IGMP Institut für Gewebemedizin und Pathologie

Institut für Gewebemedizin und Pathologie

www.igmp.unibe.ch

Jahresbericht 2023

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>>> Das Wichtigste in Kürze

Liebe Leserin, lieber Leser

Ich freue mich, dass Sie den ersten Jahresbericht des IGMP in Händen halten. **IGMP – Institut für Gewebemedizin und Pathologie** ist unsere Namenserweiterung, die wir im 2023 formalisiert haben.

Mehr Mitarbeitende des IGMP befassen sich mit künstlicher Intelligenz und molekularen Methoden als mit der klassischen Autopsie, welche leider den Begriff Pathologie sehr stark füllt. Für uns ist diese Namenserweiterung mit dem Begriff Gewebemedizin ein Beginn eines «re-branding», welches die Patientennähe betont und die Integration moderner Methoden in der Zuhilfenahme zur Untersuchung von Gewebeproben bei Hochhalten der morphologischen Methoden vorantreibt.

In diesem Sinne haben wir 2023 begonnen, in der Routine digital und im Pathojet zu arbeiten und vermehrt Tumorberichte strukturiert zu erfassen. Ich bin auch stolz, dass die ersten Patientinnen und Patienten im Rahmen unserer neuen gewebemedizinischen Erklärungs-Sprechstunde in unser Institut zugewiesen wurden. In der molekularen Diagnostik im clinical genomics lab können wir jetzt mit Liquid biopsies Tumormutationen im zirkulierenden Blut nachweisen, und weitere molekulare Marker, die bei der Indikation von Immuntherapien helfen wie TMB routinemässig anbieten.

Unsere Mitarbeiterin PD Dr. Yara Banz hat ein Teilzeitengagement bei der Organisation der Lehre des Inselspital eingenommen, auch innerhalb unseres IGMP wird sie sich vermehrt um übergeordnete Lehrerorganisation mit modernen «Teach-the Teacher» Konzepten kümmern. Besonders stolz sind wir über Wahl von Prof. Lugli als **Teacher of the year** im Masterstudiengang.

Um in der gewebsmedizinischen Forschung unserem Anspruch **«We want to make a difference in medicine»** noch stärker gerecht zu werden, überdenken wir unsere Organisationsform und führen Methoden des agilen Managements ein, wie im Fokus detaillierter dargestellt.

Ich bin stolz auf unser Team, das diese Flexibilität beibehält und mit Engagement im Sinne der Patientinnen und Patienten arbeitet, wie Sie auf den nächsten Seiten sehen können,

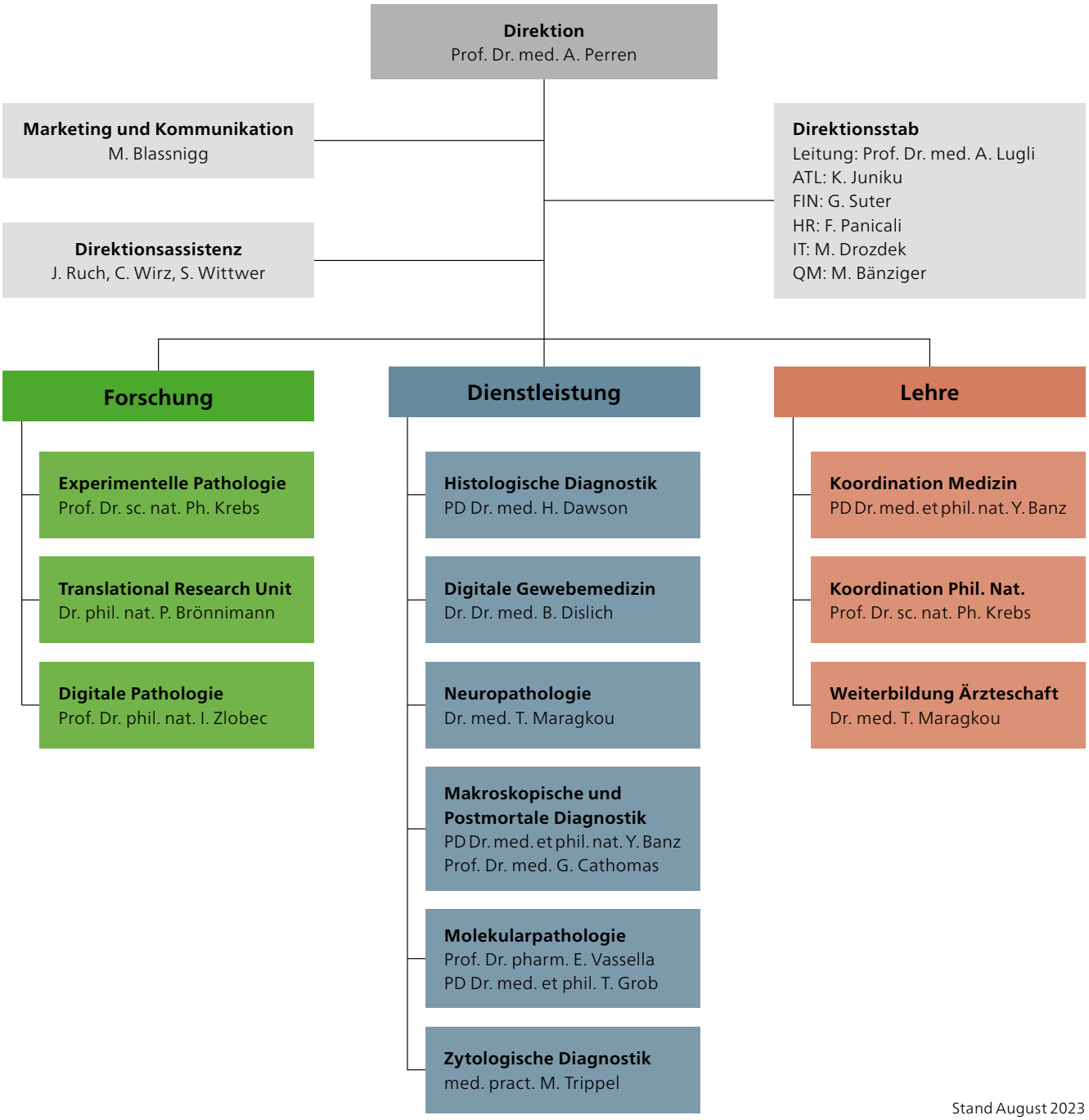
Ich wünsche Ihnen viel Freude bei der Lektüre

Herzliche Grüsse

Aurel Perren, Direktor


IGMP

>>> Organigramm



Stand August 2023

>>> Dienstleistung

1 Klinische Pathologie

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

Die Ärzteschaft und die Laborteams sind innerhalb der Gewebemedizin in den Bereichen der Histologischen, Zytologischen, Postmortalen und Molekularpathologischen Diagnostik tätig.

1.1 Ärzteschaft

Histologische Diagnostik (PD Dr. med. H. Dawson)
Das Ärzteteam besteht aus 21 FachärztInnen und 9 AssistenzärztInnen, welche zusammen das gesamte Spektrum der universitären Pathologie inklusive Zytopathologie und molekulare Pathologie abdecken. Unser Institut ist integraler Bestandteil zahlreicher interdisziplinärer Veranstaltungen des Inselspitals und externer Spitäler.

Ganz im Sinne des Konzeptes der Gewebemedizin und der Modernisierung unseres Fachs konnten 2023 einige Projekte innerhalb der Ärzteschaft realisiert werden. Mit der Patientensprechstunde Gewebemedizin/Pathologie besteht seit Herbst 2023 ein neues Angebot für Patienten, welche sich einen vertieften Einblick in ihre Erkrankung wünschen. Es handelt sich hierbei um eine Dienstleistung, welche bislang weltweit lediglich an wenigen Instituten angeboten wird. Im Gespräch mit den PatientInnen werden Fragen zu gewebsmedizinischen Aspekten beantwortet und entsprechende Präparate am Mikroskop oder am Bildschirm erläutert.

Die digitale Gewebemedizin hat auch 2023 weiterhin Einzug in die Routinediagnostik gehalten. Mittels einem kürzlich hausintern publizierten Algorithmus können Lymphknoten in Resektaten kolorektaler Karzinome auf Metastasen überprüft werden. Der Abgleich mit den Ergebnissen des Algorithmus geschieht nach der initialen Befundung durch die GewebemedizinerIn, um die Qualität der Diagnostik noch weiter zu stärken.

2023 konnten die ersten synoptischen Berichte in automatisierter Form übermittelt werden. Nebst der Sicherstellung einer vollständigen Berichterstattung gemäss den Kriterien der ICCR werden durch diese Berichtserstellung strukturierte Daten hinterlegt, welche die gezielte Extraktion aller relevanten Parameter erlaubt. So können beispielsweise Angaben im Rahmen der UCI-Zertifizierung oder Daten für das Krebsregister oder Forschungsarbeiten automatisch generiert werden. Im Jahr 2024 wird der inhaltliche und formelle Ausbau dieser synoptischen Berichte angestrebt.

Neuropathologie
(Dr. med. Theoni Maragkou)
Im Jahr 2023 untersuchten wir mehr als 1500 neurochirurgische und neuromuskuläre Proben, davon 400 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) des Inselspitals durchgeführt werden. In Zusammenarbeit mit dem Neuromorphologischen Labor der Neurologischen Klinik des Inselspitals wurden rund 90 Muskelbiopsien untersucht. Die postmortale Diagnostik mit über 80 Hirnsektionen. Entsprechend dem Charakter der Neuropathologie als Schnittstelle zwischen den klinischen Neurofächern, der Labordiagnostik und translationaler Forschung war der Fachbereich Neuropathologie auch im Jahr 2023 in zahlreichen Veranstaltungen insbesondere in Zusammenarbeit mit Kliniken des Inselspitals engagiert. Darüber hinaus ist das Fach Neuropathologie Teil des Neuroonkologischen Tumorzentrums und einer der Schwerpunkte des SIWF und der Medizinischen Allianz Basel/Bern (MBB).

Postmortale Diagnostik
(PD Dr. med. et phil. nat. Y. Banz)
Die Abteilung der postmortalen Diagnostik konnte auch 2023 ihre Aufgaben Dank des gut eingespielten und motivierten Teams wahrnehmen, trotz des nicht unerwarteten Rückgangs der Autopsiezahlen auf Werte um 90, wie in den Jahren vor 2022. Insbesondere Dank einer exzellenten Zusammenarbeit mit Spitälern der Region diente die Aufarbeitung von Autopsien nicht nur der Klärung der unmittelbar relevanten medizinischen Fragestellungen, sondern auch der klinisch-pathologischen Fallbesprechungen sowie der studentischen Lehre. In einer zunehmend digitalisierten Welt liegt die Stärke der seit Jahrzehnten durchgeführten Autopsietätigkeit immer noch in der einfachen Tatsache, dass Krankheiten und die Auswirkungen auf den Organismus, auf das Individuum, fassbar und begreifbarer werden.

Die Aufarbeitung der makroskopischen Präparate und Fotodokumentation zum Zweck der Lehre konnte auch 2023 weitergeführt werden. Sie wird dazu dienen die 2023 begonnenen Projekte zur Erstellung von Lehrvideos zur Komplementierung bestehender Teachingformate, weiterführen und abschliessen zu können.

2023 konnte das durch den schweizerischen Nationalfonds unterstützte Forschungsprojekt zur postmortalen Bildgebung in Zusammenarbeit mit dem Institut für Rechtsmedizin der Universität Bern abgeschlossen werden. Die grossen Datenmengen werden zurzeit noch analysiert und sollten hoffentlich 2024 veröffentlich werden können.

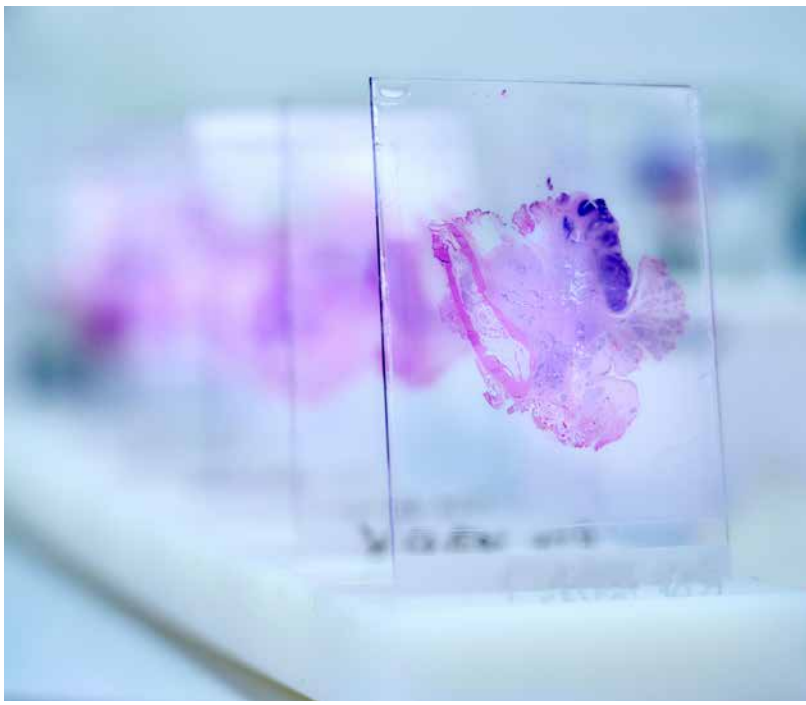
Ein Blick nach vorne sei erlaubt. Auch 2024 wollen wir am Standort Bern in der Abteilung für postmortale Diagnostik eine hochstehende Diagnostik, aufschluss- und lehrreiche interdisziplinäre Fallbesprechungen, sowie studentische Lehre auf höchstem Niveau garantieren. Durch eine enge Zusammenarbeit mit den Fachkolleg:innen im IGMP Team, mit den Kolleg:innen der Rechtsmedizin und mit unseren klinischen Kolleg:innen werden wir uns den Fragestellungen zu neuropathologischen Untersuchungen, Untersuchungen in der Pädopathologie und im Kontext «klassischer» Autopsien in der Erwachsenendiagnostik auch im neuen Jahr widmen.

Zytopathologie (Med. Pract. M. Trippel)
In der Zytologie lag der Fokus im Jahr 2023 klar auf der Weiterbildung der Zytotechniker:innen und Ärzte:innen. Zwei Assistenzärzte haben ihre sechsmonatige Rotation in der zytologischen Diagnostik absolviert und zwei Kandidatinnen mit bereits abgeschlossenem Facharzttitel der Pathologie haben in diesem Jahr ihre Weiterbildung für den Schwerpunkttitel der Zytopathologie begonnen. Ausserdem konnten wir eine weitere Person für die Ausbildung zur Zytotechnikerin gewinnen, so dass aktuell zwei Kandidatinnen die zweijährige Weiterbildung für das von uns angebotene kantonal-bernische Diplom für Zytotechniker:innen bei uns mit viel Engagement durchlaufen.

Leider verzögert sich der Start des geplanten Umbaus der gesamten Zytologie um ein paar Jahre. Wir sind aber gut vorbereitet auf diese intensive Zeit und freuen uns schon auf die modernen Räumlichkeiten, die ein optimalen Arbeitsablauf nach Lean ermöglichen werden.

Erfreulicherweise ist die Menge der einsandten Proben der gynäkologischen Zytologie und der extragynäkologischen Zytologie im Jahr angestiegen.

Wir können somit positiv in das kommende Jahr starten in dem wir uns wieder mit viel Begeisterung der zytologischen Diagnostik und der Weiterbildung widmen werden.



1.2. Labor

Histologische Diagnostik (Y. Hirschi)
Im ersten Halbjahr 2023 stand das Projekt IVD-Umsetzung in der IHC im Vordergrund. Die in der Routine eingesetzten AK wurden auf IVD-Kompatibilität kontrolliert und nötigenfalls durch IVD-Produkte neu validiert und ersetzt. Im weiteren Lauf des Jahres 2023 wurde zudem der Maschinenpark in der IHC aufgerüstet und die Arbeitsprozesse nach LEAN angepasst, um die zunehmende Bestellmenge der IHC ohne Verzögerung abzuarbeiten. Aktuell stehen der Routinediagnostik 300 Primärantikörper zur Verfügung.

Mit dem weiterführenden Projekt der Digitalen Pathologie wurde der Workflow in der Digitalen Diagnostik angepasst und weiter umgesetzt. In einem zweiten Schritt wurden die verschiedenen Routine-Arbeitsprozesse überarbeitet und Anpassungen durchgeführt, um einen konstanten Ablauf in der Routine zu gewährleisten.

Ab 01.08.23 gab es einen Laborleitungswechsel, Herr Yan Hirschi übernahm die Laborleitung. Aufgrund dieses Wechsels wurden im Organigramm der Histologischen Diagnostik einige strukturelle Anpassungen gemacht, die operative Ebene (Operative-Leitung) wurde von 4 Positionen auf 5 Positionen erhöht. Die neue OL-Position übernimmt Aufgaben im Bereich Administration und Digitale Pathologie. Durch die verstärkte operative Ebene besteht gezielter die Möglichkeit das Team zu unterstützen und die Kernaufgabe des Labors mit hohem Qualitätsstandart weiter und breiter auszuführen.

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 Gewebemedizin und Pathologie und des Inselspitals. Die in diesem Fachbereich verwendeten Methoden umfasst insbesondere die Hochdurchsatz-Sequenzierung mittels TruSightOncology (TSO) 500 Panel (Illumina). Neben der Erfassung von Mutationen aus über 500 Tumor-relevanten Genen erlaubt die Methode den Nachweis von Amplifikationen und Fusionstranskripten von Onkogenen. Zudem erlaubt die TSO500 Analyse den Nachweis der Tumormutationslast, der Mikrosatelliteninstabilität, ausgelöst durch den Funktionsverlust von Mismatch-Reparaturgenen sowie des HRD Scores als Therapieentscheid für PARP Inhibitoren. Mit dieser Schlüsseltechnologie werden prädiktive Biomarker als Therapieentscheid beim Adenokarzinom der Lunge, kolorektalem Karzinom, malignen Melanom, GIST, Ovarialkarzinom und Gliom abgedeckt und dient zur Diagnostik von Pankreaszysten. Ein erweitertes RNA Fusionspanel ist für die Diagnostik von Sarkomen hilfreich. Daneben verwenden wir in der Routine-Diagnostik die Sanger-Sequenzierung, Pyrosequenzierung, verschiedene PCR-Analysen, Fluoreszenz In situ Hybridisierung und Array-basierte Methoden. Dieses breite Methodenspektrum dient der Genotypisierung der Blasenmole, Risikostratifizierung Mammakarzinom, Abklärung Mikrosatelliteninstabilität, B- und T-Zellklonalität, Methylierungsanalyse als Classifier für ZNS-Tumore sowie Nachweis spezifischer Erreger. Die molekulardiagnostischen Befunde werden am molekularen Tumorboard des Inselspitals besprochen. Das CGL ist seit Anfang dieses Jahrs unter der ISO-Norm 15189 akkreditiert.

Nach initial starkem Anstieg der Aufträge für NGS-Analysen seit der Gründung des CGLs, blieben die Zahlen im diesem Jahr gegenüber dem Vorjahr weitgehend konstant. Deutlich zugenommen hat hingegen die Zahl der Aufträge für die Genom-weite Methylierungsanalyse (InfiniumEPIC) (+50%). Im letzten Jahr haben wir die Methode zum Nachweis des HRD Scores im CGL mittels einem erweiterten TSO500 Panels etabliert. Der HRD Score wird mittels eines Algorithmus von Myriad Genetics berechnet und dient als Therapieentscheid beim rezidivierten Ovarialkarzinom. Die TSO500 Analyse kann nun auch automatisiert mit Hilfe eines Liquid Handlers durchgeführt werden. Die TSO500 ctDNA Analyse zum Nachweis von Tumormutationen aus der Flüssigbiopsie sowie Whole Exome Sequencing (WES) wurde für die Forschungsdienstleistung etabliert. Die Weiterentwicklung der Bioinformatikpipeline für die TSO500 Analyse sowie WES haben uns auch in diesem Jahr beschäftigt.

Im nächsten Jahr wird uns insbesondere die Einführung der Mutationsanalyse an Flüssigbiopsien für die Routine-Diagnostik beschäftigen.

