IBD to mycobacterial infections to cancer Inaugural lecture/ Antittsvorlesung, Institute of Pathology University of Bern

Mario P. Tschan
- 29.05.19: Biology and Treatment of Acute Myeloid Leukemias University of Konstanz, Germany, Invited Seminar
- 13.06.19: First Retreat of the Bern Cancer Research Cluster (BCRC), Bern, Co-organizer and Chair
- 26.06.19: Autophagy Pathways Active During APL Differentiation Swiss Oncology and Hematology Congress (SOHC), Zurich, Invited talk
- 13.09.19: First LS2 section autophagy meeting, Fribourg, Co-Organizer and Chair
- 24.04.19: Autophagy Biomarker Discovery Session, Annual Meeting COST Action Transautophagy, Sofia, Bulgaria, Co-Organizer and Chair
- 27.09.19: ALK-targeted therapy triggers protective autophagy in EML4-ALK positive lung cancer cell GBM/DGZ Fall Conference, Invited talk
- 30.10.19: Targeting autophagy in cancer Molecular Partners, Zurich, Invited Seminar
- 20.11.19: Annual Meeting of the French Autophagy Association CFATG, Strasbourg, France, Co-organizer and Chair
- 03.12.19: Autophagy pathways active during acute promyelocytic leukemia (APL) differentiation Biotechnology Institute Thurgau (BITg) at the University of Konstanz, Invited Seminar

Erik Vassella
- 16.05.19: Molecular markers glioma Neurochirurgie Inselspital, Invited talk

Sabina Berezwoska
- 24.02.19: Diagnostics of Interstitial Lung Diseases in the Multidisciplinary Team
  International, Academy of Pathology, German Division – half day seminar during the sping symposium, Bonn
- 16.11.19: Update on PD-L1 – 2019
  Organization of the seminar and talk: PD-L1 in NSCLC 1-day seminar under the auspices of the Swiss Society of Pathology, Bern
- 21./22.11.2018: Differential diagnosis in hypersensitivity pneumonitis
  International Academy of Pathology, German Division – half day seminar during the sping symposium, Bonn, Talk

Rupert Langer
- 28.01.19: Tumor Regression of Gastrointestinal Cancers
  CHUV, Lausanne, Invited talk
- 08.–11.05.2019: How can pathologists help in the selection of patients for target therapy – Immunotherapy
  International Gastric Cancer Congress, Prag, Invited talk
- 08.–11.05.2019: Don't be afraid of new molecular technologies within the topic Gastric Cancer genetics and translational research
  International Gastric Cancer Congress, Prag, Chair
- 29.06.19: International survey on TRG used in gastric and EGJ adenocarcinoma
  Verona Workshop on Signet Ring Cell gastric adenocarcinoma, Invited talk
- 07.–11.09.2019: Tumour regression grading – anything new?
  European Pathology Congress, Nice, France, Invited talk
- 07.–11.09.2019: Joint Session Digestive Diseases Pathology & UEG: Challenging issues of post-treatment conditions in GI cancer pathology
  European Pathology Congress, Nice, France, Chair
- 07.–11.09.2019: Best Poster Session Digestive Diseases Pathology
  European Pathology Congress, Nice, France, Chair
- 16.11.19: Update in PD-L1 – Gastrointestinal Carcinomas
  Update in PD-L1, Bern, Invited talk

Inti Zlobec
- 23.01.19: Digital Pathology and Tissue Collectives: the Bern Experience
  Boehringer-Ingelheim, Vienna, Austria, Invited talk
- 07.02.19: Use of digital pathology and tissue micro array in translational sarcoma research and for reference pathology
  FORTRESS meeting, Leuven Belgium, Invited talk
- 17.05.19: Pathology on the move! Toward a digital future
  Swiss Histotech Meeting, Invited talk
- 04.06.19: Colorectal cancer: nipping the tumor in the bud
  Institute for Genetics and Molecular Medicine, University of Montpellier, France, Invited talk
- 06.06.19: The story of how nipping the (tumor) bud led to a million digital images
  HESO Seminar, Sierre, Switzerland, Invited talk
- 04.09.19: Next-generation pathology
  Lausanne Cancer Research Center Summer School, Lausanne, Switzerland, Invited talk
- 08.11.19: Clinical Implementation of Digital Pathology
  Swiss and Austrian Scoiety of Pathology Meeting, Lucerne, Switzerland, Invited talk
- 29.11.19: Digital Pathology in Translational Research
  MIC Symposium, Bern, Switzerland, Invited talk
- 30.11.19: Molecular pathology of tumor budding
  Tumor Budding Course, Bern, Switzerland, Invited talk
- 04.12.19: Digital pathology in translational resarch
  Genomics Live, Basel, Switzerland, Invited talk

