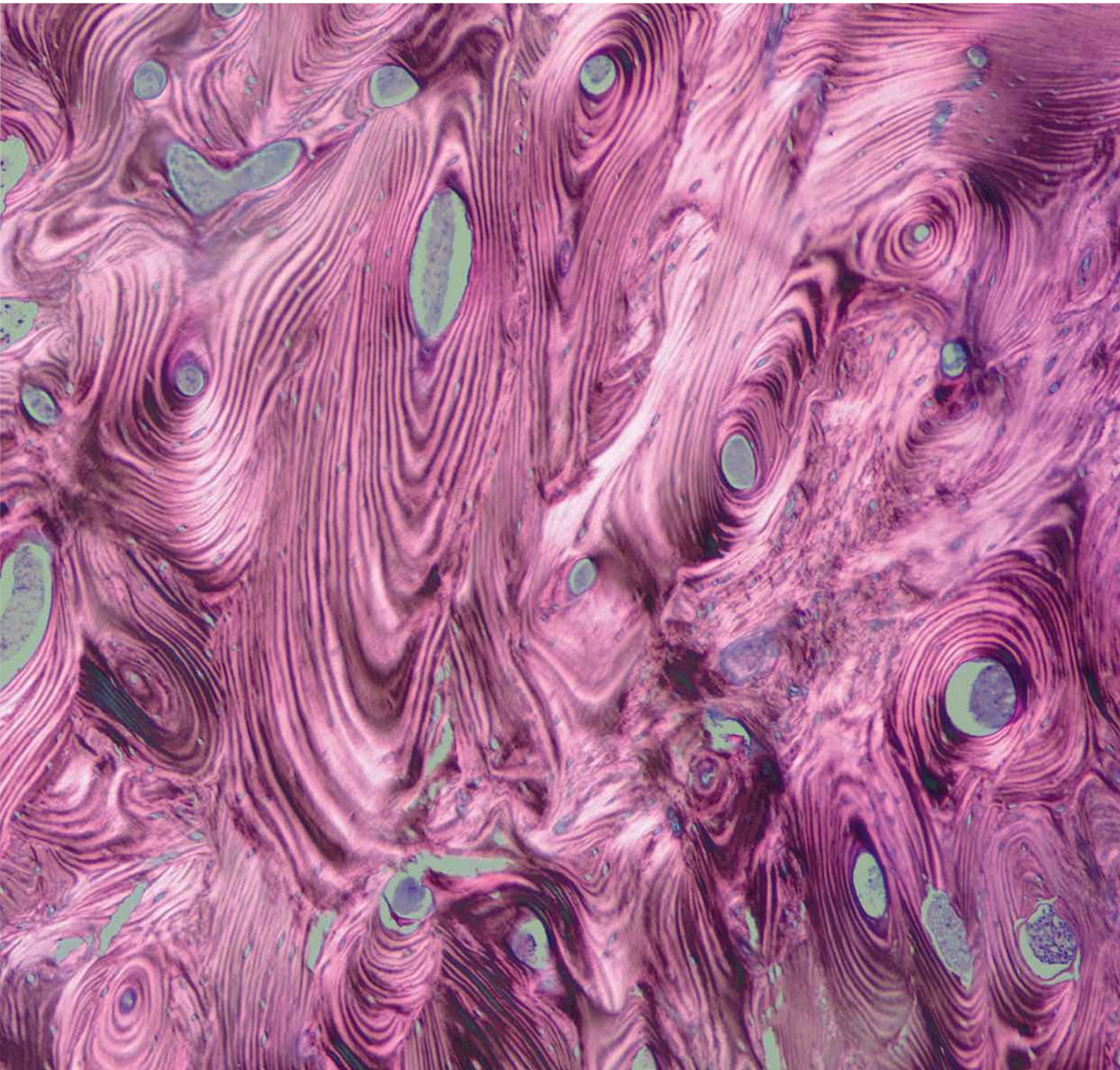
UNIVERSITÄT
BERN

Institut für Pathologie

www.pathology.unibe.ch

Jahresbericht 2017



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>>> Das Wichtigste in Kürze

Liebe Leserin, lieber Leser

Ich freue mich über Ihr Interesse am Jahresbericht 2017 des Instituts für Pathologie! Wir haben uns auf den Ebenen Dienstleistung, Forschung und Lehre weiterentwickeln können: Wir haben die Akkreditierung der Abteilung für Molekularpathologie nach ISO/IEC 17025 und ISO 15189 durch die Schweizerische Akkreditierungsstelle erfolgreich abgeschlossen und die Akkreditierung des restlichen diagnostischen Bereiches vorbereitet.

Die Einführung **synoptischer Berichte** für maligne Erkrankungen erachten wir für unsere Kunden als sichtbarste Änderung. Nach einer Testphase für Lungen- und Kolonkarzinome, welche begeistert aufgenommen wurde, haben wir inzwischen flächendeckend solche strukturierten Berichte eingeführt.