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 Institut für Gewebemedizin und Pathologie

Stand August 2023

Dermatologische Gewebemedizin	
H. Dawson	031 684 11 29
J. Wolf	031 684 11 52
O. Stanowska	031 684 11 34

Endokrinologische Gewebemedizin	
A. Perren	031 684 11 30
A. Marrazzini	031 684 11 39

Gastrointestinale Gewebemedizin	
A. Lugli	031 684 11 16
H. Dawson	031 684 11 29
G. Cathomas	031 684 11 35
B. Dislich	031 684 11 38
A. Mookhoek	031 684 11 36
M. Montani	031 684 11 25

Mamma- und gynäkologische Gewebemedizin	
W. Solass	031 684 11 33
M. Trippel	031 684 11 49
M. Montani	031 684 11 25
M. Wartenberg	031 684 11 27

Hämatologische Gewebemedizin	
Y. Banz	031 684 11 26
B. Dislich	031 684 11 38
A. Rodriguez	031 684 11 37
B. Zagrapan	031 684 11 31

Herz-, Gefäss- und rheumatologische Gewebemedizin	
Y. Banz	031 684 11 26
J. Wolf	031 684 11 52
M. Trippel	031 684 11 49
T. Losmanová	031 684 11 48

HNO-/ophthalmologische Gewebemedizin	
O. Stanowska	031 684 11 34
A. Marrazzini	031 684 11 39
M. Wartenberg	031 684 11 27

Hepatische Gewebemedizin	
M. Montani	031 684 11 25
A. Mookhoek	031 684 11 36
G. Cathomas	031 684 11 35
M. Wartenberg	031 684 11 27

Pneumologische Gewebemedizin	
J. Wolf	031 684 11 52
T. Losmanová	031 684 11 48
A. Mookhoek	031 684 11 36

Nephrologische Gewebemedizin	
A. Rodriguez	031 684 11 37
M. Montani	031 684 11 25

Neuropathologie	
T. Maragkou	031 684 11 32
B. Dislich	031 684 11 38
B. Wartenberg	031 684 11 27

Pädiatrische Gewebemedizin	
A. Marrazzini	031 684 11 39
M. Trippel	031 684 11 49
A. Mookhoek	031 684 11 36

Pankreatische Gewebemedizin	
M. Wartenberg	031 684 11 27
M. Montani	031 684 11 25
A. Perren	031 684 11 30

Urologische Gewebemedizin	
A. Rodriguez	031 684 11 37
M. Montani	031 684 11 25
T. Losmanová	031 684 11 48

Weichteil- und orthopädische Gewebemedizin	
H. Dawson	031 684 11 29
B. Dislich	031 684 11 38
W. Solass	031 684 11 33

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Y. Banz	031 684 11 26
G. Cathomas	031 684 11 35
B. Dislich	031 684 11 38
A. Marrazzini	031 684 11 39
M. Trippel	031 684 11 49
J. Wolf	031 684 11 52
B. Zagrapan	031 684 11 31

Molekularpathologie	
E. Vassella	031 684 11 63
T. Grob	031 664 11 28
H. Dawson	031 684 11 29
B. Dislich	031 684 11 38

Digitale Pathologie	
B. Dislich	031 684 11 38
H. Dawson	031 684 11 29
B. Zagrapan	031 684 11 31

Zytologische Diagnostik	
M. Trippel	031 684 11 49
Y. Banz	031 684 11 26

Direktionsstab

4 DIR-Stab

Der Direktionsstab beinhaltet die Bereiche Administrativer Support, Technischer Dienst und Logistik (ATL), Human Resources (HR), Qualitätsmanagement (QM), Informatik (IT) und Finanzen/Controlling (FIN) und stellt den Support für alle internen und externen Kunden des Instituts für Gewebemedizin und Pathologie bei deren Arbeitsprozessen und Projekten sicher.

Die definierten Qualitätsziele 2023 des Direktionsstabs beinhalten die Erstellung eines neuen und vereinfachten EMA-Prozesses, die Reorganisation der IT-Plattformen für das gesamte Institut und die Reorganisation der Untergeschosse, um die Platzverhältnisse für die Gewebeblock-Archivierung zu erfassen.

Für das Jahr 2024 ergab sich für den gesamten Direktionsstab der Fokus auf ein Qualitätsziel, nämlich die Modernisierung und Finalisierung des EMA-Prozesses, welcher operativ das gesamte Institut und zusätzlich alle Bereiche des Direktionsstabes betrifft.

Zusätzlich werden folgende Veränderungen bearbeitet:
1. Umstrukturierung des Bereiches ATL zu AFM (Administrative and Facility Management)
2. Umzug des Berichtssekretariats ins Erdgeschoss
3. Die Einführung von Jira als Plattform für das Projektmanagement

Der Direktionsstab bildet sich jährlich in zwei eintägigen Retraiten im Bereich «Leadership» fort.

5 Dienstleistungsstatistik

Klinische Pathologie

Histopathologie	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**	**2023**
Anzahl Einsendungen	43'607	45'491	48'601	46'372	48'707	49'516	**50’107**
Anzahl Lokalisationen	83'191	86'253	93'835	90'658	95'500	96'974	**96’640**
Einsendungen Schnellschnitte	1761	1784	1831	1770	1822	1585	**1529**
Proben Schnellschnitte	2264	2225	2313	2216	2295	2028	**1880**

Autopsie							
Anzahl durchgeführte Autopsien	130	134	106	99	81	114	**96**

Zytopathologie							
Anzahl Einsendungen Total	16'995	17'814	17'576	17'300	17'038	16'350	**17’584**
Anzahl Proben Total	20'519	21'949	21'787	20'384	21'301	20'006	**21’347**
Anzahl Zellblöcke	3334	3844	4011	4234	4791	4411	**4993**

Immunhistochemie							
Fälle (Blöcke) Diagnostik (Paraffin)	7681	8822	11'616	11'717	12'788	14'521	**15’118**
Färbungen Immunfluoreszenz (Nierenbiopsien)	2464	2010	2486	1980	3003	1796	**1720**
Fälle Immunzytologie am Ausstrich	258	201	246	210	154	292	**150**
Färbungen Immunzytologie am Ausstrich	364	377	353	307	204	193	**200**
Färbungen Diagnostik (Paraffin)	47'597	51'971	59'249	60'913	65'866	68'437	**75’590**

Tumorbank

Einsendungen Tumorbank	1879	1593	1823	2126	2373	2157	**1962**
Anzahl Projekteingänge TRU	602	738	850	640	787	802	**827**

>>> Forschung/Research

1 Research at the Institute of Tissue Medicine and Pathology

Research groups
Stefan Freigang, MD
Philippe Krebs, PhD
Alessandro Lugli, MD
Aurel Perren, MD & Ilaria Marinoni, PhD
& Martin Sadowski, PhD
Mirjam Schenk, PhD (since 01.1.2023, 10% at ITMP and 90% P.I. position at CK-CARE AG, Davos, Switzerland)
Mario P. Tschan, PhD
Erik Vassella, PhD
Inti Zlobec, PhD & Hannah Williams PhD

Translational Research Unit (Core Facility) (TRU) and Tissue Bank Bern
Head; Paulina Brönnimann, PhD

Organisational aspects

The eight research groups of the ITMP pursue their research projects, primarily supported by extramural funding. Major pieces of equipment are shared among the experimental research groups and, upon initial training in the appropriate use («support platforms»), can be also accessed by the research personnel of the other units of the Institute of Tissue Medicine and 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 Tissue Medicine and Pathology.
The recently created Division of Digital Pathology (Inti Zlobec) uses digital imaging and spatial technologies, along with computational analysis methods, including deep learning to investigate cancer biology, generate AI algorithms for potential diagnostic use, and support image analysis projects on various tissue types.

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.


GILSON


INTEGRA
BioConcept

1.1 ITMP Research

Head: Philippe Krebs, PhD and Inti Zlobec, PhD

Research activities

The research activities of the eight research groups in the ITMP Research are focused on three main research topics, i.e.
– Immunopathology and inflammation, and
– Experimental tumor pathology and tumor biology
– Digital Pathology

The research groups in the ITMP Research address questions related to the fundamental aspects of cell biology and to the etiopathogenesis of neoplastic, inflammatory disorders and use artificial intelligence, bioinformatics and digital pathology to investigate cellular and molecular phenotypes as well as prognostic or predictive factors from histopathology images. Translational aspects are also considered such as the identification of novel biomarkers for disease activity in cancer and in inflammatory disorders, and the development of novel vaccination strategies against solid tumors.

Personnel

In 2023 approximately 85 people were employed in the ITMP Research.

Grant Support

In 2023 the total amount of new external funding obtained by the research groups of the ITMP Research reached more than CHF 1.3 Mio (for details see: Reports of the individual research groups).

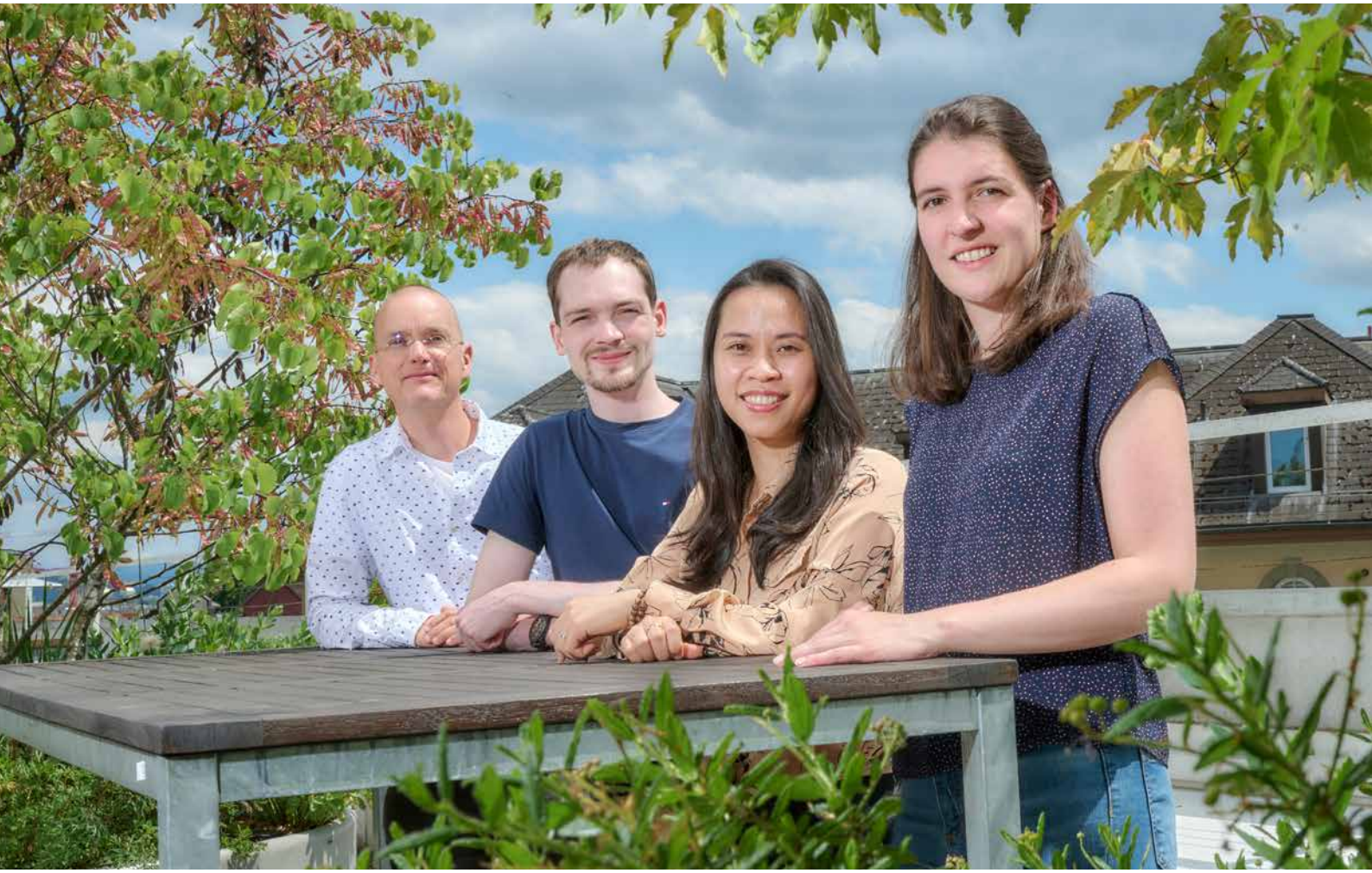
Research infrastructure and collaborations

The research activities at the Institute of Tissue Medicine and 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, as well as a MICA cell microscope for live cell time-lapse imaging at confocal resolution, also under hypoxic conditions. 2023 saw the acquisition of a MACSima™ platform for multiple immunofluorescence staining on tissue sections, that will add a novel dimension to our current histology by facilitating spatial analyses. This device can accommodate off-the-shelf conjugated anti-bodies, supporting more than 100 plex-staining protocols thanks to automated cycles of staining and antibody elution, which are consecutively applied to tissue sections. To allow optimal embedding of the MACSima™ device in our research, a specific support platform («PAPAYA») has been established to generate hyper-plex protein panels and spatial analyses within TRU and supported by the Digital Pathology research group (HyPerplex and sPAtial analYsis platform).

Moreover, we have access to core facilities provided by the Department of Biomedical Research (DBMR), including the flow cytometry (FACS) core facility, and the state-of-the-art genomics core facility. In addition, access to the microscopy centre (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 NovaSeq 6000, an illumina NextSeq 1000, an illumina MiSeq, an illumina iSeq100, a Pacific Biosciences Sequel IIe and a Pacific Biosciences Revio 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. Some of our researchers 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 ITMP Research 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 flow cytometry-based techniques in cell sorting and multi-color analysis, including spectral flow cytometry. 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 long-standing expertise in isolating and culturing primary cells, such as immune cells, primary AML blast cells, mesenchymal stromal 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.

Patents

- PCT patent application PCT/EP2023/076606
  «Temperature-triggered in situ forming lipid mesophase gel»
- S. Freigang, HTT. Gander-Bui, 05.07.2023
  Immunotherapy of fungal sepsis
  Patent application submitted, European Patent Office



Research group Stefan Freigang

Group of Stefan Freigang, MD

Dr. Thi Thuy Hang Gander, PhD, Early Postdoc
MSc Sabrina Walthert, Laboratory technician
MSc Julia Otto, PhD student (from May – October 2023)
M Med Nadja Oehninger, medical doctoral candidate
Sabrina Bertello Hernandez, MSc student

Summary of Research Activities

Immune recognition of lipids in inflammation and immunopathology

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

Research Activities

Project 1: Glycolipid-sensing by Natural Killer T cells

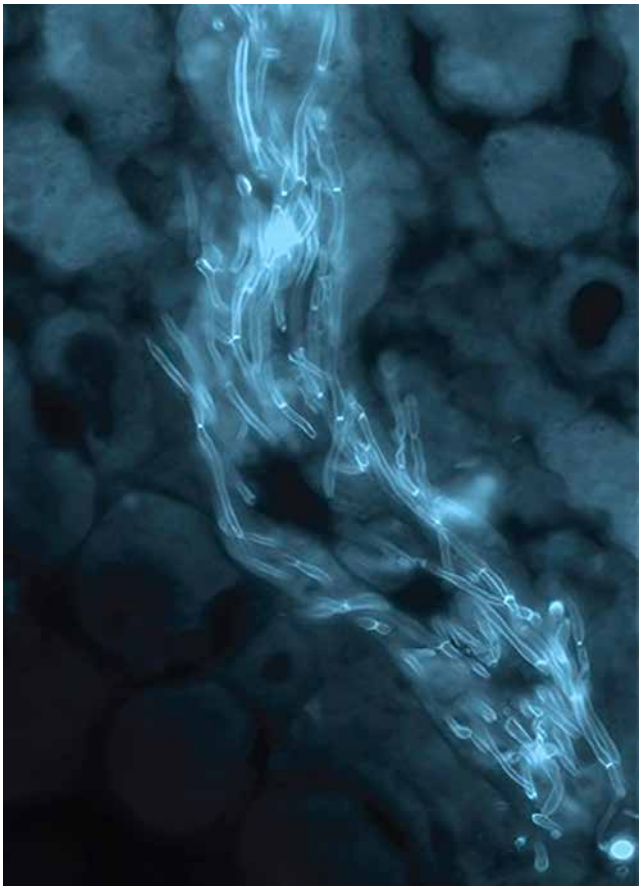
Natural killer T (NKT) cells are innate-like T cells with powerful immunoregulatory functions that recognize self and microbial glycolipids presented by CD1d molecules. While the efficacy of NKT cell agonists is currently explored in the immunotherapy of infectious diseases and cancer, the mechanisms 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: Mechanisms of metabolic adaptation in vascular immunopathology

Atherosclerosis-related diseases remain the leading cause of mortality worldwide; and chronic inflammation represents a major driver of disease progression. First clinical trials demonstrated the beneficial effects of anti-inflammatory therapies in CVD patients, a better understanding of the molecular mechanisms of vascular inflammation is required to develop more effective treatment strategies. In this project we investigate how dyslipidemia and the resulting lipid metabolism perturbation in immune cells affects physiological immune responses and contribute to vascular immunopathology in atherosclerosis.

Project 3: Cell-type specific regulation of IL-1-driven inflammation

Invasive fungal infections have high mortality rates with limited therapeutic options. We recently identified macrophage-secreted IL-1 receptor antagonist (IL-1Ra) as an innate immune checkpoint that facilitates fungal dissemination and candidiasis pathology. We showed that therapeutic IL-1Ra neutralization protects against lethal Candida sepsis, whereas interferon-driven amplification of IL-1Ra during viral infections exacerbates fungal disease. This project explores IL-1/IFN I crosstalk mechanisms, particularly IL-1Ra, as potential biomarkers and therapeutic targets in microbial infection.



Project 3: Immunofluorescence staining of an infected mouse kidney. The tissue dissemination of the fungus Candida albicans was visualized by staining of the fungal cell wall.

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

- UniBE PoC Grant, S. Freigang; PI, 2023–2024, CHF 30'000
- Swiss National Science Foundation, S. Freigang; PI, 2020–2024, CHF 632'000
- Swiss Heart Foundation, S. Freigang; PI, 2020–2023, CHF 50'000
- Swiss Lung Liga , S. Freigang; PI, 2017–2023, CHF 162'000

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 Tissue Medicine and Pathology

Publications

- Gander Thi Thuy Hang, Schläfli Joëlle, Baumgartner Johanna, Walthert Sabrina, Genitsch Vera, van Geest Geert, Galván José A, Cardozo Carmen, Graham Martinez Cristina, Grans Mona, Muth Sabine, Bruggmann Rémy, Probst Hans Christian, Gabay Cem, Freigang Stefan
  Targeted removal of macrophage-secreted interleukin-1 receptor antagonist protects against lethal Candida albicans sepsis.
  Immunity, 56(8), 1743-1760.e9. Cell Press 10.1016/j.immuni.2023.06.023
- Bertschi Nicole L, Steck Oliver, Luther Fabian, Bazzini Cecilia, von Meyenn Leonhard, Schärli Stefanie, Vallone Angela, Felser Andrea, Keller Irene, Friedli Olivier, Freigang Stefan, Begré Nadja, Radonjic-Hoesli Susanne, Lamos Cristina, Gabutti Max Philip, Benzaquen Michael, Laimer Markus, Simon Dagmar, Nuoffer Jean-Marc, Schlapbach Christoph
  PPAR-γ regulates the effector function of human T helper 9 cells by promoting glycolysis.
  Nature Communications, 14(1), p. 2471.
  Springer Nature 10.1038/s41467-023-38233-x

Research group Philippe Krebs

Group of Philippe Krebs, PhD

Robert Gaultney, PhD, advanced post-doc
Wen Jie (Jeremy) Yeoh, PhD, early post-doc
Vivian Vu, MSc, PhD student (until April 2023)
Anja Herbst, MSc, PhD student
Fatlind Malsiu, MSc student (until February 2023)
Aparna Ananthanarayan, MSc student (July–November 2023)
Emily Bessell, MSc, PhD student (from December 2023)
Kristýna Hlavácková, MSc, technician 90%
Coline Nydegger, technician, 70%

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

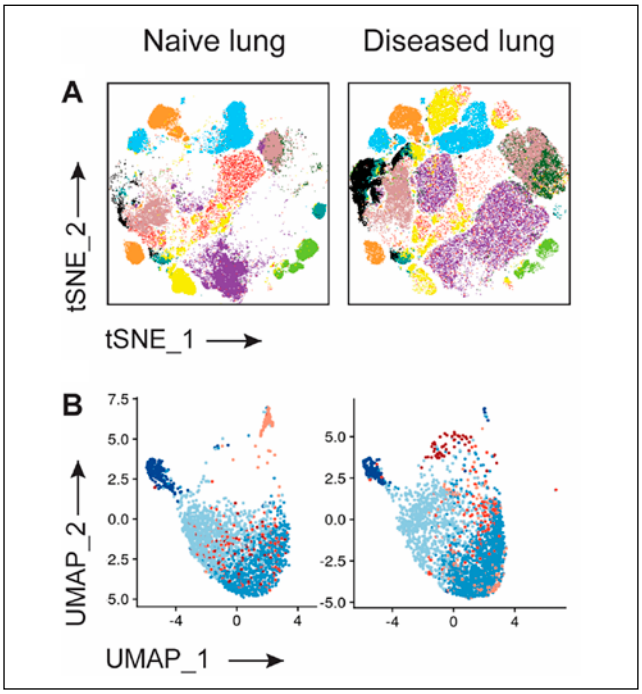
Project 1: Investigation of the local immune system regulation in COVID-19
The mechanisms leading to severe inflammatory lung disease in some COVID-19 patients are unknown. In this project, we will analyze the cells in the lung lavage of these patients and compare these findings with results from collaborators working on a mouse model of COVID-19. We hope so to reveal targets for COVID-19 therapy.