Alessandro Lugli
- 20.02.–22.02.2019: Tumour Budding in Colorectal Cancer
  Belgian Week of Gastroenterology, Antwerpen, Belgium, Invited talk
- 09.03.–11.03.2019, Should tumour budding be included in risk prediction algorithms ?
  European Multidisciplinary Colorectal Cancer Congress, Lisbon, Portugal, Invited talk
- 20.06.19: Tumour Budding in Colorectal Cancer: What clinicians should know
  Oncology Symposium, Inselspital Bern, Switzerland, Invited talk
- 22.05.–25.05.2019: The Immunoscore in Surgical Pathology; Tumour budding in Colorectal Cancer – Update 2019
  Spanish Society of Pathology, Granada, Spain, Invited talk
- 07.09.–11.09.2019: ITBCC 2.0
  ITBCC 2.0, European Society of Pathology, Nizza, France, Chair and talk
- 07.11.–09.11.2019: WHO Classification 2019 – Lower GI Tract
  Swiss and Austrian Society of Pathology, Lucerne, Switzerland, Invited talk
- 30.11.19: Tumour Budding in Preoperative Biopsies
  Tumor Budding Course, SAGIP, Bern, Switzerland, Chair and talk

Heather Dawson
- 29.01.19: Tumor Budding in Colorectal Cancer and Beyond – an Update
  Seminar Insititute for Pathology, Liestal, Switzerland, Invited talk
- 02.02.19: Applied Immunohistochemistry in Daily Practice (case presentations)
  IAP/SGPath slide seminar, Bern, Switzerland, Invited case presentations
- 24.09.19: Stains, Deposits and Buds: Update on Prognostic Factors in Colorectal Cancer
  CAP Orlando, USA, Invited talk
- 02.11.19: Tissue Handling and Assays: An Overview for Daily Routine
  Dermatopathology Essentials, Bern, Switzerland, Invited talk
- 08.11.19: Session Chair
  Poster Presentation Session, Swiss and Austrian Society of Pathology, Lucerne, Switzerland, Invited talk
- 09.11.19: Case Presentation: Mucinous Appendiceal Neoplasms
  Slide Seminar, Swiss and Austrian Society of Pathology, Lucerne, Switzerland, Invited case presentation
- 30.11.19: An Update on Tumor Budding in pT1 Colorectal Cancer
  Tumor Budding Course, SAGIP, Bern, Switzerland, talk

5 Drittmittel

S. Freigang (PI)
- Swiss Lung Liga (2017–2020), *CHF 162’000
- UniBE-ID Grant (2016–2019), CHF 150’000
- UniBE-ID Grant (2018–2020), CHF 150’000
- UniBE International 2021, J. Baumgartner (2017–2021), CHF 90’000

J. Baumgartner
- UniBE2021 PhD fellowship (2017–2021), CHF 90’000

Philippe Krebs
- Seed money project (2018–2020), CHF 10’000
- Lungenliga Bern (2018–2020), CHF 79’554
- Lungenliga Schweiz (2018–2020), CHF 79’554
- Swiss Cancer Research foundation KFS-4162-02-2017-R (2017–2020), CHF 312’500
- SNF 314730_163086 (2016–2020), CHF 525’000
- UniBE ID (Interdisciplinary) Grants (2018–2020), *CHF 75’000
- EU / Marie Skłodowska-Curie RISE (2018–2022), **Euro 904’500
- Helmut Horten (2019–2021), CHF 130’000