Wir befolgen die internationalen guidelines des ICCR (International Collaboration on Cancer reporting) oder, wenn noch nicht definiert, an die guidelines der CAP (College of American Pathologists). Dies erforderte eine mentale Umstellung der Ärzteschaft der Pathologie, dafür erleichtert es für alle nachfolgenden Bereiche die Leserlichkeit der Befunde: Jede Information ist immer an derselben Stelle im Bericht zu finden. Pathologie-intern und im Rahmen der bestehenden Anstrengungen in Richtung personalisierte Medizin bietet diese Umstellung auch die Voraussetzung, die Tumordaten detailliert in Datenbankstrukturen überzuführen.

Im Forschungsbereich haben wir viel in den Aufbau einer Struktur für digitale/computerisierte Pathologie investiert. Als Zwischenziel konnten wir Ende 2017 mit Implementierung unserer neuen Serverinfrastruktur die direkte Anbindung der Tumorboards des Inselspitals an virtuelle Slides etablieren. Wir arbeiten aktiv an den schweizweiten Projekten der Swiss Biobanking Platform (www.sbp.ch) und der SPHN Initiative (www.sphn.ch) mit.

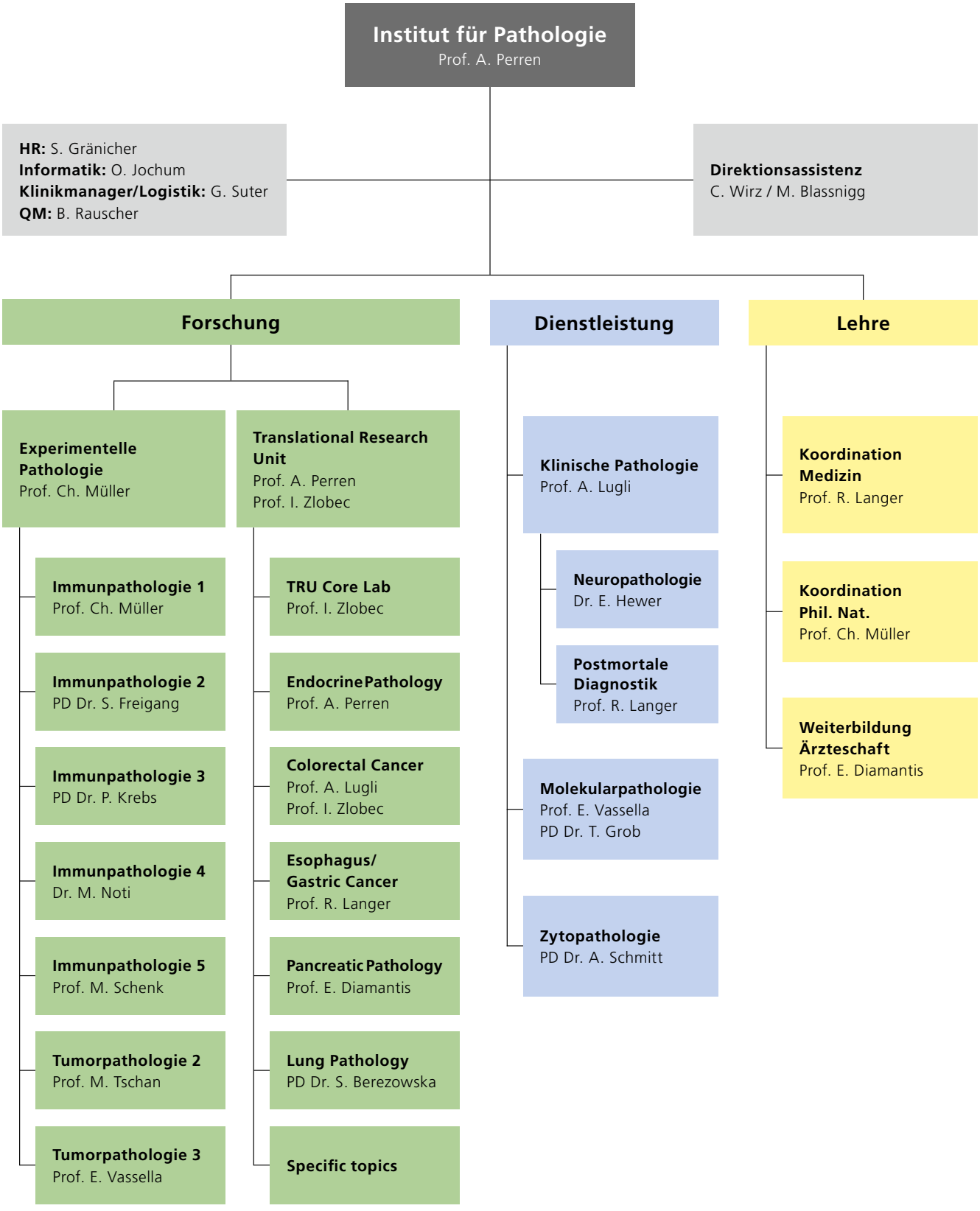
In der Lehre haben wir begonnen, uns vertieft mit dem wichtigen Instrument der Autopsie zu befassen. Unsere Strategie, den anhaltend abnehmenden Autopsiezahlen zu begegnen und ein klinisch angepassteres Angebot aufzubauen, entnehmen Sie unserem «Special topic» am Ende des Jahresberichts.