Project 2: 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; Yeoh & Vu, Cytokine, 2022). 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 3: 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 4: Immunoregulation and immunopathology

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 is responsible for memory. In this project, we use different murine models to better understand the role of specific genes in the regulation of these immune cell subsets and how disbalance in this process may lead to immunopathology in different disease contexts, including pathogen infection (Cardoso Alves, EMBO Reports, 2020).



Changes in immune infiltrate composition and transcriptomic landscape in the lungs of diseased mice with a defect in immunoregulation.
A. Immune cells were isolated from lung tissues of healthy and diseased mice and analyzed by flow cytometry to distinguish between immune cell subtypes, which are displayed in a tSNE representation.
B. Alternatively, lung innate immune lymphocytes were analyzed using single-cell RNA sequencing.

Internal Collaborations

- Christoph Mueller, PhD
- Inti Zlobec, PhD
- Yara Banz, MD, PhD
- Mafalda Trippel, MD
- Erik Vassella, PhD

External Collaborations

National

- Adrian Ochsenbein, MD; Carsten Riether, PhD, Dept. Clinical Res., University of Bern
- Andrew Macpherson, MD, 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

International

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

Grant Support

- Fondazione San Salvatore; Project grant, P. Krebs; PI, 2022–2024, CHF 170'000
- Swiss National Science Foundation Project grant, P. Krebs: PI, 2020–2024, CHF 632'000
- Swiss Life; Project grant, P. Krebs; main PI, 2021–2023, CHF 20'000
- Uniscientia; Project grant, P. Krebs; main PI;, 2021–2023, CHF 136'000
- Seal of Excellence Fund (SELF) UniBE, Fellowship; R. Gaultney, 2021–2023, CHF 128'698
- Werner und Hedy Berger-Janser Stiftung, Project grant R. Gaultney, PI, 2023, CHF 79'796
- Krebsforschung Schweiz, P. Krebs; PI; Project grant, 2023–2026, CHF 374'900
- UNIBE ID Grant, P. Krebs, PI, 2023–2025, CHF* 150'000
- Horizon Europe,Staff Exchange Program, P. Krebs; Co-Investigator, 2023–2027, Euro** 1'531'800

* total amount of funding; funding shared by PI and Co-PI; part for group Krebs is contingent on number of staff exchanges.
** total budget; part for group Krebs CHF 200'077 additional and proportional to the number of staff secondments

Administrative duties

- Biosafety Officer for research and diagnostics activities at the Institute of Tissue Medicine and 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 24 PhD students) and thesis co-advisor (total of 11 PhD students)
- Member of the Committee for the Medical and Pharmaceutical Libraries, University of Bern

Publications

- Yeoh Wen Jie, Krebs Philippe. SHIP1 and its role for innate immune regulation – novel targets for immunotherapy. (In Press). European journal of immunology (e2350446), e2350446. Wiley-VCH 10.1002/eji.202350446
- van Os Lisette, Yeoh Wen Jie, Witz Guillaume, Ferrari Dario, Krebs Philippe, Chandorkar Yashoda, Zeinali Soheila, Sengupta Arunima, Guenat Olivier. Immune cell extravasation in an organ-on-chip to model lung inflammation. European journal of pharmaceutical sciences, 187, p. 106485. Elsevier 10.1016/j.ejps.2023.106485
- Alizadeh Zeinabad Hojjat, Yeoh Wen Jie, Arif Maryam, Lomora Mihai, Banz Yara, Riether Carsten, Krebs Philippe, Szegezdi Eva. Natural killer cell-mimic nanoparticles can actively target and kill acute myeloid leukemia cells. Biomaterials, 298(122126), p. 122126. Elsevier 10.1016/j.biomaterials.2023.122126
- Ennis Sarah, Conforte Alessandra, O'Reilly Eimear, Takanlu Javid Sabour, Cichocka Tatiana, Dhami Sukhraj Pal, Nicholson Pamela, Krebs Philippe, Ó Broin Pilib, Szegezdi Eva. Cell-cell interactome of the hematopoietic niche and its changes in acute myeloid leukemia. iScience, 26(6), p. 106943. Elsevier 10.1016/j.isci.2023.106943
- Carone Marianna, Spalinger Marianne R, Gaultney Robert A, Mezzenga Raffaele, Hlavacková Kristyna, Mookhoek Aart, Krebs Philippe, Rogler Gerhard, Luciani Paola, Aleandri Simone. Temperature-triggered in situ forming lipid mesophase gel for local treatment of ulcerative colitis. Nature Communications, 14(1), p. 3489. Springer Nature 10.1038/s41467-023-39013-3
- Grabherr Sarah, Waltenspühl Alexandra, Büchler Lorina, Lütge Mechthild, Cheng Hung-Wei, Caviezel-Firner Sonja, Ludewig Burkhard, Krebs Philippe, Pikor Natalia B. An Innate Checkpoint Determines Immune Dysregulation and Immunopathology during Pulmonary Murine Coronavirus Infection. Journal of immunology, 210(6), pp. 774-785. American Association of Immunologists 10.4049/jimmunol.2200533
- Gurtner Alessandra, Borrelli Costanza, Gonzalez-Perez Ignacio, Bach Karsten, Acar Ilhan E, Núñez Nicolás G, Crepaz Daniel, Handler Kristina, Vu Vivian P, Lafzi Atefeh, Stirm Kristin, Raju Deeksha, Gschwend Julia, Basler Konrad, Schneider Christoph, Slack Emma, Valenta Tomas, Becher Burkhard, Krebs Philippe, Moor Andreas E.... . Active eosinophils regulate host defense and immune responses in colitis. Nature, 615(7950), pp. 151-157. Macmillan Journals Ltd. 10.1038/s41586-022-05628-7
- Le-Trilling Vu Thuy Khanh, Ebel Jana-Fabienne, Baier Franziska, Wohlgemuth Kerstin, Pfeifer Kai Robin, Mookhoek Aart, Krebs Philippe, Determann Madita, Katschinski Benjamin, Adamczyk Alexandra, Lange Erik, Klopfleisch Robert, Lange Christian M., Sokolova Viktoriya, Trilling Mirko, Westendorf Astrid M. Acute cytomegalovirus infection modulates the intestinal microbiota and targets intestinal epithelial cells. European journal of immunology, 53(2), e2249940. Wiley 10.1002/eji.202249940
- Krebs Philippe, Peng Hui, Duhan Vikas. Editorial: Natural killer cell plasticity and diversity in antiviral immunity. Frontiers in immunology, 14(1175111), p. 1175111. Frontiers Research Foundation 10.3389/fimmu.2023.1175111




Group of Alessandro Lugli, MD

Dr. med. H. Dawson
Dr. Dr. med. B. Dislich
Dr. A. Mookhoeck, MD PhD
Dr. med. F. Mueller
Derya Sönmez, Doktorand (Medizin)
Leonie Kovacic, Masterstudentin (Medizin)
Kartik Kohli, Masterstudent (Bioinformatics and Computational Biology)

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, 2017–2023, CHF 1'600'246, Co-Applicant
- Rising Tide Fondation A combined budding/T-cell score in pT1 and stage II colorectal cancer, Heather Dawson, 2018–2023, 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 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)
- ASCO (American Society of Oncology)
- SDiPath – Swiss Digital Pathology Consortium

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-ECCO (Histopathologists of ECCO)
- ESP (European Society of Pathology)
- IBDnet (Swiss Research & Communication Network on Inflammatory Bowel Disease)

Publications

- Liu DHW, Grabsch HI, Gloor B, Langer R, Dislich B.
  Programmed death-ligand 1 (PD-L1) expression in primary gastric adenocarcinoma and matched metastases.
  J Cancer Res Clin Oncol. 2023 Nov;149(14):13345-13352.
  doi: 10.1007/s00432-023-05142-x. Epub 2023 Jul 25.
  PMID: 37491637; PMCID: PMC10587283.

Research group Aurel Perren

Group of Aurel Perren, MD

Prof. Dr. med. Aurel Perren, MD, Director, PI
PD Dr. Ilaria Marinoni, PhD, PI
Dr. Martin Sadowski, PhD, Senior Research Assistant
M Med Aziz Chouchane, Pathology Assistant
Dr. Philipp Kirchner, PhD, Staff scientist
MScRenaud Maire, Laboratory technician
Tsilla Sunier, Laboratory technician (until September 2023)
MSc Simona Avanthay, PhD student
MSc Yasmina El Fata, PhD student
(sharing with Institute of Anatomy)
Ozan Kücükkase, PhD student
MSc Umara Rafiqi, PhD student
Abdulloh Kafa Bihi, MSc student
Young Hwa Yang, MSc student
Prof. Dr. med. Eva Diamantis-Karamitopoulou,
Guest Medical Doctor
MSc Eva Mayere (from November 2023), PhD student
MSc Camilla Ullmann (from December 2023), PhD student
Marco Visani, MSc student (until 31.1.2023)
Dr. med. Konstantin Bräutigam, MD, Resident

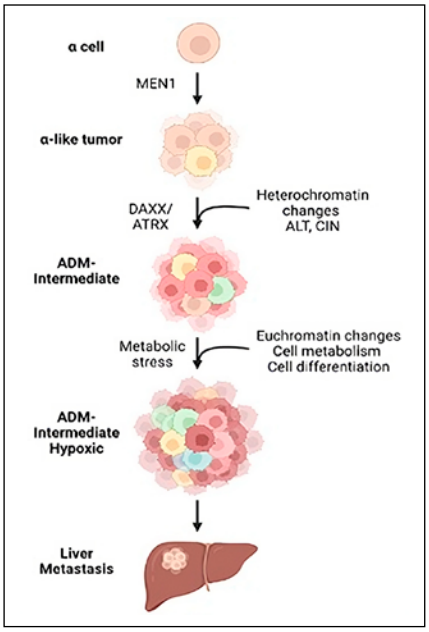
Summary of Research Activities

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.

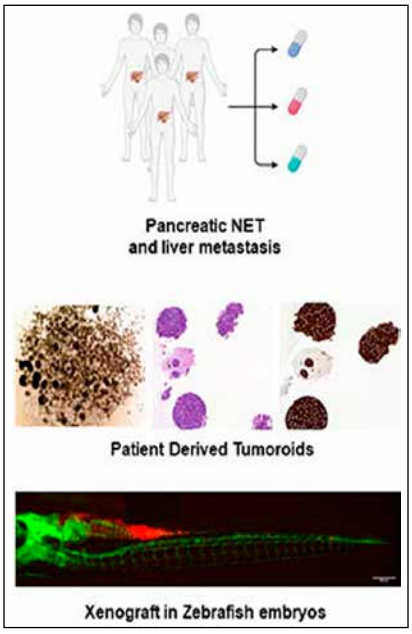


Project 1: Graphical representation of PanNET progression.

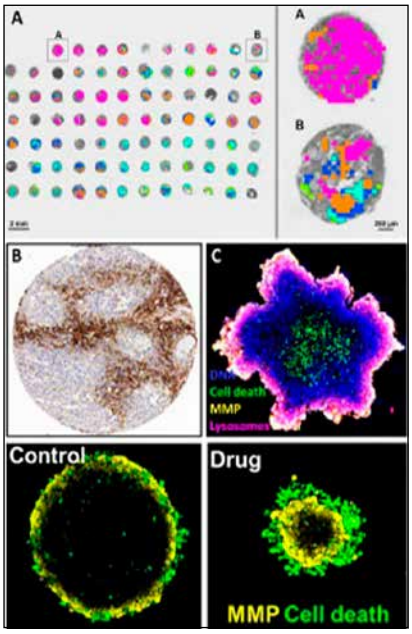
Project 2: Precision medicine approach for PanNET treatment
Up to date, no therapy prediction based on specific molecular profile is possible for PanNET patients. We recently established patient-derived tumoroid cultures from PanNEN patients which resemble features of original tumor tissue and which can be used for in vitro drug screenings. We demonstrated the utility of PanNEN tumoroids to predict patient therapy response and we identified novel epigenetic treatment options. Recently we established xenograft of PanNEN on Zebrafish embryos to further exploit in precision medicine.

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 and develop distinct metabolic subtypes. 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 PanNET stages by modern mass spectrometry, fluorescence microscopy and RNAseq data will delineate these metabolic changes and test novel therapeutic strategies.

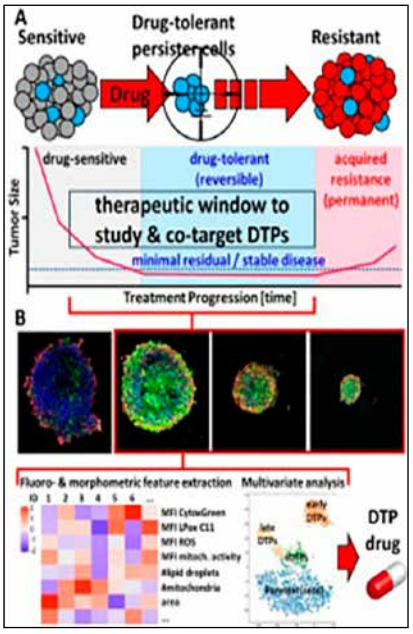
Project 4: An early offensive against acquired therapy resistance in PanNET
Acquired drug resistance (ADR) is a major clinical challenge to all current and future cancer treatments, including chemo, radiation, targeted, and immune therapies and accounts for 90% of cancer mortality. Due to the stochastic,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



Project 2: Precision medicine for PanNEN patient. PanNEN tumoroids in culture, H&E staining and synaptophysin staining of embedded tumoroids (middle). Zebrafish xenotransplant, red: tumor cells, green: endothelial cells.



Project 3: (A) Tissue mass spectrometry identified five metabolic subtypes. (B) Immunohistochemistry and (C) fluorescence microscopy show metabolic heterogeneity. Anti-metabolic drug causes spatially targeted cell death in PanNET spheroid (bottom).



Project 4: (A) DTPs precede acquired drug resistance (ADR). (B) Time-lapse fluorescence microscopy of PanNET shows therapy-induced loss of sensitive cells and emergence of DTPs. Single-cell phenotypic and molecular analysis to identify drugs for repurposing against DTPs

Internal Collaborations

- Philippe Krebs, PhD
- Erik Vassella, PhD
- Inti Zlobec, PhD
- Hannah Williams, PhD
- Mario Tschan, PhD

External Collaborations

National

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

International

- Dr. Chrissie Thirlwell, University of Exeter school of medicine, Exter, 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 Department, San Raffaele, Milan, Italy
- Dr. med. Mauro Cives, University of Bari, Bari, Italy
- Dr. Anguraj Sadanandam, ICR, The Institute of Cancer Research, London, UK.
- Prof. Gabriele Capurso, Pancreas Translational and Clinical Research Center, San Raffaele Scientific Institute Milan, Italy
- Dr. Charles Bidgood, Queensland University of Technology, Brisbane, Australia

Grant Support

- SNF 310030_188639, Aurel Perren (PI), 2020–2024, CHF 632'000
- SNF 320030_214902, Ilaria Marinoni (PI), 2023–2027, CHF 688'609
- Bern Center for Precision Medicine, Ilaria Marioni (PI), Nadja Mercader (PI), 2022–2024, CHF* 174'000
- Swiss 3RCC, Martin Sadowski (PI), 2023, CHF 5'875
- KFS-5539-02-2022, Martin Sadowski (PI), 2022–2025, 359'000

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

Administrative duties

Aurel Perren

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

Ilaria Marinoni

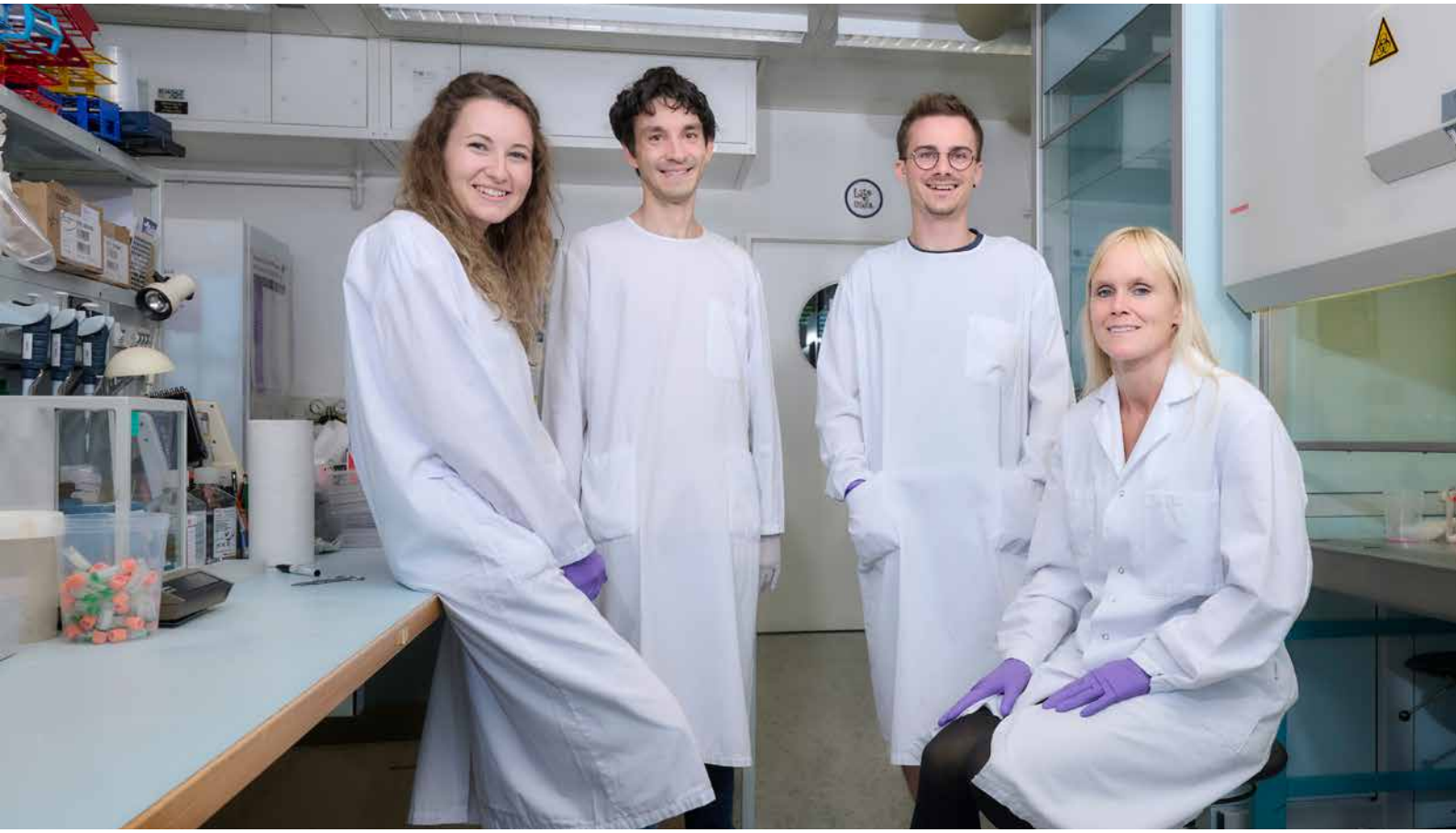
- Member of NET model consortium (Leader of the in vivo group)
- Secretary of the ENETs Basic and Translational research group

Martin Sadowski

- Coordinator MICA microscope
- Member of MIC-Committee (Microscopy Imaging Center)

Publications

- Morken Siren, Langer Seppo W, Sundlöv Anna, Vestermark Lene Weber, Ladekarl Morten, Hjortland Geir Olav, Svensson Johanna B, Tabaksblat Elizaveta Mitkina, Haslerud Torjan Magne, Assmus Jörg, Detlefsen Sönke, Couvelard Anne, Perren Aurel, Sorbye Halfdan
  Phase II study of everolimus and temozolomide as first-line treatment in metastatic high-grade gastroenteropancreatic neuroendocrine neoplasms.
  British journal of cancer, 129(12), pp. 1930-1939. Nature Publishing Group 10.1038/s41416-023-02462-0
- Karamitopoulou Eva, Wenning Anna Silvia, Acharjee Animesh, Zlobec Inti, Aeschbacher Pauline, Perren Aurel, Gloor Beat
  Spatially restricted tumour-associated and host-associated immune drivers correlate with the recurrence sites of pancreatic cancer.
  Gut, 72(8), pp. 1523-1533. BMJ Publishing Group 10.1136/gutjnl-2022-329371
- Nesti Cédric, Bräutigam Konstantin, Benavent Marta, Bernal Laura, Boharoon Hessa, Botling Johan, Bouroumeau Antonin, Brcic Iva, Brunner Maximilian, Cadiot Guillaume, Camara Maria, Christ Emanuel, Clerici Thomas, Clift Ashley K, Clouston Hamish, Cobianchi Lorenzo, Ćwikła Jarosław B, Daskalakis Kosmas, Frilling Andrea, Garcia-Carbonero Rocio; ....
  Hemicolectomy versus appendectomy for patients with appendiceal neuroendocrine tumours 1–2 cm in size: a retrospective, Europe-wide, pooled cohort study.
  Lancet oncology, 24(2), pp. 187-194. Elsevier 10.1016/S1470-2045(22)00750-1
- Knappskog Stian, Grob Tobias, Venizelos Andreas, Amstutz Ursula, Hjortland Geir O, Lothe Inger M, Kersten Christian, Hofsli Eva, Sundlöv Anna, Elvebakken Hege, Garresori Herish, Couvelard Anne, Svensson Johanna, Sorbye Halfdan, Perren Aurel
  Mutation Spectrum in Liquid Versus Solid Biopsies From Patients With Advanced Gastroenteropancreatic Neuroendocrine Carcinoma.
  JCO precision oncology, 7, e2200336. American Society of Clinical Oncology 10.1200/PO.22.00336