Christoph Mueller
- SNF 310030_170084 (2016–2019), CHF 525’000
- SNF 314730_189277 (2019–2022), CHF 516’667
- SNF 33CS30_177523 8 (SIBDCS Co-PI) (2018–2020) *CHF 304’500

Christoph Mueller / Daniel Zysset
- Monique Dornonville de la Cour Stiftung (2018–2019), CHF 52’387

Mario Noti
- Fondation ACTERIA (2018–2020), Euro 150’000

Aurel Perren
- SNF 310030-188639 (2019–2023), CHF 632’000
- Uniscientia Stiftung (2019–2021), CHF 135’000

Ilaria Marinoni
- Desirée and Niels Yde Foundation (2016–2019), CHF 51’000

Aurel Perren / Ilaria Marinoni
- Co-PI, KLS-4227-08-2017 (2018–2022), CHF 360’000

Ilaria Marinoni
- ENETS CoE Synergy Grant (2019–2021), Euro 69’700
- Wilhelm Sander Stiftung (2018–2019), CHF 210’000
- Berner Krebsliga (2019–2022), CHF 40’000

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

Mirjam Schenk
- Stiftung experimentelle Biomedizin (2016–2019), CHF 763’000
- Stiftung experimentelle Biomedizin (2019–2021), CHF 520’000
- Klinisch Experimentelle Tumorforschung (2016–2019), CHF 150’000
- Helmut Horten (2017–2020), CHF 180’000
- SNF 320030_176083 (2018–2022), CHF 566’109
- Wilhelm Sander Stiftung (2019–2020), Euro 49’700

Mario Tschan
- SNF 31003A_173219 (2017–2021) , CHF 693’600
- SNF MD-PhD 03/17, Kristina Seiler (2018–2020), CHF 180’000
- UniBE international 2021, I.Tokarchuk (2018–2020), CHF 90’000

Magali Humbert
- Bernische Krebsliga (2017–2021), CHF 85’000

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

Magali Humbert
- Stiftung Für Klinisch-Experimentelle Tumorforschung (2018–2020), CHF 20’000

Co-PI Mario Tschan
- Claudia von Schilling Foundation, R. Langer (2018–2019), *CHF 30’000
- SNF 31003A_166578, I. Zlobec (2016–2019) , *CHF 305’040
- 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

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

Erik Vassella (Co-PI) / Rupert Langer (PI)
- SAKK 75/08 (2018–2020), CHF 132’640

Sabina Berezwoska
- Swiss Cancer League (2019–2022), CHF 365’500
- Stiftung zur Krebsbekämpfung (2018–2019), CHF 20’000

Rupert Langer und José Gàlvan
- Krebsstifung Schweiz (2017–2019), CHF 15’000
- Hans-Altschüler-Stiftung (2018–2019), CHF 9’700

Rupert Langer
- Claudia von Schilling Foundation (2018–2019), CHF 30’000

Bastian Dislich
- Stiftung für Klinisch-Experimentelle Tumorforschung Bern (2019–2020), CHF 120’000

Heather Dawson (PI) / A. Fischer (Co-PI)
- Rise Tide Foundation (CCR-18-130) (2019–2022), CHF 108’984

Inti Zlobec (Co-PI) / J.P. Thiran (PI)
- Personalized Health and Related Technologies (2018–2020), CHF 182’918

Inti Zlobec (Co-PI) / D. Stroka-Keough
- Swiss National Science Foundation 316030_183501/1 (2018–), CHF 759’800

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

Inti Zlobec (Co-PI)/Alessandro Lugli (Co-PI) / Prof. Iris Nagtegaal (PI)
- Dutch Cancer Society (Consortia grant) No. 10602 (2017–2020), CHF 100’000, 1.6 Mio Euro

Inti Zlobec (Co-PI) / Prof. M. Hediger (PI)
- Swiss Cancer League KFS-3966-08-2016 (2017–2020), CHF 50’000, 196’500

Inti Zlobec (Co-PI) / S. Benhamou
- Swiss National Science Foundation 320030_163342 (2015–2018), CHF 191’117, 525’000

