IGMP Institut für Gewebemedizin und Pathologie

Institut für Gewebemedizin und Pathologie

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Jahresbericht 2022

>>> Inhalt

Organigramm 5

Dienstleistung 7

1 Klinische Pathologie 7
1.1 Ärzteschaft 7
1.2 Labor 8

2 Molekularpathologie im Clinical Genomics Lab (CGL) 10

3 Fachgruppen des Instituts für Pathologie 11

4 DIR-Stab 12

5 Dienstleistungsstatistik 13

6 eLearning 14

Forschung/Research 15

1 Forschungsberichte 15
1.1 Abteilung für Experimentelle Pathologie 17
1.2 Translational Research Unit (TRU) 36

2 Akademische Grade 47

3 Publikationen 49

4 Vorträge 54

5 Drittmittel 56

6 Preise, Ernennungen, Auszeichnungen 57

Lehre 59

Studentische Lehre 59

Weiterbildung 62

Fortbildung 63

Im Fokus 64

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>>> Das Wichtigste in Kürze

Liebe Leserin, lieber Leser

Internationalisierung und interdisziplinäres Arbeiten sind zentrale Bestandteile von tertiär-medizinischer Patientenversorgung sowie Forschung und Lehre. Wir Gewebemediziner sind in zahlreichen interdisziplinären Teams aktiv, sei es in den Tumorzentren des University Cancer Institutes Inselspitals UCI oder in Betreuung spezialisierter entzündlicher Erkrankungen (inflammatorische Darmerkrankungen, Nierenerkrankungen, Lebererkrankungen usw.) involviert. Die Abgänge von Spezialisten durch Beförderungen der letzten Jahre konnten wir durch junge, motivierte Ärzt:innen kompensieren und das Facharztteam durch Neuzugänge aus Italien, Polen, Niederlanden und Deutschland internationaler gestalten. Unsere Lean-Management-basierten Prozesse in der Dienstleistung wurden durch die Schweizer Akkreditierungsstelle in unserem ersten Re-Audit der Norm ISO: 15189 erneut akkreditiert.

Parallel zur fortschreitenden Digitalisierung im Dienstleistungsbereich, konnte das Institut für Gewebemedizin und Pathologie den Forschungsbereich in digitaler Pathologie mit dem neuen Extraordinariat Digitale Pathologie stärken. Dieser Schwerpunkt ist mit der Digitalisierungs-Strategie der Medizinischen Fakultät und der Universität verknüpft und wir gratulieren Frau Professor Inti Zlobec zu ihrer erfolgreichen Bewerbung und wünschen Ihr einen guten Start. Beim Abschiedssymposium von Prof. Christoph Müller, Leiter experimentelle Pathologie, wurden die internationalen Ambitionen mit der entsprechenden weltweiten Vernetzung apparent, wir wünschen Herrn Professor Müller alles Gute für die Zukunft.

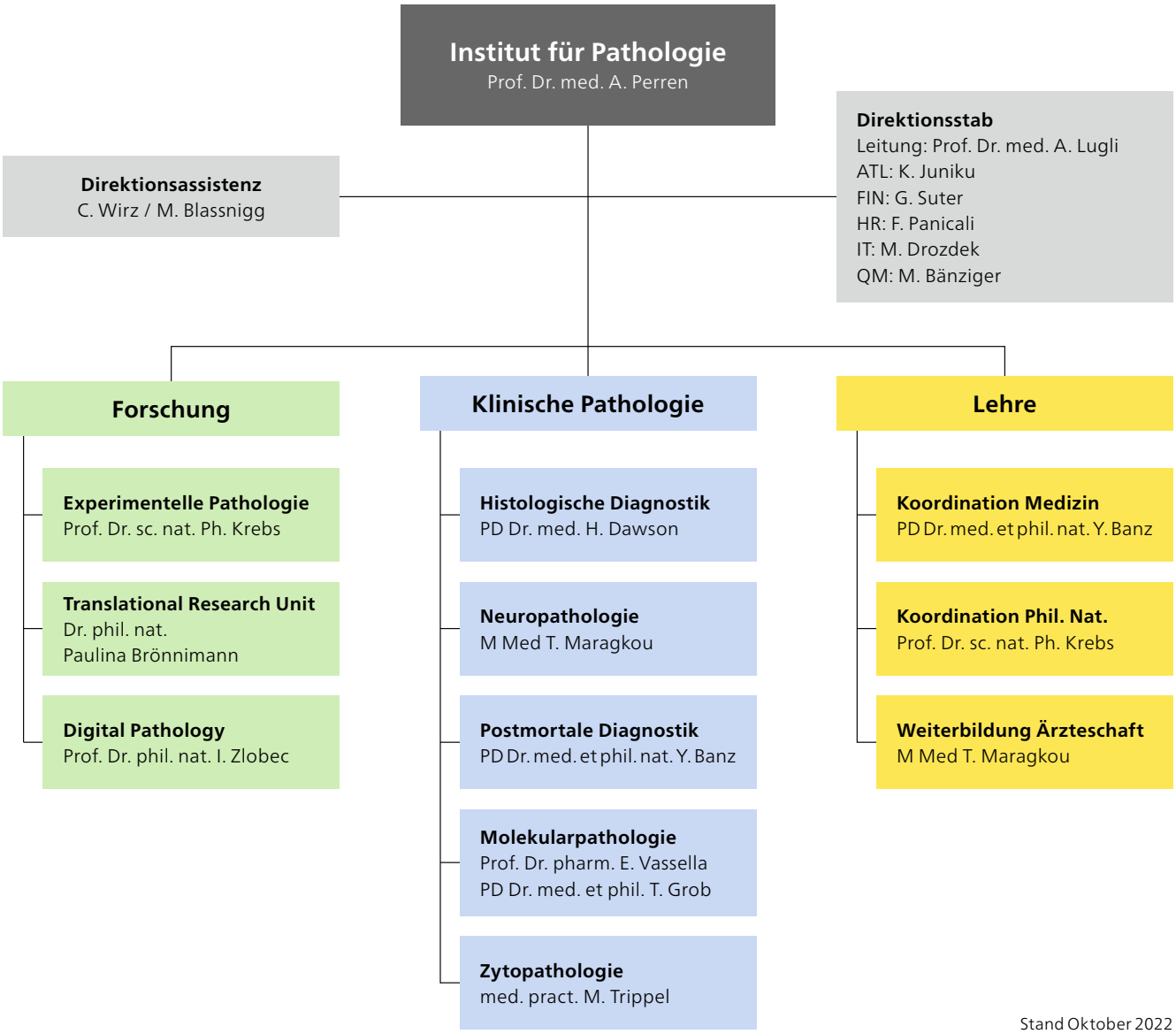
Neben der Digitalisierung gestaltet die verbreiterte Anwendung von molekularen Methoden zunehmend das Fach Pathologie. Hier sind wir, gemeinsam mit der Humangenetik, Hämatologie und klinischen Chemie des Inselspitals einen mutigen Schritt vorwärtsgegangen und haben das gemeinsame Clinical Genomics Lab (CGL) gegründet und aufgebaut. Hier haben alle Fachbereiche Zugang zu modernsten Methoden, wie den Illumina Novaseq 6000, so dass wir als erstes öffentliches Pathologie-Institut in der Schweiz eine TSO 500 Gentestung in Geweben und seit kurzem auch in Liquid Biopsy-Proben von Tumorpatienten anbieten können. Da wir glauben, dass epigenetische Analysen vom Tumor Methylom in Zukunft neben ZNS-Tumoren auch breiter diagnostisch eingesetzt werden, haben wir in eine entsprechende technologische Platform investiert. Im Sinne unserer Patienten werden wir auch weiterhin an der Front der Entwicklung dabei sein und diese Hightech-Methoden ebenfalls im Forschungssetting einsetzen. Details über die Entwicklung des CGL's entnehmen Sie bitte unserem Fokus am Ende des Jahresberichtes.

Ich wünsche Ihnen viel Freude bei der Lektüre

Herzliche Grüsse

Aurel Perren, Direktor

>>> Organigramm



Stand Oktober 2022

>>> Dienstleistung

1 Klinische Pathologie

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

Die Ärzteschaft und das Laborteam sind innerhalb der Klinischen Pathologie in den Bereichen der Histopathologischen Diagnostik, Zytopathologie, Postmortalen Diagnostik und Molekularpathologie tätig.

1.1 Ärzteschaft

Histologische Diagnostik (PD Dr. med. H. Dawson)
Das Ärzteteam besteht aus 19 Fachärzt*innen und 10 Assistenzärzt*innen, welche zusammen das gesamte Spektrum der universitären Pathologie inklusive Zytopathologie und molekulare Pathologie abdecken. Unsere Pathologie ist integraler Bestandteil zahlreicher interdisziplinärer Tumorboards des Inselspitals und externer Spitäler. Durch den beförderungsbedingten Weggang einiger Kollegen im Jahre 2021 entstand bei den Fachärzt*innen ein Engpass, der vor allem im Frühjahr und im Sommer 2022 zu spüren war. Dieser konnte zum einen durch den eigenen Nachwuchs und den Eintritt neuer Kollegen in unser Team behoben werden. Die entstandene Diversität und Internationalität stellt eine Bereicherung für die Ärzteschaft dar. Ebenso können im Sinne der Nachwuchsförderung unseren jungen Patholog*innen Ausbildungen in den Schwerpunktbereichen Zytopathologie und molekulare Pathologie angeboten werden.

Für das 2023 Jahr stehen im Rahmen der Digitalisierung weitere Herausforderungen an – zum einen der Ausbau standardisierter (synoptischer) Berichte in Zusammenarbeit mit anderen Pathologieinstituten der Schweiz, um die Erstellung strukturierter Daten gemäss der ICCR (International Collaboration on Cancer Reporting) zu ermöglichen. Zudem ist unser Institut am Grossprojekt der Erneuerung des Klinikinformationssystems des Inselspitals (EPIC) beteiligt. Als Kooperationspartner streben wir eine innovative und moderne Anbindung an das EPIC-System an, welche den Ärzten im diagnostischen Alltag unterstützen wird.

Neuropathologie (Dr. Martin Wartenberg,
Dr. Theoni Maragkou, Dr. Bastian Dislich)
Im Jahr 2022 untersuchten wir mehr als 1500 neurochirurgische und neuromuskuläre Proben, davon 350 intraoperative Schnellschnitte. Wir zählen damit weiterhin zu den diagnostisch aktivsten Neuropathologien in der Schweiz. Eine immer grössere Rolle spielt die molekulare Diagnostik von Hirntumoren. Wir bieten ein sehr breites Spektrum an molekularen Analysen, einschliesslich Next-Generation Sequencing (NGS TSO500) und Genom-weite DNA Methylierungsanalyse (EPIC Array), welche hausintern im Clinical Genomics Lab (CGL) durchgeführt werden. In Zusammenarbeit mit dem Neuromorphologischen Labor der Neurologischen Klinik des Inselspitals wurden rund 80 Muskelbiopsien untersucht. Die postmortale Diagnostik mit über 70 Hirnsektionen. Entsprechend dem Charakter der Neuropathologie als Schnittstelle zwischen den klinischen Neurofächern, der Labordiagnostik und translationaler Forschung war der Fachbereich Neuropathologie auch im Jahr 2022 in zahlreichen Veranstaltungen insbesondere in Zusammenarbeit mit Kliniken des Inselspitals engagiert. Darüber hinaus ist das Fach Neuropathologie Teil des Neuroonkologischen Tumorzentrums.

Postmortale Diagnostik (PD Dr. med. et phil. nat. Y. Banz)
Werden wir je wieder die Menge an postmortalen Untersuchungen machen, die wir vor 10 Jahren gemacht haben? Nein, wahrscheinlich nicht.

Wäre dies wünschenswert? Nicht unbedingt. Die Aufgabe der postmortalen Diagnostik hat sich verändert. Die Fragestellungen sind oft deutlich komplexer geworden. Das Ziel ist nicht primär über Quantität zu punkten, sondern sich mit Qualität auszeichnen zu können.

Die Zahl postmortaler Untersuchungen 2022 hat dennoch zum ersten Mal seit langem gegenüber den Vorjahren leicht zugenommen und liegt bei über 100 Patienten. Die Gründe hierfür sind unklar – aber wir begrüssen diesen möglichen Trend. Bei aller Qualität, die wir als gut eingespieltes Team aus Fachärzten, Assistierenden und Präparatoren bieten können, braucht es ein Minimum an postmortalen Untersuchungen, damit wir eine hochstehende Diagnostik, interdisziplinäre Fallbesprechungen, studentische Lehre und Forschungsprojekte in Zusammenarbeit mit dem Institut für Rechtsmedizin der Universität Bern garantieren können. Und längerfristig wird uns genau dieser Punkt beschäftigen – wie garantieren wir, dass wir die Ausbildung der Medizinstudierenden aufrechterhalten können, unsere Fachassistierenden weiterbilden können und das Fachwissen in der postmortalen Diagnostik erhalten können, wenn die Zahl postmortaler Untersuchungen so

tief bleibt? Das wird ein Thema sein, welches uns in der Zukunft am Standort Bern, und ganz allgemein in der Fachgesellschaft für Pathologie schweizweit beschäftigen wird.

Die Zusammenarbeit mit den klinischen Kolleg:innen sowohl auf dem Campus als auch den regionalen und überregionalen Spitälern konnte auch 2022 fortgeführt werden – so wurden weiterhin Lehrveranstaltungen im Kontext klinisch-pathologischer Fallbesprechungen durchgeführt – sei dies mit Fragestellungen zu neuropathologischen Untersuchungen, Untersuchungen in der Pädopathologie oder im Kontext «klassischer» Autopsien in der Erwachsenendiagnostik. Das Fachteam der postmortalen Diagnostik strebt auch weiterhin die enge Zusammenarbeit mit den anderen Fachspezialisten des Teams für Pathologie an, um auch im postmortalen Setting eine hochstehende und moderne Diagnostik anbieten zu können.

Die Modernisierung bzw. Digitalisierung der Lehre im Bereich der postmortalen Diagnostik sollen in Zukunft weiter vorangetrieben und ausgebaut werden um dem wichtigen Ziel der qualitativ hochstehenden Lehre im Fachbereich der speziellen Pathologie gerecht zu werden – sei dies im Kontext des Unterrichts für Medizinstudierende als auch Studierende anderer Fachrichtungen.

Zytopathologie (Med. Pract. M. Trippel)
Durch den inzwischen routinierten Umgang mit Covid, konnten wir uns 2022 wieder auf andere Aufgaben konzentrieren.

Im Fokus stand das Projekt zur Machbarkeitsstudie und Vorbereitung des Antrags zum Umbau der gesamten Zytologie in Zusammenarbeit mit der Planungskommission der Universität Bern und den zuständigen Architekten.

Die in die Jahre gekommene Infrastruktur soll für die veränderten Ansprüche einer innovativen Zytologie modernisiert werden. Dies bedeutet, dass alte Laboreinrichtungen entfernt und mehr Raum für die heute obligatorischen Apparate eines modernen Labors geschaffen und zugleich nach Lean ein optimaler Arbeitsablauf ermöglicht werden kann. Die organisatorischen und bauplanerischen Vorarbeiten konnten abgeschlossen werden. Bei Bewilligung sollte der Umbau 2024 starten können.

Den Arbeitsplatz und die Laborumgebung modern und attraktiv zu gestalten ist das eine, ein weiteres wichtiges Thema ist aber, wie in allen medizinischen Berufen, die Ausbildung von Nachwuchs, dem sich die Abteilung Zytologie seit jeher verschrieben hat. Wie schon in der Vergangenheit, engagierten wir uns im Jahr 2022 in der Fort- und Weiterbildung der Ärzt*innen und der Zytotechniker*innen. Zwei Assistenzärzt*innen haben ihre sechsmonatige Rotation in der zytologischen Diagnostik mit viel Engagement absolviert und ein Kandidat mit bereits abgeschlossenem Facharzttitel der Pathologie erwarb Mitte Jahr erfolgreich den Schwerpunkttitel der Zytopathologie. Ausserdem konnten wir eine Absolventin des von uns angebotenen kantonal-bernischen Diploms für Zytotechniker/innen feiern und in unser Team übernehmen. Die nun wieder vakante Ausbildungsstelle für die zweijährige Weiterbildung wurde Ende Jahr erfreulicher Weise wieder besetzt. Wir können somit positiv in das kommende Jahr starten.

1.2. Labor

Histologische Diagnostik (J. Ramseier)
Im ersten Halbjahr 2022 stand das Projekt zur Überarbeitung des IHC-Workflows an. Im ersten Schritt wurde die Antikörper Logistik nach LEAN neu strukturiert. Durch einheitliche Beschriftung der Container, Standardisierung der Verdünnungsmenge und Digitalisierung der Verdünnungskarten wurden Fehlerquellen reduziert. Der zweite Schritt bestand in der Umstellung von einem Batch-basierten System auf eine kontinuierliche Beladung der Geräte. Neu werden die Geräte tagsüber fortlaufend beladen und entladen. Um zukünftig auch bei grossen Bestellmengen keine Verzögerungen zu generieren, wurde im Laufe des Projekts entschieden im Jahr 2023 ein zusätzliches Gerät anzuschaffen. Dies gewährleistet eine rasche Abwicklung der Aufträge und Ausgabe an die Ärzteschaft.

Um die Einführung der Digitalen Pathologie in die Routine Diagnostik voranzutreiben, wurde eine Hybrid-Stelle mit der Translational Research Unit geschaffen. Ziel der Stelle ist die Mitgestaltung des Workflows, Betreuung der Geräte und die Schulung der Mitarbeiter. Durch die Arbeit in der TRU können neue Schritte wie z.B. ein Tool zur Qualitätsprüfung zielgerichtet in die Routine transferiert werden. Wir freuen uns mit Philipp Schneider einen bestens geeigneten und sehr engagierten Mitarbeiter für die Stelle gefunden zu haben.

In der KW20 wurden 1110 Fälle in der Histologischen Diagnostik verarbeitet. Der Rekord von 1088 Fällen aus dem Jahr 2018 wurde somit abgelöst und die Direktion bedankte sich mit einem kleinen Event am Weltlabortag für den ausserordentlichen Einsatz. Die steigenden Fallzahlen gaben auch Anlass, den Prozess wieder einmal zu beobachten und Anpassungen vorzunehmen. Die kleinen Korrekturen wurden durch das Team als entlastend wahrgenommen und haben auch zur Ebnung von Arbeitspeaks im Prozess geführt.

Nachdem sich die Zahlen im Jahr 2021 bereits von der Corona-Pandemie erholt haben, verzeichnet die Histologische Diagnostik im Jahr 2022 wieder steigende Zahlen.

Insgesamt stiegen die Einsendungen um 0,3% im Vergleich zum Vorjahr. Der Rückgang von 4.3% bei den Operationspräparaten wurde durch eine Zunahme von 3.5% bei den Biopsien ausgeglichen.

2 Molekularpathologie im Clinical Genomics Lab (CGL)

Prof. Dr. pharm. Erik Vassella,
Fachverantwortlicher molekulare Pathologie
PD Dr. med. Tobias Grob,
medizinischer Leiter molekulare Pathologie
Labor: Mitarbeiterinnen Clinical Genomics Lab

Die Dienstleistung der Molekularpathologie im Clinical Genomics Lab ist eine Zusammenarbeit des Instituts für Pathologie und des Inselspitals. Die in diesem Fachbereich verwendeten Methoden umfasst insbesondere die Hochdurchsatz-Sequenzierung mittels TruSightOncology (TSO) 500 Panel (Illumina) als Therapieentscheid bei soliden Tumoren. Neben der Erfassung von Mutationen aus über 500 Tumor-relevanten Genen erlaubt die Methode den Nachweis von Amplifikationen und Fusionstranskripte (insbesondere NTRK-, ALK, ROS-, FGFR2 und RET Fusionen) von Onkogenen, den Nachweis der Tumormutationslast sowie der Mikrosatelliteninstabilität, ausgelöst durch den Funktionsverlust von Mismatch-Reparaturgenen. Neben dieser Schlüsseltechnologie verwenden wir in der Routine-Diagnostik die Sanger-Sequenzierung, Pyrosequenzierung, verschiedene PCR-Analysen und Fluoreszenz In situ Hybridisierung. Mit diesem breiten Methodenspektrum werden prädiktive Biomarker als Therapieentscheid beim Adenokarzinom der Lunge, kolorektalem Karzinom, malignen Melanom, GIST, Ovarialkarzinom und Gliom abgedeckt. Genotypisierung der Blasenmole, Risikostratifizierung Mammakarzinom, Abklärung Mikrosatelliteninstabilität, B- und T-Zellklonalität, Diagnostik von Pankreaszysten, Methylierungsanalyse als Classifier für ZNS-Tumore, Nachweis diagnostisch relevanter Fusionstranskripte bei Sarkomen sowie Nachweis spezifischer Erreger sind weitere Analysen. Die Tests können an Formalin-fixiertem und Paraffin-eingebetteten Gewebe durchgeführt werden. Die molekulardiagnostischen Befunde werden am molekularen Tumorboard des Inselspitals besprochen.

Die Umstellung der NGS-Analysen auf das TSO500 Panel hat dazu geführt, dass die Zahl der Aufträge für NGS-Analysen deutlich zugenommen hat. Im letzten Jahr wurden insgesamt 1788 TSO500 Analysen im Molekularpathologielabor durchgeführt, der Hauptanteil davon betraf die diagnostische Dienstleistung (+25%). Die Zahl der Aufträge für die Genom-weite Methylierungsanalyse (InfiniumEPIC) hat ebenso deutlich zugenommen, die anderen Analysen blieben weitgehend konstant. Neben der Diagnostik hat uns die Weiterentwicklung der Bioinformatikpipeline zur Annotation und Beurteilung (Tier System, OncoKB) der Alterationen, die mit dem TSO500 Panel erfasst wurden, weiterhin beschäftigt. Diese Pipeline ist gleichzeitig eine integrierte Datenbank für annotierte Alterationen zur erleichterten Befundung und Qualitätskontrolle. Dies erlaubt uns, die NGS-Befundung speditiv und mit hoher Qualität durchzuführen.

Im nächsten Jahr wird uns insbesondere die Etablierung der TSO500 ctDNA Analyse zum Nachweis von Tumormutationen aus der Flüssigbiopsie sowie der Nachweis des HRD-Scores als Therapieentscheid beim rezidivierten Ovarialkarzinom beschäftigen. Zudem ist geplant, die TSO500 Analyse automatisiert mit Hilfe eines Liquid Handlers durchzuführen. Das CGL-Labor steht kurz vor einer Neuakkreditierung; diese musste im Fachbereich Molekularpathologie auf Grund der Fusion mit den anderen Bereichen vorübergehend sistiert werden.

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.

3 Fachgruppen des Instituts für Pathologie der Universität Bern

Stand Januar 2023

Dermatologische Gewebemedizin	
H. Dawson	031 632 99 60
J. Wolf	031 632 49 37
O. Stanowska	031 632 52 55

Endokrinologische Gewebemedizin	
A. Perren	031 632 32 23
A. Marrazzini	031 632 99 01

Gastrointestinale Gewebemedizin	
A. Lugli	031 632 99 58
H. Dawson	031 632 99 60
G. Cathomas	031 632 26 52
B. Dislich	031 632 71 90
A. Mookhoek	031 632 99 20
M. Montani	031 632 32 67

Mamma- und gynäkologische Gewebemedizin	
W. Solass	031 632 32 48
M. Trippel	031 632 32 76
M. Montani	031 632 32 67
M. Wartenberg	031 632 49 76

Hämatologische Gewebemedizin	
Y. Banz	031 632 88 75
B. Dislich	031 632 71 90
A. Rodriguez	031 632 99 69
B. Zagrapan	031 632 87 51

Herz-, Gefäss- und rheumatologische Gewebemedizin	
Y. Banz	031 632 88 75
J. Wolf	031 632 49 37
M. Trippel	031 632 32 76
T. Losmanová	031 632 31 91

HNO-/ophthalmologische Gewebemedizin	
O. Stanowska	031 632 52 55
A. Marrazzini	031 632 99 01
M. Wartenberg	031 632 49 76

Hepatische Gewebemedizin	
M. Montani	031 632 32 67
A. Mookhoek	031 632 99 20
G. Cathomas	031 632 26 52
M. Wartenberg	031 632 49 76

Pneumologische Gewebemedizin	
J. Wolf	031 632 49 37
T. Losmanová	031 632 31 91
A. Mookhoek	031 632 99 20

Nephrologische Gewebemedizin	
A. Rodriguez	031 632 99 69
M. Montani	031 632 32 67

Neuropathologie	
T. Maragkou	031 632 32 49
B. Dislich	031 632 71 90
B. Wartenberg	031 632 49 76

Pädiatrische Gewebemedizin	
A. Marrazzini	031 632 99 01
M. Trippel	031 632 32 76
A. Mookhoek	031 632 99 20

Pankreatische Gewebemedizin	
M. Wartenberg	031 632 49 76
M. Montani	031 632 32 67
A. Perren	031 632 32 23

Urologische Gewebemedizin	
A. Rodriguez	031 632 68 56
M. Montani	031 632 32 67
T. Losmanová	031 632 31 91

Weichteil- und orthopädische Gewebemedizin	
H. Dawson	031 632 99 60
B. Dislich	031 632 71 90
W. Solass	031 632 32 48

Postmortale Diagnostik und Makropathologie	
Y. Banz	031 632 88 75
B. Dislich	031 632 71 90
M. Trippel	031 632 32 76
A. Marrazzini	031 632 99 01

Molekularpathologie	
E. Vassella	031 632 99 43
T. Grob	031 664 04 78
H. Dawson	031 632 99 60
B. Dislich	031 632 71 90
A. Rodriguez	031 632 68 56

Digitale Pathologie	
B. Dislich	031 632 71 90
H. Dawson	031 632 99 60
B. Zagrapan	031 632 87 51

Zytologische Diagnostik	
M. Trippel	031 632 32 76
Y. Banz	031 632 88 75

Direktionsstab

4 DIR-Stab

Der Direktionsstab besteht aus den Bereichen Administrativer Support, Technischer Dienst und Logistik (ATL), Human Resources (HR), Qualitätsmanagement (QM), Informatik (IT) und Finanzen/Controlling (FIN) und unterstützt alle internen und externen Kunden des Instituts für Pathologie bei deren Aufgaben und Projekten.