Research group Mirjam Schenk

Group of Mirjam Schenk, PhD

Steve Robatel, PhD student
Lukas Bäriswyl, technician (50%)
Ivanina Mutisheva, MSc, technician (until July 2023)

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 immunophenotyping 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 ther efore 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

- Kaspar Z'Graggen, MD, Department of Surgery, Clinic Beau-Site, Bern
- Charlotte Brüggen, MD, Department of Dermatology, University Hospital Zürich
- Li Tang, PhD, Institute of Bioengineering, Institute of Materials Science and Engineering EPFL, Lausanne
- Michel Gilliet, MD, Department of Dermatology, CHUV Lausanne
- Robert Hunger, MD, Department of Dermatology, Inselspital, University of Bern

International

- Robert Modlin, MD, David Geffen School of Medicine, Dermatology, UCLA, Los Angeles, USA
- Delphine Lee, MD, The Lundquist Institute for Biomedical Innovation, Torrance, California, USA
- Feiyange Ma, PhD, Department of Cell and Developmental Biology, Feinberg School of Medicine, Northwestern University, Chicago, USA

Grant Support

- Novartis , Mirjam Schenk (PI), 2021–2024, CHF 52'000
- CK-CARE, Christine Kühne Foundation for Allergy, Research and Education, Mirjam Schenk, 2023–2025, CHF 160'000

Administrative duties

- Member of the Expert Committee Cell Biology, Graduate School for Cellular and Biomedical Sciences (GCB), University of Bern
- Member of the Mass Cytometry steering committee, University of Bern, Switzerland
- Member of the Nomination Committee for Professorship at the Medical Faculty, University of Bern, Switzerland

Publications

- Aydin Sidar, Pareja Javier, Schallenberg Vivianne M, Klopfstein Armelle, Gruber Thomas, Page Nicolas, Bouillet Elisa, Blanchard Nicolas, Liblau Roland, Körbelin Jakob, Schwaninger Markus, Johnson Aaron J, Schenk Mirjam, Deutsch Urban, Merkler Doron, Engelhardt Britta
  Antigen recognition detains CD8+ T cells at the blood-brain barrier and contributes to its breakdown.
  Nature communications, 14(1), p. 3106. Nature Publishing Group 10.1038/s41467-023-38703-2
- von Werdt Diego, Gungor Bilgi, Barreto de Albuquerque Juliana, Gruber Thomas, Zysset Daniel, Kwong Chung Cheong K C, Corrêa-Ferreira Antonia, Berchtold Regina, Page Nicolas, Schenk Mirjam, Kehrl John H, Merkler Doron, Imhof Beat A, Stein Jens V, Abe Jun, Turchinovich Gleb, Finke Daniela, Hayday Adrian C, Corazza Nadia, Mueller Christoph
  Regulator of G-protein signaling 1 critically supports CD8+ TRM cell-mediated intestinal immunity.
  Frontiers in immunology, 14, p. 1085895.
  Frontiers Research Foundation 10.3389/fimmu.2023.1085895
- Wallimann Alexandra, Schenk Mirjam
  IL-32 as a potential biomarker and therapeutic target in skin inflammation.
  Frontiers in immunology, 14(1264236), p. 1264236.
  Frontiers Research Foundation 10.3389/fimmu.2023.1264236

Research group Mario P. Tschan

Group of Mario P. Tschan, PhD

Anna Bill, PhD postdoc, 70%
Nils Bodmer, PhD student (shared Inti Zlobec)
Yasmeen Mady, MD-PhD student
Rina Mehmeti, MD-PhD student (shard Inti Zlobec)
Shun Yi, MD student
Jun Xu, MD-PhD student
Bürgler Alexandra, MMed (until May 2023)
Carmen Kalbermatter, MSc student (until April 2023)
Tanja Muralt, MSc student (until April 2023)
Ana Quirós González, MSc student
Mengyu Zhou, MSc student
Maarii Khan, MSc student
Deborah Krauer, technician, 80%

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 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 mRNA 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* 660'000
- UniBE ID grant, Co-PIs: B. Towbin; M.P. Tschan, 2021–2024, 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 PI, 2022–2025, CHF 90'000
- CDM Fellowship Egypt (Yasmeen Mady), M.P. Tschan PI, 2022–2026, CHF 120'000

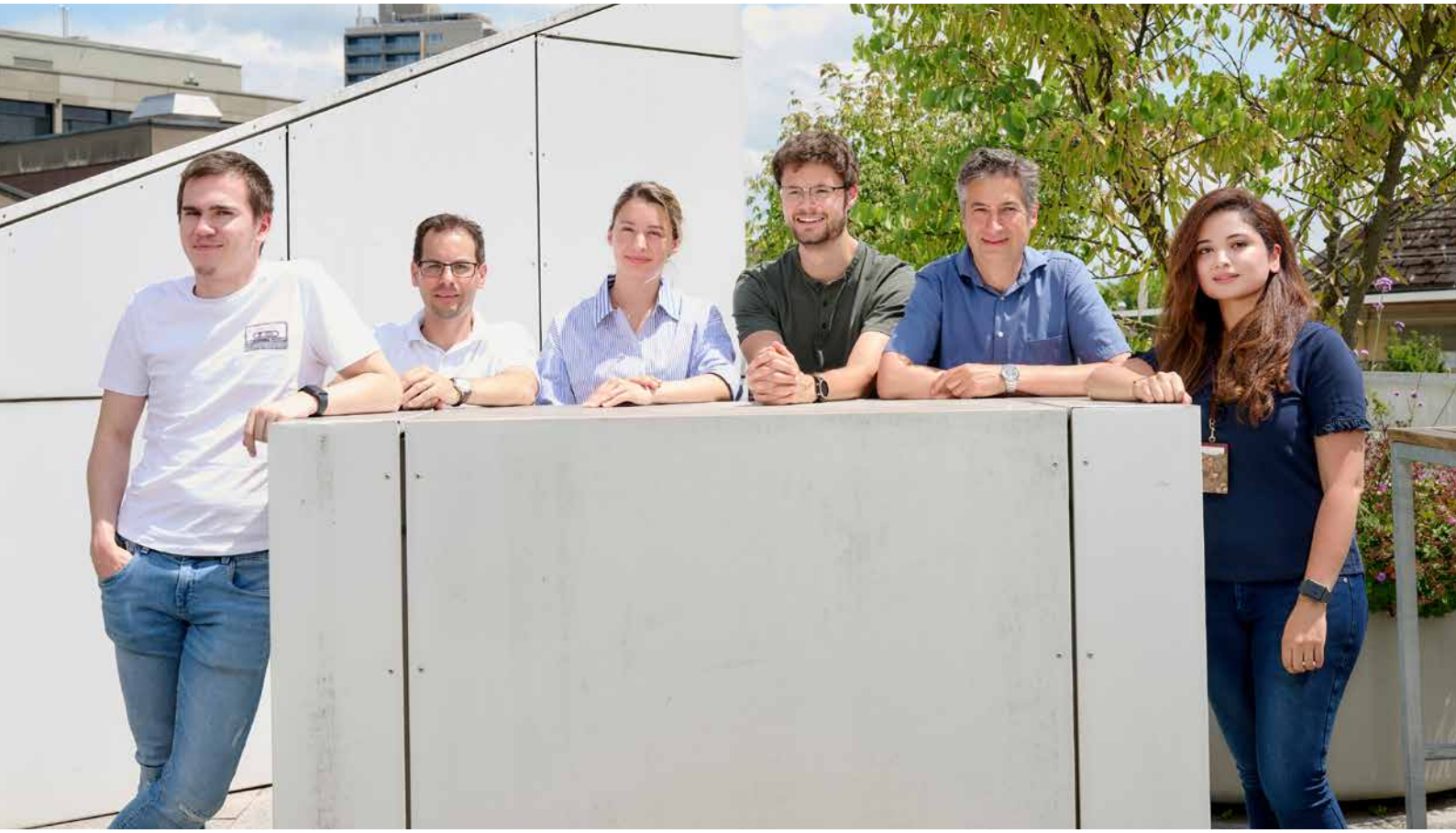
* total amount of funding; funding shared by PI and Co-PIs

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»
- President Life Sciences Switzerland LS^2

Publications

- Losmanová Tereza, Tschan Mario P, Galván José A, Berezowska Sabina
  Immunohistochemical Detection of the Chaperone-Mediated Autophagy Markers LAMP2A and HSPA8 in Formalin-Fixed and Paraffin-Embedded Tissues.
  Methods in molecular biology, 2566, pp. 141-147.
  Springer 10.1007/978-1-0716-2675-7_11



Research group Erik Vassella

Group of Erik Vassella, Dr. pharm.

Dr. med. Theoni Maragkou, Consultant Neuropathologist
Dr. Elham Kashani, PhD, Staff Scientist
Dr. Massimo Maiolo, PhD, Advanced Postdoc
Jaison Phour, Laboratory technician
MSc Romain Alexandre Gros, PhD student
MD Philipp Zens, PhD student (until August 2023)
Catarina Bieler, Master student Med
Luca Rickli; Master student Med
Evelina Parvanova, MSc 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 inter-

vals, 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: Clinical, pathological and molecular characterization of adult medulloblastomas for targeted therapy: a multicenter cohort study including primary and relapse cases

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 are currently studying 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.

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. 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

- 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, 2019–2024, CHF 365'500
- Krebsliga Bern, Theoni Maragkou (PI), 2022–2024, CHF 67'500
- Bern Center for Precision Medicine (BCPM), Erika Vassella Co-PI, Prof. Ren-Wang Peng, 2022–2024, CHF 130'000
- Stiftung für klinisch-experimentelle Tumorforschung, Theoni Maragkou (PI), 2022–2024, CHF 32'500

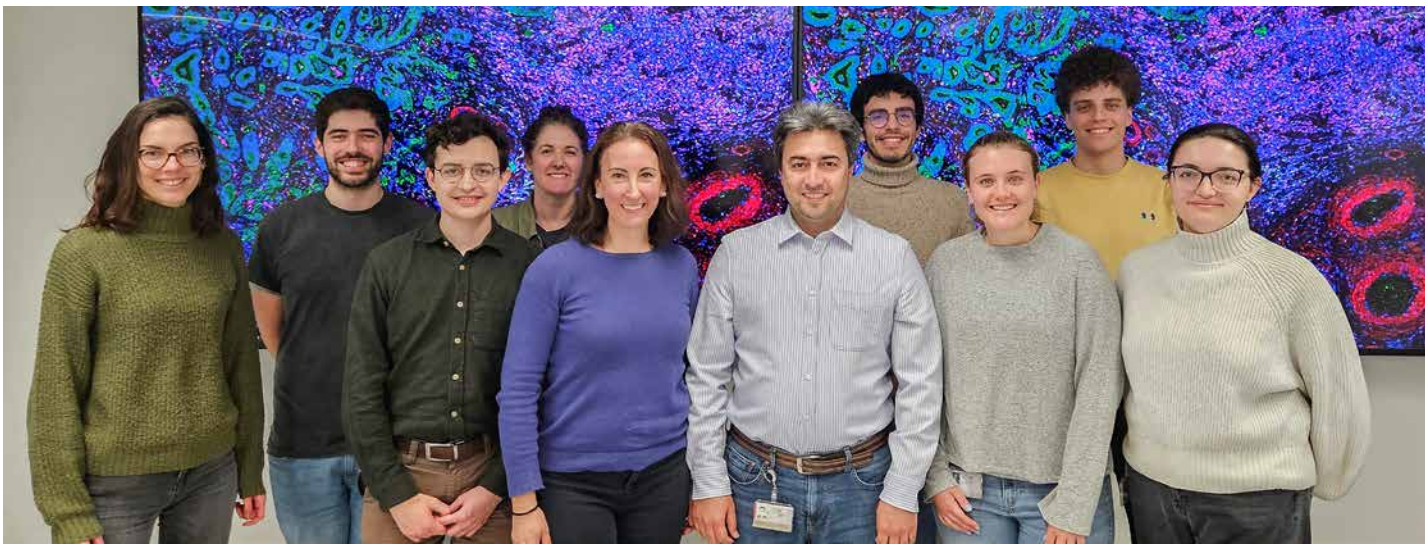
Administrative duties

Maragkou

- Member of the Steering Committee of the Young Clinical Neuroscientists (YouCliN) Network (SFCNS)
- Co-responsible for the education of medical residents, Institute of Tissue Medicine and Pathology, University of Bern, Switzerland, and organizer of the teaching activities

Publications

- Maragkou Theoni, Reinhard Stefan, Jungo Patric, Pasquier Baptiste, Neuenschwander Maja, Schucht Philippe, Vassella Erik, Hewer Ekkehard Walter
  Evaluation of MTAP and p16 immunohistochemical deficiency as surrogate marker for CDKN2A/B homozygous deletion in gliomas.
  Pathology, 55(4), pp. 466-477.
  Elsevier 10.1016/j.pathol.2023.01.005
- Kashani Elham, Schnidrig Désirée, Hashemi Gheinani Ali, Ninck Martina Selina, Zens Philipp, Maragkou Theoni, Baumgartner Ulrich, Schucht Philippe, Rätsch Gunnar, Rubin Mark A, Berezowska Sabina, Ng Charlotte K Y, Vassella Erik
  Integrated longitudinal analysis of adult grade 4 diffuse gliomas with long-term relapse interval revealed upregulation of TGF-β signaling in recurrent tumors.
  Neuro-Oncology, 25(4), pp. 662-673.
  Oxford University Press 10.1093/neuonc/noac220
- Gros Romain, Rodríguez-Núñez Omar, Felger Leonard, Moriconi Stefano, McKinley Richard, Pierangelo Angelo, Novikova Tatiana, Vassella Erik, Schucht Philippe, Hewer Ekkehard, Maragkou Theoni
  Effects of formalin fixation on polarimetric properties of brain tissue: fresh or fixed?
  Neurophotonics, 10(2), 025009. SPIE 10.1117/1.NPh.10.2.025009



Research group Inti Zlobec

Group of Inti Zlobec, PhD

Inti Zlobec, PhD
Hannah Williams, PhD, Junior Group Leader
Cristina Graham Martinez, PhD, Research assistant
Amjad Khan, PhD, post-doc
Cansaran Saygili Demir, PhD, post-doc (until May)
Christian Abbet (PI: Jean-Philippe Thiran, EPFL)
Elias Baumann, PhD student
Nils Bodmer, PhD student (shared Mario Tschan)
Ana Leni Frei, PhD student
Mauro Gwerder, PhD student
Rina Mehmeti, MD, PhD student (shared Mario Tschan)
Linda Studer, PhD student (PI: Heather Dawson)
Philipp Zens, MD, PhD student (PI: Sabina Berezowska, CHUV)
Stefan Reinhard, ICT staff
Caroline Hammer, Administration

Master and dissertation students (MSc or Medicine):
Meisam Asgari, Master of Computer Science (PI: Andreas Fischer, Uni Fribourg)
Javier Garcia Baroja Master of Biomedical Engineering, Bioimaging, ETH Zurich
Joël Baumann, MMed (PI: Bastian Dislich)
Mansour Faye Mohamed (PI: Hannah Williams)
Jérémy Rotzetter (PI: Hannah Williams)
Kartik Kohli Master of Computer Science (PI: Aart Mookhoek)
Josh Müller, MMed
Luca Noti, Dissertation MMed
Chris Rüttimann, Master of AI in Medicine (CAIM) (PI: Amjad Khan)

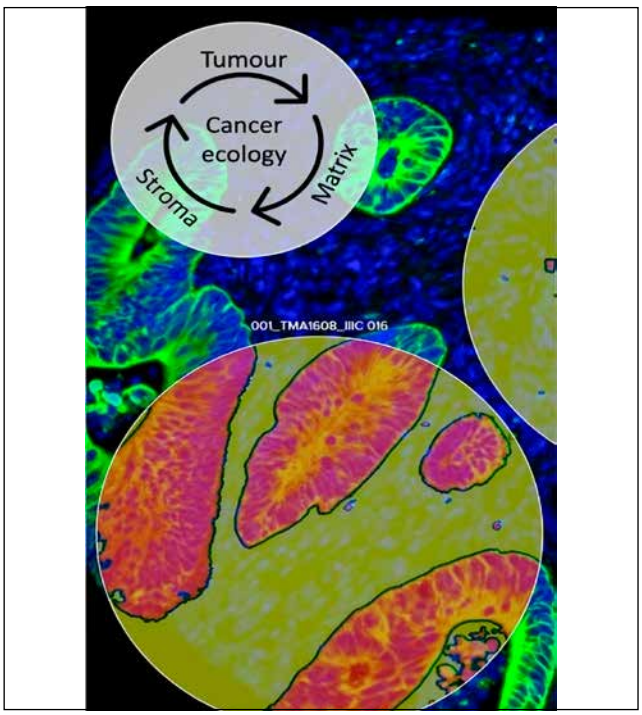
Summary of research activities

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: Spatial omics for deep characterisation of the cancer ecosystem and its association with disease prognostication and treatment response prediction

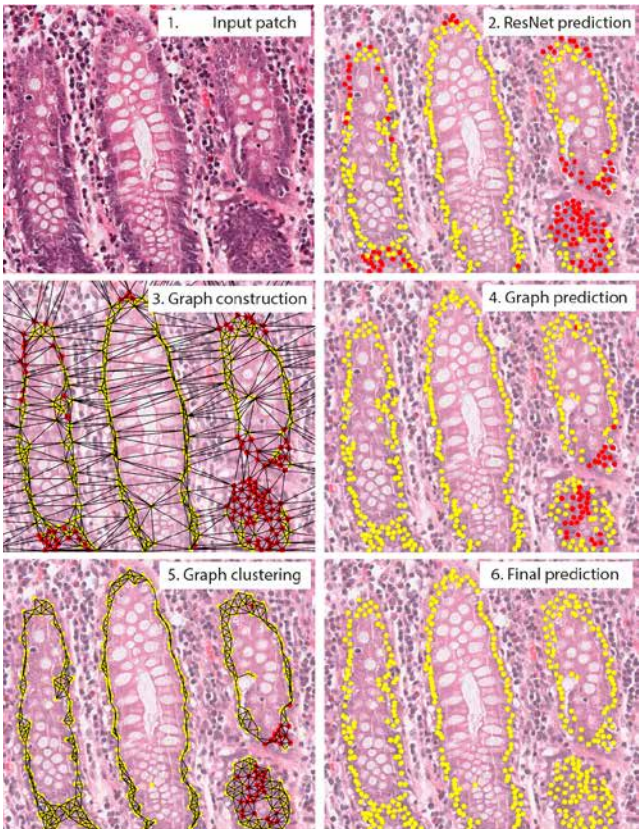
The cancer ecosystem comprises tumour, stroma (cellular component) and extracellular matrix (ECM), together the stroma and ECM make the tumour microenvironment (TME). The Williams group utilises spatially resolved technologies including Nanostring GeoMx Digital Spatial Profiler (DSP), CosMx Spatial Molecular Imager (SMI) and MACSima plat-



Project 1: Spatially resolved transcriptomic profiling of the cancer ecosystem in colorectal cancer. Primary antibodies for tissue visualisation –Green: PanCK (epithelium), Blue: DNA (nuclei). Region of interest selection – Red: tumour, Yellow: tumour microenvironment.