Alessandro Lugli (PI) / Heather Dawson (Co-PI)
- Swiss Cancer League (2017–2019), CHF 139’450

6 Preise, Ernennungen, Auszeichnungen

Aurel Perren
Wahl zum Mitglied der Leopoldina
Nationale Akademie der Wissenschaften

Vera Imboden
März 2019: CSL Behring Preis für die beste Masterarbeit im Biomedical Sciences 2019
«Autophagy functions in immune-mediated thrombotic thrombocytopenic prupura (iTTP) pathology»

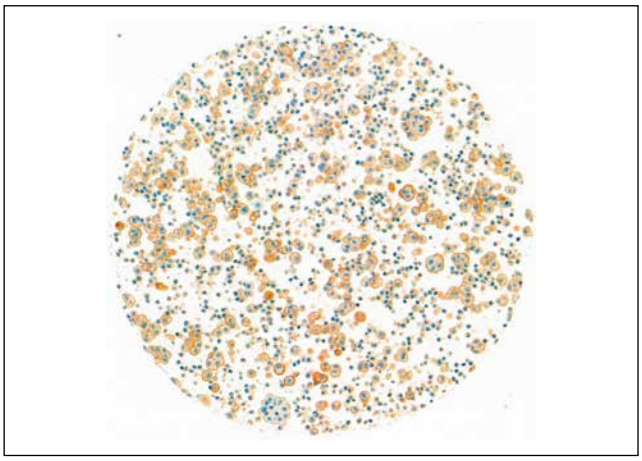
Ekkehard Hewer
März 2019: Forschungspreis der Deutschen Gesellschaft für Zytologie für die Arbeit «The 'don't eat me' signal CD47 is a novel diagnostic biomarker and potential therapeutic target for diffuse malignant mesothelioma»

Tereza Losmanová
04.7.2019: Posterpreis der Pathologischen Gesellschaft UK & Irland
12th Joint Meeting of the British Division of the International Academy of Pathology and the Pathological Society of Great Britain & Ireland

Lester Thoo Sin Lang
29–31 August 2019: Award for the best poster
12th MIM Retreat 2019, ETH Zürich/Universität Zürich

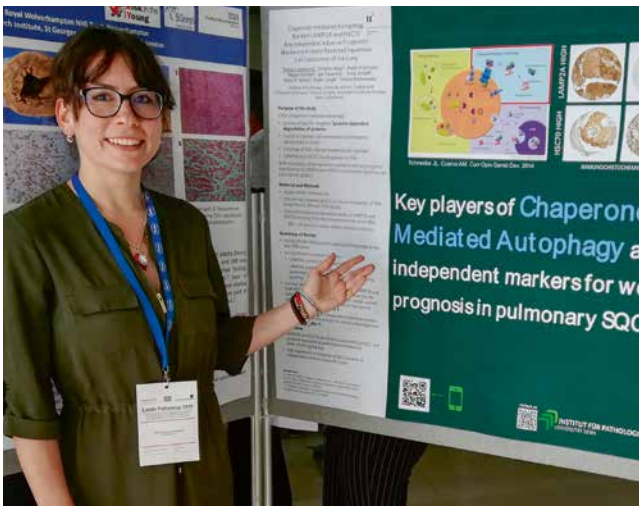
Philipp Zens
13.11.2019: Preis für das beste Projekt eines Medizinstudenten am Tag der BioMedizinischen Forschung 2019, Department for BioMedical Research (DBMR)

Vera Imboden, CSL Behring Preis.



Ekkehard Hewer, Forschungspreis der Deutschen Gesellschaft für Zytologie .

Philipp Zens, Preis für das beste Projekt eines Medizinstudenten am Tag der BioMedizinischen Forschung 2019.



Tereza Losmanovà, Posterpreis der Pathologischen Gesellschaft UK & Irland.

>>> 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 organbezogene Pathologie angewendet. Hierbei wird ein systematisches Curriculum durchlaufen, das alle Organsysteme und ihre wichtigsten Erkrankungen abdeckt. Es besteht aus theoretischen Vorlesungen und praktischen Kursen, in denen die Studierenden sich mittels Makroskopie und Mikroskopie vertiefende Kenntnisse aktiv erarbeiten. Ergänzend finden 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 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.