Ich wünsche Ihnen viel Spass bei der Lektüre.

Ihr Aurel Perren, Direktor

Institut für Pathologie.

>>> Organigramm

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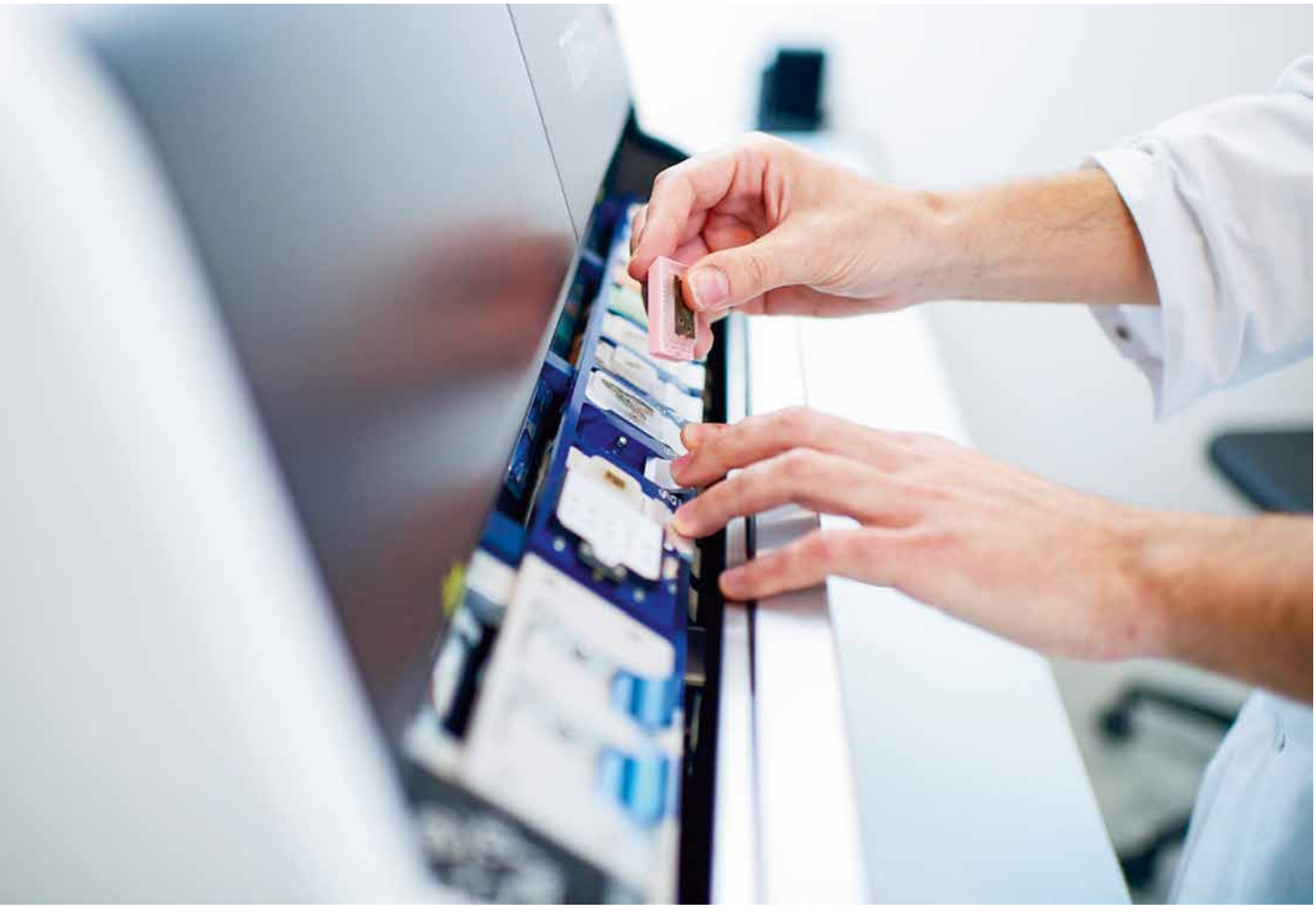


>>> Dienstleistung

1 Klinische Pathologie

Leiter: Prof. Dr. med. Alessandro Lugli

Im Jahre 2017 lag der Fokus auf Abteilungsebene in der Etablierung der beiden synergistischen Ansätze LEAN und Qualitätsmanagementsystem im Hinblick auf die bevorstehende Akkreditierung im Jahre 2018. In Kollaboration mit der «Translational Research Unit (TRU)» wurde die erste Phase des Projektes «Digital Pathology» vorbereitet, welche auf die Digitalisierung der histologischen Fallpräsentationen bei den interdisziplinären Tumorkonferenzen fokussiert ist. Die Ziele der Klinischen Pathologie für das Jahr 2018 leiten sich dementsprechend wie folgt ab: Intensivierung der Zusammenarbeit zwischen den Fachgruppen der Pathologie und den Kliniken, Einführung der Spracherkennung im Patientenmanagementsystem, Optimierung der LEAN Prozesse in den Labors und im Berichtwesen.