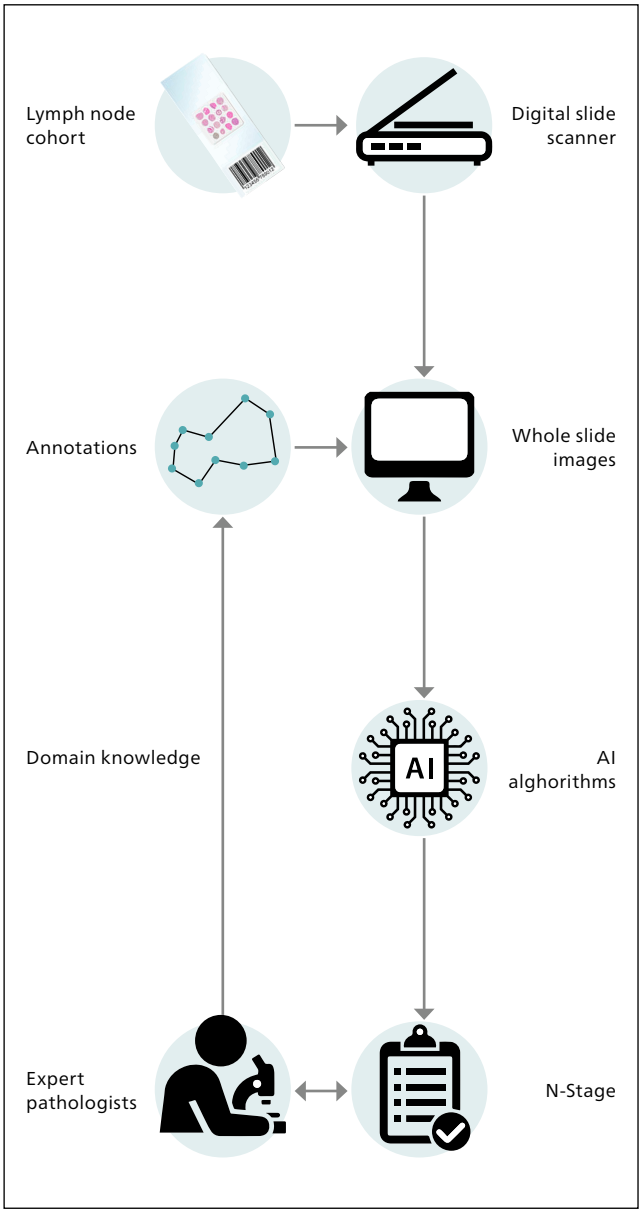
forms to examine how the composition and architecture of the cancer ecosystem defines disease phenotypes.
Current projects include: Examination of TME heterogeneity and its association with epithelial identity and plasticity in colorectal cancer. Deep characterisation of the biochemical and structural properties of the ECM for predictive and prognostic biomarker identification

Project 2. Digital pathology & AI to gain novel insights into colorectal cancer
Our Sinergia project uses AI to gain new insights into the biology of colorectal cancers. We investigate morphomolecular relationships, including the molecular subtypes 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 transcriptional subtypes using spatial transcriptomic and spatial protein expression analysis. The TME, 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: 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 generating a pan-lymph node metastasis algorithm using state-of-the-art deep learning methods. We then streamline processes from the lab to data analysis, and on to visualisation of results and interaction of our algorithms with pathologists scores and feedback. Together with our expert pathologist colleagues, we collaborate on a variety of algorithms including PD-L1 (Tereza Losmanova), H. pylori (Bastian Dislich), IBD scoring (Aart Mookhoek), tumor budding- CD8 scores (Heather Dawson), breast biomarkers (Wiebke Solass) and pancreas pathology (Martin Wartenberg).



Project 3: Computational analysis of colorectal cancer metastases in lymph nodes.

Internal Collaborations

- Mario Tschan, PhD
- Philippe Krebs, PhD
- Bastian Dislich, MD
- Philipp Kirchner, PhD
- GIPAR research group, ITMP

External collaboration

National

- Sinergia Co-PI's and project partners:
  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
- Thibaud Koessler, Claudia Corro and Giacomo Puppa, HUG, Geneva
- Jean-Philippe Thiran, EPFL, Lausanne
- Andrew Janowcyzk, CHUV, Lausanne

International

- Nigel Jamieson, University of Glasgow, UK
- Joe Yeong, Agency for Science, Technology and Research, Singapore
- Thomas Cox, Garvan Institute of Medical Research, Sydney
- Iris Nagtegaal & Team, Radboud Medical Center, Netherlands
- Norman Zerbe, Charité Berlin, Germany
- Tilman Rau, Pathologie, Düsseldorf
- Jerome Galon & Immunoscore Team, INSERM, France
- Lunaphore Technologies, Switzerland
- Indica Labs, USA
- Aiforia AI for Image Analysis, Finland

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, CHF 353'100
- Swiss Cancer Leage als Co-Applicant mit Prof. Matthias Hediger, I. Zlobec (PI), 2022–2024, CHF 96'930
- Werner und Hedy Berger-Janser Foundation, H. Williams (PI), 2023–2024, CHF 80'000
- Swiss Cancer Leage KLS 5611, Zlobec (PI), 2023–2026, CHF 371'950

Administrative duties

I.Zlobec

- Member of the Medical Faculty, providing support in commissions and Habilitation processes
- Executive Team Member, Center for AI in Medicine, responsible for Pillar 4 (research) and working group on Diversity for AI in Medicine (DAIM)
- Board member Bern Center for Precision Medicine
- Representative at the Commission for Equal Opportunities, at the Medical Faculty (IFKG)
- Mentor for PhD students, Graduate School of Cell Biology
- President of Swiss Digital Pathology Consortium (SDiPath)
- Chair of the Working Group for Digital & Computational Pathology, European Society of Pathology
- Reviewer Swiss Data Science Center proposals

H. Williams

- SPatial Omics Consortium (SPOC)

Publications

- Janowczyk A, Zlobec I, Walker C, Berezowska S, Huschauer V, Tinguely M, Kupferschmid J, Mallet T, Merkler D, Kreutzfeldt M, Gasic R, Rau TT, Mazzucchelli L, Eyberg I, Cathomas G, Mertz KD, Koelzer VH, Soldini D, Jochum W, Rössle M, Henkel M, Grobholz R. Swiss Digital Pathology Consortium. Swiss digital pathology recommendations: results from a Delphi process conducted by the Swiss Digital Pathology Consortium of the Swiss Society of Pathology.
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  Computer-Assisted Diagnosis of Lymph Node Metastases in Colorectal Cancers Using Transfer Learning With an Ensemble Model.
  Mod Pathol. 2023 May;36(5):100118. doi: 10.1016/j.modpat.2023.100118. Epub 2023 Feb 2. PMID: 36805793.
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1.2 Translational Research Unit (TRU)

Head of TRU:
Dr. Paulina Brönnimann

Administration:
Caroline Hammer (50%)

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

Consultation:
Prof. Inti Zlobec

Group Translational Research Unit (TRU)

Overview

The Translational Research Unit (TRU) is a tissue-based core facility of the Institute of Tissue Medicine and Pathology, University of Bern. We provide services for researchers and use innovative technologies to support translational projects conducted on human and animal tissues. We collaborate with researchers not only from the University of Bern but also participate in national and international scientific projects. Our portfolio includes histopathology services, establishment of methods for tissue «visualization», digital pathology and image analysis, and next-generation Tissue Microarraying (www.ngtma.com). 2023 brought an exciting innovation in our core facility with an implementation of spatial biology technology (acquired by Prof. Inti Zlobec). MACSima from Miltenyi was inclosed in our lab to facilitate

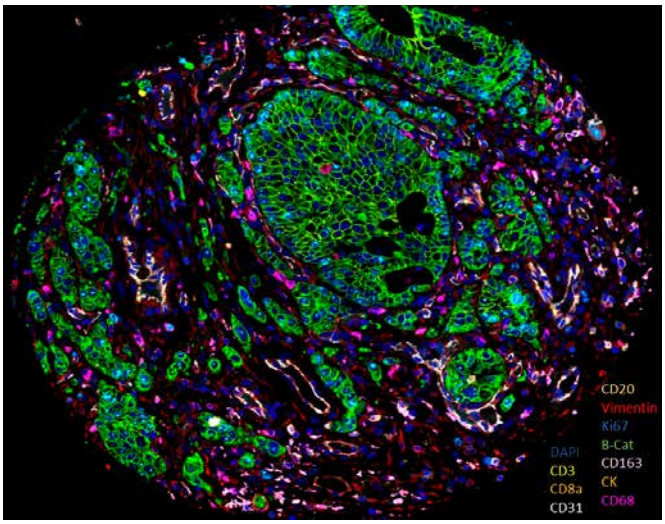
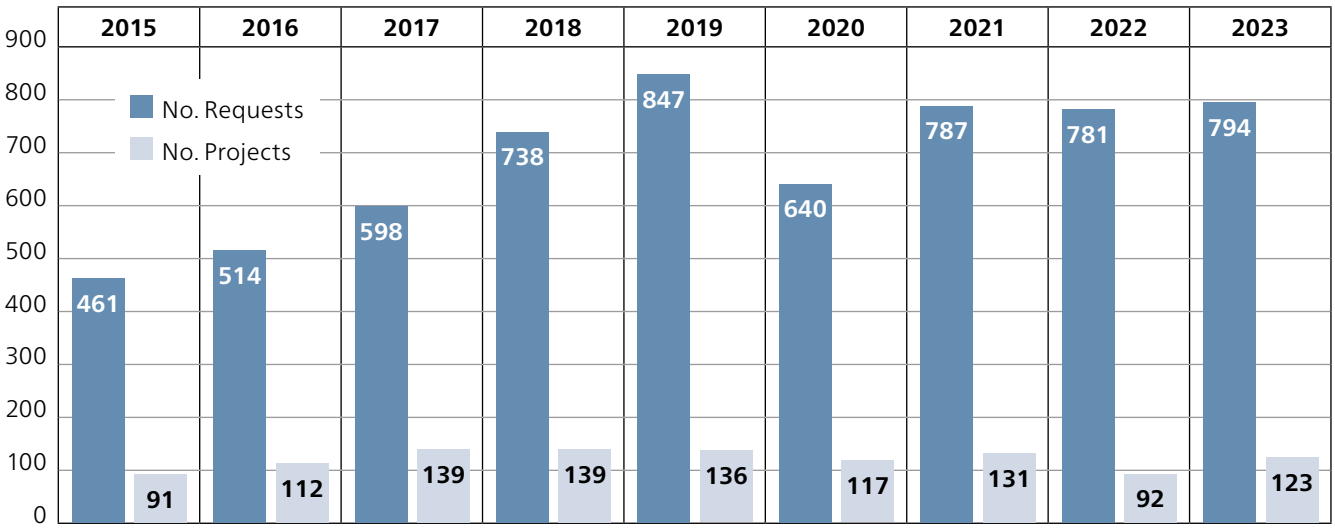
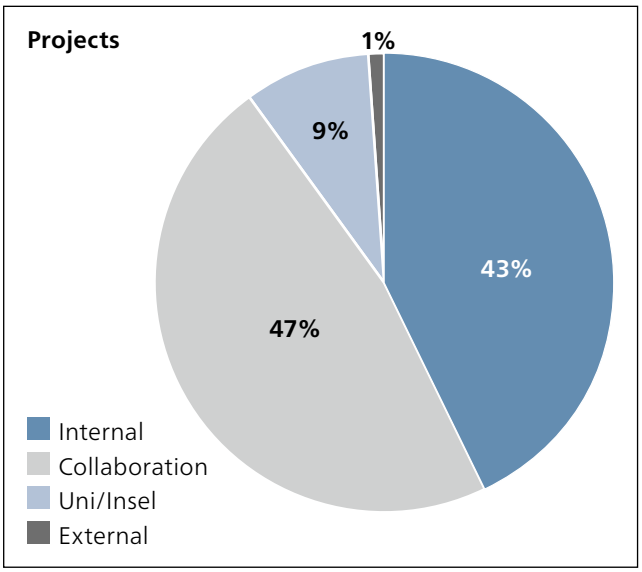
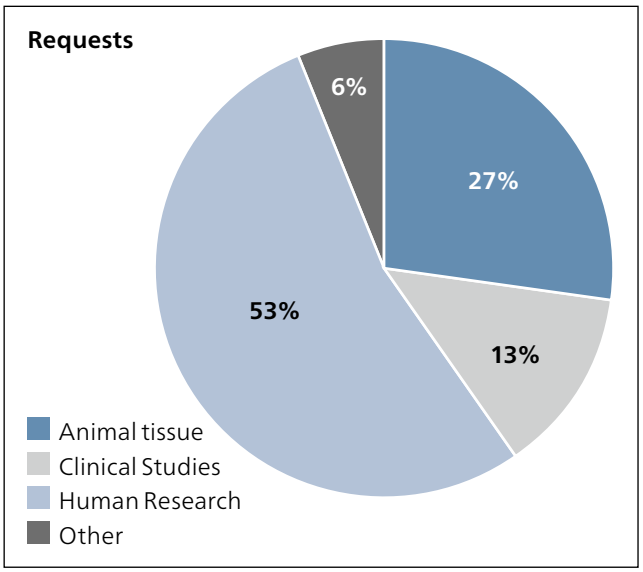


Fig. 1: MACSima instrument in TRU facility (left) and outcome of first panel establishment on the multitissue TMA (right).







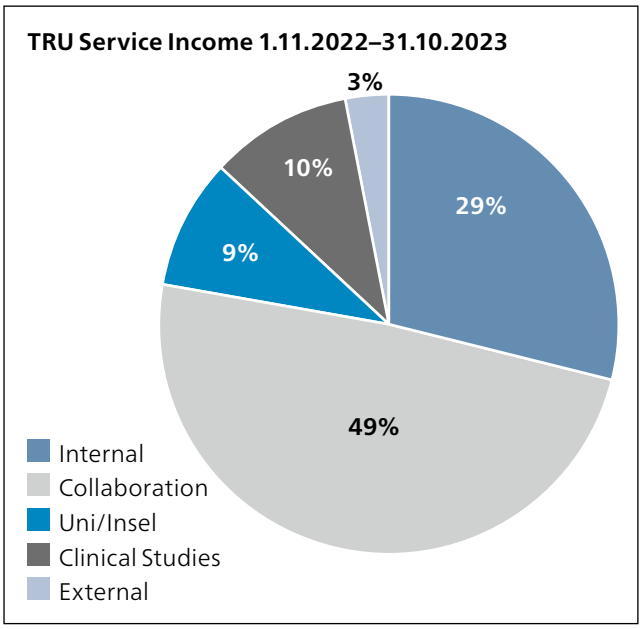


Fig. 2: Number of projects (and associated requests) managed by TRU in 2023 and distribution of funding sources this year.

understanding of complex cellular phenotypes and their interactions in the spatial context of the tissue microenvironment. MACSima platform is a fully automated fluorescence instrument utilizing MACSima Imaging Cyclic Staining technology: cyclic staining with different fluorochrome-conjugated antibodies in 3 steps: staining, imaging and erasing (photobleaching or fluorochrome release). We have started with establishment of the backbone immune marker panel that was designed to cover a range of different cell phenotypes and tissue types (Fig 1).

Projects and requests for services

In 2023, we could support 123 projects from 794 separate requests including 43% from internal researchers, whereas 47% were collaborations (together with those with industry) and 9% were from the Inselspital /DBMR (Fig. 2).
TRU requests include approximately 53% human samples, 27% animal tissue and 13% clinical studies (including SAKK or trials with primary investigators at the Inselspital). The remaining are other tissue-related requests.

Histology Lab and Scanning

Our lab has expertise in histology techniques and tries to personalize each research project. Furthermore, sections are cut for many other purposes including: DNA/RNA extraction, immunohistochemistry, immunofluorescence, spatial biology techniques and other special downstream methodologies. Histology is the basis of all the work performed in TRU. This year, we have cut thousands of slides for H&E or special stains (n = 3570), immunohistochemistry, single or double staining (n = 4648). Additionally, we have sectioned 64 frozen tissue on the cryostat.

With the increasing importance of digital pathology and the expansion of AI algorithms, it become essential to digitalize traditional slides. We have scanned this year 11895 H&E and IHC slides for further research purposes. Moreover, we scan each ngTMA slide after H&E or immunostaining creating a valuable digital archive for further use to train AI algorithms for prediction of clinical outcomes, molecular subtypes or other endpoints.

Tissue Visualisation Lab

TRU has expertise in tissue visualisation methods, including assays for immunohistochemistry (IHC), mRNA in situ hybridisation (ISH), immunofluorescence (IF), TUNEL or multiplexing technologies such as OPAL, OmniVue from Ultivue and COMET from Lunaphore.
We have expanded our expertise on COMET specifically investigating the innate immune response to microbial infection in mice. Currently, we focus on establishing a 20-plex immune panel to assess pathogen replication, myeloid cell populations and parameters of inflammation (Fig 3).
This year, TRU has added an additional 48 new antibodies to its repertoire, and has performed 4384 single stains, 216 double stains and 25 OPAL assays.

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

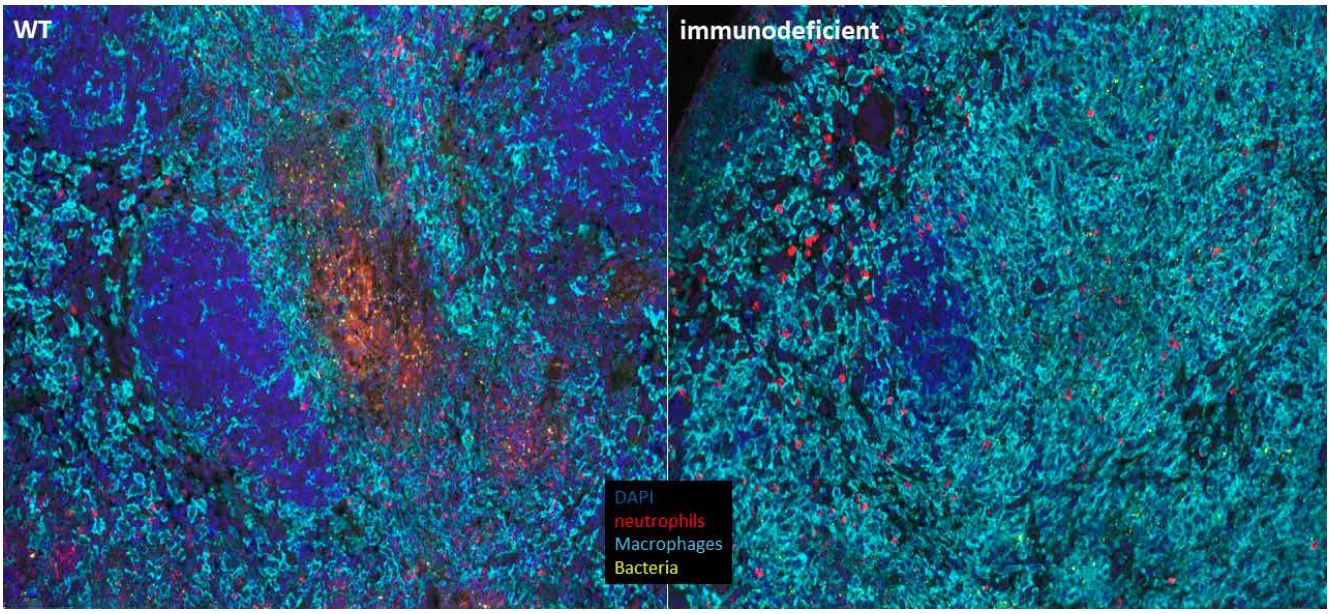
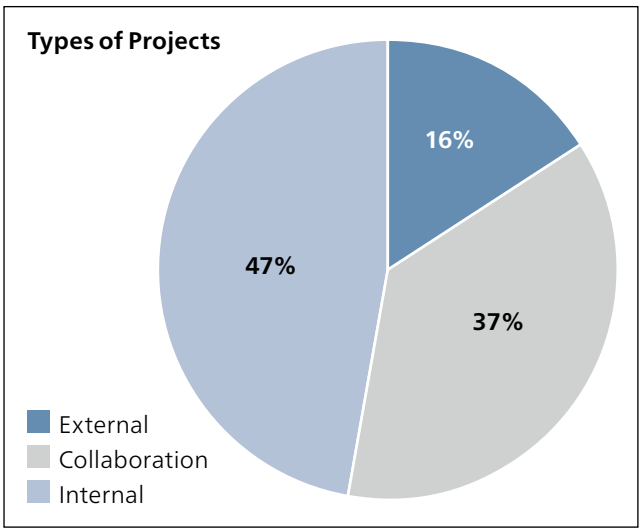


Fig. 3: Multiplex staining performed on tissue biopsies from infected wild type and immunodeficient mice. Stains: blue: DAPI; yellow: bacteria; red: neutrophils; cyan: macrophages

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.



Up to now, TRU has created 912 ngTMA blocks comprising 174869 punches. In 2023, we have constructed TMAs of urothelial tract, lower gastrointestinal cancers, liver, brain tumors, dermatitis or several multitissue TMAs (Fig 4). We were part of few animal research projects constructing TMA with mice samples from liver, lung and spleen. 19 ngTMA projects were conducted including 36 ngTMA blocks with total 3052 punches from 1132 donorblocks. Additionally, 232 cores were punched for downstream molecular analysis.

Recently, we have completed a complex project on lymphoma cohort from 354 cases, totalling 1416 punches and we are in progress to complete matching biopsies TMAs. We have participated also in 2 neurological projects contributing with construction of TMAs from brain tumors and brain metastasis from prostate.

ngTMA was a topic during a webinar organized by Standard BioTools together with our partnering lab in Bern – Imaging Mass Cytometry and Mass Cytometry Platform.