Zusätzlich zu den bisherigen Veranstaltungen, die im Rahmen der Studienplatzerhöhung («+100») inhaltlich überarbeitet wurden, arbeiten wir derzeit an einem Pilotprojekt «Fallbasiertes interaktives online-basiertes Lernen im Fach Pathologie», das von der Universität im Rahmen der «Förderung Innovative Lehre» unterstützt wird.

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)
– Bern Immunology Club, BIC (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.

General overview of the course:

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.

>>> Weiterbildung

Auf die kontinuierliche Weiterbildung der Mitarbeitenden auf dem Weg zum Facharzttitel für Pathologie legen wir grossen Wert.

Täglich findet nach dem allgemeinen Morgenrapport eine Weiterbildungsveranstaltung statt. Dabei wird jede Woche von einem Fachspezialisten oder einer Fachspezialistin ein ausgewähltes Thema strukturiert besprochen. Am ersten Tag zum Einstieg in die Thematik anhand eines theoretischen Vortrages und an zwei folgenden Tagen mittels histologischer Schnittpräparte, welche die Thematik vertiefen. Auch zyto- und molekularpathologische Themen werden im Rahmen dieser morgendlichen Veranstaltung von FachspezialistInnen besprochen.

Ein Tag der Woche ist reserviert für interessante Fälle aus dem diagnostischen Alltag. So lernen alle von illustrativen oder seltenen Fällen und es ergibt sich die Gelegenheit offene Fragen zu diskutieren. Zudem können insbesondere Pathologinnen und Pathologen in Ausbildung diese Fälle ausgiebiger studieren und die Fallpräsentation am Mikroskop üben.

Mehrmals jährlich führen wir eine Journal Club Woche durch, in der die Assisiterenden die Möglichkeit haben eine Publikation ihrer Wahl mit Unterstützung einer Fachärztin oder eines Facharztes zu präsentieren und im Plenum zu diskutieren.

Tiefer in ein Thema eintauchen können alle in Ausbildung bei den jeden Monat stattfindenden abendlichen Seminaren für Assistierende, bei denen ein Gebiet der Pathologie ausführlicher besprochen wird. Alle können sich in die Thematik einlesen, diese wird dann anhand eigener Schnittsammlungen oder mit Hilfe von Lehrserien der Internationalen Akademie für Pathologie systematisch besprochen.

Die makroskopische Aufarbeitung von Operationspräparten ist ein grosser Bestandteil des Arbeitsalltages in der Pathologie, insbesondere während der Ausbildung. Es ist wichtig, dass auch in diesem Bereich die Weiterbildung einen zentralen Platz einnimmt. Jeden Mittag treffen sich daher alle Assistierenden mit einer zuständigen Fachperson und diskutieren anhand aktueller Präparate Techniken und Fragen der makroskopischen Begutachtung und des Zuschnittes.

Die Weiterbildung zur Fachpathologin/zum Fachpathologen kann aber nicht ohne die routinemässige histopathologische Diagnostik des klinischen Alltags stattfinden. Dabei werden neben der, zentralen histopathologischen Beurteilung am Mikroskop, weitere Fertigkeiten im Umgang mit Fällen erlernt, welche für die spätere eigenständige Fallbearbeitung sehr wichtig sind. Bei unserer Arbeitsorganisation mit Signout-Teams bestehend aus Fachpathologen und Auszubildenden im selben Raum, sind die Auszubildenden dauernd in den gesamten diagnostischen Prozess involviert und können so alle Schritte der Diagnostik erlernen.