1.1 Ärzteschaft

Die in Fachgruppen organisierte Ärzteschaft besteht aus 16 Fachärztinnen und Fachärzten und wird von 10 Assistierenden unterstützt. Die Fachärzteschaft vertritt die Pathologie als Disziplin an den zahlreichen wöchentlichen Tumorboards/Fallbesprechungen innerhalb des Inselspitals und in aus₤wärtigen Spitälern. Das Fachwissen wird durch den Besuch nationaler und internationaler Kongresse auf dem neuesten Stand gehalten und die Forschungsaktivität durch die Translational Research Unit (TRU) und die Experimentelle Pathologie unterstützt.

1.2. Neuropathologie

Im Jahr 2017 untersuchte der Bereich Neuropathologie mehr als 1307 neurochirurgische Proben. Dies entspricht einer Zunahme von nahezu 10% und ist u.a. durch einen zusätzlichen hochmodernen Operationssaal bedingt, der im Jahr 2017 durch die Neurochirurgie des Inselspitals mit erheblicher Resonanz auch in Schweizer Medien in Betrieb genommen wurde. Mit mehr als 300 intraoperativen Untersuchungen trägt die Neuropathologie weiterhin überdurchschnittlich zu den am Institut durchgeführten Schnellschnitten bei. Wir zählen damit weiterhin zu den diagnostisch aktivsten Neuropathologien in der Schweiz.

Von weiterhin zunehmender Bedeutung in der Klassifikation primärer Hirntumore ist die molekulare Diagnostik, vermehrt auch mittels der «next generation sequencing». Hinzu kommen zahlreiche Einsendungen weiterer Disziplinen aus dem Bereich des peripheren Nervensystems. In Zusammenarbeit mit dem Neuromorphologischen Labor (Leiter: Prof. K. Rösler) der Neurologischen Klinik des Inselspitals wurden rund 70 Muskelbiopsien untersucht.

Im Bereich der Postmortalen Diagnostik führten wir einschliesslich konsiliarischer Untersuchungen im Auftrag des Instituts für Rechtsmedizin 87 Hirnsektionen durch. Entsprechend dem Charakter der Neuropathologie als Schnittstelle zwischen den klinischen Neurofächern, der Labordiagnostik und translationaler Forschung war der Fachbereich Neuropathologie auch im Jahr 2017 in zahlreichen Veranstaltungen insbesondere in Zusammenarbeit mit Klinken des Inselspitals engagiert. Darüber hinaus ist das Fach Neuropathologie Teil des Neuroonkologischen Tumorzentrums und einer der Schwerpunkte der Medizinischen Allianz Bern/Basel (MBB).