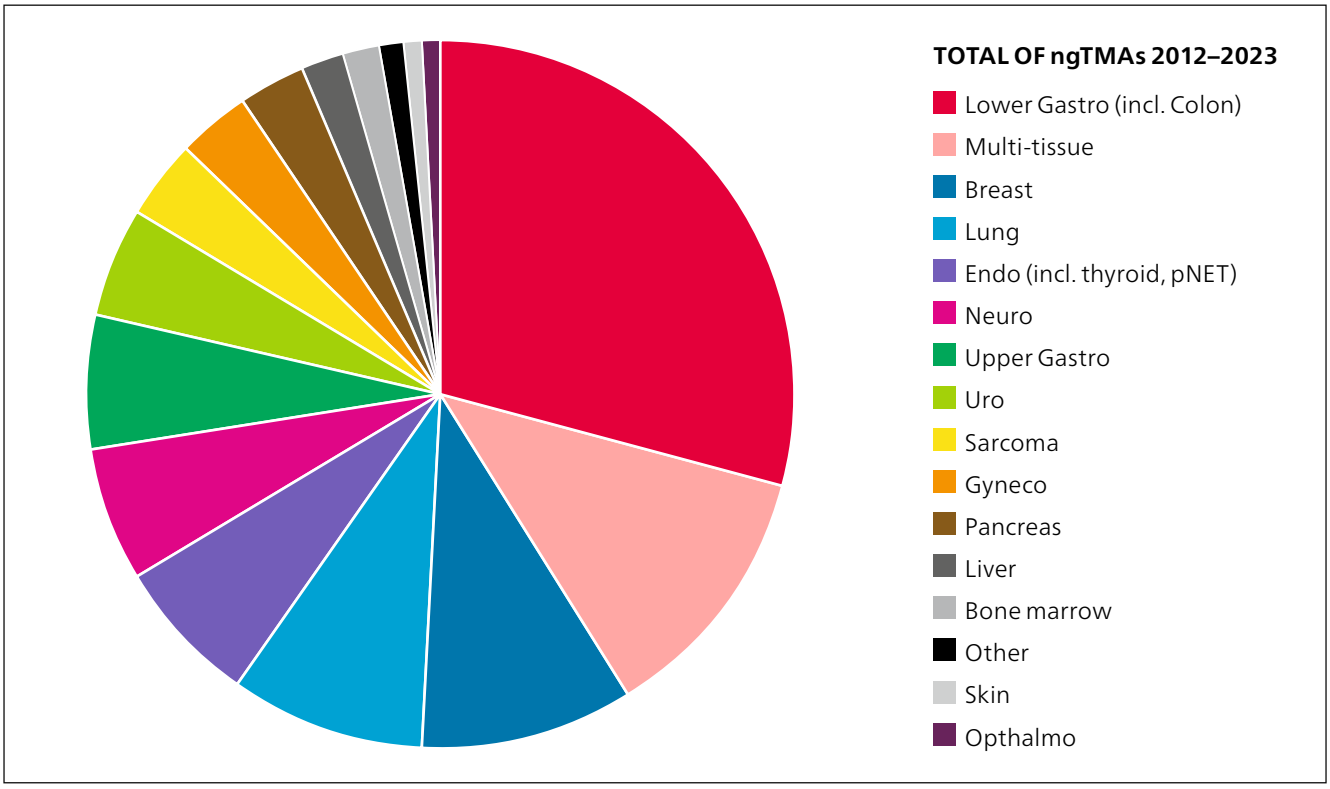


Fig. 4: ngTMA project types in 2023: internal 47%, collaboration 37% and external 16% (upper). Tissue-specific distribution of ngTMA projects since 2012 until 2023 (lower).

Publications

TRU and ngTMA supported many projects that were published this year. Here list of selected scientific articles were the support of TRU was employed:

1. Deng H, Ge H, Dubey C, Losmanova T, Medová M, Konstantinidou G, Mutlu SM, Birrer FE, Brodie TM, Stroka D, Wang W, Peng RW, Dorn P, Marti TM.
   An optimized protocol for the generation and monitoring of conditional orthotopic lung cancer in the KP mouse model using an adeno-associated virus vector compatible with biosafety level 1.
   Cancer Immunol Immunother. 2023 Dec;72(12):4457-4470. doi: 10.1007/s00262-023-03542-z. Epub 2023 Oct 5. PMID: 37796299; PMCID: PMC10700219.
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   Targeted removal of macrophage-secreted interleukin-1 receptor antagonist protects against lethal Candida albicans sepsis.
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3. Bräutigam K, Reinhard S, Wartenberg M, Forster S, Greif K, Granai M, Bösmüller H, Klingel K, Schürch CM.
   Comprehensive analysis of SARS-CoV-2 receptor proteins in human respiratory tissues identifies alveolar macrophages as potential virus entry site.
   Histopathology. 2023 May;82(6):846-859. doi: 10.1111/his.14871. Epub 2023 Feb 21. PMID: 36700825
4. Alizadeh Zeinabad H, Yeoh WJ, Arif M, Lomora M, Banz Y, Riether C, Krebs P, Szegezdi E.
   Natural killer cell-mimic nanoparticles can actively target and kill acute myeloid leukemia cells.
   Biomaterials. 2023 Jul;298:122126. doi: 10.1016/j.biomaterials.2023.122126. Epub 2023 Apr 15. PMID: 37094524.
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. Karamitopoulou E, Wenning AS, Acharjee A, Zlobec I, Aeschbacher P, Perren A, Gloor B.
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   Gut. 2023 Aug;72(8):1523-1533. doi: 10.1136/gutjnl-2022-329371. Epub 2023 Feb 15. PMID: 36792355.
7. Khan A, Brouwer N, Blank A, Müller F, Soldini D, Noske A, Gaus E, Brandt S, Nagtegaal I, Dawson H, Thiran JP, Perren A, Lugli A, Zlobec I.
   Computer-Assisted Diagnosis of Lymph Node Metastases in Colorectal Cancers Using Transfer Learning With an Ensemble Model.
   Mod Pathol. 2023 May;36(5):100118. doi: 10.1016/j.modpat.2023.100118. Epub 2023 Feb 2. PMID: 36805793.
8. Grüter BE, Canzanella G, Hägler J, Rey J, Wanderer S, von Gunten M, Galvan JA, Grobholz R, Widmer HR, Remonda L, Andereggen L, Marbacher S.
   Topographic distribution of inflammation factors in a healing aneurysm.
   J Neuroinflammation. 2023 Aug 2;20(1):182. doi: 10.1186/s12974-023-02863-1. PMID: 37533024
9. Maragkou T, Reinhard S, Jungo P, Pasquier B, Neuenschwander M, Schucht P, Vassella E, Hewer EW.
   Evaluation of MTAP and p16 immunohistochemical deficiency as surrogate marker for CDKN2A/B homozygous deletion in gliomas.
   Pathology, 55(4), pp. 466-477. Elsevier 10.1016/j.pathol.2023.01.005
10. Ferguson L P, Gatchalian J, McDermott M L, Nakamura M, Chambers K, Rajbhandari N, Lytle N K, Rosenthal S B, Hamilton M, Albini S, Wartenberg M, Zlobec I, Galván H, José A, Karamitopoulou E, Vavinskaya V, Wascher A, Lowy A M, Schürch C M, Puri P L, Bruneau B G.
    Smarcd3 is an epigenetic modulator of the metabolic landscape in pancreatic ductal adenocarcinoma.
    Nature Communications, 14(1), p. 292. Springer Nature 10.1038/s41467-023-35796-7

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

Additional members: Translational research Unit (TRU), IT and Histology Diagnostic of the Institute of Tissue Medicine and Pathology (ITMP)

The use of high-quality human specimens plays a crucial role in medical research advances, particularly in the field of precision medicine.

The Tissue Bank Bern (TBB) is a human diseased-related, solid tissue bio-repository, that provides researchers with access to high quality human tissue samples and related data in compliance to the Federal Human Research Act and Ordinance, 2014 and Swiss Biobanking Platform standards. This is done through optimal and standardized sample collection, storage, distribution and documentation as well as a strong quality management system.

TBB services are, since October 2016, being performed together with the Translational Research Unit (TRU) thus, personnel and resources are shared.

Workflow

The requirements to use the samples include 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. The estimated timelines and processes are displayed in figure 1.

REQUEST FORM	ORDER PROCESSING	SAMPLE DELIVERY
Content details Project description Sample and data requirements Ethical approval	Feasibility check Technical acceptance Clinical acceptance Patient's consent proofing	Tisssue content evaluation Material transfer agreement (only for external researchers) Material transfer to the researcher
1–8 weeks	**2–3 weeks**	**1–2 weeks**

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

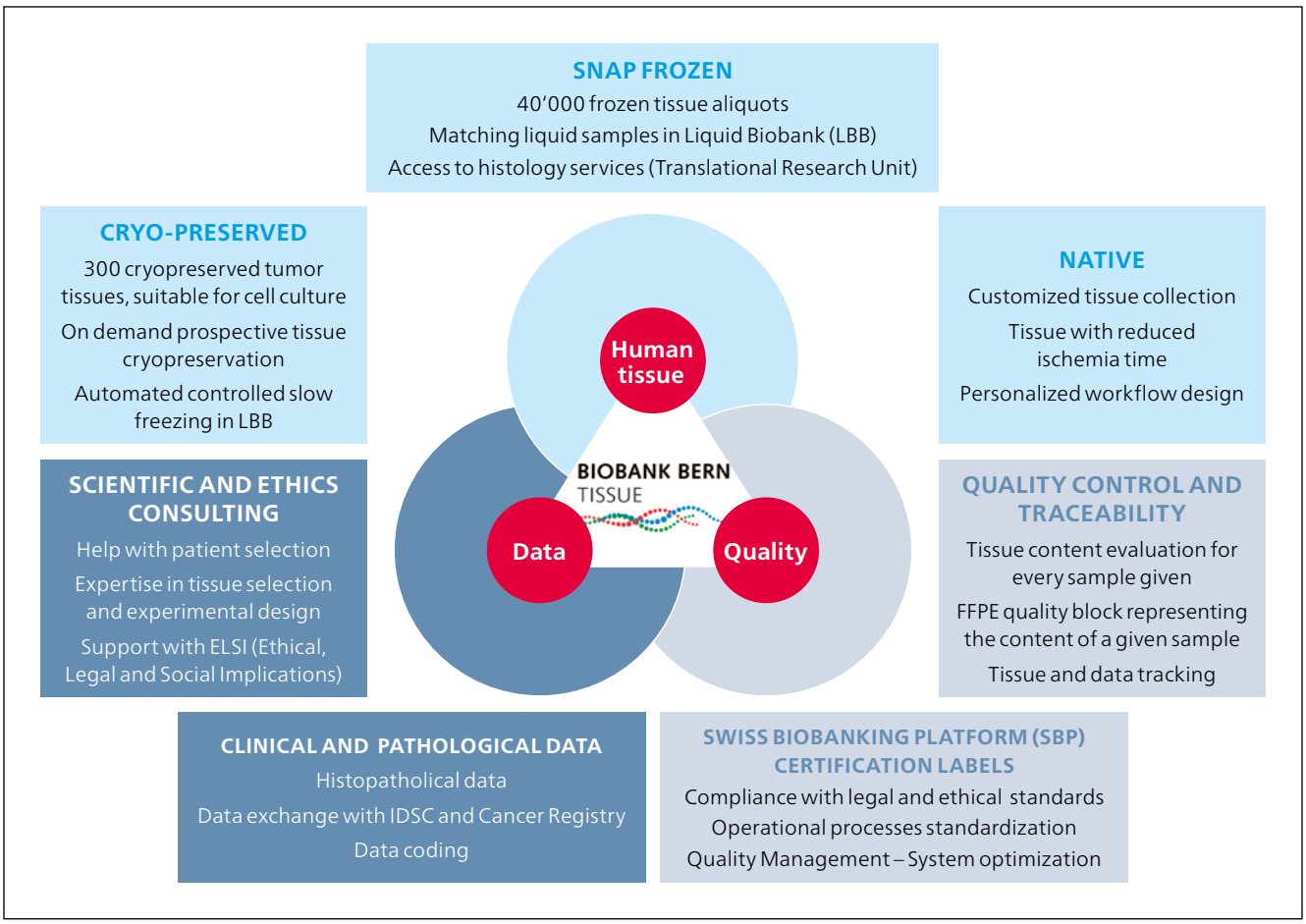


Fig. 2: Main TBB activities.

TBB activities

In 2023, we have continued providing tissues from the snap frozen and cryopreserved collection and native tissues in a prospective manner.

The cryopreservation is performed following an automated controlled slow freezing protocol in LBB (Liquid Biobank) at Inselspital, preserving the viability of the cells, what makes the collection suitable 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 around 300 cryopreserved tumor tissues from colon, liver, pancreas, ovary, breast and metastasis from different primaries.

The TBB is not only a high-quality tissue collection but also an active core facility, focused on the continuous development of workflows to meet the researcher's tissue requirements. On this regard, the close collaboration with clinics and researchers facilitates a thorough understanding of the tissue special needs and the access to the resources to fulfill them. This year, in addition to the ongoing collaborations with HNO and Angiology we have started new customized projects with the EPFL (École Polytechnique Fédérale de Lausanne) and different private partners.

Additionally, we have 10 ongoing prospective project involving native tissue form different tissue types: lung, prostate, liver, colon, pancreas, adrenal gland, neuroendocrine tumors and brain.

The principal TBB activities are summarised in figure 2.

TBB institutional collection statistics

Human biobanking has evolved into a dynamic and complex platform with more focus in quality and protocols adapted to the researchers' needs. However, the collection of frozen tissues remains important. In 2023 we have collected around 2500 aliquots from 1700 patients bringing the total collection to 57500 aliquots from more than 18000 patients from different clinics that continue their important involvement in the biobank.

The contribution per clinic can be found in the chart below, with the largest amount of samples deriving from the gynecology clinic, followed by the clinics of visceral surgery, neurosurgery, thoracic surgery as well as urology.

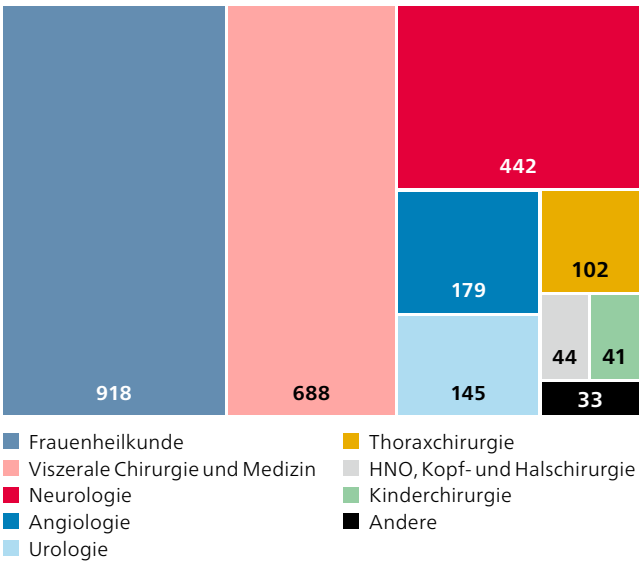


Fig. 3: Distribution of incoming tissue specimens for biobanking.

Project by Tissue Bank Bern 2023

The number of TBB projects continues to rise. In 2023, we received 77 requests for tissue and/or data.

Usage of tissue samples in 2023

During this year we have provided scientists with 133 frozen tissues. Additionally, 317 aliquots of native tissue were given in a prospective manner. The usage of frozen samples was equally distributed between researchers at the ITMP and researchers out of the University of Bern. The native tissue was mainly used by researchers from Inselspital and the Departament of BioMedical Research (DBMR) at the University of Bern.

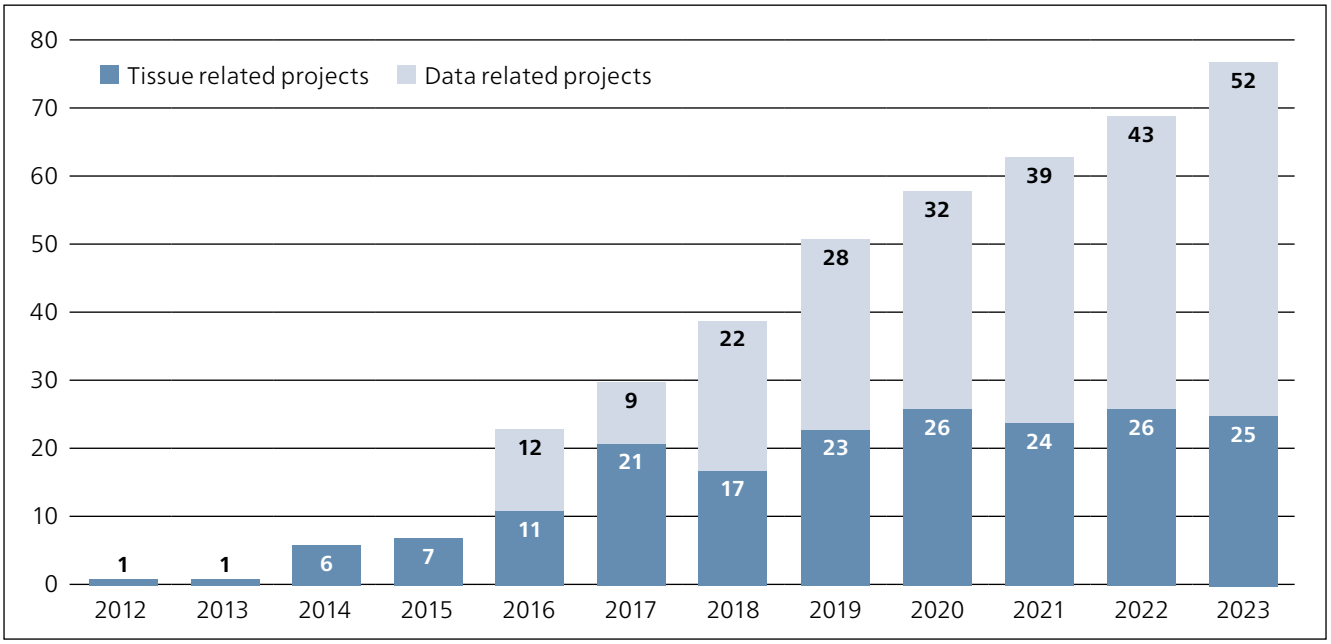


Fig. 4: Number of TBB requests for tissues/data showing increase over the last years.

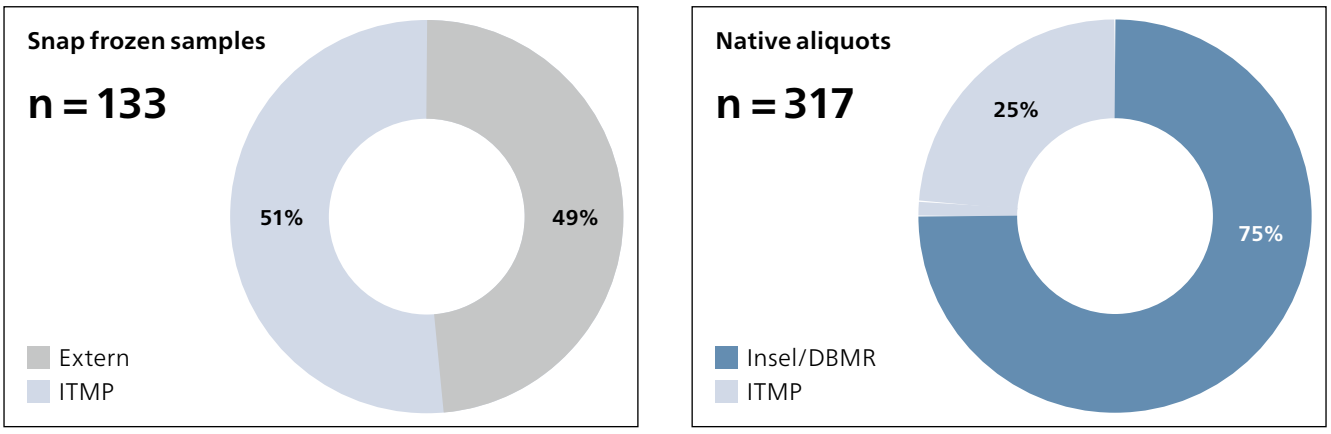


Fig. 5: Summary of tissue usage by internal, Inselspital/University of Bern (incl. DBMR) or external researchers for prospective and retrospective (frozen collection) projects in 2023.

Fig. 6: SBP labels achieved by TBB.

Towards the best quality of service

The delivery of optimal quality tissues to researchers is one of the main aims of TBB.

With a growing concern about reproducibility, not only in research but also in diagnostics, the need to standardize workflows and monitor pre-analytical variables becomes imperative, due to its impact on the tissue quality.

The preanalytical phase encompasses the processing of biological material previous to the analytical phase. In this time frame, the variables playing a role in tissue quality such as ischemia and fixation times, transport, processing and storage temperatures are meticulously documented in TBB.

This close monitoring facilitates the identification of critical points and continuous improvement according to LEAN optimization, whose main principle is the reduction of time spent on non-value-added tasks (unnecessary operations or transport, waiting times, etc.), causes of poor quality. The result is a significant reduction and homogenization of different variables such as the turnaround times, that have a major impact in tissue quality.

This strategy, together with the establishment of quality controls in crucial spots has led to the accomplishment of the Swiss Biobanking Platform (SBP) standards, acknowledged by the acquisition of the SBP Norma and Optima label in December 2019. Additionally, the collection and storage of the TBB samples are included under the Institute of Tissue Medicine and Pathology accreditation by the Swiss Accreditation Service (SAS) according to ISO 15189:2012.

Beside this, 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).

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.