Die Ende 2021 definierten Qualitätsziele 2022 des Direktionsstabs beinhalten die Reorganisation des Direktionsstabs im Erdgeschoss, die Überarbeitung des EMA (Eintritt, Mutation, Austritt) -Prozesses und die Optimierung der IT-Dienstleistung gemäss unserem Projekt- und LEAN-Management. Die Mitarbeitenden des Direktionsstabs arbeiten seit Mitte Jahr im Erdgeschoss, was eine optimale Kommunikation und pragmatische Arbeitsprozesse ermöglicht. Bezüglich EMA-Prozess und IT-Dienstleistungsoptimierung wurde der IST-Zustand akkurat erfasst. Aus den Qualitätszielen 2022 konnten dementsprechend folgende Qualitätsziele für das Jahr 2023 herauskristallisiert werden: 1) Erstellung eines neuen und vereinfachten EMA-Prozess; 2) Reorganisation der IT-Plattformen für das gesamte Institut und 3) die Reorganisation der Untergeschosse, um die Platzverhältnisse für die Archivierung zu erfassen.

Im Hinblick auf die Namenserweiterung hat der Direktionsstab in zwei eintägigen Retraiten für den eigenen Bereich eine Vision, Mission und Slogan erarbeitet.

5 Dienstleistungsstatistik

Klinische Pathologie

Histopathologie	**2016**	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**
Anzahl Einsendungen	42'422	43'607	45'491	48'601	46'372	48'707	**49'516**
Anzahl Lokalisationen	82'069	83'191	86'253	93'835	90'658	95'500	**96'974**
Einsendungen Schnellschnitte	1'936	1'761	1'784	1'831	1'770	1'822	**1585**
Proben Schnellschnitte	2'454	2'264	2'225	2'313	2'216	2'295	**2028**

Autopsie							
Anzahl durchgeführte Autopsien	146	130	134	106	99	81	**114**

Zytopathologie							
Anzahl Einsendungen Total	16'634	16'995	17'814	17'576	17'300	17'038	**16'350**
Anzahl Proben Total	19'193	20'519	21'949	21'787	20'384	21'301	**20'006**
Anzahl Zellblöcke	2'837	3'334	3'844	4'011	4'234	4'791	**4'411**

Immunhistochemie							
Fälle (Blöcke) Diagnostik (Paraffin)	9'094	7'681	8'822	11'616	11'717	12'788	**14'521**
Färbungen Immunfluoreszenz (Nierenbiopsien)	2'772	2'464	2'010	2'486	1'980	3'003	**1'796**
Fälle Immunzytologie am Ausstrich	158	258	201	246	210	154	**292**
Färbungen Immunzytologie am Ausstrich	486	364	377	353	307	204	**193**
Färbungen Diagnostik (Paraffin)	44'366	47'597	51'971	59'249	60'913	65'866	**68'437**

Tumorbank

Einsendungen Tumorbank	1'417	1'879	1'593	1'823	2'126	2'373	**2'157**
Anzahl Projekteingänge TRU	604	602	738	850	640	787	**802**

6 eLearning ist unabhängig von Ort und Zeit

Guido Suter

Wir nehmen die Weiterbildung ernst. Früher fanden die Weiterbildungen für neue Mitarbeitende im Frontalunterricht alle 3 Monate statt. Die Mitarbeitenden haben zwar die Bezugsperson kennengelernt, jedoch erhielten sie die Schulung oft zu spät. Die Schulungsunterlagen waren nicht zentral zugänglich und der Schulungsnachweis wurde in Papierform geführt.

2020 haben wir eine eLearning Plattform auf ILIAS entwickelt und eingeführt. Die Mitarbeitenden können sich eine Videoschulung anschauen und anschliessend mit einem Multiple Choice Test das Training abschliessen. So können sie die Schulungen unabhängig von Zeit und Ort mit dem Computer, einem Tablet oder Mobile erledigen. Uns gibt es die Möglichkeit die Schulungen zu kontrollieren, und bei einem externen Audit können wir jederzeit einen Schulungsnachweis vorweisen.

Unsere Mitarbeitenden sind uns wichtig, deshalb entwickeln wir die Schulungen weiter und lassen die vielen Feedbacks, die wir von Mitarbeitenden erhalten haben in die Anpassungen einfliessen. Anfang 2023 werden wir eine überarbeitete Version präsentieren. Mit den Schulungen leisten wir einen wichtigen Beitrag zur Arbeitssicherheit, der Qualität, dem Datenschutz und der Finanzkontrolle am IGMP. Nach unseren Informationen sind wir das erste Institut an der Universität Bern mit einer solch fortschrittlichen Weiterbildung zu diesen Themen. Bedanken möchte ich mich beim ILUB-Team der Universität Bern, den Referentinnen und Referenten der Fachbereiche und bei unserem Human Resources Team.

Arbeitssicherheit
Dienstarzt
Datenschutz
Qualitätsmanagement

Training
Grundmodul Modul A

Chemische Sicherheit
Biologische Sicherheit
Strahlenschutz

Training
Labor Modul C

Work safety
Doctor on duty
Data protection

Training
Basic module B

Chemical safety
Biological safety
Radiation protection

Training
Laboratory module D

Data Protection Research

Training
Module E

Internes Kontrollsystem

Training
Module F

Biosafety level 2 (BLS2)

Training
Laboratory module BLS2

Radiation Laboratory

Training
Laboratory module C Lab

eLearning auf ILIAS.

>>> Forschung/Research

1 Research at the Institute of Pathology

Research groups Experimental Pathology
Stefan Freigang, MD
Philippe Krebs, PhD
Christoph Mueller, PhD (since 01.08.2022: emeritus)
Aurel Perren, MD & Ilaria Marinoni, PhD
Mirjam Schenk, PhD (since 01.11.2022, 90% P.I. position at CK-CARE AG, Davos, Switzerland)
Mario P. Tschan, PhD
Erik Vassella, PhD

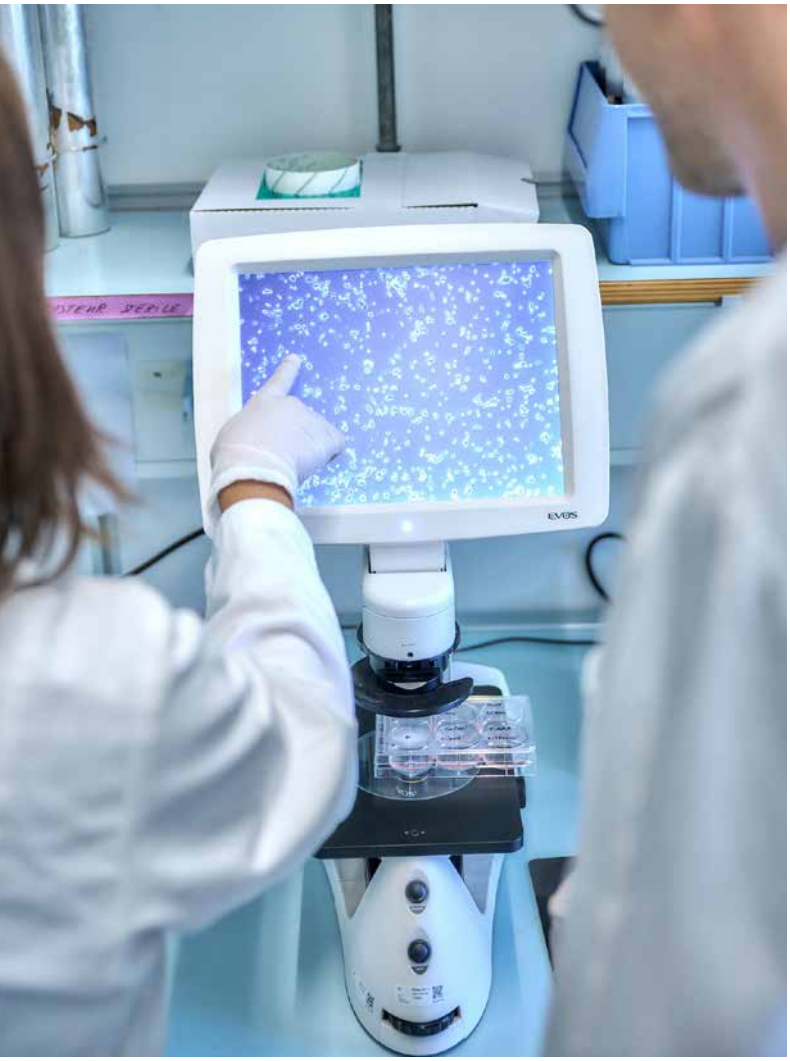
Translational Research Unit (Core Facility) (TRU)
Research groups supported by TRU
Alessandro Lugli, MD
Inti Zlobec, PhD

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 appropriate use («support platforms»), can be also accessed by the research personnel of the other units of the Institute of Pathology. This allows an efficient use of the limited financial resources and also foster scientific collaborations and exchanges 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, image analysis and next-generation Tissue Microarray construction (www.ngtma.com). TRU also provides partner with Tissue Bank Bern (TBB: https://www.biobankbern.ch). and collaborates with researchers from the University of Bern including the Department for BioMedical Research (DBMR) and the University Hospital / Inselspital, as well as other researchers in Switzerland and abroad.


EVOS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1.1 Division of Experimental Pathology

Head: Christoph Mueller, PhD
(01.01.2022–31.07.2022)
Head: Philippe Krebs, PhD
(01.08.2022–31.12.2022)

Research activities

The research activities of the seven research groups in the Division of Experimental Pathology are focused on two main research topics, i.e.
– Immunopathology and inflammation, and
– Experimental tumor pathology and tumor biology

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, and inflammatory disorders. Nevertheless, translational aspects are also considered in our research activities, such as the identification of novel biomarkers for disease activity in cancer and in remitting – relapsing inflammatory disorders, and the development of novel vaccination strategies against solid tumors.

Personnel

In 2022 approximately 70 persons were working in the Division of Experimental Pathology.

Grant Support

In 2022 the total amount of new external funding obtained by the research groups of the Division of Experimental Pathology was more than CHF 1.6 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, digital pathology, confocal microscopy, Cell-IQ® continuous live cell imaging and analysis system and a Nanostring® Platform for multiplexed assays for gene expression and mutation analysis. Moreover, we recently acquired a MICA cell microscope for live cell time-lapse imaging at confocal resolution, also under hypoxic conditions. In addition, we have access to core facilities provided by the Dept. of Biomedical Research, including the flow cytometry (FACS) 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, an illumina NovaSeq 6000, and a Pacific Biosicences Sequel IIe device) and have access to the recently established Imaging Mass Cytometry (IMC) Platform (with a Helios and a Hyperion instrument) of the DBMR, University of Bern. 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 miR's and their target sequences in normal, and diseased tissues, the assessment of autophagy, and several distinct transfection systems, including lentivirus-based transduction systems, and mRNA expression profiling from small numbers of cells and microdissected tissues are available (e.g. scRNA sequencing on the 10X Genomics platform; NanoString® analysis). 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.

Farewell Symposium of Christoph Mueller on July 1, 2022 – a truly memorable event!

After more than 30 years of active research at the Institute of Pathology, with the last 15 years as Head of the Division of Experimental Pathology, Prof. Christoph Mueller retired from his academic function by the end of July and became Prof. emeritus starting from August 2022. To mark the event, internationally renowned speakers and long-time colleagues and friends from around the world (UK, DE, USA and CH) were invited to a special and very inspiring Scientific Farewell Symposium entitled «Immunity: A journey from the Thymus to the Gut». We are very thankful to Prof. Christoph Mueller for his great contribution to our Institute and wish him all the best for his retirement.


GELATERIA


Passione
Cioccolato
Vaniglia
Caramel
Fleur de Sel


GELATERIA

Institute Research Retreat 2022

On September 13th all the staff involved in research gathered at Unitobler (University of Bern) for a one-day Institute Research Retreat. The aim of the retreat was to increase networking and awareness to favor potential collaborations within the different research groups of the Institute of Pathology.

The day started with a poster section in which PhD students and postdocs had the opportunity to present and discuss their projects. In addition, there were posters presenting an overview of our different core facilities (presented by technicians) and services (presented by TRU).

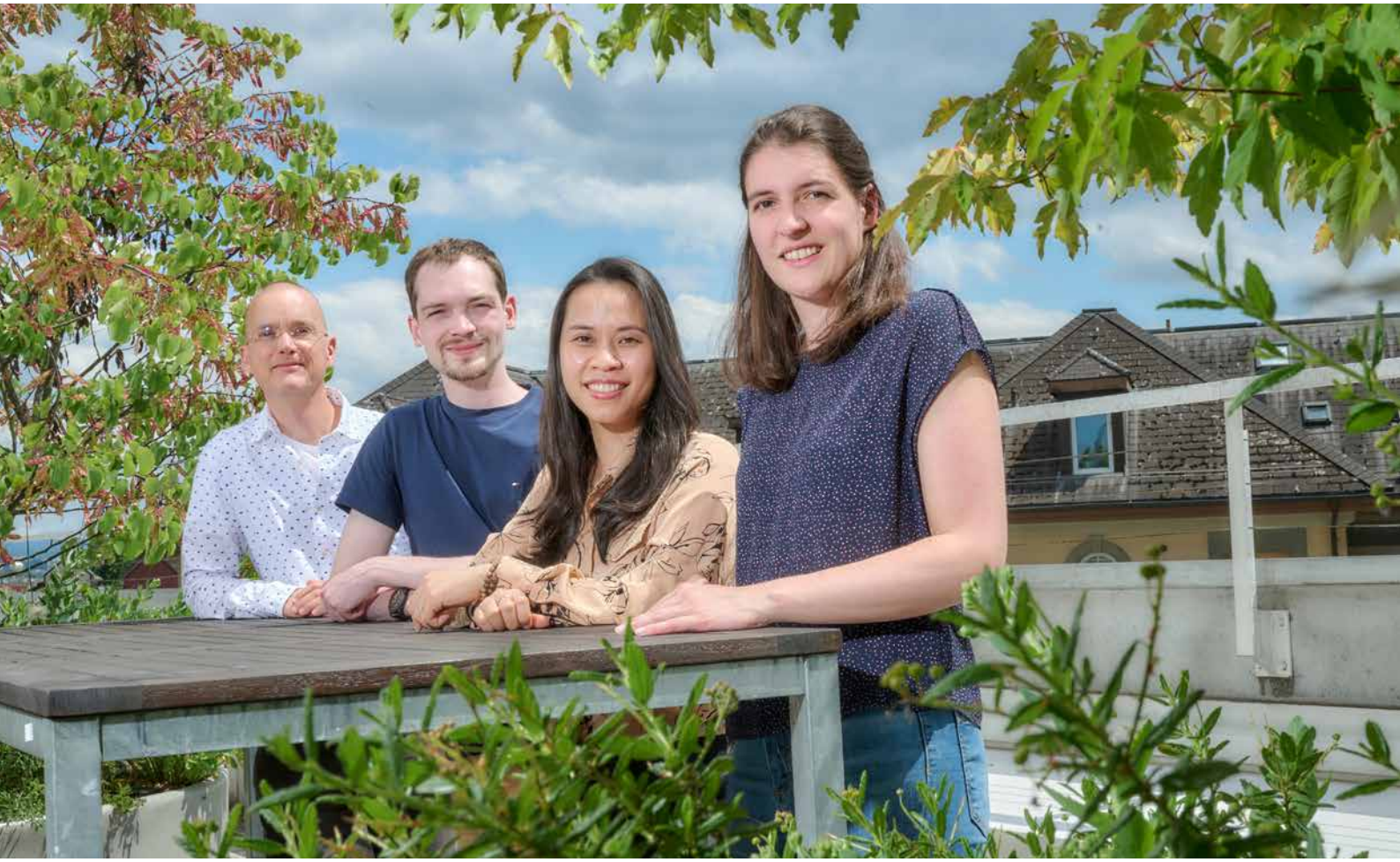
After the poster section we had an interactive activity. All participants were divided into six teams, whose composition was selected to have the highest mix between different expertise, seniority and belonging to research groups. The task of each team was to design an interdisciplinary research project, in which each member of the workshop group contributed, and which used at best the platform services of the Institute of Pathology.

At the end of this interactive workshop the teams presented their project in front of all the participants who could vote for the best one. The criteria to select the best project were as follows: 1) Interdisciplinarity, 2) Best usage of the Institute's resources, 3) Feasibility and 4) Involvement and balanced contribution of the workshop members.

All the participants actively took part in the activity. In a survey sent a few days after the retreat, ca. 70% of the participants said that they felt very engaged during the event! People particularly enjoyed the team activity and the interactions with members of different research groups.

Overall, the research retreat was an inspiring event, which revealed great potential of collaboration across the different research groups. It also highlighted the availability at our Institute of many cutting-edge technologies as well as broad expertise.

The organizers:
Ilaria Marinoni, Cornelia Mileto, Philippe Krebs



Research group Stefan Freigang

Group of Stefan Freigang, MD

MSc Quentin Pascal Bugnon, PhD student
Dr. Thi Thuy Hang Gander, PhD, Early Postdoc
Martina Kaufmann, MSc student
M Med Nadja Oehninger, medical doctoral candidate
Joëlle Schläfli, MSc student
MSc Sabrina Walthert, Laboratory technician

Summary of Research Activities

Immune recognition of lipids in inflammation and immunopathology

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

Research Activities

Project 1: Glycolipid-sensing by Natural Killer T cells

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

Project 2: 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 3: 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.

Internal Collaborations
- Vera Genitsch, MD

External Collaborations
National
- Cem Gabay, MD, Dept. Of Medicine, University of Geneva, Switzerland
- Georgia Konstantinidou, PhD, Inst. of Pharmacology, University of Bern, Switzerland
- Manfred Kopf, PhD, Federal Institute of Technology Zürich (ETHZ), Switzerland
- Philippe Renaud, PhD, Dept. Chemistry and Biochemistry, University of Bern, Switzerland

International
- Hans-Christian Probst, University of Mainz, Germany

Grant Support
- Swiss National Science Foundation, S. Freigang (PI), 2020–2024, CHF 632'000
- Swiss Heart Foundation, S. Freigang (PI), 2020–2022, CHF 50'000
- Swiss Lung Liga, 2017–2022, S. Freigang (PI), CHF 162'000

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

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

Publications

- Bertschi, Nicole L; Steck, Oliver; Luther, Fabian; Bazzini, Cecilia; von Meyenn, Leonhard; Felser, Andrea; Keller, Irene; Friedli, Olivier; **Freigang, Stefan;** Begré, Nadja; Lamos, Cristina; Gabutti, Max Philip; Benzaquen, Michael; Laimer, Markus; Simon, Dagmar; Nuoffer, Jean-Marc; Schlapbach, Christoph. *PPAR-γ regulates the effector function of human TH9 cells by promoting glycolysis (bioRxiv).* Cold Spring Harbor Laboratory 10.1101/2022.08.16.503972

Research group Philippe Krebs

Group of Philippe Krebs, PhD

Hojjat Alizadeh Zeinabad, MSc, PhD student (visiting student, until 04/2022)
Lukas Bauer, MD doctoral student (until 04/2022)
Océane Derivaz, MSc student (until 01/2022)
Silvio Eugster, MSc student (until 03/2022)
Robert Gaultney, PhD, post-doc
Kristýna Hlavácková, MSc, technician 90%
Fatlind Malsiu, MSc student
Coline Nydegger, technician, 90%
Wen Jie (Jeremy) Yeoh, MSc, PhD student
Vivian Vu, MSc, PhD student
Anja Herbst, MSc, PhD student (starting from 09/2022)
Sara Lenart, MSc, visiting PhD student (Swiss-European Mobility Program; from 05/2022 to 07/2022)

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 and immunopathology
– Immunopathology

Research Activities

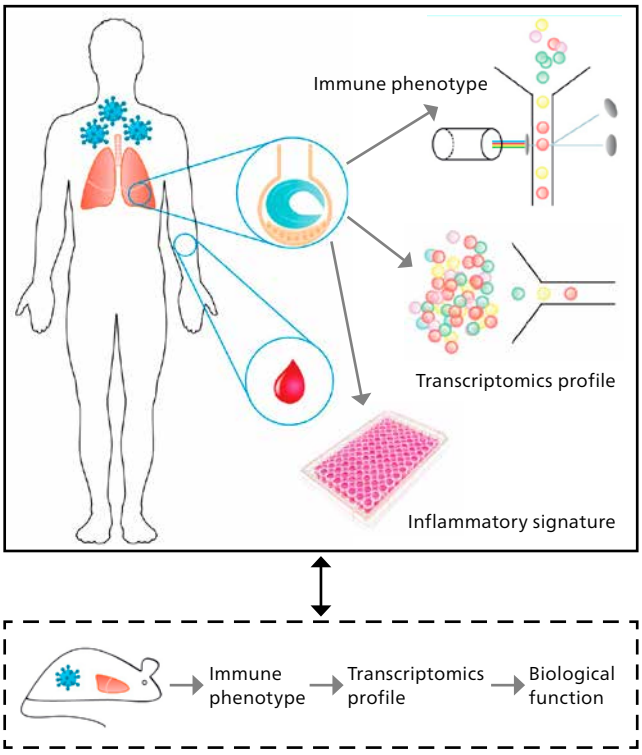
Project 1: Role of cytokine signaling for immunopathology and tumor development

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 IL-33-dependent CRC. For these studies, we use patient-derived samples and mouse models.

Project 2: mRNA splicing and epithelial integrity
The intestinal barrier is often disrupted during intestinal diseases, causing gut leakiness. We have recently shown that the protein ESRP1, a regulator of mRNA splicing in epithelial cells, has a critical function to maintain the integrity of the intestinal barrier (Mager et al., eLife, 2017). In this project, we further investigate how loss or reduction of ESRP1 leads to intestinal homeostasis and pathogenesis, including inflammatory bowel disease and 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, 2020) or sterile (e.g. for tumor surveillance) situations.

Project 4: Investigation of the local immune system regulation in COVID-19
The mechanisms leading to severe inflammatory lung disease in some COVID-19 patients are unknown. In this project, we will analyze the cells in the lung lavage of these patients and compare these findings with results from collaborators working on a mouse model of COVID-19. We hope so to reveal targets for COVID-19 therapy.



Graphical abstract to project 4.

Internal Collaborations
- Christoph Mueller, PhD
- Inti Zlobec, PhD
- Yara Banz, MD, PhD
- Mafalda Trippel, MD

External Collaborations
National
- Adrian Ochsenbein, MD; Carsten Riether, PhD, Dept. Clinical Res., University of Bern
- Burkhard Ludewig, DVM, Natalia Pikor, PhD, Institute of Immunobiology, Cantonal Hospital St.-Gallen
- Nicolas Bonadies, MD; Alicia Rovó, MD; Vera U. Bacher, University Hospital of Bern
- Manuela Funke-Chambour, MD; University Hospital of Bern

International
- Kathy McCoy, PhD, University of Calgary, Canada
- Astrid Westendorf, PhD, Universitätsklinikum Essen, Germany

Grant Support
- Swiss National Science Foundation Project grant, P. Krebs: PI, 2020–2024, CHF 632'000
- EU / Marie Skłodowska-Curie RISE grant Project grant, P. Krebs: co-Investigator, 2018–2022 , Euro* 904'500
- Werner und Hedy Berger-Janser Stiftung; Project grant main PI, R. Gaultney, 2022, CHF 79'796
- Swiss Life; Project grant, P. Krebs (main PI), 2021–2023, CHF 20'000
- Uniscientia; Project grant, P. Krebs (main PI), 2021–2022, CHF 136'000
- Seal of Excellence Fund (SELF) UniBE; Fellowship to R. Gaultney, P. Krebs (PI), 2021–2023, CHF 128'698
- Fondazione San Salvatore, Project grant, P. Krebs (PI), 2022–2024, CHF 170'000

* total amount of funding; funding shared by PI and Co-PI; part for group Krebs is contingent on number of staff exchanges.

Administrative duties
- Biosafety Officer for research and diagnostics activities at the Institute of Pathology, University of Bern
- Member of the Expert Commission of the Graduate School for Cellular and Biomedical Sciences of the University of Bern; mentor (total of 20 PhD students) and thesis co-advisor (total of 7 PhD students)
- Member of the Committee for the Medical and Pharmaceutical Libraries, University of Bern

Publications

- Alessandra Gurtner, Costanza Borrelli, Ignacio Gonzalez-Perez, Karsten Bach, Ilhan E Acar, Nicolás G Núñez, Daniel Crepaz, Kristina Handler, Vivian P Vu, Atefeh Lafzi, Kristin Stirm, Deeksha Raju, Julia Gschwend, Konrad Basler, Christoph Schneider, Emma Slack, Tomas Valenta, Burkhard Becher, **Philippe Krebs,** Andreas E Moor*, Isabelle C Arnold*. *Active eosinophils regulate host defense and immune responses in colitis.* Nature. 2022 Dec 12. doi: 10.1038/s41586-022-05628-7. Online ahead of print.
- Vu Thuy Khanh Le-Trillinga, Jana-Fabienne Ebel, Franziska Baier, Kerstin Wohlgemuth, Kai Robin Pfeifer, Aart Mookhoek, **Philippe Krebs,** Madita Determann, Benjamin Katschinski, Alexandra Adamczyk, Erik Lange, Robert Klopfleisch, Christian M. Lange, Viktoriya Sokolova, Mirko Trilling & Astrid M. Westendorf. *Acute cytomegalovirus infection modulates the intestinal microbiota and targets intestinal epithelial cells.* Eur J Immunol. 2022 Oct 17. doi: 10.1002/eji.202249940. Online ahead of print
- Noti L, Galván JA, Dawson H, Lugli A, Kirsch R, Assarzadegan N, Messenger D, **Krebs P,** Berger MD, Zlobec I. *A combined spatial score of granzyme B and CD68 surpasses CD8 as an independent prognostic factor in TNM stage II colorectal cancer.* BMC Cancer. 2022 Sep 16;22(1):987. doi: 10.1186/s12885-022-10048-x




Group of Alessandro Lugli, MD

Dr. med. H. Dawson
Dr. Dr. med. B. Dislich
Dr. A. Mookhoeck, MD PhD
Dr. med. F. Mueller

Summary of Research Activities

The GI-pathology research group's focus lies on three research topics: first, the clinico-tissue medical aspects of tumor budding in colorectal cancer, the histologic scoring systems in inflammatory bowel disease as well as the prognostic/predictive biomarkers in tumors of the upper gastrointestinal tract.