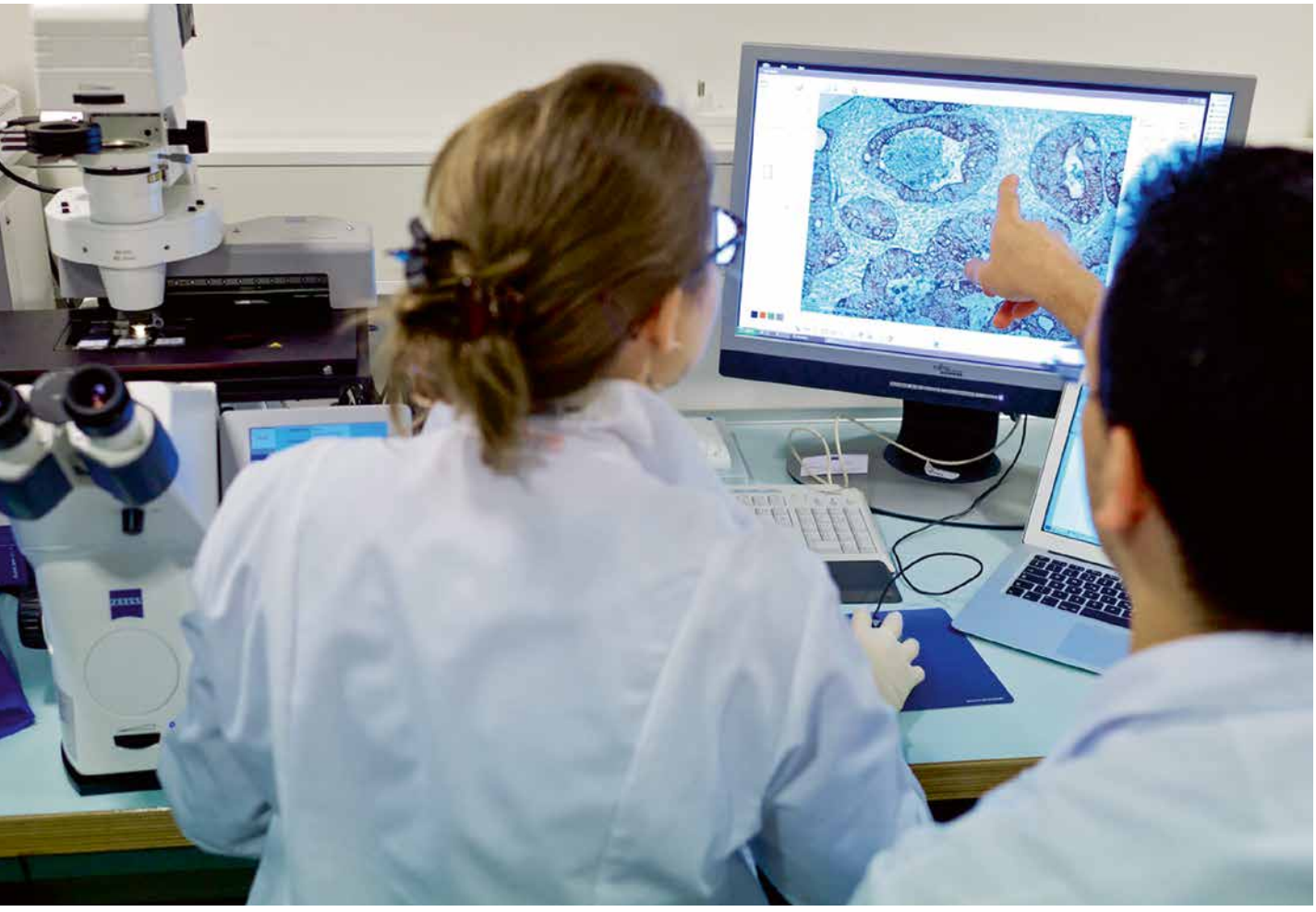
1.3. Postmortale Diagnostik

Das Projekt «Postmortale Diagnostik» wird im Jahresbericht 2017 in der Rubrik «Im Fokus» präsentiert.

1.4. Labor Histopathologie und Immunhistochemie

2017 lag der Fokus des Histopathologielabors bei der Erarbeitung der Dokumente und Schulung des Teams zur bevorstehenden Akkreditierung im Jahr 2018. Auch wurde nochmals eine Optimierung des LEAN Prozesses vorgenommen. In diesem Zusammenhang wurden drei grössere Projekte erfolgreich abgeschlossen: Anpassung des Organigramms, Personaleinsatzplanung und das Lean Six Sigma Projekt zur Workflow-Optimierung der Fallbearbeitung.

Anfang 2017 wurden die bestehenden Bereichsleiterstrukturen in eine operative Ebene umgeformt, welche nun die Laborleitung bei den operativen Tätigkeiten unterstützt und die Mitarbeiter so direkt unterstützt. Das Lean Six Sigma Projekt war auch Grundstein bei der diesjährigen Personaleinsatzplanung. Hier wurden durch die Workflow-Optimierung neue Ressourcen generiert, welche eine Anpassung unumgänglich machten. So konnten nicht nur die einzelnen Dienste, son-



dern auch die Dienstzeiten angepasst resp. verlängert werden. Die Nummernkreisumstellung wurde im 4. Quartal vollzogen und wird im Jahr 2018 weiter ausgebaut. 2017 wurden total 43'600 Einsendungen verarbeitet, was einem erneuten Zuwachs von über 3% entspricht gegenüber 2016 (42'200 Einsendungen). Rückläufig war die Zahl der Schnellschnitte von 2400 (im Jahr 2016) auf 2200 (im Jahr 2017), hingegen konnte die Anzahl Proben mittels Schnellschnittfahrzeug leicht gesteigert werden.

Durch den Umzug der Abteilung Immunhistochemie in das topmoderne Labor der klinischen Pathologie im Sommer 2017 greifen die Arbeitsprozesse optimal ineinander und erleichtern die Kommunikation und Zusammenarbeit der beiden Labore Immunhistochemie und Histopathologie deutlich. Damit erfüllt sich ein weiterer Schritt im LEAN Konzept des Instituts. Im Weiteren befasst sich die IHC intensiv mit der bevorstehenden Akkreditierung im Jahre 2018 und nutzt den Umzug, um die ersten Anpassungen an die Hand zu nehmen. Die neue Fachgruppe der Immunhistochemie, bestehend aus drei Fachärzten/innen und der IHC- Leitung widmet sich insbesondere der Validierung neuer Primärantikörper und der Qualitätssicherung. Das Team der IHC hat an 7681 Fällen insgesamt 47597 immunhistochemische Färbungen vorgenommen und mit 224 nativen Nierenbiospien etwas weniger Fälle bearbeitet als im vergangen Jahr. Zurzeit sind in der Immunhistochemie 254 Primärantikörper für diagnostische Untersuchungen verfügbar.