Partnerships

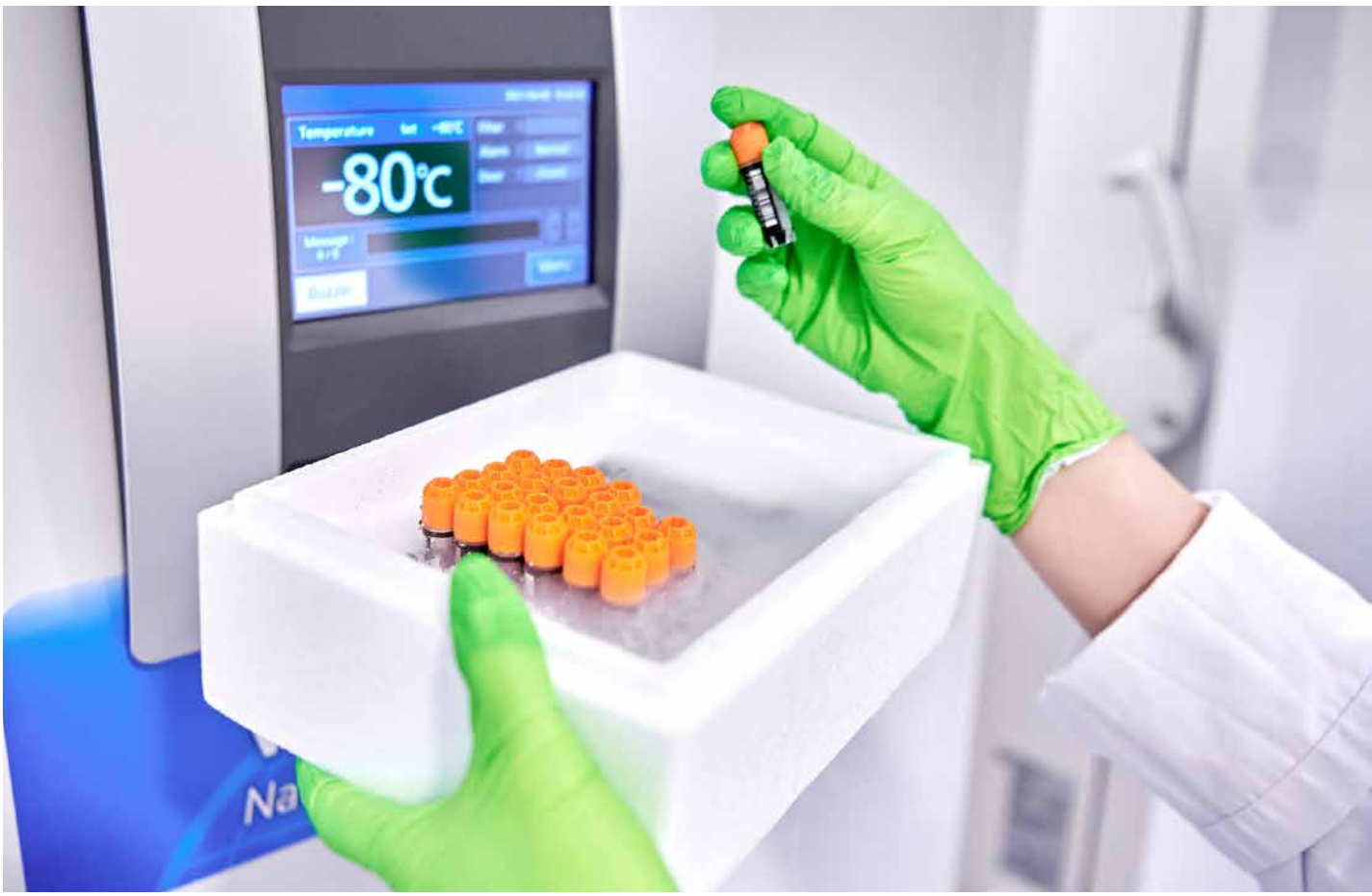
Excellence in biobanking is a multi-institutional and cross-departmental goal. We work in close collaboration with the Histology Diagnostic department of the ITMP for sample acquisition; with Liquid Biobank Bern for collaborative projects liquid-tissue and harmonisation of processes and with the Swiss Biobanking Platform for quality monitoring and process standardization.

The clinics that continue to send samples for biobanking and participating actively in the implementation of «fit for purpose» collections are invaluable as are the medical doctors and technical staff of the Clinical Pathology Lab at the Institute of Tissue Medicine and Pathology. Support from the IT department is of upmost importance to ensure high quality and LEAN processes.

Additionally, the multidisciplinary co-work with the Insel Data Science Center and Cancer Registry Bern-Solothurn completes the toolbox to improve not only the quality of biological material resources but also the quality of the associated data.

TBB also participates in scientific seminars such us the Day of Clinical research 2023 in which a poster with our main activities was presented.

Fig. 7: Collection procedure of peripheral artery disease tissue samples in the surgical theatre.



References

The TBB has been referenced in several articles in the last year, some of them are listed below:

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2 Akademische Grade

PhD Students

- *Christian Abbet*
  Self-Supervised Learning for Patient Stratification and Survival Analysis in Computational Pathology : An Application to Colorectal Cancer
  Fakultät: Med
  Supervisor: Jean-Philippe Thiran (EPFL)
  Co-supervisor: Inti Zlobec
- *Francis Bruehlmann*
  Theileria effectors transforming host cells into cancerlike cells
  Fakultät: Vetsuisse
  Supervisor: P. Olias
  Mentoren: M.P. Tschan/D.Soldati-Favre
- *Christina Cismaru*
  The M2 protein LC3-interacting region and its role in influenza A virus assembly and morphogenesis
  Fakultät: Vetsuisse
  Supervisor: G. Zimmer
  Mentoren: M.P.Tschan/P. Plattet
- *Benedetta De Ponte Conti*
  Probing gut-tumor axis during therapy with immune checkpoint inhibitors by modulating intestinal extracellular ATP
  Fakultät: Medicine
  Supervisor: Fabio Grassi
  Co-Advisor: Philippe Krebs
- *Lisa Dietsche*
  Implications of SMAD1 Loss and TGF-β Signaling in MLL-Rearranged Acute Myeloid Leukemia
  Fakultät: Uni Zürich
  Supervisor: Alexandre Theocharides
  External Reviewer: Philippe Krebs
- *Martin Gonzalez Fernandez*
  Charting the chemogenetic landscape of taxane response in BRCA1-deficient mammary tumors
  Fakultät: Med.
  Supervisor: S. Rottenberg
  Mentoren: M.P. Tschan/P. Meraldi
- *Marjolaine Hugonnet*
  Sweet control: Sialoglycans in lymphocyte-mediated immunity.
  Supervisor: Stephan von Gunten
  Mentor: Stefan Freigang
- *Laura Laloli*
  Characterization of the innate immune response in the respiratory epithelium of human, porcine, and bovine during influenza virus infection
  Fakultät: Medicine
  Supervisor: Ronald Dijkman
  Mentor: Philippe Krebs
- *Haapreet Mandhair*
  Subtype-specific role of autophagy associated protein ULK1 in Diffuse Large B-cell Lymphomas
  Fakultät: Med.
  Supervisor: U. Novak
  Mentoren: C. R. Largiader/M.P. Tschan
- *Martina Minoli*
  Developing new tools for precision medicine in bladder cancer
  Fakultät: Med.
  Supervisoren: M. Kruithof-de Juliio/R. Seiler
  Mentoren: M.P. Tschan/ C.Riether
- *Vivian Pham Vu*
  The Role of IL-33/ST2 Signaling in Inflammation-induced Immunopathologies
  Fakultät: Medicine
  Supervisor: Philippe Krebs
  External Reviewer: Grégory Verdeil
- *Kevin Plattner*
  On the role of IgE glycosylation in the protection against anaphylaxis by IgG anti-IgE antibodies
  Fakultät: Medicine
  Supervisor: Monique Vogel
  Co-Advisor: Philippe Krebs
- *Vera Tscherrig*
  The therapeutic potential of microRNAs from small extracellular vesicles derived from Wharton's jelly mesenchymal stromal cells in premature white matter injury
  Fakultät: Medizin
  Supervisoren: Prof. Daniel Surbek, Prof. Andreina Schoeberlein, Dr. Marianne Jörger
  Co-Advisor: Erik Vassella
- *Wen Jie Yeoh*
  The Role of Alarmins in Immunoregulation during Lung Inflammation and Viral Infection
  Fakultät: Medicine
  Supervisor: Philippe Krebs
  External Reviewer: Christoph Klose
- *Liang Zhao*
  A non-canonical function of LDHB promotes glutathione metabolism and protects against ferroptosis in KRAS-driven lung cancer
  Fakultät: Med.
  Supervisor: T. Marti/R. Schmid
  Mentoren: M.P. Tschan/T. Kaufmann

MSc Master of Science

- *Abdulloh Kafa Bihi,*
  MCT1, MCT4, and ACSS2 as Potential Novel Therapeutic Targets Against Metabolic Heterogeneity in Pancreatic Neuroendocrine Tumors
  Fakultät: Life Science
  Supervisor: Dr. Martin Sadowski
- *Ana Quiros Gonzalez*
  Hexokinase 3 modulates gene transcription and lactate production via PKM2 alternative splicing in acute myeloid leukemia
  Fakultät: Faculty of Science
  Supervisor: M.P. Tschan
  Mentor: A. Schläfli
- *Carmen Kalbermatter*
  Non-canonical functions of Hexokinase 3 in myeloid cell death
  Fakultät: Faculty of Science
  Supervisor: M.P. Tschan
  Mentor: A. Schläfli
- *Fatlind Malsiu*
  Investigating the role of alternative splicing in colorectal cancer development
  Fakultät: Medicine
  Supervisor: Philippe Krebs
  Co-Advisor: Robert Gaultney
- *Tanja Muralt*
  Non-canonical functions of Hexokinase 3 in therapy response of myeloiproliferative neoplasms
  Fakultät: Faculty of Science
  Supervisor: M.P. Tschan
  Mentor: A. Schläfli
- *Chris Rüttimann*
  Development of a User Interface for Deep-zoom Whole Slide Images to Overlay Predictions from Deep Learning Models
  Fakultät: Med
  Supervisor: Inti Zlobec
  Mentor: Amjad Khan
- *Young Hwa Yang*
  Understanding the progression from primary to metastasis in Pancreatic Neuroendocrine Tumors (PanNET) in vitro
  Fakultät: Life Science
  Supervisor: PD.Dr. Ilaria Marinoni

M Med Master of Medicine

- *Alexandra Bürgler*
  Sensitization of MCF-7 cells to differentiative therapy with ATRA by knockdown of HDAC genes
  Fakultät: Med.
  Supervisor: M. P. Tschan
  Mentor: A. Schläfli
- *Nico-Alessandro Mognetti*
  Establishment of a next generation tissue microarray of malignant lymphomas
  Fakultät: Med
  Supervisor: Yara Banz
- *Luca Noti*
  A combined spatial score of granzyme B and CD68 surpasses CD8 as an independent prognostic factor in TNM stage II colorectal cancer
  Fakultät: Med
  Supervisor: Inti Zlobec

MD Doctor of Medicine

- *Leonard Alexander Felger*
  Robustness of the wide-field imaging Mueller polarimetry for brain tissue differentiation and white matter fiber tract identification in a surgery-like enviroment: an ex-vivo study
  Fakultät: Medizinische Fakultät Bern
  Supervisor: Philippe Schucht
  Co-supervisor: Theoni Maragkou
- *Livia Spörri*
  Zwei Klinisch-Pathologische Fälle für Studierende der Humanmedizin – Mediendissertation
  Fakultät: Med
  Supervisor: Yara Banz


IGMP
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Gewebemedizin
und Pathologie
Hörsaaltrakt

3 Publikationen

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Review In-House

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Übrige Publikationen

- Berezowska S, Galván JA
  Immunohistochemical Detection of the Autophagy Markers LC3 and p62/SQSTM1 in Formalin-Fixed and Paraffin-Embedded Tissue.
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- Kaderli RM, Nesti C, Bräutigam K, Zwahlen M, Perren A
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- Raabe C, Dettmer M, Baumhoer D, Suter VGA
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Nicht klassifiziert

Tagungsbeitrag

- Frei AL, Khan A, Studer L, Zens P, Lugli A, Fischer A, Zlobec I
  Local and global feature aggregation for accurate epithelial cell classification using graph attention mechanisms in histopathology images
  In: Medical Imaging with deep Learning 2023 (Hg.) , S.
- Frei AL, Khan A, Zens P, Lugli A, Zlobec I, Fischer A
  GammaFocus: An image augmentation method to focus model attention for classification
  In: Medical Imaging with Deep Learning 2023 (Hg.) , S.

Rezension

- Berezowska S, Cathomas G, Grobholz R, Henkel M, Jochum W, Koelzer VH, Kreutzfeldt M, Mertz KD, Rössle M, Soldini D, Zlobec I, Janowczyk A
  Digital image analysis and artificial intelligence in pathology diagnostics-the Swiss view.
  Pathologie, 44(Suppl 3): 222-4
- Bowee S, Matter SB, Dawson H, Inglin RA
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  GASTROENTEROL REP, 11(goad002): goad002
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  J NEUROENDOCRINOL, 35(12): e13343
- Lincke JB, Christe L, Unterlauft JD, Zinkernagel MS, Zysset-Burri DC
  Microbiome and retinal vascular diseases.
  AM J PATHOL, 193(11): 1675-82

4 Vorträge

Yara Banz
- 02.12.23, «IAP Tautopsie Seminar – Kardiovaskuläre Pathologie und Hämatopathologie»
  IAP Herbstututorials 2023: 588. Tutorial - Autopsie: Fallbezogene Diskussion relevanter Krankheitskomplexe in der postmortalen Diagnostik
- 11.11.23, «Slide Seminar 2 – Hematopathology – Part II – Case presentation»
  Annual Meeting of the Swiss Society of Pathology, Lausanne
- 10.11.23, «SAMO Interdisciplinary Workshop on Lymphoma – WHO versus ICC»
  Swiss Acadamy of Multidisciplinary Oncology, Interdisciplinary Workshop on Lymphoma 2023, Lucerne
- 23.06.23, «VEXAS Syndrome – a multidisciplinary case presentation»
  Swiss Society of Hematology Annual Diagnostic Meeting 2023, Bern

Heather Dawson
- 08.03.23, «Molecular Pathology of Gastrointestinal Cancer»
  SSMP/IAP Molecular Pathology Training School, Basel
- 30.03.23, «AI in Pathology»
  Neuroseminar Vetsuisse, Bern
- 25.05.23, «The role of quality standards in tissue medicine in improving patient care in colorectal cancer»
  Institute for Gastroenterological Tumors of Croatia
- 09.11.23, «Novel insights in lower gastrointestinal neoplasia»
  88th Annual Congress of the Swiss Society of Pathology

Stefan Freigang
- 07.07.23, «Targeted removal of macrophage-secreted i nterleukin-1 receptor antagonist protects against lethal Candida albicans sepsis»
  World Immune Regulation Meeting, Davos
- 15.03.23, «Molecular mechanisms of interleukin-1 regulation in fungal sepsis»
  Seminar Series, Universitätsklinik RIA, Inselspital Bern

Robert Gaultney
- 27.11.23, «Host epithelial alternative splicing directs the outcomes of antibiotic treatment on the gut flora»
  Bern PacBio Revio Launch Day, UniBE NGS facility symposium, Bern

Benjamin Goeppert
- 13.08.23, «Risk factors and morphomolecular changes in cholangiocarcinogenesis»
  FASEB Conference, The Cholangiocarcinoma Conference: Molecular Drivers, Microenvironment and Precision Medicine, Palm Springs, CA, USA

Anja Herbst
- 23.08.23, «Investigation of the role of IL-33 for intestinal tumorigenesis»
  SYIS (Swiss Young Immunologists Society) Annual Symposium 2023, Bern

Philippe Krebs
- 30.10.23, «Testimonial on participation to EU RISE / MSCA Staff Exchange projects»
  Information Event on the Marie Skłodowska-Curie Staff Exchange call 2023 & Swiss Participation, Bern
- 07.06.23, «Immunoregulation at mucosal sites»
  Immunology Lunch Meeting, Bern
- 12.10.23, «Immunoregulation during inflammatory lung disorder»
  Seminar, Biotechnology Institute Thurgau, Kreuzlingen
- 24.08.23, «Symposium 2c: T Cells and Immune Regulation»
  SSAI (Swiss Society for Allergology and Immunology) Annual Congress 2023, Bern, Session Chair
- 04.–06.07.2023, École Doctorale Environnements-Santé, Université de Bourgogne/Franche-Conté, Jury member

Tereza Losmanova
- 06.12.23, «Digital Pulmonary Pathology: From PD-L1 Evaluation to Innovations in Digital Cytology»
  User Group Meeting, Indica Labs, London, UK
- 12.09.23, «Cytology takes off with AI, in-house experience with evaluation of BAL samples»
  35th European Congress of Pathology, Dublin, Ireland

Alessandro Lugli
- 21.12.23, «Mit Napoleon auf Du und Du»
  Weihnachtsfortbildung UKH-HZL Inselspital Bern

Theoni Maragkou
- 24.05.23, «Histopathological considerations and classification of adult-type gliomas»
  Intractranial Glioma Workshop: From A to Z, Athens, Greece
- 24.05.23, «The role of methylation profiling in glioma classification»
  Intractranial Glioma Workshop: From A to Z, Athens, Greece
- 26.05.23, «WHO classification of gliomas in children »
  Intractranial Glioma Workshop: From A to Z, Athens, Greece

Ilaria Marinoni
- 22.03.23, «Epigenetics in NENs, role in oncogenesis and clinical potential»
  ENETs Basic and Translational NET Research. Vienna , Austria
- 14.05.23, «Epigenomics of Neuroendocrine Tumors»
  European Congress of Endocrinology, Istanbul, Turkey
- 19.06.2023, «Epigenetic of Pancreatic Neuroendocrine Tumors (PanNETs)»
  NET Symposium, Rhue Operandi, Paris, France
- 04.10.23, «Zebrafish Model in NET»
  NANETs Annual conference, Montreal, Canada
- 28.11.23, «Genetic and Epigenetic of PanNETs»
  Quality and Innovation in Personalized Pancreatic Care, Milano, Italy

Aart Mookhoek
- 02.03.23, «Surgical specimens in CD: Pathologist perspective»
  18th Congress of European Crohn's and Colitis Organisation
- 03.03.23
  «Case 3: Upper GI IBD»
  «Scoring systems in UC»
  «Practical examples of scoring systems»
  18th Congress of European Crohn's and Colitis Organisation
- 12.09.23, «Eosinophilic esophagitis and gastroenteritis. Can we rely on eosinophils?»
  35th European Congress of Pathology

Mirjam Schenk
- 05.04.23, «Discovering novel mechanism of tumor immune responses using high dimensional data»
  Immunology Meeting, University Clinic for Rheumatology and Immunology, Universitätsklinik RIA, Bern
- 27.04.23, «BCG-hydrogel as immunotherapy in melanoma»
  Swiss Society of Young Immunologists (SYIS), Seminar series, Davos
- 07.07.23, «Treatment and diagnosis of immune disorders»
  WIRM, World Immune Regulation Meeting, Davos

Aurel Perren
- 22.03.23, «Session A: Diagnostic challenges & dilemmas in NEN medicine »
  ENETS PG Course, Vienna, Austria
- 24.03.23, «Moderator: Basic and translational science abstracts»
  20th ENETS Conference, Vienna, Austria
- 05.05.23, «Molekulare Pathologie und Genetik von NEN des Pankreas: Meilensteine, Gegenwart und Zukunft»
  17. Interdisziplinäres NEN-Symposium 2023, Essen, Germany
- 09.06.23, «What's new in the thyroid pathology»
  SCS, Swiss College of Surgeons Annual Meetings 2023, Basel, Switzerland
- 11.09.23, «Neuroendocrine tumours of the appendix: recent insights and clinical implications»
  ECP, Dublin, Ireland
- 23.11.23, «Endokrine Pathologie»
  Juniorakademie IAP, Bonn, Germany
- 28.11.23, «Liquid and Digital – A new area for pathology?»
  6th Meeting, Quality & Innovation in Personalised Pancreatic Care, Milan, Italy

Martin Sadowski
- 28.06.23, «Discovery powered by the speed of light: Multiparametric quantitative single-cell imaging (mqSCI) of 2D and 3D cancer models»
  MIC Research Day, Bern, Switzerland
- 01.09.2023, «Discovery powered by the speed of light: Multiparametric quantitative single-cell imaging (mqSCI) of 2D and 3D cancer models»
  Workshop Tschan-Brunner Labs, Säntis, Switzerland

Wiebke Solass
- 04.02.–06.02.23
  «Pathology: PRGS How and Why ?»
  «Molecular And Histological Classification of Appendiceal Tumor»
  «Histological Classification of Mesothelioma»
  «Histological And Molecular Implication in Ovarian Pm»
  Middle East Conference on Peritoneal Surface Oncology, Jeddah, Saudi Arabia
- 04.04.23, «STK11 mutated adnexal tumor»
  Course on Molecular Pathology and Targetes Therapy on Gynecological Cancers, London UK
- 05.05.23, «Rare Cause of peritoneal metastasis»
  ISSPP translational & basic science peritoneum workshop Paris
- 01.06.23, «STK11 mutated adnexal tumor»
  Deutsche Gesellschaft für Pathologie Jahrestagung Leipzig
- 08.06.23, «Is chemotherapy working? What the pathologist can tell you?»
  Swiss College of Surgeons – Annual Meeting Basel