Research Activities

Project 1: Tumor budding in gastrointestinal neoplasms
The main aim of the GI Tissue Medicine research group concerning tumor budding in CRC is the following: to identify potential target molecules in tumor buds and develop an anti-budding therapy. The focus lies on four clinical scenarios: pT1 CRC, stage II CRC, rectal cancer (preoperative) and colorectal liver metastases. Additionally, our group is also a member of the International Budding Consortium (IBC).

Project 2: Biopsy-based prediction and prognosis in inflammatory bowel disease
Our group works on extracting information from colorectal tissue biopsies to aid prognosis of disease evolution and prediction of therapy success in patients with inflammatory bowel disease (IBD). In Bern, we are working on implementing the IBD-DCA score in clinical practice. In parallel, we are establishing its prognostic value and develop an AI algorithm to automatize the scoring. In collaboration with gastroenterologists in Europe (Switzerland, Netherlands), we hope to identify tissue-based markers that allow a personalized treatment strategy in asymptomatic patients diagnosed with IBD during colorectal cancer screening.

Project 3: Influence of neoadjuvant therapy on the immune profile of esophageal adenocarcinomas
Immune checkpoint inhibitors are increasingly used in the adjuvant therapy of locally advanced, neoadjuvantly treated adenocarcinomas of the esophagus. Reliable predictive biomarkers are essential to identify the patient population that shows a significant response to immune checkpoint inhibitors. We are studying the transcriptome, methylome and immunohistochemical expression profile of immunomodulatory molecules in human tumor samples. The aim is to identify key molecules that may influence the response to therapy. In addition, the impact of neoadjuvant therapy on these immunomodulatory molecules will be investigated.

External Collaborations

International
- Prof. Iris Nagtegaal, Nijmegen
- Prof. Magali Svrcek, Paris
- Prof. Michael Vieth, Bayreuth
- Prof. Maurice Loughrey, Belfast
- Prof. Kieran Sheahan, Dublin
- Prof. Fatima Carneiro, Porto
- Prof. Luigi Terracciano, Milan
- PD Dr. Pascal Juillerat, Bern
- Prof. Rupert Langer, Linz
- Prof. Christian Schürch, Tübingen
- Prof. Richard Kirsch, Toronto

Grant Support

- Swiss Cancer Research, A. Lugli (PI), M. Schürch (Co-PI), 2021–2023, CHF 331'500*
- Dutch Cancer Society, A. Lugli, 2017–2022, CHF 1'600'246, Co-Applicant
- Rising Tide Fondation A combined budding/T-cell score in pT1 and stage II colorectal cancer, Heather Dawson, 2018–2022, CHF 108'984
- Stiftung für klinisch-experimentelle Tumorforschung Influence of neoadjuvant chemotherapy on the immunogenicity of esophageal adenocarcinomas, Bastian Dislich, 2019–2023, CHF 120'000*

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

Administrative duties

Alessandro Lugli
- Member of the SGPath
- Member of the DGP
- Member of the SFP
- Member of the USCAP
- Member of the AGA
- Member of the ASCO
- Member of the SAGIP
- Member of the ESP

Heather Dawson
- SGPath (Swiss Society of Pathology)
- SAGIP (Swiss Working Group of Gastrointestinal Pathology; President)
- IAP (International Academy of Pathology; President of Swiss Division)
- SSMP (Swiss Society of Molecular Pathology; Member of Advisory Board)
- SwissNET (Swiss Neuroendocrine Tumor Society)
- USCAP (United States and Canadian Academy of Pathology)
- ASCO (American Society of Oncology)

Bastian Dislich
- SDiPath – Swiss Digital Pathology Consortium
- USCAP- United States and Canadian Academy of Pathology

Aart Mookhoek
- SGPath (Schweizerische Gesellschaft für Pathologie)
- SAGIP (Swiss Association of Gastrointestinal Pathology)
- ECCO (European Crohn's and Colitis Organisation)
- H-EDDO* (Histopathologists of ECCO)
- IBDnet (Swiss Research & Communication Network on Inflammatory Bowel Disease)

*gewähltes Mitglied

Publications

- Khan A, Janowczyk A, Müller F, Blank A, Nguyen HG, Abbet C, Studer L, **Lugli A,** Dawson H, Thiran JP, Zlobec I. *Impact of scanner variability on lymph node segmentation in computational pathology.* J Pathol Inform. 2022 Jul 25;13:100127. doi: 10.1016/j.jpi.2022.100127. PMID: 36268105; PMCID: PMC9577043.
- Mlecnik B, Torigoe T, Bindea G, Popivanova B, Xu M, Fujita T, Hazama S, Suzuki N, Nagano H, Okuno K, Hirohashi Y, Furuhata T, Takemasa I, Patel P, Vora H, Shah B, Patel JB, Rajvik KN, Pandya SJ, Shukla SN, Wang Y, Zhang G, Yoshino T, Taniguchi H, Bifulco C, **Lugli A,** Lee JJ, Zlobec I, Rau TT, Berger MD, Nagtegaal ID, Vink-Börger E, Hartmann A, Geppert CI, Kolwelter J, Merkel S, Grützmann R, Van den Eynde M, Jouret-Mourin A, Kartheuser A, Léonard D, Remue C, Wang J, Bavi P, Roehrl MHA, Ohashi PS, Nguyen LT, Han S, MacGregor HL, Hafezi-Bakhtiari S, Wouters BG, Masucci GV, Andersson E, Zavadova E, Vocka M, Spacek J, Petruzelka L, Konopasek B, Dundr P, Skalova H, Nemejcova K, Botti G, Tatangelo F, Delrio P, Ciliberto G, Maio M, Laghi L, Grizzi F, Marliot F, Fredriksen T, Buttard B, Lafontaine L, Maby P, Majdi A, Hijazi A, El Sissy C, Kirilovsky A, Berger A, Lagorce C, Paustian C, Ballesteros-Merino C, Dijkstra J, Van de Water C, van Lent-van Vliet S, Knijn N, Mușină AM, Scripcariu DV, Marincola FM, Ascierto PA, Fox BA, Pagès F, Kawakami Y, Galon J. *Clinical Performance of the Consensus Immunoscore in Colon Cancer in the Asian Population from the Multicenter International SITC Study.* Cancers (Basel). 2022 Sep 6;14(18):4346. doi: 10.3390/cancers14184346. PMID: 36139506; PMCID: PMC9497086.
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- Loughrey MB, Webster F, Arends MJ, Brown I, Burgart LJ, Cunningham C, Flejou JF, Kakar S, Kirsch R, Kojima M, **Lugli A,** Rosty C, Sheahan K, West NP, Wilson RH, Nagtegaal ID. *Dataset for Pathology Reporting of Colorectal Cancer: Recommendations From the International Collaboration on Cancer Reporting (ICCR).* Ann Surg. 2022 Mar 1;275(3):e549-e561. doi: 10.1097/SLA.0000000000005051. PMID: 34238814; PMCID: PMC8820778.

Research group Christoph Mueller

Group of Christoph Mueller, PhD

Juliana Barreto de Albuquerque, PhD, post-doc (till March 2022)
Regina Berchtold, technician, 80%
Antonia Ferreira, MSc (till May 2022)
Bilgi Gungor, PhD, post-doc
Beat Imhof, PhD, visiting scientist

Summary of Research Activities

Our group has a longstanding interest in the complex immunoregulatory mechanisms that are operative in the intestinal mucosa during homeostasis, and in the potential events leading to disruption of these mutualistic interactions between host and microbiome during inflammatory conditions as typically seen in inflammatory bowel diseases (Crohn's disease, ulcerative colitis). The importance of the intestinal microflora in shaping the differentiation of the local immune system, but also on 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 the associated metabolic changes. While we often use experimental mouse models to test our hypotheses, we also validate these experimental findings using state-of-the-art technologies with patient materials initially obtained from the SIBDCS biobank.

Specific research interests

The research interests of our research 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 neurodegenerative disorders

Research Activities

Project 1: Functional changes in local T cells during onset vs. remission vs. relapse of colitis

Understanding the mechanisms that drive remission and relapsing of intestinal inflammation is a prerequisite for treating patients with inflammatory bowel diseases. We have recently established a reversible, relapsing-remitting mouse model of colitis with reproducible onset of intestinal inflammation, induction of remission and repeated flares of inflammation (Brasseit et al., Mucosal Immunol 2016). In this model we monitor the functional changes induced in the CD4 T cells during induction of colitis, during remission, and relapse of colonic inflammation at the single cell level, and in distinct CD4 T cell clones with identical T cell receptor. 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 in immunosurveillance 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. 2014) to determine the Trem1-mediated effects in atherosclerosis (Zysset et al., Nat Comms 2016) and the development of colitis-associated colorectal carcinoma (Saurer and Zysset et al., Sci Rep 2017). Current research interests include collaborative efforts on the involvement of TREM-1 in neurological disorders, such as stroke (Liu et al., Nat Immunol 2019), and neurodegenerative disorders.

Project 3: Functional plasticity and retention of tissue-resident T-cells in the intestinal mucosa

Understanding the functions and the regulation of intestinal T cell subsets is one of our long-standing research objectives. Some of these T cells in the intestine 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 the protective immunity against pathogens (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 either result in protective immunity, or inflammatory pathologies.

Project 4: Differential CD8+ T cell priming following oral vs. intestinal antigen exposure

Food, airborne particles, and commensal bacteria and pathogens enter the gastrointestinal tract through the mouth. We investigate how microbes and other antigens are sensed locally, and how the immune reaction initiated in the oral cavity may differ from an immune response induced by intestinal antigens. We identified the mandibular lymph nodes as sentinel lymphoid organs for oral antigens, which are well-equipped to intercept potential pathogens and rapidly induce a cellular immune response. In contrast to CD8+ T effector cells which are primed during an intestinal infection with Listeria monocytogenes in mesenteric lymph nodes, these mandibular lymph node-derived CD8+ T effector cells do not preferentially traffic to the small intestine, but rather support a systemic T-cell mediated immunosurveillance. This provides further evidence for the regional specialization of the immune system of the gastrointestinal tract (Science Immunology 7, eabf1861 (2022).

Internal Collaborations

- Stefan Freigang, MD
- Philippe Krebs, PhD
- Mirjam Schenk, PhD

External Collaborations

National

- Andrew Macpherson, MD, Julien Limenitakis, PhD, 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
- Jens Stein, PhD, University of Fribourg

International

- Katrin Andreasson, MD, Neurology and Neurosciences, Stanford University Medical Center, USA
- Klaas von Gisbergen, PhD, Sanquin Research, Amsterdam, The Netherlands
- Sebastian Zundler, MD, Department of Medicine 1, Friedrich-Alexander-Universität (FAU) Erlangen-Nürnberg, Erlangen, Germany
- John Kehrl, NIAID, Bethesda, MD, USA
- Bärbel Stecher, PhD, Max von Pettenkofer Institute of Hygiene and Medical Microbiology, Ludwig-Maximilians-University of Munich, Germany

Grant Support

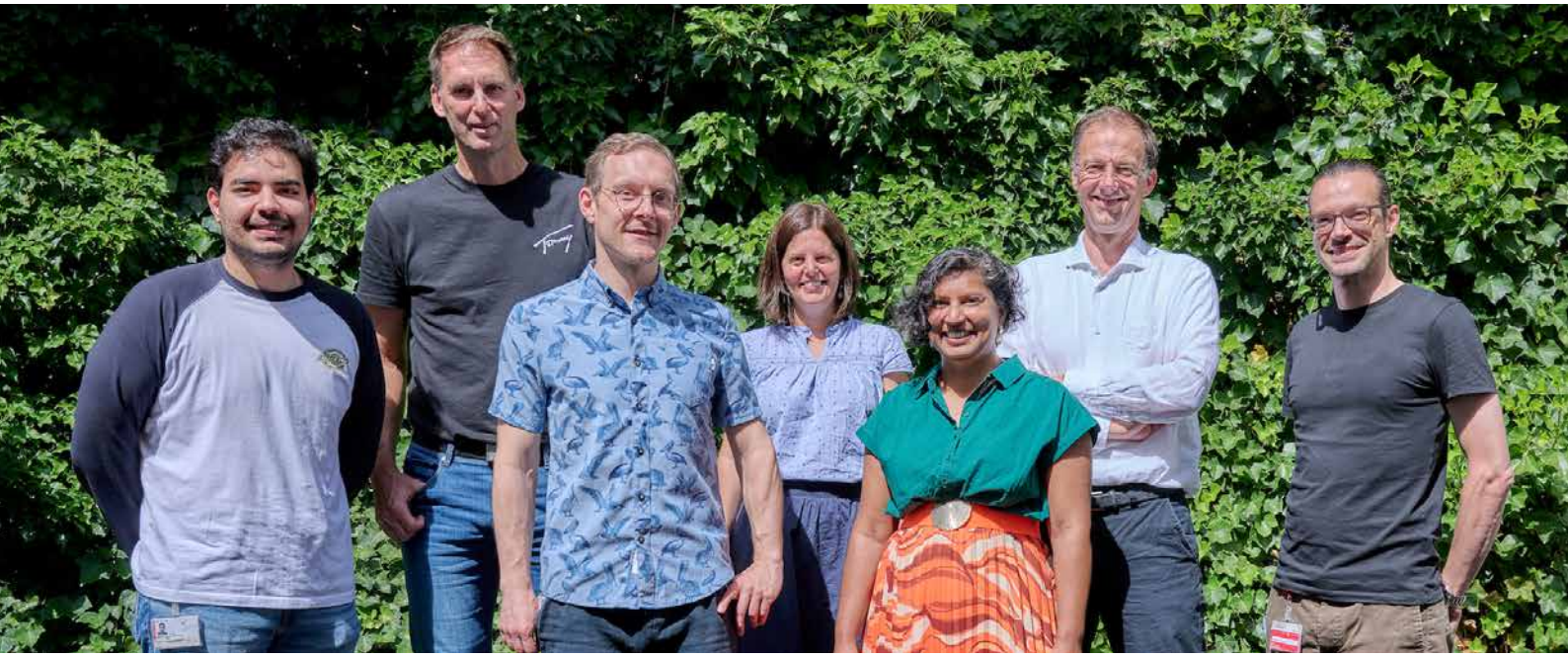
- SNF 314730_189277, Christoph Müller, 2019–2022, CHF 516'667
- Novartis, Juliana Barreto de Albuquerque, 2021–2022, CHF 51'182

Administrative duties

- Chair, Program Board «Certificate of Advanced Studies in Research Management» (CAS «Forschungsmanagement»), University of Bern (till May 2022)
- Head, Biobank, Swiss IBD Cohort Study (SIBDCS)
- Stiftungsratspräsident, Stiftung für klinisch-experimentelle Tumorforschung Bern
- Member of the Committee on the Novo Nordisk Foundation Challenge Programme, Denmark
- Member of several faculty committees

Publications

- Juliana Barreto de Albuquerque ,Lukas M Altenburger, Jun Abe, Diego von Werdt, Stefanie Wissmann, Jose Martínez Magdaleno, David Francisco, Geert van Geest, Xenia Ficht, Matteo Iannacone, **Christoph Mueller,** Jens V Stein.
  Microbial uptake in oral mucosa-draining lymph nodes leads to rapid release of cytotoxic CD8+ T cells lacking a gut-homing phenotype.
  Sci Immunol. 2022 Jun 24;7(72):eabf1861. doi: 10.1126/sciimmunol.abf1861. PMID: 35714202
- Zu dieser Publikation wurde auch ein Editorial in der gleichen Zeitschrift (Science Immunology) verfasst, das die Ergebnisse gut zusammenfasst:
  Williams DW, Hajishengallis G, Moutsopoulos NM.
  Regional specification of oral mucosal immunity.
  Sci Immunol. 2022 Jun 24;7(72):eabp8632. doi: 10.1126/sciimmunol.abp8632. PMID: 35714199



Research group Aurel Perren

Group of Aurel Perren, MD

Ilaria Marinoni, PhD, Co-PI
Aziz Chouchane, M Med, guest scientist
Martin Sadowski, PhD, Senior Research Assistant
Martin Wartenberg MD, Staff pathologist
Philipp Kirchner, Staff scientist
Renaud Maire, MSc, Laboratory technician
Tsilla Sunier, Laboratory technician
Simon April, MSc, PhD student
Umara Rafiqi, MSc, PhD student
Young Hwa Yang, MSc student
Marco Visani, MSc student
Bräutigam, MD, Resident
Simona Avanthay

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.

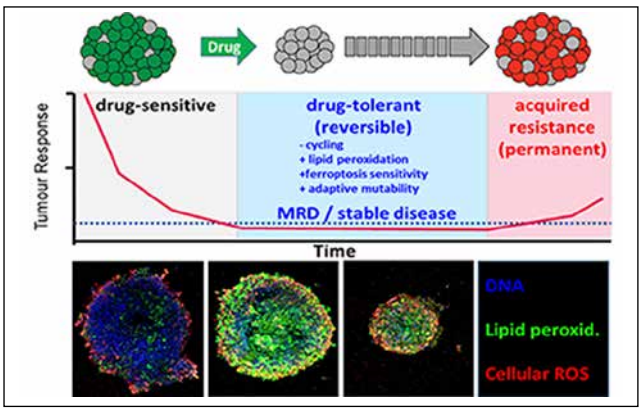
Research Activities

Project 1: Epigenetic changes and tumor cell heterogeneity in the progression of PanNETs
We focus on understanding epigenetic changes occurring in PanNET and their impact on progression and metastasis formation. Based on DNA methylation we identified subgroups of PanNETs with: specific cell of origin, genetic background and clinical outcome. Integrating epigenetic and transcriptomic profiles we found that cell dedifferentiation and metabolic changes characterize progression from small PanNET to more advanced ones. We are currently investigating spatial and temporal heterogeneity of PanNET using multi-omic approaches.

Project 2: Precision medicine approach for PanNET treatment
Up to date, no therapy prediction based on specific molecular profile is possible for PanNET patients. We recently established patient-derived tumoroid cultures from PanNET patients which resemble features of original tumor tissue and which can be used for in vitro drug screenings. We are currently assessing the utility of PanNET tumoroids to predict patient therapy response and to identify novel epigenetic treatment options. Also, we aim at identifying specific molecular profiles through DNA sequencing, methylation- and gene expression analysis to predict therapy response in vitro and on the patients.

Project 3: Metabolic changes in PanNET
Critical metabolic changes are early hallmarks of cancer cells. Emerging epigenetic, transcriptional and translational data suggest that PanNET cells undergo substantial metabolic reprogramming. However, the identity, functional consequences and therapeutic potential of metabolic changes in PanNET remain up until now largely unknown and untested. Our multimodal, integrated analysis of PanNET cell culture and tissue samples of various stages of tumor development by modern mass spectrometry, fluorescence microscopy and RNAseq data will delineate these metabolic and test novel therapeutic strategies.

Project 4: An early offensive against acquired therapy resistance in PanNET
Acquired drug resistance (ADR) is a major clinical challenge to all current cancer treatments, including chemo, radiation, targeted, and immune therapies and accounts for 90% of cancer mortality. Given the stochastic, mutation-driven nature of ADR, multiple different resistance mechanisms often co-evolve within in the same tumour or across metastatic lesions in the same patient, requiring individualized



Project 4: Graphical description of the three phases of acquired drug resistance and associated phenotypes (top) with corresponding micrographs (bottom) of chronically treated PanNET spheroids showing hallmarks of DTPs (enhanced lipid peroxidation).

therapeutic approaches. This project seeks to identify and test novel strategies to target drug-tolerant persister cells (DTPs), which comprise an early, reversible bottleneck phase of ADR. RNAseq and high content imaging-guided molecular and phenotypic analysis will delineate the early dynamic changes during DTP development in 2D and 3D ADR models of PanNET.

Internal Collaborations

- Philippe Krebs, PhD
- Erik Vassella, PhD
- Inti Zlobec, PhD
- Corina Kim-Fuchs Universitätsklinik für Diabetologie, Endokrinologie
- Ernährungsmedizin & Metabolismus (UDEM) Inselspital

External Collaborations

National

- Beat Gloor, MD, Department of Visceral Surgery, Insel University Hospital, Bern
- Holger Moch, MD, Department of Pathology, University Hospital, Zurich
- Corina Kim-Fuchs Universitätsklinik für Diabetologie, Endokrinologie, Ernährungsmedizin & Metabolismus (UDEM), Inselspital
- Prof. Nadia Mercader, Institute of Anatomy, University of Bern

International

- Dr. Chrissie Thirlwell, University of Exeter school of medicine, Exeter, UK
- Prof. Bertram Wiedenmann, Charité, University Hospital, Berlin, Germany
- Prof. Anne Couvelard and Dr. Jérôm Cros, Department of Pathology, Hospital Beaujon, Clichy, France
- Prof. Marianne Pavel, head of Endocrinology and Diabetes department, Erlangen Germany
- Prof. Massimo Falconi, Surgery Departement, San Raffaele, Milan, Italy
- Dr. med. Mauro Cives, University of Bari, Bari, Italy
- Dr. Anguraj Sadanandam, ICR, The Institute of Cancer Research, London, UK

Grant Support

- SNF 310030_188639, Aurel Perren (PI), 2020–2024, CHF 632'000
- ENETs CO-Synergy Award, Ilaria Marinoni (PI), 2019–2022, Euro 69'700
- KLS-4227-08-2017, Aurel Perren (PI), Ilaria Marinoni (Co-PI), 2018–2022, CHF 395'450*
- Bern Center for Precision Medicine , Ilaria Marioni, 2022–2024, CHF 174'000
- Swiss Cancer League, Martin Sadowski , 2022–2025, CHF 359'000

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

Administrative duties

Aurel Perren

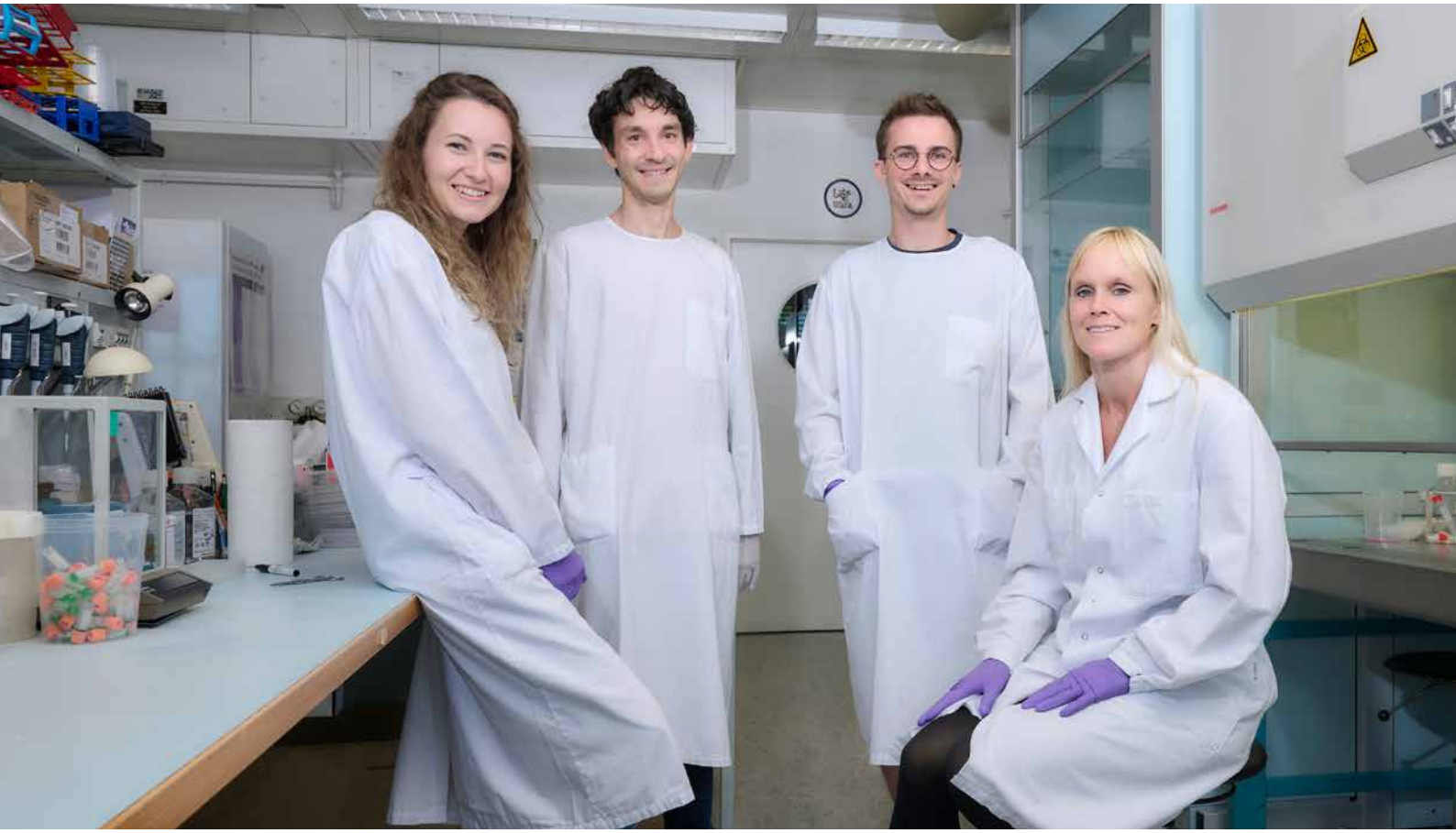
- Stellvertreter des Dekans Medizinische Fakultät
- Mitglied Direktorium CCC Inselspital
- Co-Pi und Vize-Präsident Swiss Biobanking Platform (SBP)
- Mitglied Forschungskommission Krebsliga Bern
- Advisory Board, Mitglied, European Neuroendocrine Tumor Society (ENETS)
- Leiter Krebsregister Bern und Solothurn (KRBESO)
- Stiftungsrat NICER
- Vorstandsmitglied der Deutschen Gesellschaft für Pathologie (DGP)
- Mitglied Forschungskommission SKL
- Einzelmitglied Senat SAMW
- Mitglied der Leopoldina Nationale Akademie der Wissenschaften
- Mitglied Education Committee IAP, Sektion Deutschland