1.5. Berichtswesen

Im Januar 2017 zog das Sekretariat der Zytopathologie in den zweiten Stock ins Grossraumbüro. Die Zusammenarbeit der beiden Sekretariate hat sich mit dem Schritt der räumlichen Zusammenlegung optimal entwickelt, nicht zuletzt auch dank der Implementierung des LEAN Konzeptes. Die Kommunikation mit den beiden Labors und mit der Ärzteschaft hat sich ebenfalls weiter intensiviert.

2 Molekularpathologie

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

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

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

Das Analysenspektrum des PCR-Labors umfasst den Nachweis von Mutationen, Promoter-Methylierung, Mikrosatelliteninstabilität, B- und T-Zellklonalität sowie den Nachweis spezifischer Erreger. Die Tests haben diagnostische oder prädiktive Implikation und können an Formalin-fixiertem und Paraffin-eingebetteten Gewebe durchgeführt werden. Die Schlüsseltechnologie in der Molekularpathologie ist die «Next-Generation Sequencing» (NGS), welche die gleichzeitige Sequenzierung multipler Gene (als Genpanels) in einer Reaktion ermöglicht. Diese Methode wird für den Entscheid einer zielgerichteten Therapie bei Krebspatienten eingesetzt. Zudem führen wir einen auf der Nanostring-Technologie basierenden Genexpressionstest für den Therapieentscheid beim Mammakarzinom (PAM50-Analyse) durch. Die FISH Analyse erlaubt den Nachweis von Translokationen oder Amplifikationen bei unterschiedlichen Tumoren. Im letzten Jahr haben wir insbesondere in die Etablierung neuer Genpanels/Fusionspanels mittels NGS sowie die Analyse von Human Papillomavirus (HPV) mittels eines quantitativen PCR Assays (Anyplex II HPV28, Seegene) investiert. Das Molekularpathologie-Labor dient auch als Ausbildungsstätte für Assistenzärzte sowie für Pathologen zur Erlangung des FMH-Subtitels in Molekularpathologie. Eine Vorlesungsreihe in Molekularpathologie im Rahmen des Masterprogramms Molecular Life Sciences sowie der Graduate School wird jährlich durchgeführt.

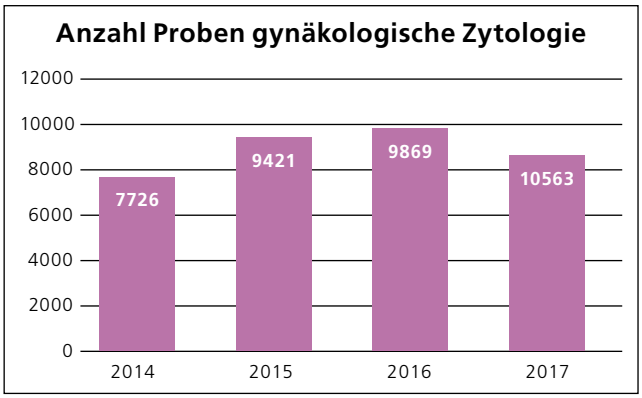
Ende dieses Jahres wird die Zusammenlegung von vier diagnostischen Labors auf dem Insel-Campus, der Molekularen Pathologie des Instituts für Pathologie, der Hämatologischen molekularen Diagnostik der Universitätsklinik für Hämatologie, der Pharmakogenetik des Universitätsinstituts für Klinische Chemie sowie des Labors der Humangenetik, Inselspital, geplant. Zukünftig sollen diese Labors in einer neuen Einheit, dem Clinical Genomics Lab (CGL) organisiert sein. Die Kompetenzen der verschiedenen Fachbereiche werden zusammengeführt, um in der neu aufgebauten Einheit das gesamte Spektrum der klinischen molekularen Diagnostik auf höchstem Niveau anzubieten. Das CGL wird zudem ein zentrales Standbein des geplanten Zentrums für Precision Medicine und wird zukünftig als Core Facility für Hochdurchsatzsequenzierung des Zentrums für Precision Medicine die klinische und translationale Forschung am Standort Bern stärken. Das CGL wird im 6. OG der Murtenstrasse 31 entstehen. Die Teilprojekte Laborорganisation, NGS Core Facility für Precision Medicine, IT, Finanzen, Bau und Netzwerk sind in Bearbeitung.