Seminare für Assistierende

Monat	Referierende	Thema
Januar	Sabina Berezowska und Anja Roden	**Mediastinum**
Februar	Yara Banz	**Hämatopatohlogie: Maligne Lymphome**
März	Martin Wartenberg	**HNO**
April	Mafalda Trippel	**Plazenta**
Mai	Rupert Langer	**Knochentumore**
Juni	Christina Neppl	**Zytologie**
Juli	Vera Genitsch	**Hodentumoren**
August	Matteo Montani	**Leber, nicht-neoplastisch**
September	Vera Genitsch	**Prostatapathologie**
Oktober	Annika Blank	**Leber, neoplastisch**
November	Tilman Rau	**Mammapathologie**
Dezember	Inti Zlobec und José Galvan	**SPSS**

>>> Fortbildung

Wie auch in den Vorjahren konnten wir 2019 ein attraktives und vielseitiges Angebot an Vorträgen im Rahmen der wöchentlichen Fortbildungen anbieten.

Montag- und Donnerstagsseminare

Datum	Titel	Referent/-in
21.01.	Slide seminar: Lesions in the Anterior Mediastinum – Don't Be Afraid	Prof. Anja Roden Mayo Clinic Rochester
14.02.	Tissue micro processing: a proposal for local analysis of tumors for multi-omic profiling	Dr. Govind Kaigala IBM Research Zurich
21.02.	Image normalization and data augmentation in quantitative digital pathology	Christine Decaestecker, PHD Ecole Polytechnique de Bruxelles
28.02.	Exploiting B cell autophagy-lysosomal dysfunctions as a therapeutic target in auto-inflammatory diseases	Prof. Sylviane Muller University of Strasbourg, Institute for Advanced Study, Strasbourg, France
21.03.	Genotype-phenotype correlations in cleft lip/palate (CLP) patient-derived cells	Dr. Martin Degen, PhD Oral Molecular Biology Lab, Medical Faculty, School of Dental Medicine, University of Bern
11.04.	Targeting Oxidation-specific Epitopes in Sterile Inflammation and Atherothrombosis	Christoph J. Binder MD, PhD, Professor of Atherosclerosis Research Medical University of Vienna, Dept. of Laboratory Medicine & Research Center for Molecular Medicine of the Austrian Academy of Sciences
02.05.	Flotillins organise endocytic recycling of the T-cell receptor to promote T-cell activation	Dr. Jérémie Rossy, Group leader Biotechnology Institute Thurgau, University of Konstanz, Kreuzlingen
16.05.	Differentiation of tissue-resident memory T cells in primary and secondary immune responses	Klaas van Gisbergen Department of Hematopoiesis, Sanquin Research and Landsteiner Laboratory, Amsterdam and Department of Experimental Immunology, Amsterdam UMC, University of Amsterdam, Netherlands
23.05.	From Neuroendocrine tumours to Colorectal cancer metastases biomarkers	Dr. Jorge Barriuso, MD, Clinical Senior Lecturer & Honorary Consultant in Medical Oncology Division of Cancer Sciences, School of Medical Sciences, Faculty of Biology, Medicine and Health, University of Manchester, The Christie NHS Foundation Trust
04.06.	Peripheral responses to brain and intestinal immunogens	Katrin I. Andreasson, MD, Professor of Neurology Department of Neurology and Neurological Sciences and Stanford
04.06.	Hedgehog signaling: mechanism and role in regeneration and malignancy	Philip A. Beachy, PhD The Ernest and Amelia Gallo Professor in the School of Medicine, Professor of Urology and of Developmental Biology Institute for Stem Cell Biology and Regenerative Medicine, Stanford University Medical School, Stanford CA, USA