Ilaria Marinoni

- Member of NET model consortium (Leader of the in vivo group)
- Secretary of the ENETs Basic and Translational research group

Publications

- Gulde, Sebastian; Foscarini, Alessia; April-Monn, Simon L; Genio, Edoardo; Marangelo, Alessandro; Satam, Swapna; Helbling, Daniel; Falconi, Massimo; Toledo, Rodrigo A; Schrader, Jörg; **Perren, Aurel; Marinoni, Ilaria;** Pellegata, Natalia S. *Combined Targeting of Pathogenetic Mechanisms in Pancreatic Neuroendocrine Tumors Elicits Synergistic Antitumor Effects.* Cancers, 14(22) MDPI AG 10.3390/cancers14225481
- Simon, Tincy; Riemer, Pamela; Jarosch, Armin; Detjen, Katharina; Di Domenico, Annunziata; Bormann, Felix; Menne, Andrea; Khouja, Slim; Monje, Nanna; Childs, Liam H; Lenze, Dido; Leser, Ulf; Rossner, Florkin; Merkel, Murkus; Blüthgen, Nils; Puvel, Muriunne; Horst, Duvid; Cupper, Duvid; Murinoni, Iluriu; **Perren, Aurel;** ... *DNA methylation revea/s distinct cells of origin for pancreatic neuro-endocrine carcinomas and pancreatic neuroendocrine tumors.* Genome medicine, 14(1), S. 24. BioMed Central 10.1186/s13073-022-01018-w
- Depoilly, Thomas; Leroux, Raffaele; Andrade, Dafne; Nicolle, Remy; Dioguardi Burgio, Marco; Marinoni, Ilaria; Dokmak, Safi; Ruszniewski, Philippe; Hentic, Olivia; Paradis, Valerie; De Mestier, Louis; **Perren, Aurel;** Couvelard, Anne; Cros, Jeröme. *Immunophe-notypic and molecular characterization of pancreatic neuroendo-crine tumors producing serotonin.* Modern pathology, 35(11), S. 1713-1722. Springer Nature 10.1038/s41379-022-01110-x
- Battistella, Anna; Partelli, Stefano; Andreasi, Valentina; **Marinoni, Ilaria;** Palumbo, Diego; Tacelli, Matteo; Lena, Marco Schiavo; Muffatti, Francesca; Mushtaq, Junaid; Capurso, Gabriele; Arcidia-cono, Paolo Giorgio; De Cobelli, Francesco; Doglioni, Claudia; **Perren, Aurel;** Falconi, Massimo. *Preoperative assessment of microvesse/ density in nonfunctioning pancreatic neuroendocrine tumors (NF-PanNETs).* Surgery, 172(4), S. 1236-1244. E lsevier 10.1016/j.surg.2022.06.01717
- Karamitopoulou, Eva; Andreou, Andreas; Wenning, Anna Silvia; Gloor, Beat; **Perren, Aurel.** *High tumor mutational burden (TMB) identifies a microsatellite stable pancreatic cancer subset with prolonged survival and strong anti-tumor immunity.* European journal of cancer, 169, S. 64-73. Elsevier 10.1016/j.ejca.2022.03.033



Research group Mirjam Schenk

Group of Mirjam Schenk, PhD

Lukas Bäriswyl, technician (50%)
Ivanina Biserova Mutisheva,
MSc student Steve Robatel, PhD student

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.

Project 3: Highly multiplex, spatially resolved immuno-phenotyping of PDAC for biomarker discovery

The tumor immune microenvironment in pancreatic ductal adenocarcinoma (PDAC) is diverse, comprising various cell types that may either enhance or attenuate tumor immunity and disease progression, as well as response to therapies. It is therefore essential to dissect the immunological landscape in human PDAC tissues and to assess the correlation of various cell subsets and tumor-derived immunosuppressive factors to patient survival and other clinical parameters. Utilizing a novel approach to perform spatially resolved multiplex immunohistochemistry, we intend to delineate the phenotypes of tumor-infiltrating immune subpopulations in exquisite detail. Integrating these findings with transcriptomic data and tumor genotype signatures will allow us to unravel the mechanistic and prognostic relevance of certain immune markers in PDAC.

Internal Collaborations

- Martin Wartenberg, 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
- S Morteza Seyed Jafari, MD, Department of Dermatology, Inselspital, University of Bern

International

- Robert Modlin, MD, David Geffen School of Medicine, Dermatology, UCLA, Los Angeles
- Delphine Lee, MD, Division of Dermatology, Department of Medicine Harbor-UCLA Medical Center, Los Angeles Biomedical Research Institute

Grant Support

- SNF 320030_176083, Mirjam Schenk (PI), 2018–2022, CHF 566'109
- Stiftung experimentelle Biomedizin, Mirjam Schenk (PI), 2016–2022, CHF 1.3 Mio
- Novartis, Mirjam Schenk (PI), 2021–2024, CHF 52'000

Administrative duties

- Member of the Flow Cytometry & Cell Sorting Core Facility Working Group, University of Bern
- Member of the Nomination Committee for an Associate Professorship at the Medical Faculty, University of Bern, Switzerland
- Member of the Mass Cytometry steering committee, University of Bern, Switzerland

Publications

- Ivanina Mutisheva, Steve Robatel, Lukas Bäriswyl, **Mirjam Schenk.** *An Innovative Approach to Tissue Processing and Cell Sorting of Fixed Cells for Subsequent Single-Cell RNA Sequencing.* Int J Mol Sci. Sep 6;23(18):10233 (2022).
- Mirela Kremenovic, Alfred A. Chan, Bing Feng, Lukas Bäriswyl, Steve Robatel, Thomas Gruber, Li Tang, Delphine J. Lee, **Mirjam Schenk.** *BCG hydrogel promotes CTSS-mediated antigen processing and presentation, thereby suppressing metastasis and prolonging survival in melanoma.* The Journal for ImmunoTherapy of Cancer (JITC), Jun;10(6):e004133 (2022).
- Steve Robatel and **Mirjam Schenk.** *Current Limitations and Novel Perspectives in Pancreatic Cancer Treatment.* Cancers, Feb 16; 4(4):985 (2022).

Research group Mario P. Tschan

Group of Mario P. Tschan, PhD

Anna Bill, PhD post-doc, 70%
Nils Bodmer, PhD student
Carmen Kalbermatter, MSc student
Mengyu Zhou, MSc student
Deborah Krauer, technician, 80%
Rina Mehmeti, MD, PhD student
Tanja Muralt, MSc student
Ana Quirós González, MSc student
Yasmeen Mady, PhD student
Jun Xu, MD-PhD student
Shun Yi, MD, PhD student
Bürgler Alexandra, Medical Doctoral candidate

Summary of Research Activities

Cancer Autophagy Group: My research team investigates molecular mechanisms involved in the survival of acute myeloid leukemia cells (AML). Currently, we are deciphering the function of alternative splicing, the non-metabolic functions of glycolytic enzymes and autophagy recycling pathway in AML cell survival. Additional research projects address the function of autophagy in cell migration and metastasis of breast cancer cells. 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: Unravel the functions of autophagy in breast cancer motility

Metastasis formation accounts for the majority of deaths from breast cancer, making it imperative to better understand the mechanisms driving the metastatic cascade in order to develop therapeutic interventions to target it. We earlier discovered an oncogenic splice variant of a transcription factor and named it DMTF1β. We now show that DMTF1β promotes invasion and tumor-initiating capacity of breast cancer cells by activating autophagy. It has also been shown that inhibition of autophagy can have undesirable effects in some cancer types and induce epithelial to mesenchymal transition (EMT), one of the early steps of metastasis. Our aim is to identify breast cancer subtypes or cellular conditions in which autophagy inhibition will decrease migration, and those in which the inhibition of autophagy will promote invasiveness.

Project 2: PU.1 and alternative splicing

The transcription factor PU.1 (SPI1) plays a key role in myeloid differentiation as well as in myeloid cell survival. Aberrant low PU.1 expression contributes to an immature myeloid phenotype, e.g., acute myeloid leukemia (AML). Interestingly, two studies indicate that high PU.1 protein levels were associated with alternative splicing promoted by either direct binding to splice factors or by RNA binding. Our data indicate that PU.1 controls splicing of the anti-apoptotic CFLAR (cFLIP) gene, and thereby regulates cell death during myeloid differentiation.

Project 3: Reducing FASN expression facilitates AML differentiation

Apart from glycolysis and OXPHOS, lipid metabolism is frequently reprogrammed in leukemic cells to support cellular growth. Particularly, the protein important for de novo lipid synthesis, fatty acid synthase (FASN), is frequently upregulated in tumor cells. We found that high FASN expression in acute myeloid leukemia (AML) cells is associated with an immature hematopoietic phenotype. Decreasing FASN levels by RNAi or epigallocatechin-3-gallate (EGCG) treatment, but no blocking its enzymatic function, resulted in improved response of AML cells to differentiation therapy.

Internal Collaborations

- Inti Zlobec, PhD
- Lucine Christe, 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
- Sabina Berezowska, MD, Institute of Pathology, University of Lausanne

International

- Bruce E. Torbett, PhD, TSRI, La Jolla, CA, USA
- Rupert Langer, MD, Institute of Pathology and Molecular Pathology, University of Linz, Austria
- 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_310030_197786, Co-PIs: I. Zlobec; M. Tschan, 2020–2024, CHF 632'000*
- SNSF_31003A_173219, Mario Tschan (PI), 2017–2021, CHF 694'000
- UniBE ID grant, Co-PIs: B. Towbin; M.P. Tschan, 2021–2023, CHF 109'000*
- China Scholarship Council Fellowship, J. Xu; M. P. Tschan, PI, 2021–2024, CHF 90'000*
- Swiss Government Excellence Scholarship, Co-PIs: I. Zlobec; M.P.Tschan, 2021–2024, CHF 90'000*
- China Scholarship Council Fellowship (Shun Yi), M.P. Tschan, 2022–2025, CHF 90'000

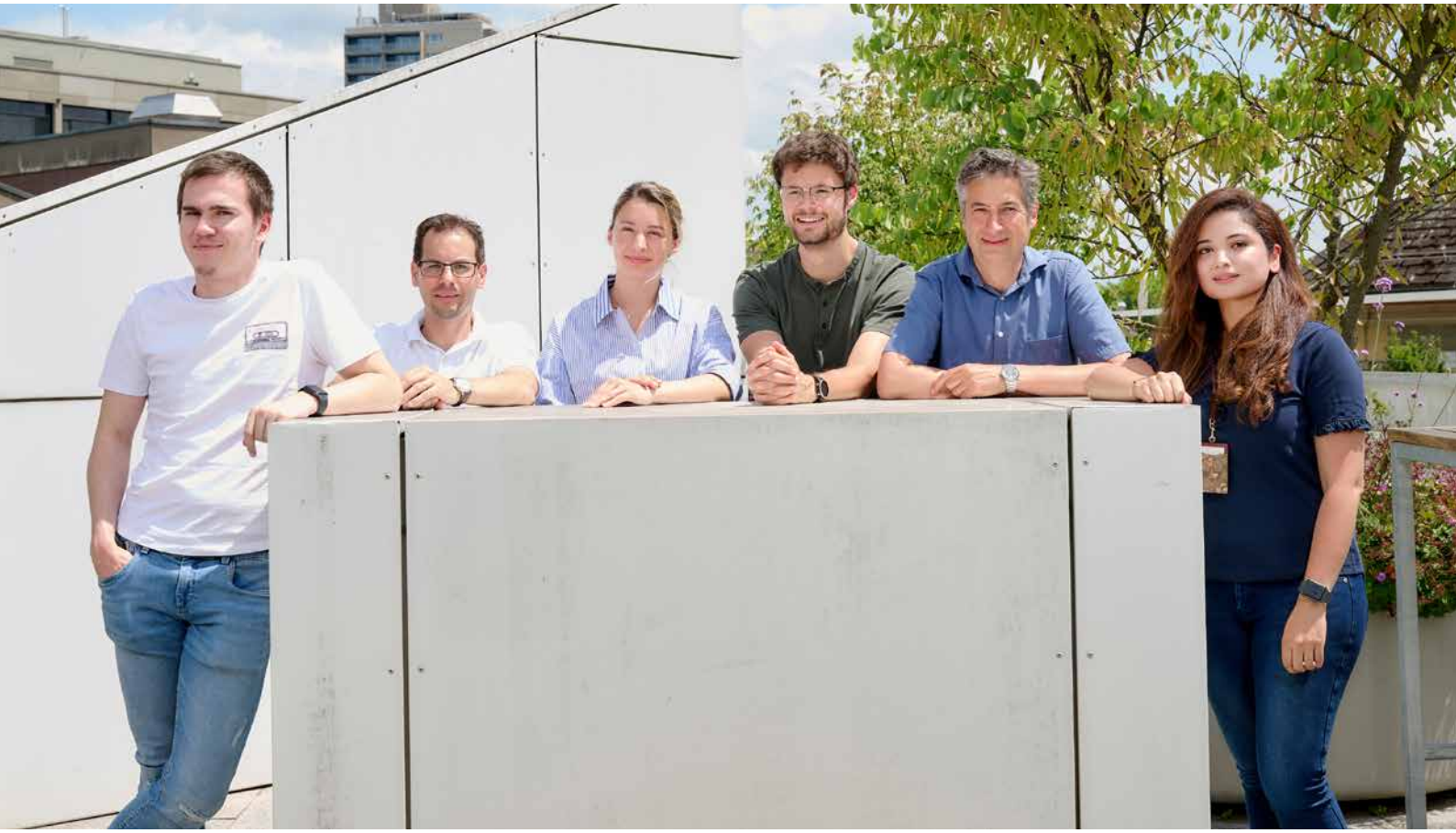
* total amount of funding; funding shared by PI and Co-PIs

Administrative duties

- 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
- 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»
- Life Sciences Switzerland LS2 Vice-president

Publications

- Seiler K, Humbert M, Minder P, Mashimo I, Schläfli AM, Krauer D, Federzoni EA, Vu B, Moresco JJ, Yates JR 3rd, Sadowski MC, Radpour R, Kaufmann T, Sarry JE, Dengjel J, **Tschan MP*,** Torbett BE*.
  *shared last authorship
  Hexokinase 3 enhances myeloid cell survival via non-glycolytic functions.
  Cell Death Dis. 2022 May 11;13(5):448. doi: 10.1038/s41419-022-04891-w.PMID: 35538058 Free PMC article.
- Pied N, Daussy CF, Deniz Z, Ragues J, Faure M, Iggo R, **Tschan MP,** Roger B, Rayne F, Wodrich H.
  TBK1 is part of a galectin 8 dependent membrane damage recognition complex and drives autophagy upon Adenovirus escape.
  PLoS Pathog. 2022 Jul 20; 18(7):e1919736. doi: 10.1371/journal ppat. 1010736. eCollection 2022 Jul.
  PMID: 35857795 Free PMC article.
- Giann' M, Coracci L, Schlaefli A, Di Veroli A, Kurosaki M, Guarrera L, Bolis M, Foglia M, Lupi M, **Tschan MP,** Cruciani G, Terao M, Garattini E.
  Role of cardiolipins, mitochondria and autophagy in the differentiation process activated by all-trans retinoic acid in acute promyelocytic leukemia.
  Cell Death Dis 2022 Jan 10; 13(1):30. doi: 10.1038/S41419-021-04476-Z. PMID: 350131142 Free PMC article.



Research group Erik Vassella

Group of Erik Vassella, Dr. pharm.

Catarina Bieler, Master student
MSc Romain Alexandre Gros, PhD student
Dr. Elham Kashani, PhD, Staff Scientist
Dr. Massimo Maiolo, PhD, Advanced Postdoc
M Med Theoni Maragkou, Staff Neuropathologist
Jaison Phour, Laboratory technician
Luca Rickli; Master student
Elia Rossini, Master student
Huijuan Wang, Master student
Dr. med. Philipp Zens, PhD student

Summary of Research Activities

Gliomas and medulloblastomas are the most common aggressive brain tumours in adults and children, most of which are associated with a fatal prognosis. The focus of our research group includes the molecular characterisation of glioblastomas and adult medulloblastomas with the aim of further defining the molecular profile of these tumours for the development of targeted therapy. To this end, we perform whole exome sequencing, genome-wide methylation and transcriptome analyses as well as microRNA and CRISPR/CAS9 library screens.

Research Activities

Project 1: Role of serine-threonine phosphatases in temozolomide resistance of glioblastoma

We followed 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. miRNAs identified by this screen showed downregulation of serine-threonine phosphatases, which in turn caused enhanced phosphorylaton of ERK and AKT, modulated the activity of DNA repair enzymes, and thereby confer resistance to TMZ response.

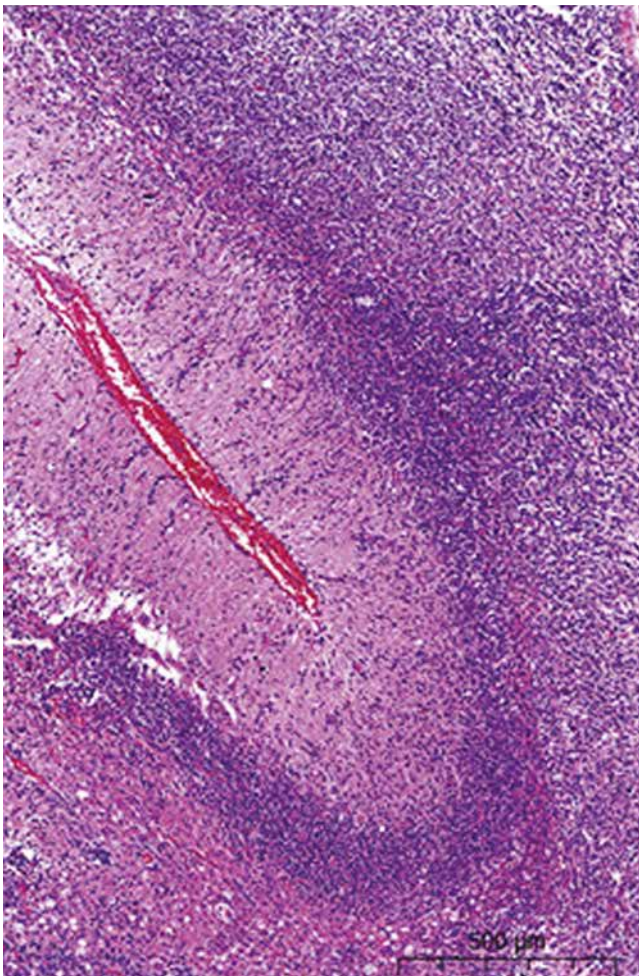
Project 2: Molecular characterization of recurrent glioblastoma

Glioblastoma (GBM) is the most heterogeneous and aggressive primary brain tumors, and represents a particular challenge of therapeutic intervention. In a single-center retrospective study of 43 matched initial and post-therapeutic GBM cases with exceptionally long recurrence period, we performed whole exome sequencing in combination with mRNA and microRNA expression profiling with the aim to identify processes altered in recurrent GBM. Seven mRNAs coding for proteins implicated in Epithelial to Mesenchymal Transition (EMT) and 13 miRNAs implicated in Tumor Necrosis Factor (TNF) and Wnt signaling pathways were significantly dysregulated. To the best of our knowledge, this is the largest cohort of recurrent GBM with long-

term resection intervals, that has been analyzed by multi-omics approaches In future, this approach may help for the development of new personalized medicine. This project is currently supported by the Swiss National Science Foundation.

Project 3

Medulloblastomas are the most common aggressive pediatric brain tumors, molecularly defined by different groups and subgroups. Although medulloblastoma is a rare disease, it has been also described in postpubertal and adult patients. The lack of studies exclusively on adult medulloblastomas means that the therapeutic approach in these patients is mainly based on existing data from studies on pediatric medulloblastomas. For these reasons and given that adult patients do not have a satisfactory clinical outcome after therapy, we would like to study a large cohort of adult medulloblastomas and medulloblastoma relapses on a clinical, pathological and molecular level in order to further characterize the biology of these tumors for developing a targeted therapy adapted to their molecular profile.



Project 3: Classic histomorphology of an adult medulloblastoma.

Internal Collaborations

- Prof. Dr. Philippe Krebs
- PD Dr. Ilaria Marinoni and Prof. Dr. Aurel Perren

External Collaborations

National

- Prof. Dr. Sabina Berezowska, Institut universitaire de pathologie, CHUV, Lausanne
- Prof. Dr. Iris Baumgartner, Universitätsklinik für Angiologie, Inselspital
- Prof. Dr. Markus Lüdi, Universitätsklinik für Anästhesiologie, Inselspital
- Prof. Dr. med. Philippe Schucht, Neuroonkologie, Inselspital
- Prof. Dr. med. Ekkehard Hewer, Institut für Pathologie, CHUV, Schweiz
- Dr. med. Regina Reimann, Institut für Neuropathologie, USZ, Schweiz

International

- Prof. Dr. Rupert Langer, Kepler Universitätsklinikum, Linz
- Prof. Dr. Pascal O. Zinn, MD, PhD, University of Pittsburgh
- Prof. Dr. med. Christine Stadelmann-Nessler, Institut für Neuropathologie, UMG, Deutschland

Grant Support

- SNF (31003A_175656), Erik Vassella; PI, 2018–2022, CHF 408'509
- SAKK 75/08 Rupert Langer, Rupert Langer (PI), Erik Vassella (Co-PI), 2018–2025, CHF 132'640
- Swiss Cancer League, Sabina Berezowska (PI), Erik Vassella (Co-PI), 2019–2022, CHF 365'500
- Krebsliga Bern, Theoni Maragkou (PI), 2022–2023, CHF 67'500
- Bern Center for Precision Medicine (BCPM), Theoni Maragkou (PI), Erika Vassella (Co-PI), 2022–2024,CHF 130'000
- Stiftung für klinisch-experimentelle Tumorforschung, Theoni Maragkou (PI), 2022–2023, CHF 32'500

Publications

- Kashani E, Schnidrig D, Hashemi Gheinani A, Ninck MS, Zens P, Maragkou T, Baumgartner U, Schucht P, Rätsch G, Rubin MA, SOCIBP consortium, Berezowska S, Ng CKY and **Vassella E.** *Integrated longitudinal analysis of adult grade 4 diffuse gliomas with long-term relapse interval revealed upregulation of TGF-β signaling in recurrent tumors.* Neuro Oncol. 2022:noac220. Online ahead of print. PMID: 36124685
- Kashani E, **Vassella E.** *Pleiotropy of PP2A Phosphatases in Cancer with a Focus on Glioblastoma IDH Wildtype.* Cancers. 2022;14:5227. PMID: 36358647.
- Kündig A, Zens P, Fung C, Scherz A, Cerciello F, Herrmann E, Ermis E, Schmid RA, **Vassella E,** Berezowska S. *Programmed Death-Ligand 1 Expression in Lung Cancer and Paired Brain Metastases-a Single-Center Study in 190 Patients.* JTO Clin Res Rep. 2022;3:100413. PMID: 36275910
- Rodriguez-Calero A, Gallon J, Akhoundova D, Maletti S, Ferguson A, Cyrta J, Amstutz U, Garofoli A, Paradiso V, Tomlins SA, Hewer E, Genitsch V, Fleischmann A, **Vassella E,** Rushing EJ, Grobholz R, Fischer I, Jochum W, Cathomas G, Osunkoya AO, Bubendorf L, Moch H, Thalmann G, Ng CKY, Gillessen S, Piscuoglio S, Rubin MA. *Alterations in homologous recombination repair genes in prostate cancer brain metastases.* Nat Commun. 2022;13:2400. PMID: 35504881
- Guse K, Hagemann N, Thiele L, Remlinger J, Salmen A, Hoepner R, Keller I, Meyer P, Grandgirard D, Leib SL, **Vassella E,** Locatelli G, Hermann DM, Chan A. *CNS Antigen-Specific Neuroinflammation Attenuates Ischemic Stroke With Involvement of Polarized Myeloid Cells.* Neurol Neuroimmunol Neuroinflamm. 2022:e1168. PMID: 35676093.

Group Translational Research Unit (TRU)

1.2 Translational Research Unit (TRU)

Head of TRU: Dr. Paulina Brönnimann

Consultant: Prof. Inti Zlobec

Administration: Caroline Hammer (50%)

Technical and Scientific Staff:
Carmen Cardozo
Dr. Irene Centeno
Loredana Daminescu
Cristina Graham Martinez
Philipp Schneider
Jérémy Valentin
Therese Waldburger

Overview

The Translational Research Unit (TRU) is a core facility of the Institute of Pathology, University of Bern. We provide tissue-based services for researchers and use innovative technologies to support translational projects conducted on human and animal tissues.