Mario Tschan
- 05.03.23, «Autophagy Mechanisms Active in Acute Myeloid Leukemia Differentiation Therapies»
  3rd Institut du Medicament Strasbourg Scientific Meeting, Strasbourg
- 13.11.23, «Unexpected Role for Hexokinase 3 in Acute Myeloid Leukemia Cell Survival»
  Blood Research Program Research Day, Bern
- 09.08.23, «Anti-apoptotic, non-glycolytic function of hexokinase 3 (HK3) in AML cell therapy response»
  12th SWISS APOPTOSIS AND AUTOPHAGY MEETING, Bern
- 10.09.23, «The oncogenic DMTF1β splice variant promotes autophagy-dependent cancer cell motility»
  11th Scientific Days on Autophagy, CFATG11, Lyon

Erik Vassella
- 07.09.23, «Grundlagen und aktuelle Entwicklung der molekularen Biomerker-Testung in der Onkologie»
  PathoEvent, Bern (Merck)

Hannah Wiliams
- 26.04.23, «Spatially resolved transcriptomic characterisation of high-risk morphologies in lung adenocarcinoma»
  2nd International Spatial Biology Congress
- 07.07.23, «Spatially resolved transcriptomic characterisation of high-risk morphologies in lung adenocarcinoma»
  European Congress of Pathology, Dublin
- 12.09.23, «Spatially resolved transcriptomic characterisation of high-risk morphologies in lung adenocarcinoma»
  MIC Symposium
- 17.11.23, SPatial Omics Consortium

Janina Wolf
- 12.09.23, «What on earth is this?! Challenging cases in mediastinal pathology»
  European Congress of Pathology, Dublin, Ireland

Inti Zlobec
- 18.01.23, «Perception of utility and current use of spatial methodologies in the clinical and research setting: where do we stand?»
  AGORA Spatial Symposium
- 20.01.23, «AI applications in colorectal cancer»
  24. Bamberger Morphologietage
- 19.04.23, «Where clinical needs inspire AI research»
  Milano Lectures in Digital Pathology
- 05.05.23, «Digitale Pathologie: Was das Labor wissen muss»
  Swiss Histotech Society
- 12.09.23, «Does it really help? Results from a Swiss national slide seminar on AI-assisted tumor cell fraction»
  European Congress of Pathology, Dublin
- 30.09.23, «The Swiss landscape of digital pathology»
  Austrian Society of Pathology (ÖGPath)
- 10.11.23, «Multiplexed imaging and the case of tumor budding»
  Swiss Society of Pathology (SGPath)
- 20.11.23, «What is holding us back from using DP and AI in clinical routine?»
  EMPAIA Symposium- Shaping a Sustainable Association
- 08.12.23, «Swiss Digital Pathology Initiative (SDPI)»
  Nanostring Summit

5 Drittmittel

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

H. Dawson
- Rising Tide Fondation, 2018–2023, CHF 108'984

B. Dislich
- Stiftung für klinisch-experimentelle Tumorforschung, 2019–2023, CHF 120'000

S.Freigang, PI
- Swiss National Science Foundation, 2020–2024, CHF 632'000
- Swiss Heart Foundation, 2020–2023, CHF 50'000
- Swiss Lung Liga, 2017–2023, CHF 162'000*
  * total amount of funding; funding shared by PI and Co-PI
- UniBE Proof-of Concept Grant, 2023–2024, CHF 30'000

R. Gaultney, PI, Project grant
- Werner und Hedy Berger-Janser Stiftung, 2023, CHF 79'796

Gaultney, Fellowship
- Seal of Excellence Fund (SELF) UniBE, 2021–2023, CHF 128'698

P. Krebs, PI
- Fondazione San Salvatore; Project grant, 2022–2024, CHF 170'000
- Swiss National Science Foundation Project grant, 2020–2024, CHF 632'000
- Krebsforschung Schweiz, Project grant, 2023–2026, CHF 374'900
- UNIBE ID Grant, 2023–2025, CHF 150'000
  total amount of funding CHF 150'000, part for group Krebs CHF 75'000

P. Krebs, main PI
- Swiss Life; Project grant, 2021–2023, CHF 20'000
- Uniscientia; Project grant, 2021–2023, CHF 136'000

P. Krebs, Co-Investigator, Staff Exchange Program
- Horizon Europe, 2023–2027, Euro 1'531'800*
  * total budget; part for group Krebs CHF 200'077 additional and proportional to the number of staff secondments

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

A. Lugli, PI/M. Schürch, Co-PI
- Swiss Cancer Research, 2021–2023, CHF 331'500

A. Lugli
- Dutch Cancer Society, 2017–2023, CHF 1'600'246, Co-Applicant

Theoni Maragkou
- Krebsliga Bern, 2022–2024, CHF 67'500
- Stiftung für klinisch-/experimentelle Tumorforschung, 2022–2024, CHF 32'500

Ilaria Marinoni, PI/Nadja Mercader, PI
- Bern Center for Precision Medicine, 2022–2024, CHF 174'000
  * total amount of funding; funding shared by I. Mariconi and N. Mercader

Ilaria Marinoni, PI
- SNF 320030_214902, 2023–2027, CHF 688'609

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

Martin Sadowski, PI
- KFS-5539-02-2022, 2022–2025, CHF 358'900
- Swiss 3RCC - Knowledge Transfer KT-2022-002, 2023, CHF 5'875

M. Schenk
- Novartis, Foundation for medical-biological research, Project grant, 2021–2024, CHF 52'000
- CK-CARE, Christine Kühne Foundation for Allergy, Research and Education, Project grant, 2023–2025, CHF 160'000

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
- CDM Fellowship Egypt (Yasmeen Mady), 2022–2026, CHF 120'000

M.P.Tschan, Co-PI/B. Towbin, Co-PI
- UniBE ID Grant, 2022–2024, CHF 109'000
  * total amount of funding; funding shared B. Towbin and M.P. Tschan, extended 2024

E. Vassella, Co-PI/Prof. Ren-Wang Peng
- Bern Center for Precision Medicine (BCPM); Co-PI, 2022–2024, CHF 130'000

Wiebke Solass, PI
- Protected Research Time, 2023–2025, CHF 80'000
- Stiftung für Klinisch experimentelle Forschung, 2023–2024, CHF 50'000

H. Williams, PI
- Werner und Hedy Berger-Janser Stiftung, 2022–2023, CHF 80,000*
  *total amount of funding

I. Zlobec, PI/M. Anisimova/MMRodriguez/B.Snjider
- Swiss National Science Foundation- SINERGIA, 2020–2024, CHF 2'875'765

I. Zlobec, Co-PI/M.P. Tschan, Co-PI
- SNSF_310030_197786, 2020–2024, CHF 660'000
  * total amount of funding; funding shared I. Zlobec and M.P. Tschan
- Swiss Government Excellence Scholarship, 2021–2024, CHF 90'000
  * total amount of funding; funding shared I. Zlobec and M.P. Tschan

I. Zlobec, PI, Co-Applicant mit Prof. Matthias Hediger
- Swiss Cancer Leage, 2022–2024, CHF 96'930

I. Zlobec, PI
- Swiss Cancer League, 2023–2026, CHF 371'950
  *total amount of funding; funding shared by PI and co-PI equally
- Swiss Cancer League KFS-5534-02-2022-R, 2022–2025, CHF 353'100

I. Zlobec, Co-PI
- Innosuisse, 2021–2023, CHF 450'540

6 Preise, Ernennungen, Auszeichnungen

Romain Gros, PhD student: best Student Paper Award, SPIE Photonics WEST Congress 2023, San Fransisco (January 2023)

Philipp Zens received the Best Poster Award in the category of pathology/tumor biology during the European Lung Cancer Congress 2023 in Copenhagen (1.4.2023)

elcc European Lung Cancer Congress

Dr. Antonio Rodriguez Calero received the 2023 Benjamin Castleman Award during the USCAP 112th Annual Meeting on March 2023 in New Orleans. This award was granted in recognition of his paper published in Nature Communications. (1.3.2023)

- *PD Dr. Ilaria Marinoni:* Second Prize for Best Oral Basic Science Abstract at 20th t ENETs annual conference. Vienna (24.3.2023)

Ana Leni Frei, PhD student: Best poster prize, MIDL conference 2023, Nashville (5.5.2023)

- *Elias Baumann,* PhD student: 3rd best e-poster prize, Swiss Society of Pathology (11.11.2023)

2023 wurden erstmals zwei Teacher of the year gewählt, je einen für Bachelor- und Masterstudium.

Prof. Dr. med. Alessandro Lugli wurde Teacher of the year im Master-studiengang. Er überzeugte die Studierenden mit: Innovativer Lehre; investigativen Autopsiedemokursen sowie seiner Vorlesungsgestaltung.

www.fsmb.ch/toy

- *Lucine Christe* hat die Facharztprüfung bestanden
- *Konstantin Bräutigam* hat die Facharztprüfung bestanden

>>> Studentische Lehre

Yara Banz und Philippe Krebs

«Education is what survives when what has been learned is forgotten»

B.F. Skinner

Über 1000 Stunden Lehrleistungen – Vorlesungen, PBL-Praktika, Kurse und Vertiefungsseminare: Auch 2023 haben sich zahlreiche Mitarbeitende am Institut für Gewebemedizin und Pathologie für die studentische Lehre eingesetzt. Dabei geht es nicht nur darum Fachwissen zu übermitteln, sondern die Begeisterung für das Fach Pathologie, für biologische Mechanismen der Krankheitslehre, für die klinischen Aspekte der Gewebemedizin und die zellulären Details verschiedener Erkrankungen weiterzugeben.

Die Lehre stellt auch 2023 nebst der Forschung und Dienstleistung eines der drei Pfeiler des Instituts für Gewebemedizin und Pathologie dar. Die Ausbildung der Medizinstudierenden, der Studierenden der Zahnmedizin, Studierenden der Pharmazie wie auch der Studierenden anderer Studiengänge, z.B. der philosophisch-naturwissenschaftliche Fakultät, nimmt viel Zeit in Anspruch, gibt aber auch viel zurück. Nur dank der exzellenten Zusammenarbeit zwischen dem Team der Fachärzt:innen, jungen Kolleg:innen in der fachspezifischen Weiterbildung, Mitarbeitenden in den Forschungsgruppen, Laborpersonal und Assissten:innen in der Lehre, ist eine solche Arbeit überhaupt möglich.

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 bekommen Sie die Möglichkeit in einem mehrjährigen strukturierten Unterricht, ihre Kenntnisse und ihr Verständnis für Mechanismen, Zusammenhänge und Morphologie von Erkrankungen zu vertiefen. Die Grundlagen werden nach wie vor im 3. Studienjahr gelegt, wo im Kontext von themenorientierten Vorlesungen, Praktika in «Problem Based Learning» (PBLs) und Fachseminaren am digitalen Mikroskop der erste wichtige Kontakt mit dem Fach vermittelt wird. Im 4. und 5. Studienjahr geht es darum, die speziellen Inhalte des Faches zu vermitteln. Die makroskopischen Kurse im 4. Studienjahr, die zwischenzeitlich stark überarbeitet wurden und in Zukunft nochmals mittels ergänzter digitaler Medien modernisiert werden, dienen dabei der Vertiefung der Inhalte der Vorlesungen. Komplementär hierzu werden den Studierenden in interaktiven Kursen mittels digitaler Mikroskopie die Erkrankungen nähergebracht und klinisch-pathologische Zusammenhänge besprochen. Autopsie Demonstrationen, bei denen anhand aktueller Fallbeispiele die aktive Erarbeitung pathophysiologischer Zusammenhänge und Sequenzen verschiedenster Krankheiten im Vordergrund steht, runden das vielseitige interaktive Angebot ab. Diese stets gut besuchten Veranstaltungen sind nach wie vor ein essenzieller Eckpfeiler in der Ausbildung junger Medizinstudierender. Auch wenn *virtual reality* und *augmented reality* sinnvollerweise Einzug finden in der heutigen Ausbildung, kann manchmal das simple «Ertasten» eines erkrankten Organs viel schneller helfen etwas wirklich zu begreifen – wortwörtlich.

Nebst einer Führung durch das Institut mit realistischer Präsentation des Arbeitsalltags als Fachpatholog:in im Kontext des Vertiefungsseminars im 3. Studienjahr, bieten wir den Studierenden auch am Ende des Medizinstudiums, kurz vor dem Staatsexamen im 6. Studienjahr, die Möglichkeit das Wahlstudienjahrpraktikum am Institut für Gewebemedizin und Pathologie zu absolvieren. 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. In Zukunft werden 2024 weitere interaktive Seminare angeboten zum Thema digitale Pathologie und artifizielle Intelligenz.

Eine Vielzahl von Masterarbeiten wurden 2023 begleitet und erfolgreich abgeschlossen. Das Angebot reichte von translationaler zu experimenteller Forschung, über Projekte in der Lehre bis hin zu AI *(artificial intelligence)* und digitale Medizin.

Das Engagement in der Ausbildung Studierender der Zahnmedizin im 3. und 5. Studienjahr hält weiterhin an. In einer Vorlesungsserie wird den jungen Kolleg:innen nebst wichtigen Themen der oralen Pathologie die essenziellen Gebiete der allgemeinen und speziellen Pathologie weiterer Organsysteme vermittelt. Ein engagiertes Team begleitet die Studierenden bis zu den jeweiligen Prüfungen. Studierenden des Studiengangs Bachelor Pharmazeutische Wissenschaften werden im Kontext einer kleinen Vorlesungsserie wichtige Grundsteine der Pathologie – im engeren Sinne der Krankheitslehre – vermittelt. Weitere Angebote in zusätzlichen Lehrgängen der Philosophisch-Naturwissenschaftliche Fakultät ergänzen das reiche Angebot an Lehrleistungen (mehr hierzu unteren Abschnitt).

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 Gewebemedizin und Pathologie folgende Vorlesungsreihen im Modulformat angeboten und koordiniert:

2.1. Allgemeine Pathologie und Histologie

Koordinator: Philippe Krebs
Dozierende: aus dem Institut für Gewebemedizin und 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 Gewebemedizin und 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 Gewebemedizin und 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 Gewebemedizin und 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 Gewebemedizin und 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 Gewebemedizin und 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 is 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 Gewebemedizin und 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 breakthroughs 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 Gewebemedizin und 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 Zellbiologie (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.

Kontinuierliche Verbesserung der Organisation und des Inhalts unserer Vorlesungen basierend auf dem Feedback der Studierenden

Die Evaluation unserer Lehrveranstaltungen wird regelmässig und automatisch durch anonyme Online-Umfragen der Fachstelle Lehrveranstaltungsevaluation der Universität Bern durchgeführt. Diese Umfragen bewerten eine gesamte Vorlesungsreihe und enthalten einen umfangreichen Fragenkatalog. Bisher war die Rückmeldungsquote bescheiden, und schriftliche Kommentare bezogen sich auf wenigen Dozentinnen und Dozenten, insbesondere solche, die ihre Vorlesung am Ende der Reihe hielten.

Um detaillierteres Feedback zu jeder Vorlesung und ihren Dozent:innen zu erhalten, haben einige Kurse für Medizinstudierenden sowie die Vorlesungsreihe «Histologie und allgemeine Pathologie» ein innovatives Konzept eingeführt. Dieses ermöglicht ein schnelles, gezieltes und nützliches Feedback nach jeder Vorlesung und jedem Praktikum, mit den unten aufgeführten Fragen. Die Rückmeldungsquote war bisher sehr gut, und die Rückmeldungen waren im Allgemeinen konstruktiv. Unsere Dozent:innen haben somit die Möglichkeit gezielte Verbesserungen im Folgejahr zu implementieren. Daher wird diese Initiative auch im nächsten Studienjahr beibehalten.

Feedback

Gestellte Fragen:

1. Wie schätzen Sie heute ihren persönlichen Lernzuwachs ein?
   Von kein Zuwachs (1) bis sehr grosser Zuwachs (6)
2. Wie würden Sie die heutige Vorlesung insgesamt bewerten?
   Von sehr schlecht (1) bis sehr gut (6)
3. Erläutern Sie die vorangehenden Antworten oder geben Sie weitere konstruktive Rückmeldungen und konkrete Optimierungsideen.

>>> Weiterbildung

Das Institut für Gewebemedizin und 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 ein 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, Nephro-pathologie, Uropathologie, HNO-/Ophthalmopathologie, Endokrinopathologie, Hämatopathologie, Weichteil- und Knochenpathologie, Herz-, Gefäss- und Rheumapathologie, Leberpathologie, Pankreaspathologie, Lungenpathologie, Dermatopathologie, Pädopathologie sowie Neuropathologie.

In diesem vierten Jahr der Pandemie fanden Weiterbildungen für Ärztinnen und Ärzte überwiegend 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 von 08:30 bis 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	H. Dawson	**Weichteilpathologie**
Februar	J. Wolf	**Lungenpathologie**
März	Y. Banz	**Hämatopathologie**
April	B. Dislich / P. Brönnimann	**Knochen- und Gelenkpathologie / Tissue Biobank Projekte**
Mai	W. Solass	**Ovar- und Tube-Pathologie**
Juni	A. Perren	**Schilddrüse- und Nebenschilddrüse-Pathologie**
Juli	H. Dawson	**Hautpathologie**
August	A. Rodriguez	**Harnblase- und Niere-Pathologie**
September	A. Lugli	**Oberer GI-Trakt-Pathologie**
Oktober	W. Solass	**Zervix-, Vulva- und Vaginapathologie**
November	M. Montani	**Neoplastische und nicht-neoplastische Leberpathologie**
Dezember	M. Trippel	**Zytologie**

>>> Fortbildung

In den während des Semesters montags stattfindenden Seminaren (08:30 bis 09:00 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.

Montagsseminare für Ärzteschaft

Datum	Referierende	Titel
14.08.	Prof. Dr. Christoph Klose	**Non-redundant functions of group 2 innate lymphoid cells**
16.10	PD Dr. med. Franziska Siegenthaler	**Endometriumkarzinom: One size does not fit all**
20.11.	PD. Dr. Salvatore Piscuoglio	**Patient-derived models to enhance precision oncology**
04.12.	Alexis Jourdain, PhD Assistant Professor	**Nucleotides and RNA as Unconventional Energy Sources**
11.12.	Dr. Bernadette Jana Stolz-Pretzer	**Topology and learning for transitions in spatial biomedical data**
18.12.	Dr. med. Thomas Albrecht	**Deep learning-enabled diagnosis of liver adenocarcinoma**

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.

Fortbildungen für nicht-ärztliche Mitarbeitende

Datum	Referierende	Titel
07.02.	J. Wolf	**Lungentumoren**
07.03.	Y. Banz	**Postmortale Diagnostik**
05.04.	W. Solass	**Organschulung Gallenblase**
02.05.	B. Dislich	**Hämato-Pathologie**
06.06.	M. Wartenberg	**Fragestellungen aus der Klinik (Infekt, Malignität, etc.)**
04.07.	A. Rodriguez	**Organschulung Niere**
08.08	T. Losmanova	**Organschulung Harnblase und Harnblasentumoren**

>>> Im Fokus: «One Research» at ITMP

From silo mindset to agile leadership

ITMP includes several research teams with scientific and technical expertise in their research fields. So far, the various groups have worked on distinct research topics with few thematic overlaps and in-house collaborations. The ITMP has the vision of «One Research» and has set up the following project to identify paths towards a more interactive, communicative, interest-stimulating and collaborative environment, which transcends disciplines and institutional departments /units to promote a more united, stronger and impactful research.

Steps towards this goal began with the Institute retreat in September 2022, where a number of initiatives were initiated at ITMP to improve the communication and interdisciplinary exchanges between our researchers and foster scientific interactions. A series of research strategy meetings guided by an external coach (Christian Polz, www.3p-leadership.de) were organized throughout 2023, and are still on-going. These research strategy meetings bring together established research group leaders, senior postdoctoral fellows, and research-oriented senior physicians.

During these workshops, participants began by exploring various leadership types, determining by consensus that a so-called «agile leadership» would be optimal for carrying out multidisciplinary research projects at ITMP.

In a second step, top-down suggestions for initiatives to enhance scientific exchanges and communication within ITMP were proposed. These measures included physical rearrangements of offices and meeting spaces, communication opportunities through research «hubs», and financial incentives for Institute-internal interdisciplinary projects.

An overview of current and future tools, such as the newly institutionalized research seminars as well as a «retro-analysis» of group discussions during the workshop, aimed to further improve interactions. The team discussions in this workshop explored the rationale behind adopting agile leadership and working collaboratively, emphasizing synergies between basic scientists and clinicians.

Two projects were identified for practical implementation of the «agile» methodology, namely a solution on how to enhance communication at ITMP, as well as measures to ameliorate the active participation of younger researchers in our weekly research seminars.

Although these improvements have already helped to strengthen the communication and scientific exchange at the ITMP, we pursue the vision of one research into 2024.

To make a difference in medicine together

This sentence has been formalized as the overarching goal for the new vision and mission of the Institute. This shared vision is encapsulated in the Institute's Charter, reinforcing the commitment to impactful and collaborative research at ITMP.

Agile leadership is self-organising, creative teamwork towards a common goal.

>>> Situationsplan

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