3 Klinische Zytopathologie

Leiterin: PD Dr. med. A. Schmitt Kurrer

Die Zytologie ist als minimal-invasive und gleichzeitig maximal effiziente und kostengünstige Methode zukunftsweisend. Sie ist somit für die Anforderungen der modernen Medizin mit ihren immer sensitiver und spezifischer werdenden prädiktiven und prognostischen Tests ein bedeutender Partner sowohl in der gynäkologischen als auch der extra-gynäkologischen Diagnostik. Dies spiegelt sich in den kontinuierlich zunehmenden Zahlen zytologischer Einsendungen wider (Abbildung 1).

Die Zytologie ist jedoch nicht «nur» am Mikroskop für die PatientInnen engagiert. Im Rahmen der Ende 2016 gegründeten interdisziplinären Schilddrüsensprechstunde an der Universitätsklinik für Diabetologie, Endokrinologie, Ernährungsmedizin & Metabolismus (UDEM) des Inselspitals besetzt die Zytologie ein 10%-Pensum für Feinnadelpunktionen von Schilddrüsenknoten mit direkter mikroskopischer Beurteilung der Proben im Sinne einer «rapid on-site evaluation», ROSE. Somit erhält der Patient im Normalfall eine sofortige Diagnose, so dass das weitere Vorgehen direkt mit dem Patienten besprochen und eingeleitet werden kann. Dieses Vorgehen wird sowohl von den zuweisenden KollegInnen als auch den PatientInnen geschätzt: Im Jahr 2017 wurden in der Abteilung für Zytologie nahezu 33% mehr Schilddrüsenproben verarbeitet und diagnostiziert als im Jahr 2016 (2016: 1357 Proben; 2017: 1804 Proben; +32.9%).



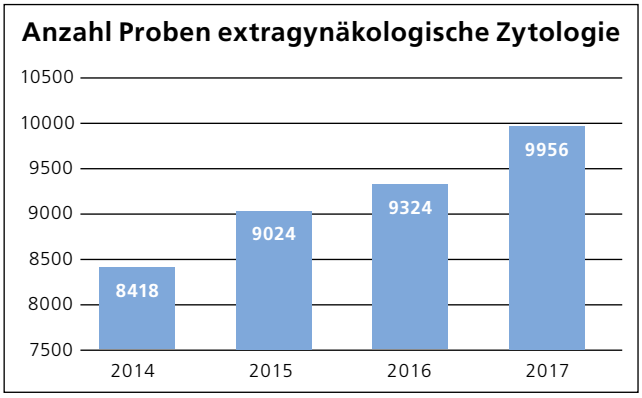


Abbildung 1: Entwicklung der Einsendungen gynäkologischen und extragynäkologischen Zytologie 2014–2017

Auch für PatientInnen mit zystischen Pankreasläsionen und ihre behandelnden ÄrztInnen hat es 2017 Neuerungen gegeben: Während zuvor das mittels endoskopisch-ultraschallgesteuerter Feinnadelpunktion (EUS-FNP) gewonnene Material rein morphologisch nach der Papanicolaou-Klassifikation beurteilt wurde, wurde in einem gemeinsamen Projekt mit dem Bauchzentrum des Inselspitals sowie der Gastroenterologie des Tiefenauspitals der Überstand des Materials im Jahre 2017 zunächst im Rahmen einer Pilotstudie molekularpathologisch mittels NGS auf wegweisende Mutationen untersucht. Die Ergebnisse der Pilotstudie sind vielversprechend, so dass zukünftig die weiteren Therapieentscheide nicht nur morphologisch, sondern auch molekular abgestützt werden können.

Um auch in Zukunft eine qualitativ hochstehende zytologische Diagnostik anbieten zu können, engagiert sich die Zytologie auch in der Fort- und Weiterbildung von ÄrztInnen und von technischen MitarbeiterInnen. Hervorzuheben ist hier die Würdigung der verantwortungsvollen Tätigkeit von ZytotechnikerInnen mit dem 2017 neu etablierten eidgenössisch anerkannten Titel «HFP ExpertIn für Zytodiagnoastik». Als eine von drei Pionierinnen hat eine unserer Mitarbeiterinen die hierzu erforderliche Prüfung mit Präsentation einer Diplomarbeit bestanden, sechs weitere Mitarbeiterinnen erhielten den Titel im Rahmen des Anerkennungsverfahrens. Zusätzlich erhielten zwei MitarbeiterInnen nach zweijähriger berufsbegleitender Weiterbildung Ende 2017 das kantonal-bernische Diplom als ZytotechnikerIn.