2022 is an important year for TRU and ngTMA® as we celebrate 10 years anniversary of creation. TRU initially founded as a histology lab supporting internal researchers, expanded over last years broden our expertise and knowledge. Nowaday, we collaborate with researchers not only from the University of Bern but also participate in national and international scientific projects. Our portfolio includes

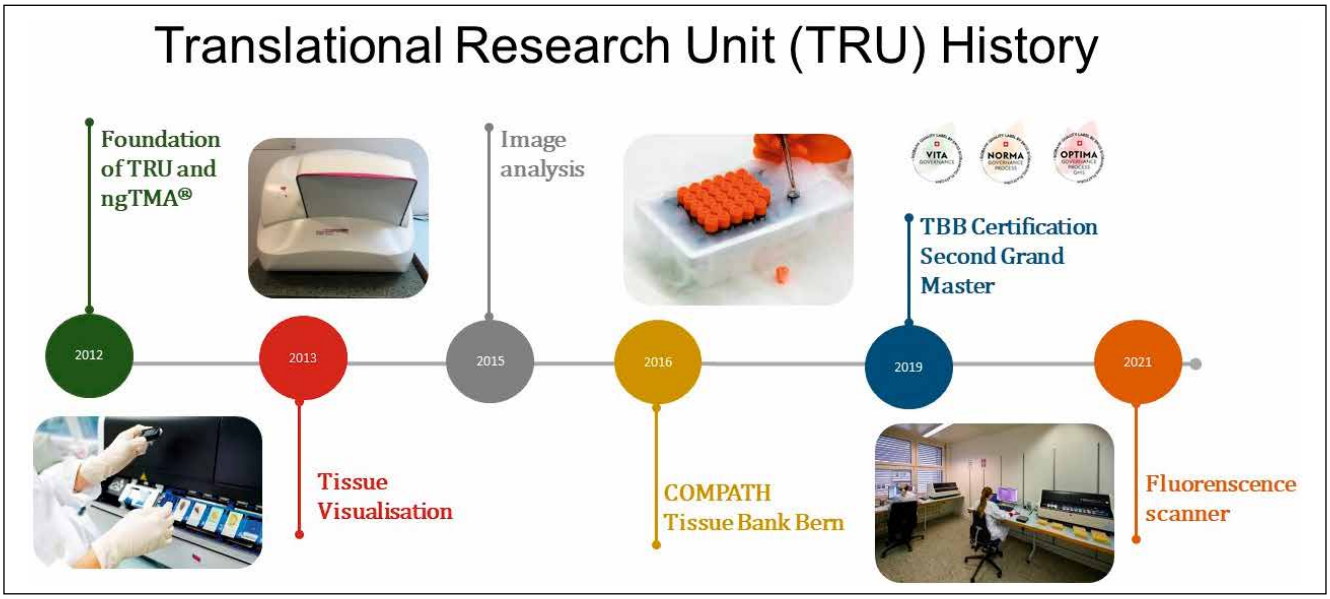


Fig. 1: History and development of TRU expertise since 2012. Since its foundation in 2012, TRU and ngTMA has expanded expertis over years.

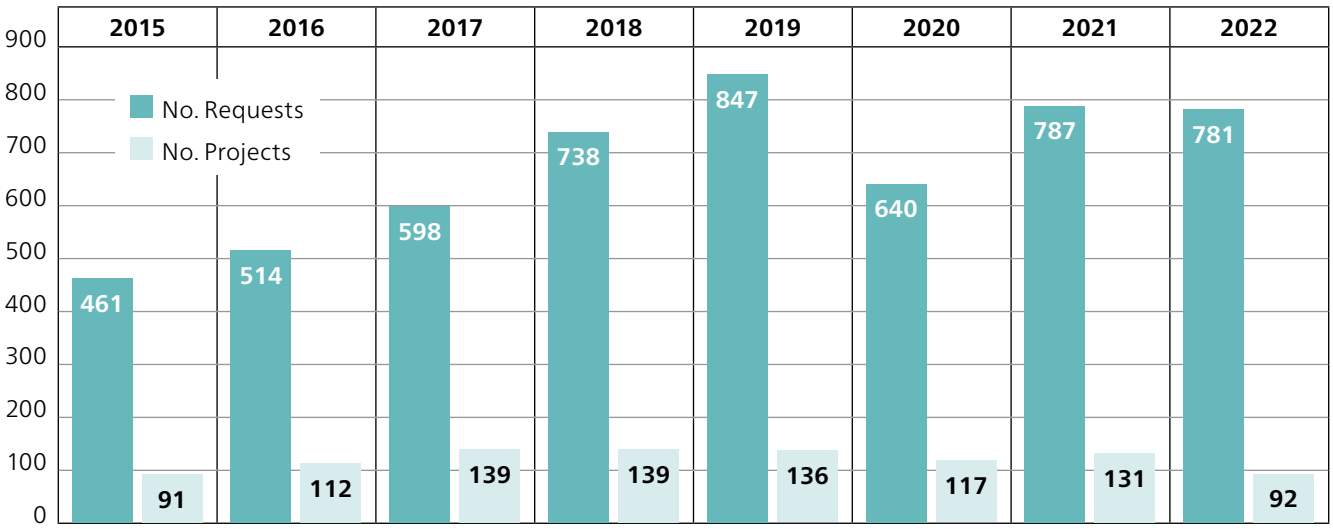
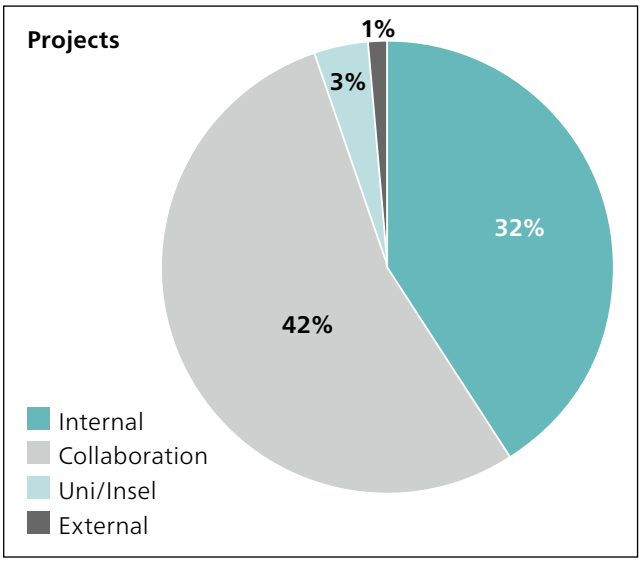
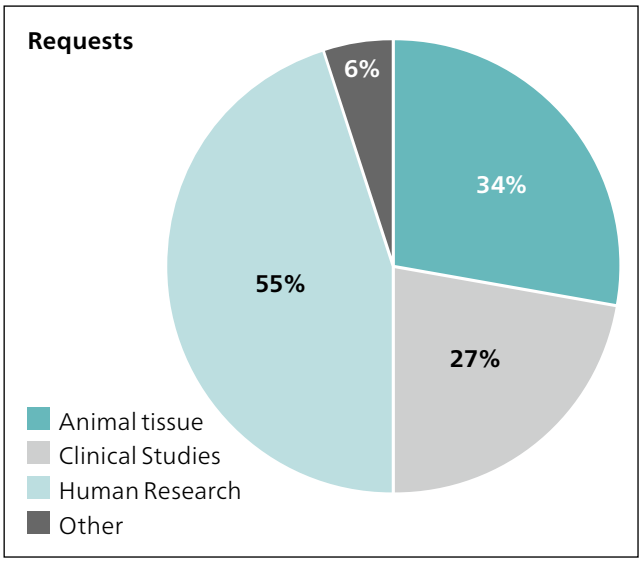
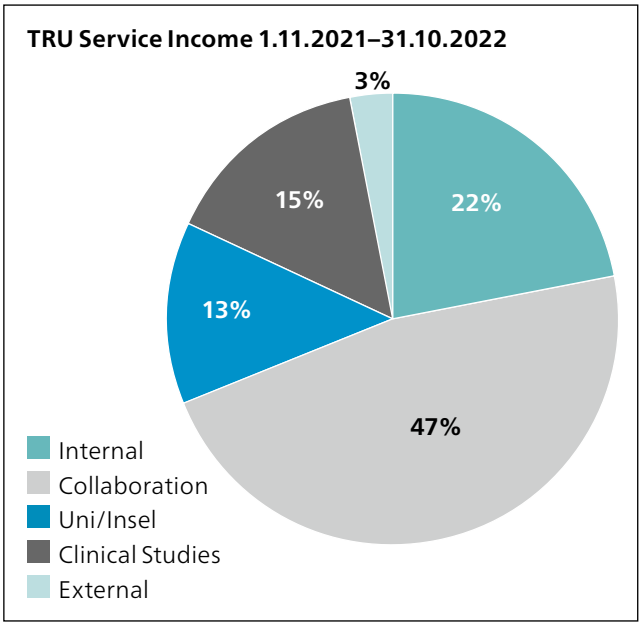


Fig. 2: Number of projects (and associated requests) managed by TRU in 2022 and distribution of funding sources this year.







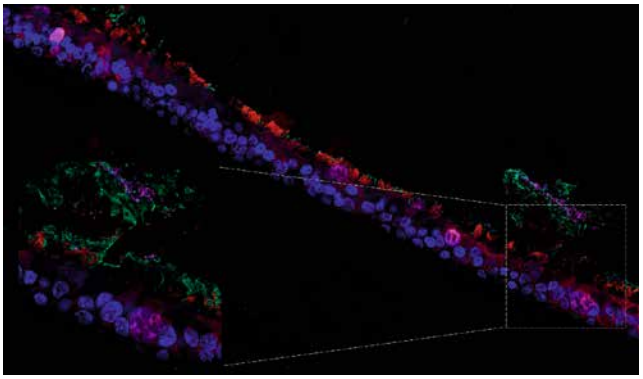


Fig. 3: Visualization of topically applied IgG and mucin 5AC in a Mucil-AirTM cell culture from a COPD donor. IF staining of Carnoy-fixed, paraffin-embedded epithelial ALI cells. blue: DAPI; red: β-Tubulin; violet: Mucin 5AC; green: IgG .
Source: CSL Behring AG, Research Bern, Stefanie Graeter

histopathology services, establishment of methods for tissue «visualization», digital pathology and image analysis, and next-generation Tissue Microarraying (www.ngtma.com). Moreover, we further support research by working together and providing access to patient material for research purposes through our certified partner biobank, Tissue Bank Bern (TBB: www.biobankbern.ch). In 2016, TRU has partnered with the Vetsuisse to create a service platform for comparative pathology (COMPATH). An overview on the last 10 years with more examples can be seen in Figure 1.

Projects and requests for services

In 2022, we could support 92 projects from 781 separate requests (excluding those in TBB) with 47% from internal researchers, whereas 41% were collaborations, including those with industry, and 6% were completed for researchers from the Inselspital /DBMR (Fig. 2). The number of service requests from investigators outside of the University/hospital occurred only in a small percentage of cases (1%).

TRU requests include approximately 55% human samples, 34% animal tissue and 27% clinical studies (including SAKK or trials with primary investigators at the Inselspital). The remaining are tissue-related requests.

Histology Lab

Our lab has expertise in histology techniques and tries to personalize each research project. This year we have established histology protocol including embedding and sectioning of a lung epithelial cells on the membrane (Fig. 3). Furthermore, sections are cut for many other purposes including: laser capture microdissection, DNA/RNA extraction, immunohistochemistry, immunofluorescence, spatial biology techniques 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 1982 (2020 n=2882) blocks, and cut thousands of slides for H&E or special stains (n=2952; 2020 n=3788 slides), immunohistochemistry, TUNEL or in situ hybridization (n=2201; 2020 n=4550). Additionally, we have sectioned 329 frozen tissue on the cryostat.

Tissue Visualisation Lab

TRU has expertise in tissue visualisation methods, including assays for immunohistochemistry (IHC), mRNA in situ hybridisation (ISH), immunofluorescence (IF), TUNEL or OPAL (Fig. 4).

This year TRU, has expanded expertise in tissue visualisation starting a collaboration with Ultivue, specialists in multiplexing tools and novel image analysis solutions. InSituPlex® technology enables advanced exploration and interrogation of tissue samples for precision medicine research (Fig. 5).

This year, TRU has added an additional 56 new antibodies to its repertoire, and has performed 2005 single stains, 139 double stains, 33 ISH and 4 OPAL assays. Moreover, 52% of all slides were stained for internal researchers from the Institute of Pathology, 31% were part of collaboration projects, and 36% were performed as a service for the University/Insel researchers. In addition, about 33% of all slides stained were animal tissues.

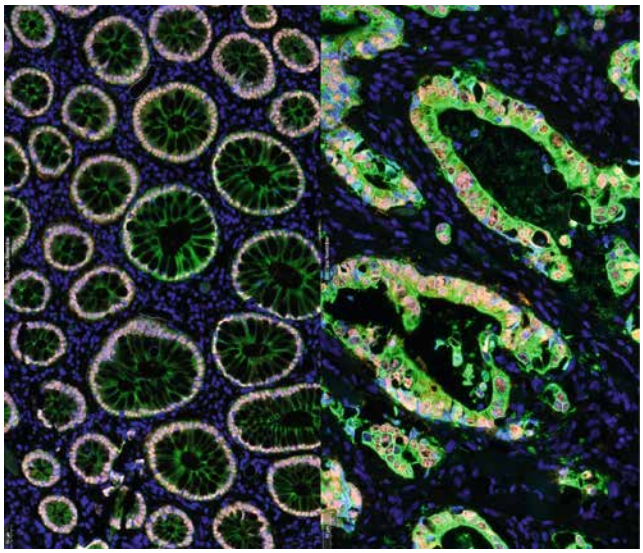


Fig. 4: Immunofluorescence staining performed with OPAL, technology from Akoya, on a CRC tumor sample: Normal (left) and tumor (right); blue: DAPI; red: E-cadherin; yellow: CDX2; green: Cytokeratin.

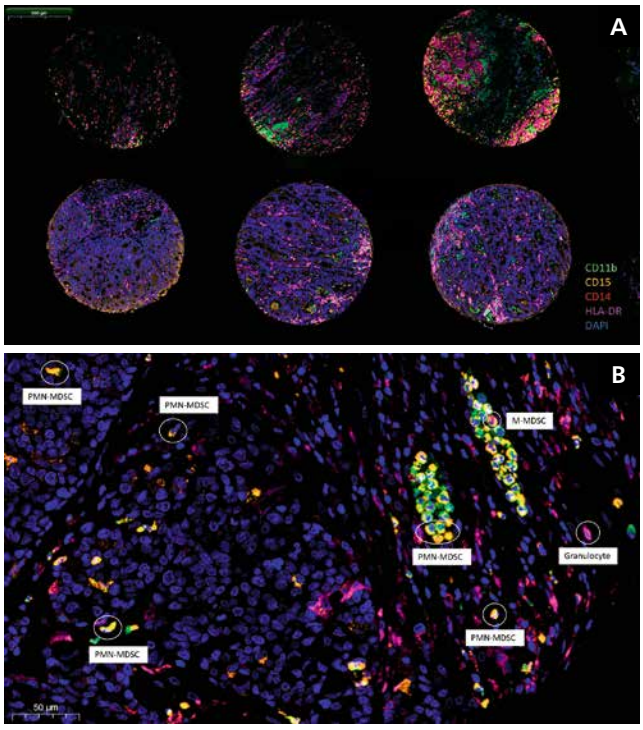


Fig. 5: Myeloid-derived suppressor cells (MDSCs) FixVUE panel from Ultivue. Example image done on CRC TMA and scanned with P250 fluorescence scanner (left). Cell phenotypeing done with MDSC panel enabling identification of monocytic MDSCs (M-MDSCs) and polymorphonuclear MDSCs (PMN-MDSCs) or granulocytes (right); blue: DAPI; red: E-cadherin; yellow: CDX2; green: Cytokeratin.

Next-generation Tissue Microarrays (ngTMA®) Lab

Our ngTMA 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. We use ngTMAs to study protein biomarkers by standard immunohistochemistry, but also have used probes for mRNA, miRNA, non-coding RNA, or immunofluorescence for studies related to precision medicine, tumor heterogeneity, rare diseases, or animal models. ngTMA this year was employed for development of new methodologies, such as multiplexed immunofluorescence e.g. Hyperion, LabSat (Lunaphore), OPAL (Akoya), PhenoCycler (Akoya), MIBI-TOF or Ultivue.

Recent updates and news on our ngTMA platform can be find every time on the website: www.ngtma.com.

Since it's inception in 2012, TRU has created more than 876 ngTMA blocks, totaling more than 154300 punches in recipient blocks and 6929 punches for tubes, and hence downstream molecular analysis. In 2022, we have constructed TMAs of upper and lower gastrointestinal cancers, pancreas, lung including MPM tumors or synovitis among others. 12 ngTMA projects were conducted including 88 ngTMA blocks with total 11925 punches from 1708 donorblocks. Additionally, 2518 cores form 767 donor blocks were punched for downstream molecular analysis (Fig. 6).

Recently, we have completed a lengthy project on colon cancer cohort constructing 54 blocks with 6980 TMA punches and 3114 DNA/RNA punches for downstream molecular analysis. Those were specially design to investigate spatial organization of tumor microenviorement components and immune cells expression and spatial distribution (first results can be seen with InSituPlex® technology from Ultivue on Fig. 5).

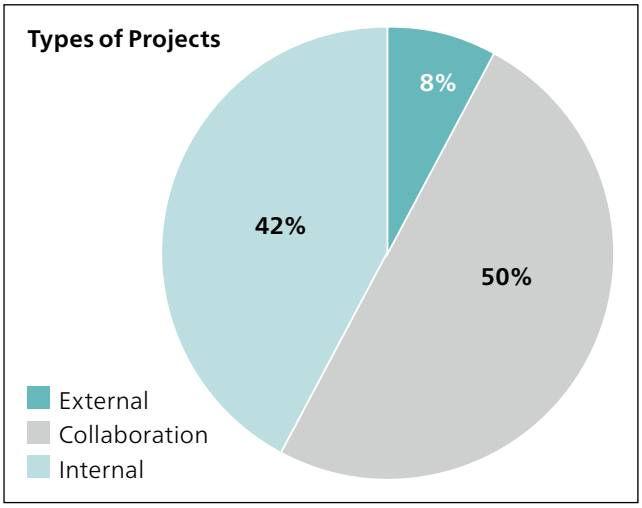


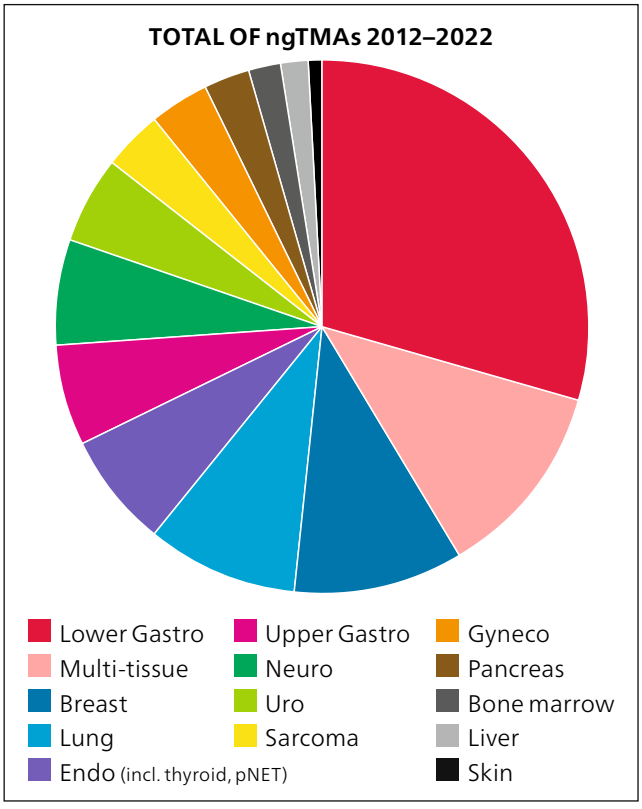
Fig. 6: ngTMA project types in 2022 (upper):internal (42%, collaboration (50%) aand external (8%). Tissue-specific distribution of ngTMA projects since 2012 until 2022 (lower).

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.

ngTMA was also the topic of several invited talks at various events, virtually or in-person, including the European Congress of Pathology in Basel, European Congress of Veterinary Pathologist in Bern, European Congress of Digital Pathology in Berlin or 3DHistech Symposium on AACS in New Orleans.

Data Management and Image Analysis

Modern pathology goes hand-in-hand with digitisation. TRU has been working on digital pathology on different fronts. One of them is slide scanning, a service used for various purposes, namely for education, to produce publication-quality images, for digital image analysis and development of artificial intelligence algorithms, for construction of next-generation Tissue Microarrays, sharing of images with research collaborators, or even archiving of slides digitally. TRU offers access to the Case Center for external users. Here, digital slides can be uploaded and viewed from outside the Institute.



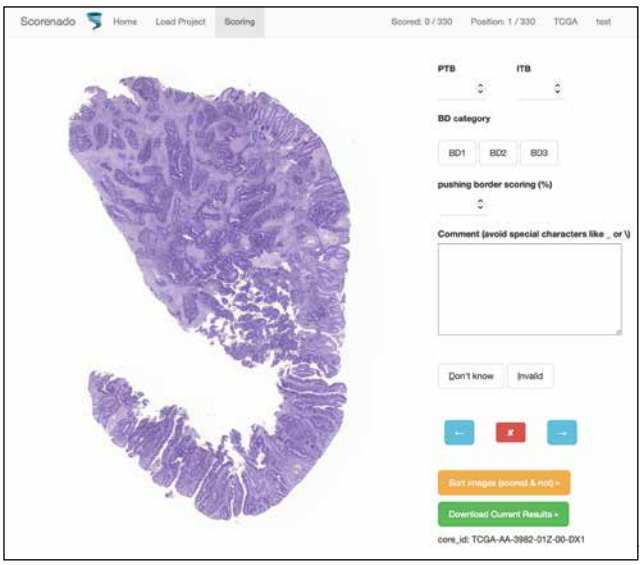


Fig. 7: Screenshot of Scorenado setup to score TCGA dataset.

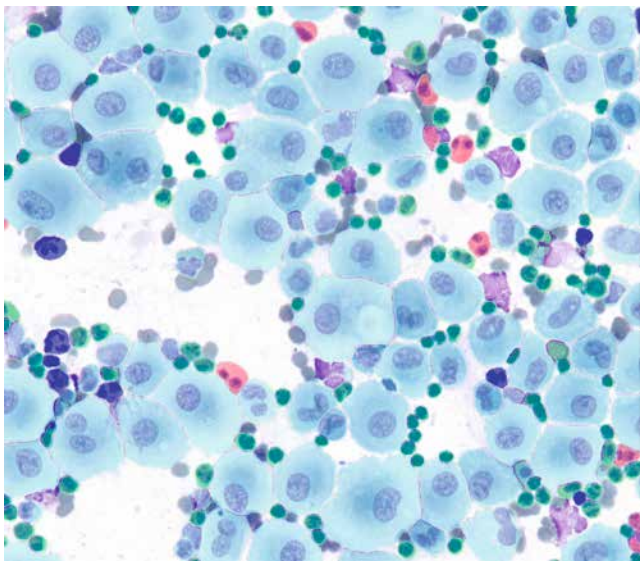


Fig. 8: Phenotyping cells and classification thereof in Halo AI on cytology slide (BAL).

Last year, we have acquired an upgrate to our Panoramic P250 scanner with 5 immunofluorescence (IF) filters including: DAPI, FITC, TRITC, Cy5 and Cy7 filters.

TRU provides access to "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 (Fig 7). The current version has been redesigned to run on a public web server to allow external collaborators to score with Scorenado. Since its test launch, a total of 73 Scorenado projects, including 817 slide scans, were set up for research conducted in-house, at Inselspital, and at other institutes in Switzerland and abroad. Overall, 240'797 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. For multiple publication the scores were processed and statistical analysis done.

TRU is also supporting researchers by providing training in image analysis using the free, open-source tool QuPath and commercial Indica Labs Halo and Halo AI (Fig. 8). This year, 6 different projects could be supported. In addition, a collection of scripts facilitating image analysis in QuPath and TMA data handling was populated.

Publications

TRU and ngTMA played an important role in several research publications this year including:

1. Pour Farid P, Eckstein M, Merkel S, Grützmann R, Hartmann A, Bruns V, Benz M, Schneider-Stock R, Geppert CI. Novel Criteria for Intratumoral Budding with Prognostic Relevance for Colon Cancer and Its Histological Subtypes. Int J Mol Sci. 2021 Dec 3;22(23):13108. doi: 10.3390/ijms222313108. PMID: 34884913; PMCID: PMC8658236.
2. Noti L, Galván JA, Dawson H, Lugli A, Kirsch R, Assarzadegan N, Messenger D, Krebs P, Berger MD, Zlobec I. A combined spatial score of granzyme B and CD68 surpasses CD8 as an independent prognostic factor in TNM stage II colorectal cancer. BMC Cancer. 2022 Sep 16;22(1):987. doi: 10.1186/s12885-022-10048-x. PMID: 36114487; PMCID: PMC9482175.
3. Jiang S, Mukherjee N, Bennett RS, Chen H, Logue J, Dighero-Kemp B, Kurtz JR, Adams R, Phillips D, Schürch CM, Goltsev Y, Hickey JW, McCaffrey EF, Delmastro A, Chu P, Reader JR, Keesler RI, Galván JA, Zlobec I, Van Rompay KKA, Liu DX, Hensley LE, Nolan GP, McIlwain DR. Rhesus Macaque CODEX Multiplexed Immunohistochemistry Panel for Studying Immune Responses During Ebola Infection. Front Immunol. 2021 Dec 6;12:729845. doi: 10.3389/fimmu.2021.729845. PMID: 34938283; PMCID: PMC8685521.
4. Zeng Q, Saghafinia S, Chryplewicz A, Fournier N, Christe L, Xie YQ, Guillot J, Yucel S, Li P, Galván JA, Karamitopoulou E, Zlobec I, Ataca D, Gallean F, Zhang P, Rodriguez-Calero JA, Rubin M, Tichet M, Homicsko K, Hanahan D. Aberrant hyperexpression of the RNA binding protein FMRP in tumors mediates immune evasion. Science. 2022 Nov 18;378(6621):eabl7207. doi: 10.1126/science.abl7207. Epub 2022 Nov 18. PMID: 36395212.
5. Losmanová T, Tschan MP, Galván JA, Berezowska S. Immunohistochemical Detection of the Chaperone-Mediated Autophagy Markers LAMP2A and HSPA8 in Formalin-Fixed and Paraffin-Embedded Tissues. Methods Mol Biol. 2023;2566:141-147. doi: 10.1007/978-1-0716-2675-7_11. PMID: 36152248.
6. Berezowska S, Galván JA. Immunohistochemical Detection of the Autophagy Markers LC3 and p62/SQSTM1 in Formalin-Fixed and Paraffin-Embedded Tissue. Methods Mol Biol. 2023;2566:133-139. doi: 10.1007/978-1-0716-2675-7_10. PMID: 36152247.