Datum	Titel	Referent/-in
06.06.	Cell cycle regulation and specific translation in Haematopoiesis	Prof. Ramanjaneyulu Allam, PhD Assistant Professor SNSF, Hematology Research Group/Inselspital, DBMR, Bern
20.06.	Targeting Autophagy and Metabolic Dependencies in Leukaemic Stem Cells	Dr. Vignir Helgason Senior Lecturer in Cancer Research, Wolfson Wohl Cancer Research Centre, Institute of Cancer Sciences, University of Glasgow
19.08.	Harnessing the microbiota and immune system for the treatment of colorectal cancer	Lukas Mager, MD-PhD Department of Physiology and Pharmacology, Snyder Institute of Chronic Diseases, Cumming School of Medicine, University of Calgary, Calgary, Canada
16.09.	Inhibition of HER2 Tumorigenesis by Beclin 1 and an Autophagy-Inducing Peptide	Silvia Vega-Rubin-de-Celis, PhD NCT-DKTK School of Oncology Fellow, Institut für Zellbiologie (Tumorforschung), Universitätsklinikum Essen
23.09.	Immunoprofiling of Neuroendocrine Tumors	Liliana H. Mochmann, PhD Institut für Medizinische Immunologie, Charité, Universitätsmedizin Berlin
28.10.	Introduction to Computational Pathology for Pathologists	Prof. Andrew Janowczyk Department of Precision Oncology, CHUV, Lausanne, and Case Western Reserve University, Cleveland, OH, USA
04.11.	Digital Pathology through DNA Methylome Analysis: Clinical Implications	Dr. med Jürgen Hench Institut für Medizinische Genetik und Pathologie, Universitätsspital Basel
18.11.	Immune cell trafficking in inflammatory bowel diseases	Dr. med. Sebastian Zundler, Forschungsruppenleiter Department of Medicine 1, Kussmaul Campus for Medical Research and Translational Research Center, Friedrich-Alexander-Universität (FAU) Erlangen-Nürnberg, Erlangen, Deutschland
25.11.	Emerging Need for Prostate Cancer Genomic Testing	Prof. Dr. Mark Rubin Department of BioMedical Research, Direktor Departement Klinische Forschung
02.12.	Recent advances in morpho-molecular characterization of Head & Neck Tumors	Dr. med. Niels J. Rupp Universitätsspital Zürich, Institut für Pathologie und Molekularpathologie
09.12.	Anti-angiogenic Immunotherapy	Professor Michele de Palma, PhD Angiogenesis and Tumor Microenvironment Lab, The Swiss Institute for Experimental Cancer Research (ISREC). School of Life Sciences

>>> Im Fokus: Direktionsstab

Die Mitglieder des neu gegründeten Direktionsstabes.