Gruppe Tissue Bank Bern (TBB)

Tissue Bank Bern (TBB)

Director: Prof. Dr. med. Aurel Perren
Operative manager: Dr. Paulina Brönnimann
Senior advisor: Prof. Dr. phil. nat. Inti Zlobec
Medical advisor: Dr. med. Aart Mookhoek
Office and quality manager: Caroline Hammer
Project management and operative functions:
Dr. Irene Centeno Ramos and Loredana-Ionela Daminescu
Histological Diagnostics lab TBB responsible:
Corinne Siegenthaler
Additional members: TRU and Histological Diagnostics Department staff, IT team of the Institute of Pathology

The Tissue Bank Bern (TBB) is an active core facility providing researchers with access to high quality human tissue samples and data in compliance to the Federal Human Research Act and Ordinance 2014 and the Swiss Biobanking Platform standards. This is done through optimal sample collection, storage, distribution and documentation. TBB services are, since October 2016, being performed in a partnership with the Translational Research Unit (TRU) thus, personnel and resources are shared.

Workflow

In order to provide a sample to a researcher, TBB staff requires the following information: the description of the project, the type and characteristics of the requested tissue and essential information regarding the ethical approval. Our committee will evaluate each request and provide advice, if needed. After the technical and clinical approval, the general consent status of the patients is reviewed and the appropriate samples, with patient consent, are prepared for the delivery. To assure their quality and content an exit quality control is done, consisting in an H&E staining reviewed by an expert pathologist. For external partners a Material Transfer Agreement (MTA) is signed at the time of the delivery. These processes and the timelines are summarized in the figure 1.

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

Fig. 1.: TBB request processing, workflow and timelines.

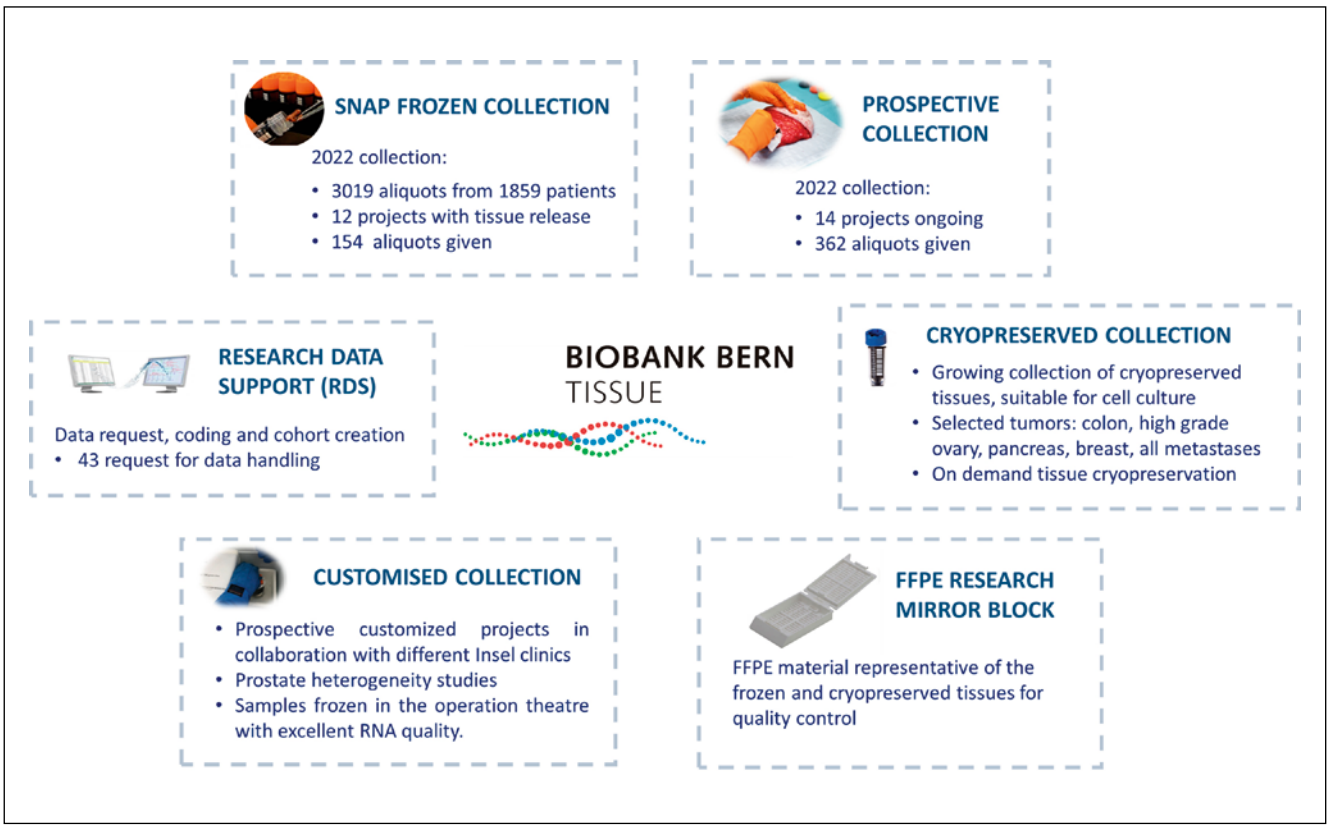


Fig. 2: Different activities performed by TBB in 2022.

TBB activities

In 2022, we have continued providing tissues from the snap frozen and cryopreserved collection and native tissues in a prospective manner. Additionally, we have a strong focus in special collections and new workflows to fulfill special needs.

As part of the Research Data Support team, we provide support for the researchers in data handling: cohort creation, clinical information requests, coding and general consent status proofing.

The principal on-going activities are summarised in the figure 2.

TBB institutional collection statistics

Human biobanking has evolved into a dynamic and complex activity with more focus in quality and protocols adapted to the researcher's needs. However, the collection of frozen tissues remains important. In 2022 we have collected around 3000 samples from almost 2000 patients bringing the total collection to almost 55000 aliquots from more than 16000 patients.

The contribution per clinic can be found in figure 5, with the largest number of samples deriving from the Gynecology Clinic, followed by the clinics of Visceral Surgery, Neurosurgery, Thoracic Surgery as well as Urology.

Regarding the cryopreserved collection, we slow freeze the selected tissues and store them in liquid nitrogen for experiments requiring living cells.

A representative part from the cryopreserved tissue is formalin fixed, paraffin embedded and H&E stained to assure an adequate vital tumor content before working with the cryopreserved material. The collection includes more than 200 cryopreserved tumor tissues, mainly from colon, liver, pancreas and breast.

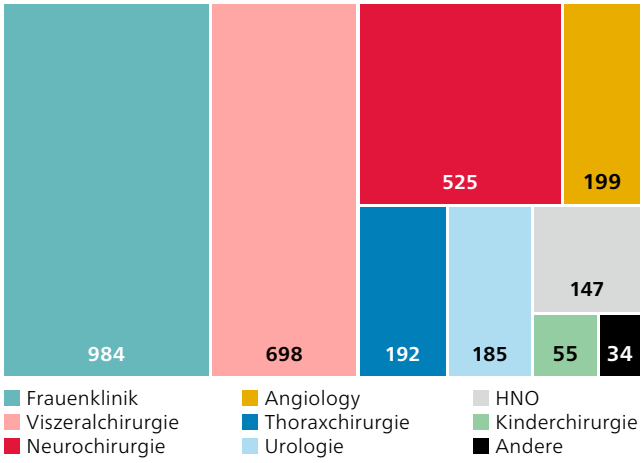


Fig. 3: Distribution of incoming tissue specimens for biobanking per clinic.

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, in addition to the ongoing collaborations with the Angiology and the Head and Neck surgery departments, we have started new projects with the Neurosurgery, the Gynecology departments and different private partners.

Project by Tissue Bank Bern 2022
The number of TBB projects continues to rise. In 2022, we received 69 requests for tissue and/or data.

Usage of tissue samples in 2022
During this year we have provided scientists with 154 frozen tissues. Additionally, 219 native tissues (362 aliquots) were given in a prospective manner. The usage of frozen samples was mainly done by internal researchers, while most of the native tissue given was used by Inselspital/DBMR researchers.

Towards the best quality of service
The delivery of optimal quality tissues to researchers is one of the main aims of TBB. The standardization of the processes, documentation of pre-analytical variables and strong quality monitoring systems are essential for the development and maintenance of the highest service quality and guarantee a continual improvement. In this field, TBB accomplish the Swiss Biobanking Platform (SBP) standards, acknowledged by the acquisition of the SBP Norma and Optima

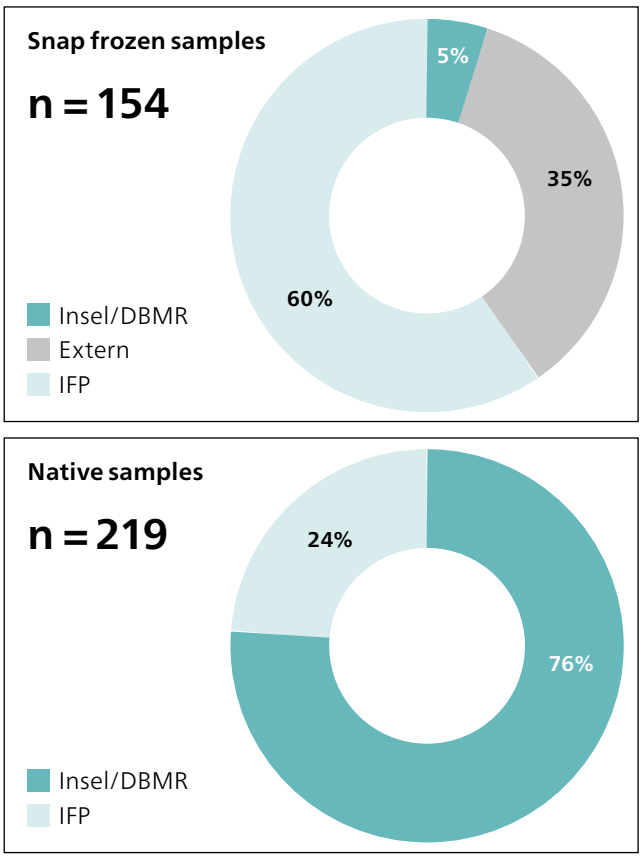


Fig. 4: Summary of tissue usage by internal, Inselspital/University of Bern (incl. DBMR) or external researchers for prospective and retrospective (frozen collection) projects in 2022.

VITA
Compliance with legal and ethical standards

NORMA
Standardization of the biobanking processes

OPTIMA
Implementation of quality assurance measures of the overall biobanking system

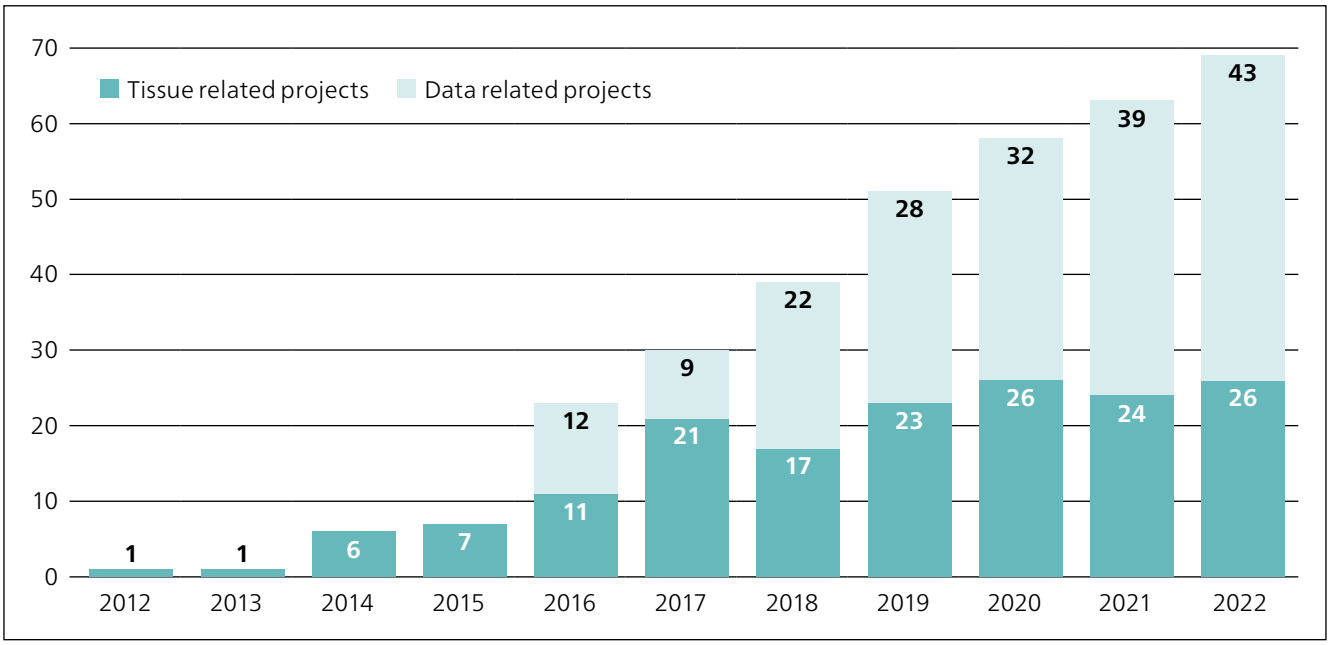


Fig. 5: Number of TBB requests for tissues/data showing increase over the last year.

Fig. 4A: OCT block creation for a customized collection.
Fig. 4B: Material for the collection procedure of peripheral artery disease tissue samples in the surgical theatre.

label in December 2019. Additionally, 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.

TBB puts a big effort in performing Human Research Act compliant workflows as evidenced by the SBP Vita Label certificate achieved already in 2018. Additionally, TBB offers support to the biomedical research activities by facilitating compliance with best practice standards and regulatory requirements relating to ethical, legal and societal issues (ELSI).

Partnerships

Excellence in biobanking is a multi-institutional and cross-departmental goal. We work in close collaboration with the Histological Diagnostics Department for sample acquisition; with Insel Data Science Center (IDSC) for general consent status and treatment related data management; with Liquid Biobank Bern for collaborative projects liquid-tissue and harmon-sation of processes; with Krebsregister for follow-up data on cancer patients and with the Swiss Biobanking Platform (SBP) for quality monitoring and process standardization. Additionally, we cooperate with the SBP sharing our expertise for document revision, appropriate BIMS selection and minimal biobank data set decision. 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 Histological Diagnostics 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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Research group Inti Zlobec

Group of Inti Zlobec, PhD

Inti Zlobec, PhD
Cristina Graham Martinez, Research assistant (from October)
Hannah Williams, post-doc (from September)
Cansaran Saygili Demir, post-doc
Amjad Khan, PhD student
Elias Baumann, PhD student
Ana Leni Frei, PhD student
Mauro Gwerder, PhD student
Linda Studer, PhD student (PI: Heather Dawson)
Rina Mehmeti, PhD student (shared Mario Tschan)
Nils Bodmer, PhD student (shared Mario Tschan)

Master students:
Chris Rüttimann
Kartik Kohli (PI: Aart Mookhoek)
Meisam Asgari (PI: Andreas Fischer, Uni Fribourg)
Christian Abbet (PI: Jean-Philippe Thiran, EPFL)

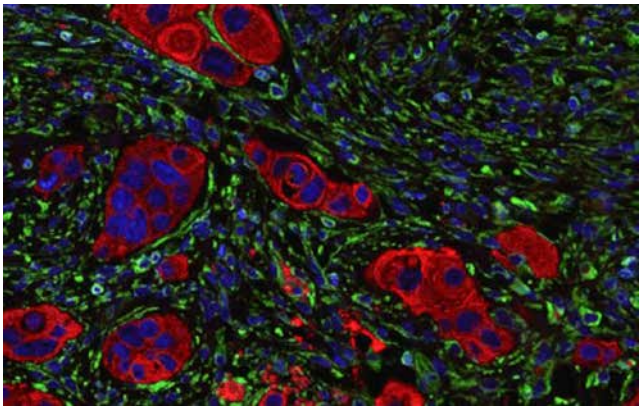
Summary of research activities

Our research group takes a deep dive into the morphomolecular and spatial biology aspects of colorectal cancer. We use digital pathology and artificial intelligence (AI) to gain insights into the multi-faceted phenomenon of «tumor budding», including the post-treatment modulation of the tumor budding microenvironment and the clinical impact of tumor heterogeneity on patient outcome.

Research Activities

Project 1: High-dimensional spatial biology approach to study tumor budding

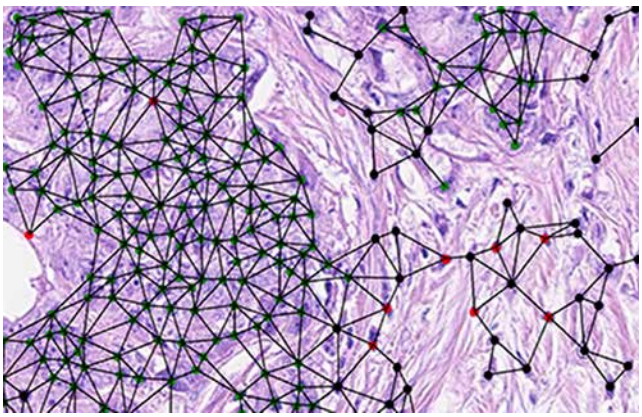
In our Innosuisse-funded project together with Lunaphore technologies, we are establishing a high-dimensional protein expression panel to investigate the nature of tumor buds and their microenvironment under native and treatment scenarios. We investigate the «active» state of tumor buds and their relationship to Epithelial-Mesenchymal Transition (EMT). Most importantly, the clinical relevance of different budding phenotypes, stromal changes and immune cell contexture by utilizing our well-documented patient collectives and ngTMA®. Data analysis is critical, and we aim to develop streamlined pipelines to evaluate these multiplexed fluorescent images using in-house deep learning algorithms and commercially available and open-source software.



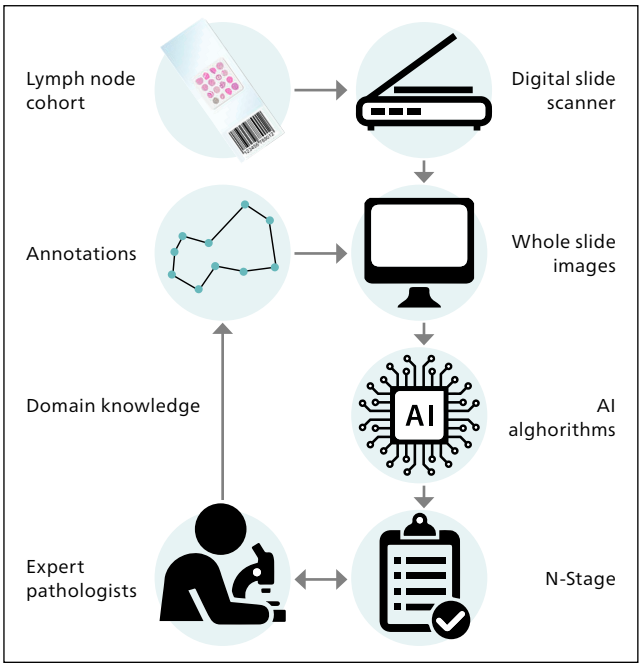
Project 1: Tumor microenvironment in colorectal cancer.
DAPI = blue, Pan-CytoKeratin = red, Vimentin = green.

Project 2. Digital pathology & AI to gain novel insights into colorectal cancer

Our Sinergia project uses AI to harness the power of histopathology images, genomics (focusing on STRs), and pharmacoscopy to gain novel insights into colorectal cancer biology and understand their impact on clinical outcomes. We investigate morphomolecular relationships, including the CMS classification, and intratumoral heterogeneity in order to learn new interpretable & clinically important features from histopathology images. We use various computational methods, including graphs and deep learning) to evaluate the structural and spatial patterns at the tumor invasion front in neoadjuvantly treated patients. We've extended our scope to understanding CMS using spatial transcriptomic and protein expression analysis. The tumor microenvironment, with its complex stromal patterns and immune contexture are important focus points. Collaborators on this project include M. Rodriguez (IBM Research), M. Anisimova (ZHAW), B. Snijder (ETH Zürich), A. Fischer (HES-SO & Uni Fribourg) and V. Koelzer (UniZürich).



Project 2: Epithelial cell and lymphocyte graphs in colorectal cancer.



Project 3: Computational Analysis of Colorectal Cancer Metastases in Lymph Nodes.

Project 3: Building tools for computer-assisted diagnostics

In addition to exploratory tissue analysis, our team builds, tests and validates in-house, open-source and commercially available algorithms for potential diagnostic use and workflow integration. We are currently running a comparative study on the impact of scanners and performance of different software for Ki-67 detection and quantification. We use deep learning methods for segmentation and metastatic detection in lymph nodes, and streamline processes lab and data analysis processes, for e.g from scanning to construction of «next-generation Tissue Microarrays®» (ngtma.com) to visual presentation of results and analysis. We use graphs and geometric deep learning to learn about tumor budding and lymphocytes, and as part of our collaboration with the International Budding Consortium, generate hot-spot detection and tumor budding quantification algorithms in early stage pT1 cancers.

Internal Collaborations

- Mario Tschan, PhD
- Alessandro Lugli, MD
- Aart Mockhoek, MD PhD
- Heather Dawson, MD
- Philippe Krebs, PhD
- Bastian Dislich, MD
- Philipp Kirchner, PhD

External collaboration

National

- Maria Rodriguez, IBM Research
- Maria Anisimova, ZHAW
- Berend Snjider, ETH Zürich
- Viktor Koelzer, CTP Lab, Institute of Pathology, Unispital Zürich
- Andreas Fischer, DIVA Group, HES-SO and Uni Fribourg
- Center for AI in Medicine (CAIM)
- Martin D. Berger, Oncology, Inselspital
- Jean-Philippe Thiran, EPFL, Lausanne
- Andrew Janowcyzk, CHUV, Lausanne
- Lunaphore Technologies, Switzerland

International

- Iris Nagtegaal & Team, Radboud Medical Center, NL
- Norman Zerbe, Charité Berlin, Germany
- Tilman Rau, Pathologie, Düsseldorf
- Jerome Galon & Immunoscore Team, INSERM, France

Grant support

- Innosuisse, I. Zlobec (Co-PI), 2021–2023, CHF 450'540
- Swiss National Science Foundation, I. Zlobec (PI)/M. Tschan, 2020–2024, CHF 632'000
- Swiss National Science Foundation- SINERGIA, I. Zlobec (PI), M. Anisimova/MMRodriguez/B.Snjider, 2020–2024, CHF 2'875'765
- Swiss Cancer League KFS-5534-02-2022-R, I. Zlobec (Co-PI), 2022–2025, 353'100
- Rising Tide Foundation for Clinical Research, I. Zlobec (PI)/P Thiran, 2018–2022, CHF 290'230
- Swiss Cancer League, I. Zlobec (PI)/JP Thiran, 2018–2022, CHF 361'250
- Swiss Cancer Leage als Co-Applicant mit Prof. Matthias Hediger, I. Zlobec, 2022–2024, 96'930

Administrative duties

- Head of Translational Research Unit (TRU), until 04.2022
- Operative Manager of Tissue Bank Bern (TBB), until 04.2022
- Executive Team Member, Center for AI in Medicine (CAIM)
- Chair, IT Working Group European Society of Pathology (ESP)
- President of the Swiss Consortium for Digital Pathology (SDiPath)
- Member of the Graduate School of Cell Biology and mentor (GCB)
- Member of the Bern Center for Precision Medicine (BCPM)
- Member of the International Budding Consortium (IBC)

Publications

- Noti L, Galván JA, Dawson H, Lugli A, Kirsch R, Assarzadegan N, Messenger D, Krebs P, Berger MD, **Zlobec I.** *A combined spatial score of granzyme B and CD68 surpasses CD8 as an independent prognostic factor in TNM stage II colorectal cancer.* BMC Cancer. 2022 Sep 16;22(1):987. doi: 10.1186/s12885-022-10048-x. PMID: 36114487; PMCID: PMC9482175.
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2 Akademische Grade

PhD Students

- *Annina Bindschedler*
  The Plasmodium Parasitophorous Vacuole Membrane: from Autophagic Targeting to Signaling Platform
  Supervisor: Prof. Volker Heussler
  Mentor: Stefan Freigang
- *Dzhangar Dzumashev*
  Liposomal targeted drug delivery to rhabdomyosarcoma
  Supervisor: Prof. Jochen Rössler
  Mentor: Stefan Freigang
- *Nikita Markov*
  The functional and metabolic consequences of mitochondrial dysfunction in macrophages
  Supervisor: H.U. Simon
  Mentor: M.P. Tschan/J-M Nuoffer
- *Marine Inglebert*
  Investigating canine mammary tumors and patient-derived organoids as a preclinical model for breast cancer
  Supervisor: S. Rottenberg
  Mentor: M.P. Tschan/R. Santoro
- *Darya Karatkevich*
  Increasing the efficiency of chemotherapy for malignant pleural mesothelioma
  Supervisor: T. Marti/R. Schmid
  Mentor: M.P. Tschan/R.B. Johnson
- *Fatemeh Safari*
  Exogenous and intrinsic regulators of bone remodelling
  Supervisor: W. Hofstetter
  Mentor: M.P. Tschan/D. Stroka
- *Mirela Kremenovic*
  Targeting tumor-associated myeloid cells in immunotherapy of melanoma
  Supervisor: M. Schenk
  Mentor: Prof. Dr. Konstantinidou/Prof. Dr. M. Fabri
- *Amjad Khan*
  Computational Analysis of Colorectal Cancer Metastases in Lymph Nodes using Deep Learning Techniques
  Supervisor: I. Zlobec
  Co-supervisor : Jean-Philippe Thiran
- *Elham Kashani*
  Therapeutic alternatives to address brain tumors, a translational and functional investigation
  Suvervisor: Prof. Dr. Pharm. Erik Vassella
  Co-advisor: PD Dr. Thomas Michael Marti
- *Lijuan Ma*
  The Role of EMT in the Alteration of Hormone Response in Endometriotic Lesions and its Contribution to the Recurrence of Endometriosis
  Supervisor: Christoph Mueller
  Co-Advisor: Michael Mueller, Thomas Andrieu

MSc Master of Science

- *Krystina Filipova*
  Mapping the metabolic landscape of pancreatic neuroendocrine tumors (PanNETs)
  Supervisor: Aurel Perren, Martin Sadowski
- *Leonie Weber*
  Histone Deacetylase inhibition in pancreatic neuroendocrine tumors
  Supervisor: Aurel Perren, Ilaria Marinoni
- *Joëlle Schläfli*
  Cell type-specific regulation of IL-1Ra in systemic Candida albicans infection
  Supervisor: Stefan Freigang
- *Fatlind Malsiu*
  Investigating the role of alternative splicing in colorectal cancer development
  Supervisor: Philippe Krebs
  Co-supervisor: Robert Gaultney
- *Silvio John Eugster*
  The differential role of IL-33 in colorectal cancer development
  Supervisor: Philippe Krebs
  Co-supervisor: Vivian Vu & Robert Gaultney
- *Océane Derivaz*
  Regulation of lymphocytic cells during inflammation and infection
  Supervisor: Philippe Krebs
  Co-supervisor: Wen Jie Yeoh
- *Ibai Lertxundi*
  Deep Learning to quantitatively study the prognostic value of the tumor stroma ratio in rectal cancer patients treated with neoadjuvant therapy. A preliminary study.
  Supervisor: Inti Zlobec
  Co-supervisor: Andrew Janowczyk
- *Elia Rossini*
  Resistance mechanisms in glioblastoma
  Supervisor: Prof. Dr. Pharm. Erik Vassella
- *Huijuan Wang*
  PARPi enhances temozolomide sensitivity in WRN-deficient glioblastoma cells
  Supervisor: Prof. Dr. Pharm. Erik Vassella

BSc Bachelor of Science

- *Danai Kokona*
  Consecutive treatment of KDM5 and HDAC inhibitors plus Cisplatin in Pancreatic Neuroendocrine Tumor cell lines
  Supervisor: Ilaria Marinoni

M Med Master of Medicine

- *Alexandra Bürgler*
  Sensitization of MCF-7 cells to differentiative therapy with ATRA by knockdown of HDAC genes
  Supervisor: M. P. Tschan
  Mentor: A. Schläfli
- *Luca Noti*
  A combined spatial score of granzyme B and CD68 surpasses CD8 as an independent prognostic factor in TNM stage II colorectal cancer
  Supervisor: Inti Zlobec
- *Melanie Bächli*
  Refining the ITBCC tumor budding scoring system with a «zero-budding» category in colorectal cancer
  Supervisor: Inti Zlobec
  Co-supervisor: Martin Berger
- *Gaëlle Rhyner Agocs*
  LAG-3 Expression Predicts Outcome in Stage II Colon Cancer
  Supervisor: Inti Zlobec
  Co-supervisor: Martin Berger

MD Doctor of Medicine

- *Lukas Bauer*
  Primary human bone marrow-derived mesenchymal stromal cells' collagen expression and proliferation in response to cytokines released by IL33-stimulated megakaryocytic cells
  Supervisor: Yara Banz & Philippe Krebs
  Mentor: Coline Nydegger

Andere

- *Antonio Rodriguez-Calero*
  Dr.med.
  Tumour heterogeneity and prognostic significance of PD-L1 expression in metastasizing urothelial bladder carcinoma
  Supervisor: Prof. Dr.med. Achim Fleischmann
- *Gian Ziegelmüller*
  Dipl. BMA
  Cloning of different DMTF1beta rescue constructs and functional analysis thereof
  Supervisor: M.P. Tschan
  Mentor: A. Schläfli

3 Publikationen

Originalarbeiten In-House

- Abbet C, Studer L, Fischer A, Dawson H, Zlobec I, Bozorgtabar B, Thiran JP
  Self-rule to multi-adapt: Generalized multi-source feature learning using unsupervised domain adaptation for colorectal cancer tissue detection.
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- Kremenovic M, Chan AA, Feng B, Bäriswyl L, Robatel S, Gruber T, Tang L, Lee DJ, Schenk M
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- Noti L, Galván J, Dawson H, Lugli A, Kirsch R, Assarzadegan N, Messenger D, Krebs P, Berger MD, Zlobec I
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4 Vorträge

Simon April
- 15.09.2022, Swiss NET Annual Conference: «Patient-derived tumoroids mimic original GEP-NENs and facilitate in vitro drug screening»

Paulina Brönnimann
- 04.09.22, European Congress of Pathology: «Next-generation Tissue Microarrays (ngTMA®): from scientific discoveries to clinical practice»

Heather Dawson
- 10.2022, Dermatopathology Essentials: «AI in Pathology»
- 09.2022, ECP Basel: «Joining forces – the Bern experience»
- 08.2022, Pathologists for Ukraine (IAP): «Challenging issues in colorectal cancer reporting»
- 03.2022, SGPath/IAP Molecular Pathology Training School: «Molecular Pathology of Gastrointestinal Tumors»
- 02.2022, DACH Symposium: «Digital Pathology: the Bern Experience»

Philippe Krebs
- 07.03.22, Seminar, Lipides Nutrition Cancer (LNC), Université Bourgogne Franche-Comté, Dijon, France: «Cytokine-dependent immunoregulation in cancer and pathology»
- 12.05.22, BCPM project update webinar, University of Bern: «Investigation of the local and systemic immune system regulation in COVID-19»
- 09.06.22, DISCOVER (consortium) meeting, Lipides Nutrition Cancer (LNC), Université Bourgogne Franche-Comté, Dijon, France: «Generation of natural killer cell-mimic nanoparticles to target tumor cells»
- 25.06.22, Villa Vigoni Cell Death Meeting, Loveno di Menaggio: «Cytokine-dependent immunoregulation in cancer and pathology»
- 30.06.22, Seminar, Clinics of Hematology, Inselspital, University Hospital Bern: «The IL-33/ST2 pathway promotes fibrosis in the MPN bone marrow»

Tereza Losmanova
- 28.10.22, Fortbildungsveranstaltung der Universitätsklinik für Pneumologie und Allergologie: Transbronchiale Kryobiopsie aus der Sicht des Pathologen: Vorteile und Limitationen

Ilaria Marinoni
- 28.04.2022, NET Cancer Foundation Monthly Seminar: «Toward precision medicine in PanNET: epigenetics and patient derived tumoroids»
- 20.05.22, NET Cancer Foundation Annual Summit: «Patient derived tumoroids as a new tool for precision medicine in Neuroendocrine Neoplasms»
- 29.06.2022, ENETs Webinar: «Role of molecular testing for individualizing therapy in GEP and thoracic NENs: Potential application in NEC»
- 15.09.2022, Swiss NET Annual Conference: «Epigenetic progression steps in alpha-lineage MEN1-DAXX/ATRX mutated Pancreatic Neuroendocrine Tumors (PanNET)»

Aart Mookhoek
- 05.09.22, 34th European Congress of Pathology: «Joint Slide Seminar Digestive Diseases Pathology in collaboration with ECCO: Complications of inflammatory bowel diseases, Case 6»

Aurel Perren
- 19.02.22, ENETS postgraduate Course, Barcelona: «Live multidisciplinary Tumorboard»
- 01.04.22, Curriculum Endokrinologie, Inselspital: «Pathologie neuroendokriner Neoplasien»
- 02.05.22, SBP Dataset Workshop, SNF Bern: «Working group Tissues in SBP Dataset Workshop»
- 10.06.22, DGP 105. Jahrestagung 2022, Münster: Moderation DGP Session «Automation»
- 01.07.22, Abschiedssymposium Prof. Müller: «A pathologist's view on immunology»
- 02.07.22, Basel Seminars in Pathology 2022, Daily Practice in Gastrointestinal Pathology: «Neuroendocrine Tumors of the GI Tract – The Essentials, Daily Practice in Gastrointestinal Pathology»
- 06.09.22, 34th European Society of Pathology, Basel: «High grade well differentiated neuroendocrine neoplasms: in every organ?»
- 15.09.22, SGG-SGVC-Kongresse, Interlaken: «Neuroendocrine Tumors, what's new in …»
- 21.10.22, Co-Creation Workshop, Penzberg: «Lean, innovativ, digital und patientennah: Wann ist die Zeit reif für eine Entwicklung der Pathologie in Richtung Gewebemedizin?»
- 24.11.22, IAP, 21. Juniorakademie, Bonn: «Endokrine Pathologie»

Mirjam Schenk
- 08.02.22, Symposium Stiftung Experimentelle Biomedizin, University of Zürich: «Mycobacteria-derived immunotherapies in the treatment of melanoma»
- 11.10.22, CK-CARE Meeting 2022, Davos: «Discovering novel mechanism of immune regulation using high dimensional data»

- 11.11.22, Research meets Clinic, Annual Meeting 2022, SCRM Platform: «Melanoma Pathology and Clinical Needs; Hydrogel treatment»

Wiebke Solass
- 13.10.22, ISSPP congress, LA, USA: «Histologic and Molecular Implications on Ovarian Cancer Treatment»
- 14.10.22, ISSPP congress, LA, USA: «Tumor Microenvironment in Peritoneal Mesothelioma»
- 11.11.22, Zürich SGPath Annual meeting: «SGPath Slide seminar- Case 1 and 2»

Mario Tschan
- 04.10.22, Feria de Investigación IMSS. Mexico: «Autophagy in Breast Cancer Cell Viability and Motility» Youtube: https://www.youtube.com/watch?v=fMj9uX7W_dE
- 14.11.2022, Blood Research Program Research Day-2022: «Non-Canonical hexokinase and autophagy functions in therapy responses of myeloid malignancies»

Erik Vassella
- 06.09.22, ESP: «Evaluation of the TruSight Oncology 500 assay for clinical research use»
- 21.06.22, 47. Hirslanden Academy: «Molekulare Marker beim Lungenkarzinom»

Jun Xu (Mario Tschan)
- 31.05.2022, CFATG9 Autophagy Meeting, Besancon: «BNIP3L/NIX, a downstream effector of oncogene-induced cancer cell autophagy and invasion»

Inti Zlobec
- 04.09.22, European Congress of Pathology: «2001: A Digital Pathology Odyssey»
- 18.09.22, MICCAI 2022 CLINIICCAI Symposuim: «Tissue Medicine Goes Digital»
- 29.09.22, European Congress of Veterinary Pathologists: «Tissue microarrays in the era of digital pathology: useful or useless»
- 24.10.22, European Congress of Computer Vision (ECCV): «2001: A Digital Pathology Odyssey»
- 04.09.22, European Congress of Pathology: «Ki-67 in breast cancer / e-validation using IBCSG8/9 clinical trials»
- 10.09.22, Clinical Neurosciences Bern: «2001: A Digital Pathology Odyssey»
- 17.06.22, European Congress of Digital Pathology: «Allied Societies: the European Society of Pathology: Working Group IT (computational)»

5 Drittmittel

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

Rupert Langer PI, Erik Vassella Co-PI
- SAKK 75/08, 2018-2025, CHF 132'640

Sabina Berezowska PI, Erika Vassella Co-PI
- Swiss Cancer League, 2019-2024, CHF 365'500

Theoni Maragkou (PI)
- Krebsliga Bern, 2022–2023, CHF 67'500
- Stiftung für klinisch-experimentelle Tumorforschung, 2022–2023, CHF 32'500

Ren-Wang Peng (PI), Erika Vassella Co-PI
- Bern Center for Precision Medicine (BCPM), 2022–2024, CHF 130'000

Antonio Rodriguez-Calero
- Prostate Cancer Foundation, 2021–2023, $ 225'000 per year

Bastian Dislich
- Stiftung für klinisch-experimentelle Tumorforschung Influence of neoadjuvant chemotherapy on the immunogenicity of esophageal adenocarcinomas, 2019–2023, CHF 120'000, Verlängerung bis 30.6.2023

Heather Dawson
- Rising Tide Fondation A combined budding/T-cell score in pT1 and stage II colorectal cancer, 2018–2022, CHF 108'984

Tereza Losmanová
- DNA Methylierungsmuster Lungenkarzinom-Hirnmetastasen, Alfred und Anneliese Sutter-Stöttner Stiftung, 2022–2023, CHF 59'221

Martin Wartenberg
- Stiftung für Klinisch-experimentelle Tumorforschung, Examining the impact of microRNA-29-family members on tumor budding, immunosuppression and desmoplastic stroma in pancreatic ductal adenocarcinoma, 2020-2023, CHF 60'000

Konstantin Bräutigam
- Expressionsanalyse von alternativen SARS-CoV-2-Rezeptor-molekülen im menschlichen Atemtrakt, Jubiläumsstiftung von Swiss Life, 2022–offen, CHF 10'000

Wiebke Solass
- HER2 low assessment in breast cancer, 12.2022–04.2023, CHF 24'964, PI: Wiebke Solass, shraed with TRU, Digital pathology department -funding by Astra seneca

Stefan Freigang (PI)
- Swiss National Science Foundation, 2020–2024, CHF 632'000
- Swiss Lung Liga, 2017–2022, CHF 162'000
- Swiss Heart Foundation, 2020–2022, CHF 50'000

Philippe Krebs
- Fondazione San Salvatore Project grant, 2022-2024, CHF 170'000
- Werner & Hedy Berger-Janser Stiftung Project grant, 2022, CHF 79'796, Main PI: Robert Gaultney
- Seal of Excellence Fund (SELF) UniBE, 2021–2023, CHF 128'698, Awarded to R. Gaultney (fellowship)
- Swiss Life Project grant, 2021–2023, CHF 20'000
- Uniscientia Project grant, 2021–2023, CHF 136'000
- Swiss National Science Foundation Project grant, 2020–2024, CHF 632'000
- EU/Marie Skłodowska-Curie RISE grant Project grant, 2018–2022, Euro 904'500*

Mirjam Schenk (PI)
- Swiss National Science Foundation, 2020–2024, CHF 566'109
- Novartis Foundation for medical-biological research, 2018–2022, CHF 52'000
- Stiftung experimentelle Biomedizin, 2016–2022, CHF 1'560'000

Inti Zlobec (Co-PI)/Mario P. Tschan (Co-PI)
- SNSF_310030_197786, 2020–2024, CHF 632'000*
- Swiss Government Excellence Scholarship, 2021–2024, CHF 90'000*
- Swiss National Science Foundation 310030_197786, 2021–2025, CHF 632'000*

B. Towbin (Co-PI)/Mario P.Tschan (Co-PI)
- UniBE ID Grant, 2022–2023, CHF 109'000*

M.P. Tschan
- China Scholarship Council Fellowship (Jun Xu), 2021–2024, CHF 90'000
- China Scholarship Council Fellowship (Shun Yi), 2022–2025, CHF 90'000

Aurel Perren (PI)
- SNF 310030_188639, 2020–2024, CHF 632'000

Aurel Perren (PI)/Ilaria Marinoni (Co-PI)
- KLS-4227-08-2017, 2018–2022, CHF 395'450*

Martin Sadowski
- Swiss Cancer League, 2022–2025, CHF 359'000

Ilaria Marinoni
- Bern Center for precision Medicine, 2022–2024, CHF 174'000, Co-Principal Investigator: Nadia Mercader, Corina Kim-Fuchs
- ENETs CO-Synergy Award, 2019–2022, Euro 69'700

Inti Zlobec (Co-PI)
- Swiss Cancer League KFS-5534-02-2022-R, 2022–2025, CHF 353'100*
- Swiss Cancer League KFS-4427-02-2018, 2018–2022, CHF 361'250
- Swiss National Science Foundation CRSII5_193832, 2020–2024, CHF 2'875765*
- Rising Tide Foundation for Clinical Cancer Research, 2019–2022, CHF 290'230*
- Innosuisse; Investigation of Tumor Budding in Colorectal Cancer for Personalized, 2021–2023, CHF 450'540

Inti Zlobec Co-Applicant mit Prof. Matthia Hediger
- Swiss Cancer Leage als Co-Applicant mit Prof. Matthia Hediger, 2022–2024, CHF 96'930*

Alessandro Lugli (PI) / M. Schürch (Co-PI)
- Swiss Cancer Research, 2021–2023, CHF 331'500*

Alessandro Lugli
- Dutch Cancer Society, 2017–2022, EUR 1'600'246, Co-Applicant

Christoph Müller (PI)
- SNF 314730_189277, 2019–2022, CHF 516'667, Project completed by December 31, 2022

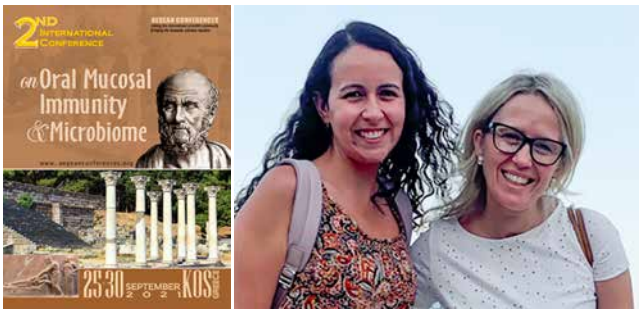
Juliana Barreto de Albuquerque (Gruppe Müller)
- Novartis, 2021–2022, CHF 51'182, Project completed by December 31, 2022

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

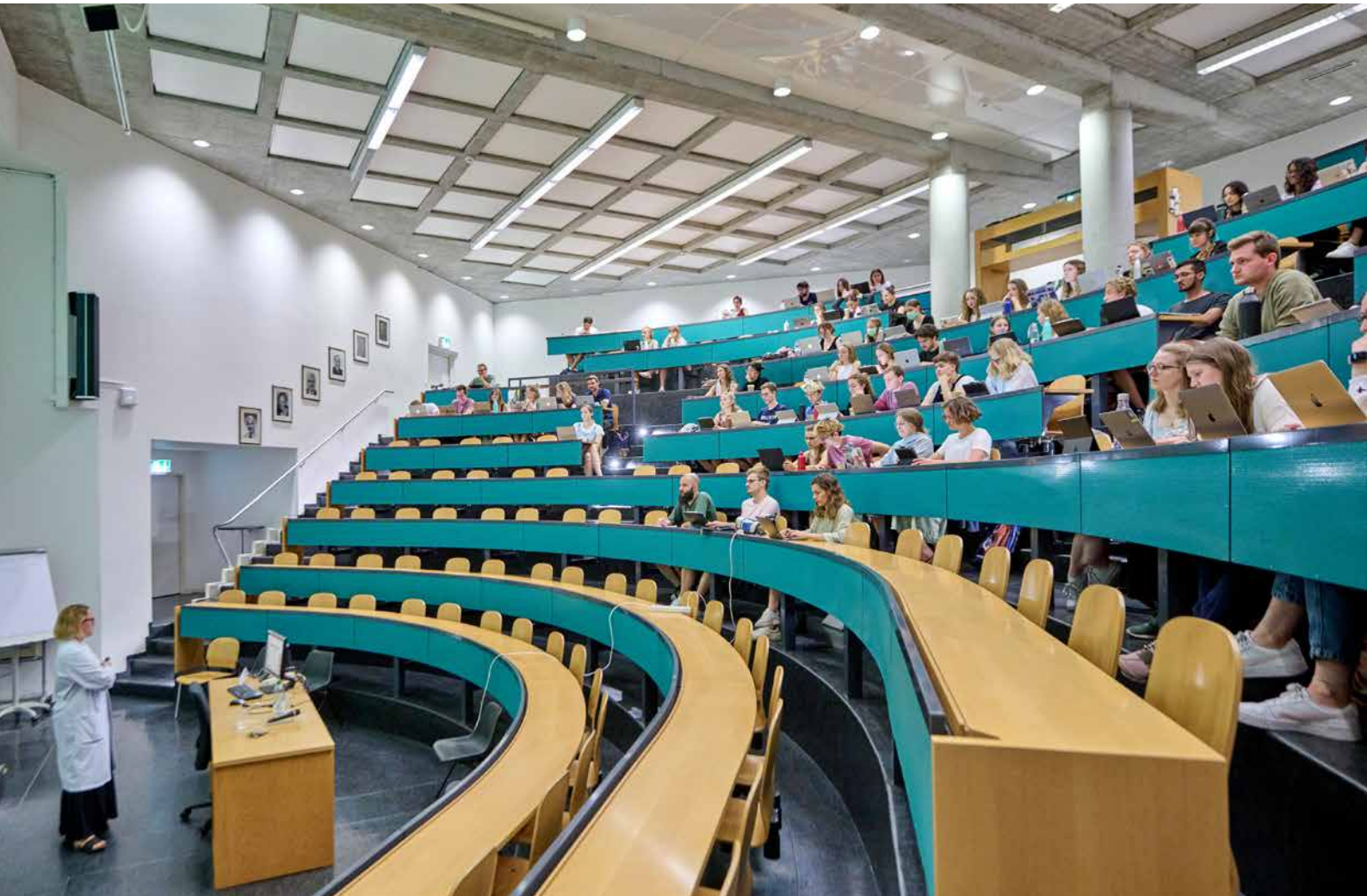
6 Preise, Ernennungen, Auszeichnungen

- Im März hat *Philipp Zens* für seine Dissertation von der Medizinischen Fakultät den Titel eines Doctor Medicinae (Dr. med.) erhalten
- *Prof. Inti Zolbec* wird offizielle Gleichstellungsbeauftragte für das Institut für Pathologie
- Per 1. April 2022: Ausserordentliche Professur für Digitale Pathologie für *Prof. Inti Zlobec*
- *Antonio Rodriguez* hat im August den Facharzttitel Pathologie erreicht
- *M Med Theoni Maragkou* hat im September das Weiterbildungsdiplom mit interdisziplinärem Schwerpunkt Neuropathologie erhalten
- *Dr. med. Tereza Losmanovà* hat im September die Facharztprüfung Pathologie bestanden
- Im Dezember hat *Simon April* seine Dissertation als PhD abgeschlossen.
- *PD Dr. Ilaria Marioni, PhD:* First Price for the best oral presentation in Basis Science, 1st International NET forum
- *Simon April:* Third Price for the best oral presentation in Basis Science, ENETs Annual conference
- *Jun Xu*, 31.5.2022, CFATG Travel Grant Award, 10th French Autophagy Meeting (CFATG) 2022
- *Juliana Barreto de Albuquerque:* Best oral presentation, 2nd International Conference on «Oral Mucosal immunity and Microbiome»

Simon April at the ENETs Annual Conference.



Juliana Barreto de Albuquerque and Nagy Bostancy (Organizer) in Greece at the 2nd International Conference on «Oral Mucosal immunity and Microbiome».



>>> Studentische Lehre

Yara Banz und Philippe Krebs

«If you think education is expensive, try ignorance"

Wer Erstautor dieser Aussage war, bleibt etwas umstritten. Unumstritten ist sicher die Tatsache, dass diese Aussage absolute Richtigkeit hat.

Das Strategieziel der Universität Bern (Teilstrategie 3; Strategie 2021 der Universität Bern) den Standplatz Bern in der Lehre zu fördern, widerspiegelt die Wichtigkeit und Wertigkeit der Lehre und ist absolut im Einklang mit den Zielen, die wir in der studentischen Lehre (und Lehre allgemein am Institut für Pathologie) schon seit Jahren verfolgen.

Das Fach Pathologie setzt den Grundstein der allgemeinen Krankheitslehre im 3. Studienjahr des Medizinstudiums und führt dann im 4. und 5. Studienjahr über in die spezielle Pathologie. Das Fach selber ist aber auch in anderen Studiengängen, so zum Beispiel in der Zahnmedizin und Studiengängen der philosophisch-naturwissenschaftliche Fakultät sehr präsent.

Ein Team aus Fachärzt:innen, jungen Kolleg:innen in der fachspezifischen Weiterbildung, Mitarbeitenden in den Forschungsgruppen, Laborpersonal und Assissten:innen in der Lehre garantiert, dass die weit über 100 Vorlesungen, Kurse und Praktika jedes Jahr problemlos koordiniert werden und das Wissen mit Fachkompetenz und Elan an die jungen Studierenden diverser Fachrichtungen weitergegeben wird. Nebst der allgemeinen und speziellen Pathologie wird Wissen in Molekularpathologie, Tumorpathologie sowie diversen Spezialgebieten wie die Zytopathologie angelehnt an die aktuellsten Forschungsdaten und relevanten Studien, weitervermittelt.

Die Herausforderungen an die Lehre in Pathologie waren auch 2022 gross. Es gilt Histologiepraktika, Kurse in Makropathologie, Vertiefungsseminare mit Führungen durch das Institut, zahlreiche Vorlesungen und Fachpraktika im klinisch-diagnostischen Alltag zu integrieren und den jungen Studierenden nicht nur das fachlich-Inhaltliche sondern auch eine reelle Abbildung des Berufsbildes und des Alltags einer universitären Pathologie zu wiedergeben.