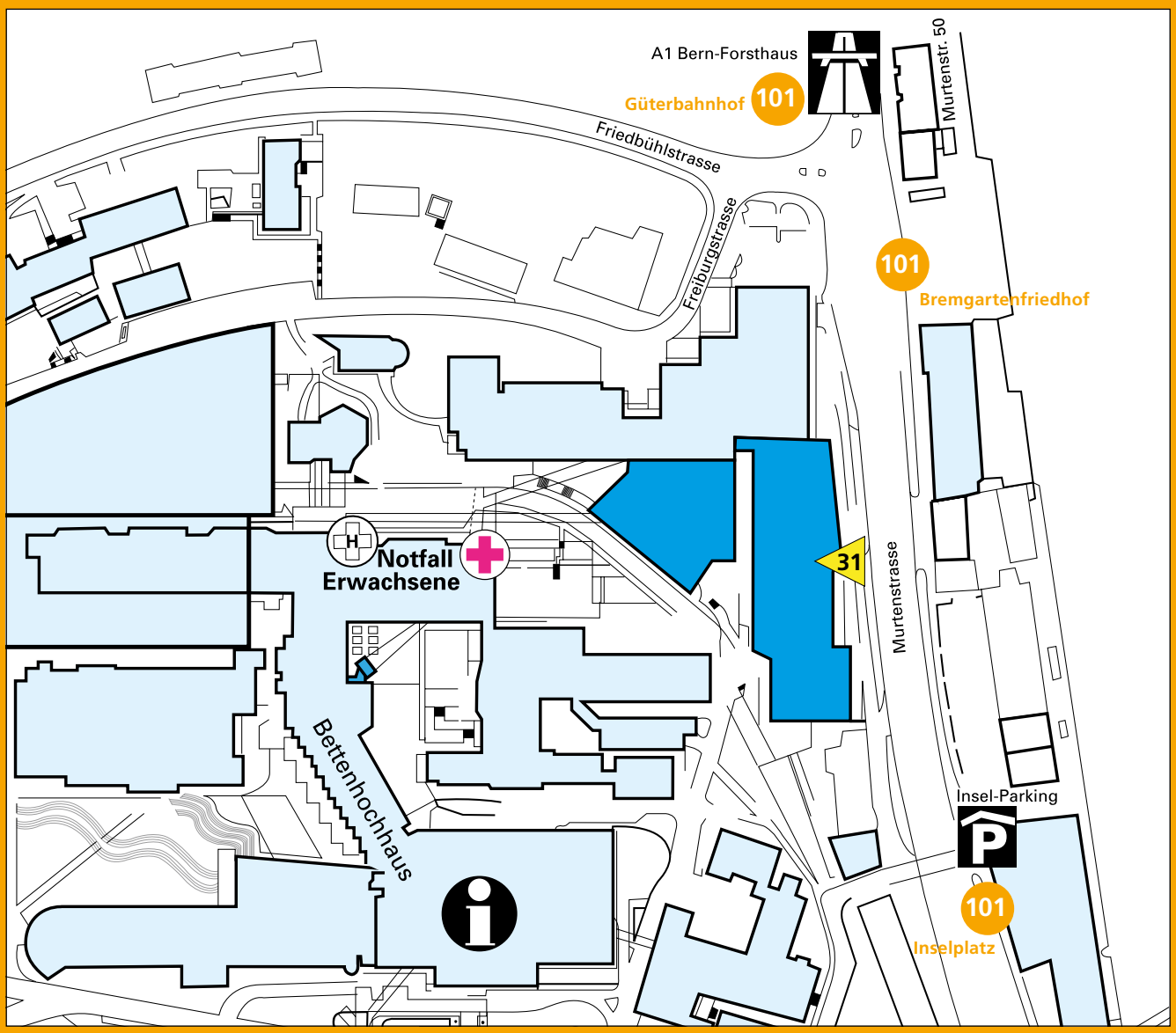
Die Dienstleistung, Lehre und Forschung sind die Hauptaufgaben des Instituts für Pathologie der Universität Bern. Daraus lässt sich pragmatisch die Vision unserer Institution ableiten: *Gewebemedizin von hoher Qualität nahe an der Forschung.* Damit diese Vision optimal erreicht werden kann, braucht es zwischen Leadership auf strategischer und Management auf operativer Ebene eine gute funktionierende Drehscheibe. Diese äusserst wichtige Position nimmt seit Januar 2019 der neu gegründete Direktionsstab ein, dessen Mission klar definiert ist: Unterstützung aller internen und externen Kunden des Instituts für Pathologie bei deren Aufgaben und Projekten.

Damit unterstützt der Direktionsstab die Direktion und die Direktionsassistenz auf operativer Ebene und umfasst fünf Bereiche: Administrativer Support (AS), Human Resources (HR), Informatik, Technischer Dienst und Logistik (ITL), Klinikmanager (KM) und Qualitätsmanagement (QM).

Der administrative Support beinhaltet das Berichtssekretariat für die Erstellung der Berichte und Organisation der Tumorboards sowie den Support Center mit den Aufgaben Kundenbetreuung, Buchhaltung und Unterstützung in der Lehre. Die Informatik ist strategisch auf die «Digitale Pathologie» ausgerichtet und garantiert durch den Zusammenschluss mit der Logistik und dem Technischen Dienst einen nach dem LEAN Management ausgerichteten Support für die interne und externe Kundschaft. Die Hauptaufgaben Finanzen, Datenschutz und Arbeitssicherheit wurden ins Klinikmanagement integriert, während das Personalbüro für die personellen Anliegen der Mitarbeitenden und für die Prozesse Eintritte, Mutationen und Austritte verantwortlich ist.

Dank dem Aufbau eines Qualitätsmanagements ist das Institut für Pathologie seit Ende November 2017 bei der Schweizerischen Akkreditierungsstelle SAS entsprechend der Internationalen Norm ISO/IEC 17025:2005 & ISO 15189:2012 und der Schweizer Norm SN EN ISO/IEC 17025:2005 & SN EN ISO 15189:2013 als Prüflaboratorium für pathologische Diagnostik akkreditiert.

>>> Situationsplan



Universität Bern
Institut für Pathologie
Murtenstrasse 31, CH-3008 Bern
Telefon +41 31 632 32 11
Fax +41 31 632 49 95
www.pathology.unibe.ch