Ruhen wir uns nicht auf den Lorbeeren der zahlreichen positiven Rückmeldungen aus, die uns in Form von strukturierten Feedbacks erreicht haben. Die Dozierenden nehmen auch kritische Stimmen wahr und so setzen wir uns als Ziel für das kommende Jahr, weiterhin auf der guten Basis aufzubauen.

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 einem mehrjährigen strukturierten Unterricht, der die Kenntnisse und das Verständnis für Mechanismen, Zusammenhänge und Morphologie von Erkrankungen vermittelt. Die makroskopischen Kurse im 4. Studienjahr dienen dabei der Vertiefung der Inhalte der Vorlesungen und erlauben es, makroskopische Präparate aus der umfassenden Sammlung zu «begreifen». Komplementär wird den Studierenden anhand eingescannter histologischer Präparate die virtuelle Mikroskopie nähergebracht und erlaubt die Besprechung weiterer wichtiger Krankheitsbilder.

Im 3. Studienjahr, dem letzten Jahr des Bachelor-Teils des Medizinstudiums werden den Studierenden die Grundlagen der allgemeinen Pathologie vermittelt (Einführungskurs 2). Diese Vorlesungen sind in interdisziplinäre Vorlesungsveranstaltungen eingebettet, wobei die verschiedenen Themen im Kontext spezieller Themenblöcke behandelt werden. Diese theoretischen Kenntnisse werden im Rahmen Fachpraktika Pathologie vertieft, wo die entsprechenden wesentlichen morphologischen Veränderungen studiert 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 folgt die systematische Aufarbeitung der speziellen Pathologie. Hier wird zunächst im 4. Studienjahr (Einführungskurs 2) sowie im 4./5. Studienjahr (BK1 und BK2) organ- bzw. systembezogene Pathologie gelehrt. Anhand von theoretischen Vorlesungen und praktischen Kursen vertiefen die Studierenden ihre Kenntnisse. Wöchentlich finden dabei nebst den Histologiekursen auch Autopsiedemonstrationen statt, bei denen anhand aktueller Fallbeispiele die aktive Erarbeitung pathophysiologischer Zusammenhänge und Sequenzen verschiedenster Krankheiten im Vordergrund steht. Diese Demonstrationen sind nach wie vor ein essentieller Eckpfeiler in der Ausbildung. Allen Multimedien und technischen Errungenschaften zum Trotz: hat man mal die Gelegenheit eine schwergeschädigte Lunge nach Covid-19 Pneumonie in die Finger zu nehmen und zu ertasten, erübrigen sich viele Erklärungen und Beschreibungen: man begreift – wortwörtlich – die Erkrankung. Dieses hautnahe Erleben und Begreifen der Erkrankungen,

diese wichtigen klinisch-pathologischen Diskussionen sollen auch in Zukunft den Studierenden helfen Grundlagen, Zusammenhänge und klinische Aspekte besser zu verstehen.

Auch am Ende des Medizinstudiums, kurz vor dem Staatsexamen im 6. Studienjahr können Studierende ihre Kenntnisse im Fach Pathologie vertiefen in Form eines Wahlstudienjahrpraktikums. Im Minimum besteht ein solches Angebot für einen Monat bis hin zu einem viermonatigen Praktikum. Während dieser Zeit wird den Studierenden ein strukturiertes Curriculum angeboten, welches ihnen erlaubt das ganze Spektrum der histopathologischen, zytopathologischen, molekularpathologischen wie auch postmortalen Diagnostik kennen zu lernen.

Dank Innovation in der Lehre, dem Aufgleisen neuer Lehrinhalte in Form von Fall-basiertem Lernen (in Form eines nun erfolgreich gestarteten Pilotprojektes), werden die 100 zusätzlichen Studierenden auch in Zukunft gut im Fachgebiet der Pathologie ausgebildet werden können. Insbesondere im Bereich der Makropathologieausbildung und der Lehre pathophysiologischer Zusammenhänge wird auf Grund der zurückgehenden Autopsien in Zukunft innovative Lehre gefördert sein.

Den Studierenden der Zahnmedizin werden im 3. Jahr sowohl die Allgemeine Pathologie, als auch die spezielle Pathologie einzelner wichtiger Organsysteme in Form einer Vorlesungsserie Pathologie vermittelt. Im 5. Studienjahr werden zudem spezielle orale Pathologien in weiteren Vorlesungen behandelt.

Studiengänge der Philosophisch-Naturwissenschaftliche Fakultät und der Graduierten Schule

Die Mitarbeitenden der experimentellen und klinischen Pathologie sind auch an der Ausbildung der Studierenden der philosophisch-naturwissenschaftlichen Fakultät (Phil.-nat.) der PhD/MD-PhD Studenten der Graduierten Schule GCB (Phil-nat., Vetsuisse, Med Fak.) beteiligt. Diese Lehrveranstaltungen werden meist in einem Modulformat angeboten, so dass Studierende verschiedener Fächer gleiche Vorlesungsreihen besuchen können.

1. Seminarreihen

- Bern Immunology Club, BIC
  (Vorträge externer Seminargäste, monatlich)
- DBMR Research Conference
  (Vorträge externer Seminargäste, monatlich)

2. Vorlesungsreihen im Fachgebiet Pathologie

Zu Gunsten der phil. nat. Fakultät der UniBE werden von Dozierenden des Instituts für Pathologie folgende Vorlesungsreihen im Modulformat angeboten und koordiniert:

2.1. Allgemeine Pathologie und Histologie

Koordinator: Philippe Krebs

Dozierende: aus dem Institut für Pathologie, aus anderen Instituten auf dem Campus vom Inselspital und aus dem Institut für Anatomie, Universität Bern.

Studierende: BSc, MSc und PhD Studierende der Zell Biologie und Biomedical Sciences.

Allgemeine Übersicht:

- General introduction to anatomy and histology
- Molecular mechanisms of pathology
- Tumor biology and molecular oncology
- Practical and interactive classes on histology and pathology

2.2. Selected Topics in Molecular Pathology

Koordinator: Erik Vassella

Dozierende: aus dem Institut für Pathologie der Universität Bern und Universitätsspital Basel, Department für Biomedizinische Forschung (DBMR) und Inselspital Bern.

Studierende: BSc, MSc und PhD Studierende der Zell Biologie und Biomedical Sciences.

Allgemeine Übersicht:

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

3. Studiengänge der Medizinischen Fakultät («Biomedical Sciences»)

Vorlesungsreihe im Fachgebiet Biomedizinische Wissenschaften (Study director: S. Rohr, Physiologie; Co-directors: A. Berzigotti, UVCHM, M.P. Tschan, Pathologie)

3.1. Tumorbiologie

Koordinator: Mario P. Tschan

Dozierende: aus dem Institut für Pathologie, Institut für Pharmakologie und Department für Biomedizinische Forschung (DBMR), Universität Bern.

Studierende: BSc, MSc Studierende Biomedical Sciences.

Allgemeine Übersicht:

- Cellular mechanisms of tumor development and metastasis
- Basics of proteomics and bioinformatics
- Animal and cell models

4. Vorlesungen und Seminare der Graduate School for Cellular and Biomedical Sciences (GCB)

4.1. Topics in Tumor Biology

Koordinator: D. Stroka, Y. Zimmer, M. P. Tschan

Dozierende: aus dem Institut für Pathologie, Department für Biomedizinische Forschung (DBMR) und Inselspital Bern, Vetsuisse, Universität Bern.

Studierende: MSc und PhD Studierende der GCB, Zellbiologie und Biomedical Sciences.

Allgemeine Übersicht:

- Basics of Tumor Biology

4.2. Translational Cancer Research

Koordinator: N. Leupin, M. P. Tschan
Dozierende: M.P. Tschan (Institut für Pathologie), N. Leupin (CMO Molecular Partners), wechselnde Dozierende aus der Privatindustrie
Studierende: MSc und PhD Studierende der GCB, Zellbiologie und Biomedical Sciences.

Allgemeine Übersicht:

- Introduction to translational cancer research
- Drug target identification and validation
- Principles and challenges of drug development
- Clinical trials
- Models of academia and industry collaborations
- Pharmaceutical start up models

4.3. Bern Cancer Research Cluster (BCRC) – progress reports

Wöchentlich, online Koordination: T. Marti (DBMR), M. Tschan (Pathologie)
Teilnehmer: Gruppenleiter, Postdocs, Master- und PhD-Studenten der folgenden Institute: Institut für Pharmakologie, Institut für Pathologie, Institut für Anatomie, Vetsuisse, Department für Biomedizinische Forschung (DBMR), Theodor Kocher Institut (TKI), Medizinische Onkologie, Nuklearmedizin.

- The main goal of these progress reports from students working in cancer research groups in Bern it to discuss their projects (including technical problems, suggestions, inputs,…) with their colleagues.

4.4. Bern Cancer Research Cluster (BCRC) – Journal Club

Monatlich, online Koordination: M. Medova (Radio-Onkologie)
Teilnehmer: Master- und PhD-Studenten der folgenden Institute: Institut für Pharmakologie, Institut für Pathologie, Institut für Anatomie, Vetsuisse, Department für Biomedizinische Forschung (DBMR), Theodor Kocher Institut (TKI), Medizinische Onkologie, Nuklearmedizin.

- This monthly «lunch» journal club will allow PhD/MSc students to discuss the latest break troughs in cancer research. Moreover, it will allow for informal networking among students during lunch.

4.5. Principles in Transgenic Mouse Technology

Zweitägiger Kurs
Koordinator: C. Benarafa (IVI), U. Deutsch (TKI), P. Krebs (Pathologie)
Introduction on transgenic mice, their usefulness in research, as well techniques used to generate genetically modified mice.
Teilnehmer: Master- und PhD-Studenten und Mitarbeitende der folgenden Institute: Institut für Pharmakologie, Institut für Pathologie, Institut für Anatomie, Vetsuisse, Department für Biomedizinische Forschung (DBMR), Theodor Kocher Institut (TKI).

5. Weitere Lehrveranstaltungen

Dozierende der Experimentellen Pathologie unterrichten zudem in Lehrmodulen, die von anderen Instituten koordiniert werden, wie im 3-wöchigen experimentellen Praktikum «Practical Course in Immunology» des Instituts für Zellbio-logie (phil. nat. Fakultät), dem Kurs «Cellular and Molecular Immunology» der Universitätsklinik für Rheumatologie und Immunologie, dem Themenblock «Blut und Abwehr» im 2. Studienjahr Medizin und dem dazu gehörenden Lerngruppenunterricht (PBL) im 2. und 3. Studienjahr. Ferner sind Dozierende des Instituts an der Ausbildung von Studierenden des «Masters in Artificial Intelligence in Medicine» und des «Masters in Bioinformatics» beteiligt.

>>> Weiterbildung

Das Institut für Pathologie der Universität Bern ist SIWF-zertifizierte Weiterbildungsstätte für das Fachgebiet Pathologie, Zytopathologie und Molekularpathologie. Das Institut ist ausserdem als Weiterbildungsstätte der Kategorie A für Neuropathologie anerkannt. Die individuelle Weiterbildung wird in erster Linie täglich mit den Assistierenden in einer 1:1 Situation am Doppelmikroskop im Rahmen der Fallabgabe geleistet, dies vor allem durch die stringente Arbeitsorganisation im Diagnostikbereich, wo jeweils eine Oberärztin oder Oberarzt mit einem Assistierenden zusammenarbeitet. Zusätzlich wird die systematische Erarbeitung der organspezifischen Themengebiete durch verschiedene Weiterbildungsangebote abgedeckt. An der sogenannten strukturierten Weiterbildung beteiligen sich sämtliche Kolleginnen und Kollegen der Methoden (Zytopathologie und Molekularpathologie) bzw. der organspezifischen Fachgruppen. Die Fachgruppen sind jeweils fokussiert auf Mamma- und Gynäkopathologie, Gastrointestinalpathologie, Nephropathologie, Uropathologie, HNO-/Ophthalmopathologie, Endokrinopathologie, Hämatopathologie, Weichteil- und Knochenpathologie, Herz-, Gefäss- und Rheumapathologie, Leberpathologie, Pankreaspathologie, Lungenpathologie, Dermatopathologie, Pädopathologie sowie Neuropathologie.

In diesem dritten Jahr der Pandemie fanden Weiterbildungen für Ärztinnen und Ärzte praktisch ausschliesslich online oder als Hybridangebot (Präsenz mit Zertifikat) statt. Die im vergangenen Jahr vorgenommene Neuausrichtung hin zu monatlich wechselnden Themengebieten ist bei allen Mitarbeitern sehr gut angekommen und hat sich als effektiv und effizient bewährt. Einerseits ergibt sich die Möglichkeit sich über eine längere Zeit vertieft mit einem Thema zu befassen und die theoretischen Grundlagen dazu zu erarbeiten oder aufzufrischen. Das Herzstück unserer strukturierten Weiterbildung ist die Zeit zwischen 08:30 und 09:00 Uhr im Rahmen des Morgenrapports. Dort werden täglich digital verfügbare Fälle zum entsprechenden Themengebiet gezeigt. Einige Veranstaltungen, wie Molekularpathologie oder digitale Bildanalyse, Organoide, neue Methoden zur Evaluation prädiktiver Marker, sind eher theoretisch. Darüber hinaus sind Vorträge über Publikationen, im Rahmen von Journal Clubs, und wissenschaftliche Resultate, im Rahmen von Progress Reports, zum entsprechenden Themengebiet integriert, sodass die Assistierende erste wissenschaftliche Erfahrungen sammeln können.

Komplementär zu Mikroskopie gibt es jeden Tag von 13:00 bis 13:15 Uhr eine Gelegenheit für alle Assistenten makroskopisch Präparate zu besprechen. Teilweise wird diese Zeit auch genutzt um systematisch das Vorgehen bestimmter OP-Präparate für jüngere 1. oder 2. Jahresassistenten zu erläutern. Davon profitieren sowohl die erfahrenen Assistenten, quasi als Tutoren, wie auch die jüngeren Assistenten. Eine Oberärztin/Oberarzt ist stets als Supervisor dabei.

Ein weiteres Angebot sind die monatlichen Seminare für Assistierende, bei welchen an einem Abend ein Thema vertieft besprochen wird. Diese wurden in Präsenz unter gegebenen Schutzmassnahmen durchgeführt.

Seminare für Ärzteschaft

Monat	Referierende	Thema
Januar	P. Brönnimann	**Translational Research Unit**
Februar	Y. Banz	**Herz-, Gefäss- und Rheumapathologie**
März	A. Perren	**Endokrinopathologie**
April	Y. Banz	**Hämatopathologie**
Mai	A. Lugli	**Gastrointestinalpathologie**
Juni	T. Maragkou	**Neuropathologie**
Juli	M. Montani/M. Wartenberg	**Leber- und Pankreaspathologie**
August	C. Saganas	**Nephropathologie**
September	M. Trippel	**Mamma- und Gynäkopathologie**
Oktober	Assistenzärzte	**Fallvorstellungen aus dem diagnostischen Alltag**
November	A. Rodriguez/T. Grob	**Uropathologie und Molekularpathologie**
Dezember	O. Stanowska	**HNO-Pathologie**

>>> Fortbildung

In den während des Semesters montags stattfindenden Seminaren (11:45 bis 12:45 Uhr) gewähren uns Referenten aus dem In- und Ausland Einblicke in ein sehr breites Themenspektrum der klinischen und experimentellen Pathologie sowie anderer Fachgebiete.

Diese Veranstaltungsreihe war in diesem Jahr teils als online und teils als hybride Veranstaltung durchgeführt, welche für alle ein wertvolles Zusammentreffen ermöglichte. Immer in Abhängigkeit von den Entscheidungen des Bundesrates und den Vorgaben der Uni wurde mehrmals wieder auf ein reines Online-Format umgestellt.

Zudem fanden für die Mitarbeitenden des Labors der klinischen Pathologie, des Sekretariats und des Krebsregisters monatliche Fortbildungsveranstaltungen zu verschiedenen Fachbereichen der Pathologie statt, welche von den jeweiligen Fachspezialistinnen und Fachspezialisten gehalten wurden.

Montagsseminare für Ärzteschaft

Datum	Titel	Referierende
24.01.	**Mycobacteria derived immunotherapies in the treatment of melanoma**	Prof. Dr. phil. nat. Mirjam Schenk
28.03.	**Friend or Foe? S100 antimicrobial peptides in inflammation and tumorigenesis**	Ronald Wolf, MD
02.05.	**Spatially-resolved single-cell assessment of pancreatic cancer expression subtypes reveals co-expressor phenotypes and profound intra-tumoral heterogeneity**	Dr. Hannah Williams
30.05.	**NFAT5 induction by the tumor microenvironment enforces CD8 T cell exhaustion**	Dr. Grégory Verdeil
27.06	**In vivo analysis of dynamic CD8+ T cell-mediated immunity**	Prof. Jens Stein, PhD
26.09.	**FcRγ promotes antitumor functions of NK cells by limiting its adaptive program linked to human cytomegalovirus infection**	Dr. Vikas Duhan
17.10.	**Investigating the role of mitochondrial energy remodelling throughout prostate cancer progression and therapeutic resistance**	Dr. Charles Bidgood
07.11.	**Introduction to ACD RNAscope technology**	Dr. Vladimir Zlateski
21.11.	**The ex ovo Chicken Chorioallantoic Membrane Assay – A Short-term in vivo Model for Cancer Research**	Dr. Nassim Ghaffari Tabrizi-Wizsy

>>> Im Fokus: Clinical Genomics Lab (CGL)

Das Clinical Genomics Lab (CGL) wurde 2019 gegründet und ist ein Zusammenschluss der molekularen Diagnostik aus den Bereichen Pathologie, Humangenetik, Hämatologie und Pharmakogenetik. Für dieses gemeinsam genutzte Labor wurde das gesamte 6. OG im Institut für Pathologie an der Murtenstrasse 31 umgebaut. Unterdessen arbeiten in dem Labor über 25 technische MitarbeiterInnen mit über 20 assoziierten AkademikerInnen aus den verschiedenen Kliniken und Instituten.

Die Grundidee des CGLs war, durch eine Bündelung der Ressourcen und des Know-hows die Voraussetzung für alle Fachbereiche zu schaffen, eine hochmoderne, innovative und effiziente molekulare Diagnostik zu betreiben. Es zeigte sich, dass die erwarteten Synergieeffekte sogar deutlich übertroffen wurden. Alleine die Zusammenlegung des Geräteparks und die gemeinsamen Investitionen in neue Geräte ermöglicht eine deutliche Steigerung der Effizienz und führte zu einem Schub in der Entwicklung neuer diagnostischer Testmethoden, da kaum Limitierungen seitens des technischen Equipments mehr vorhanden sind. Die Voraussetzungen, welche durch den Umbau geschaffen wurden erlauben es, dass Arbeitsabläufe optimal aufeinander abgestimmt werden können. Zusätzlich wurde ein modernes Laborinformationssystem eingeführt, welches alle Proben, Arbeitsschritte und Resultate digital verwaltet. Neben der Steigerung der Effizienz führten diese Massnahmen auch zu einer deutlichen Verbesserung der Qualitätssicherheit.

Eine zusätzliche Aufgabe, welche das Clinical Genomics Lab übernommen hat, ist als Dienstleister Ressourcen für klinische Forschungsvorhaben bereitzustellen. Diese Kombination aus Forschungsprojekten und diagnostischen Aufgaben stellen eine hervorragende Chance für das CGL dar: Die Etablierung von Methoden und Techniken für Forschungsprojekte ermöglicht Entwicklungen, welche später direkt in die Diagnostik überführt werden können. Dieses Konzept hat sich immer wieder bewährt und erlaubt dem CGL jederzeit moderne und innovative Diagnostik auf höchstem Niveau zu betreiben.

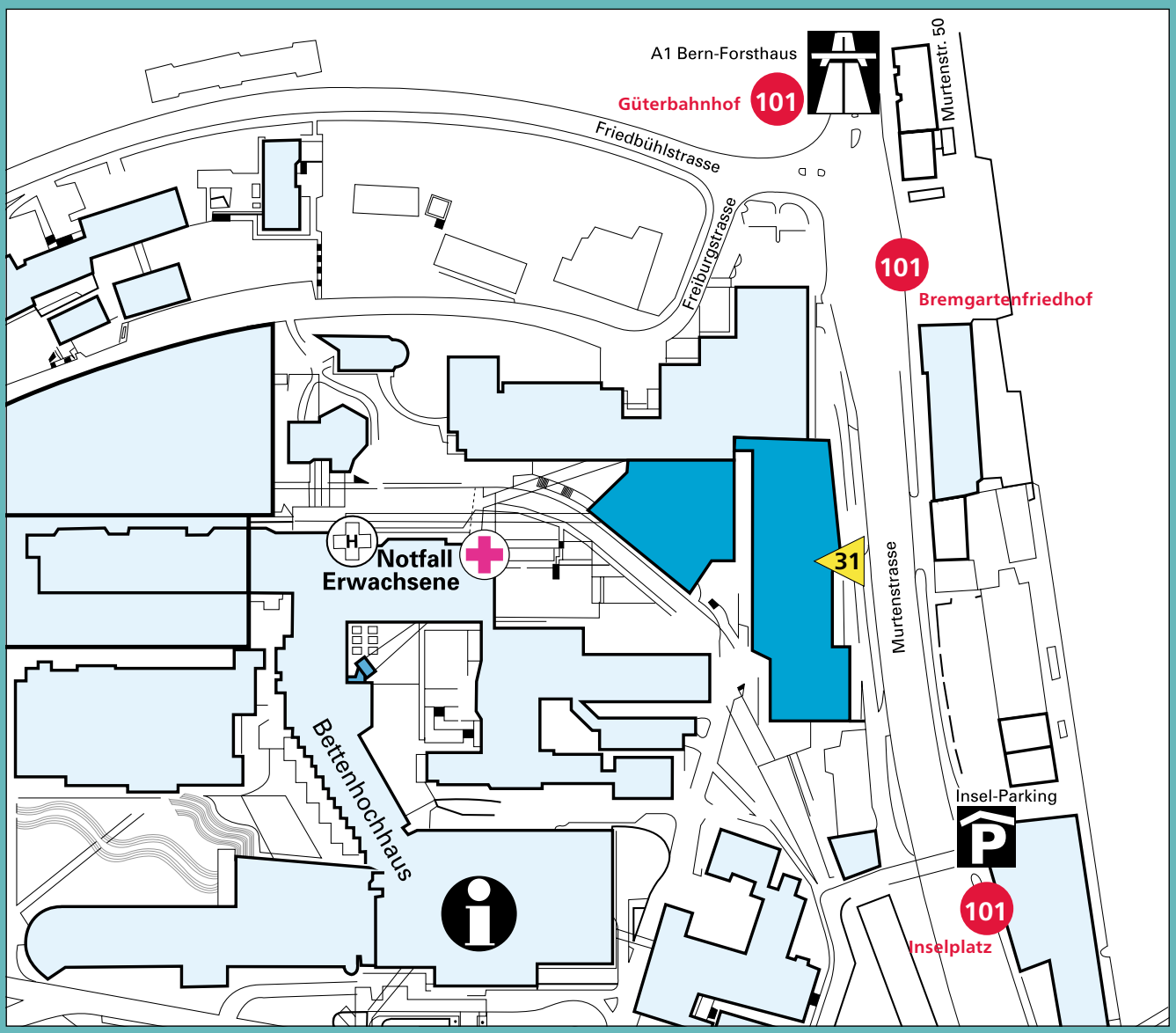
Für die Pathologie bedeutet dies, dass im CGL alle Anforderungen an prädiktive oder diagnostische Fragestellungen erfüllt werden. So wurden im letzten Jahr über 1200 Tumorsequenzierungen mittels NGS (500 Gen-Panel) durchgeführt und ausführliche Berichte über prädiktive Biomarker an die behandelnden Onkologen erstellt. Für die pathologisch-diagnostischen Fragestellungen wurde die genomweite Methylomanalyse in die Routine-Diagnostik überführt. Ebenfalls in diesem Jahr wurde ein grosses NGS Panel für die RNA-Sequenzierung etabliert, welches Fragestellungen im Bereich der Sarkomdiagnostik lückenlos abdeckt. Unterdessen wurden zusätzliche externe Einsender gewonnen. Der Bereich Pathologie betreut so nicht nur das Institut für Pathologie und das Inselspital, sondern ist für die meisten Spitäler und Pathologien im Kanton Bern das Zentrum für molekulare Untersuchungen.

Für die akademische Betreuung des Bereichs Pathologie arbeiten drei MolekularpathologInnen und ein wissenschaftlicher Mitarbeiter aus dem Institut für Pathologie im Clinical Genomics Lab. Ein weiterer Facharzt für Pathologie ist in Ausbildung zum Molekularpathologen.

Aktuell ist die Überführung der einzelnen Laborakkreditierungen in eine gemeinsame Akkreditierung des Clinical Genomics Lab für 2023 geplant. Damit kann auch eine gemeinsame Bewilligung des BAG für die Durchführung genetischer Analysen beantragt werden. Um das laufend grösser werdende Probenvolumen zu bewältigen wird im nächsten Jahr insbesondere weiter in Automatisierungslösungen investiert. Ein Roboter, welcher auch komplexe Protokolle in hohem Durchsatz bearbeiten kann wurde bereits bewilligt. Für den Bereich Pathologie steht die Überführung weiterer Sequenzierpanels für spezielle Fragestellungen in die Diagnostik an. So wird z.B. ein qualitativ hochstehender Test für die liquid Biopsy in der Tumordiagnostik eingeführt. Damit können prädiktive Tumormarker im Blut erfasst werden, wenn eine Gewebeentnahme nicht möglich oder sinnvoll ist.

Insgesamt hat sich das Konzept des Clinical Genomics Lab für alle Fachbereiche bewährt und wird immer mehr zu einem Vorzeigeprojekt des Medizinalstandort Bern.

>>> Situationsplan



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