4 Fachgruppen des Instituts für Pathologie der Universität Bern

Stand Dezember 2017

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

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

Gastrointestinalpathologie	
A. Lugli	031 632 99 58
R. Langer	031 632 32 47
A. Blank	031 632 99 01
H. Dawson	031 632 99 60
E. Diamantis	031 632 87 68
M. Montani	031 632 32 67
T. Rau	031 632 87 56

Mamma- und Gynäkopathologie	
T. Rau	031 632 87 56
M. Trippel	031 632 32 76
Y. Banz	031 632 88 75
H. Dawson	031 632 99 60
V. Genitsch	031 632 99 22
M. Montani	031 632 32 67

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

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

HNO-Pathologie	
M. Dettmer	031 632 99 69
M. Wartenberg	031 632 87 54
T. Rau	031 632 87 56

Leberpathologie	
M. Montani	031 632 32 67
E. Diamantis	031 632 87 68
A. Blank	031 632 99 01

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

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

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

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

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

Pankreaspathologie	
E. Diamantis	031 632 87 68
M. Montani	031 632 32 67
R. Langer	031 632 32 47
M. Wartenberg	031 632 87 54

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

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

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

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

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

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

5 Dienstleistungsstatistik

Klinische Pathologie

Histopathologie	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**
Anzahl Einsendungen	33'805	32'710	35'293	37'232	42'422	**43'607**
Anzahl Lokalisationen	61'015	58'795	66'420	70'286	82'069	**83'191**
Anzahl Einsendungen Schnellschnitte	1'220	1'472	1'673	1'647	1'936	**1'761**
Anzahl Proben Schnellschnitte	1'792	1'997	2'307	2'252	2'454	**2'263**
Autopsie						
Anzahl durchgeführte Autopsien	195	155	156	152	146	**130**
Zytopathologie						
Total Anzahl Einsendungen	16'946	14'237	13'788	16'043	16'634	**16'995**
Anzahl Proben Klinische Zytologie	8'218	8'361	8'418	11'582	9'324	**9'956**
Anzahl Proben Gynäkologische Zytologie	8'724	8'054	7'726	9'375	9'869	**10'563**
Total Anzahl Einsendungen Proben	16'942	16'415	16'144	20'957	19'193	**20'519**
Anzahl Zellblöcke	1'830	2'277	2'324	2'748	2'837	**3'355**
Immunhistochemie						
Anzahl Fälle (Blöcke) Diagnostik (Paraffin)	6'692	7'104	8'313	7'843	9'094	**7'681**
Anzahl Färbungen Immunfluoreszenz (Nierenbiopsien)	2'844	2'101	2'280	2'079	2'772	**2'464**
Anzahl Fälle Immunzytologie am Ausstrich	302	302	372	197	158	**258**
Anzahl Färbungen Immunzytologie am Ausstrich	672	586	–	240	486	**364**
Anzahl Färbungen Diagnostik (Paraffin)	43'436	–	52'532	47'944	44'366	**47'597**
Molekularpathologie						
Anzahl Fälle PCR-basierende Tests	1'235	1'420	1'304	1'444	1'624	**1'870**
Anzahl Fälle Lymphome	171	214	218	216	221	**227**
Anzahl Fälle Methylierungsnachweis	155	180	128	88	114	**148**
Anzahl Fälle Mutationsanalysen (EGFR, kRAS, BRAF, IH1/2 + weitere)	755	818	902	870	508	**332**
Anzahl Fälle NGS-Analysen	–	–	–	87	247	**337**
Anzahl Fälle PAM50 (Nanostring)	–	–	–	18	48	**38**
Anzahl Fälle FISH	206	287	554	627	744	**650**
Anzahl Hybridisierungen FISH	304	391	683	839	981	**715**

Tumorbank

Anzahl Einsendungen Tumorbank	727	831	894	1'030	1'417	**1'879**
Anzahl Eingänge TRU	–	166	465	457	604	**602**

>>> Forschung/Research

1 Research at the Institute of Pathology

Research groups Experimental Pathology
Stefan Freigang, MD
Philippe Krebs, PhD
Christoph Mueller, PhD
Mario Noti, PhD
Mirjam Schenk, PhD
Mario Tschan, PhD
Erik Vassella, PhD

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

Organisational aspects

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

The core lab of the Translational Research Unit

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

1.1 The Division of Experimental Pathology

Head: Christoph Mueller, PhD

Research activities

Thematically the research activities of the current 7 research groups in the Division of Experimental Pathology are focused on two main topics, i.e.

– Immunopathology and inflammation, and
– Experimental tumor pathology and tumor biology

Most of the research groups in the Division of Experimental Pathology address questions related to the fundamental aspects of cell biology and to the etiopathogenesis of neoplastic, or inflammatory disorders. Nevertheless, translational aspects are also considered in our research activities such as the identification of novel biomarkers for disease activity in remitting – relapsing inflammatory disorders and the development of novel vaccination strategies against solid tumors.

Personnel

At the end of 2017 more than 50 persons were affiliated with the 7 research groups of the Division of Experimental Pathology. In 2017 no changes in the number of independent research groups and the principal investigators occurred.

Grant Support

In 2017 the amount of new external funding obtained by the research groups of the Division of Experimental Pathology exceded CHF 3'000'000 (for details see: Reports of the individual research groups).

Research infrastructure and collaborations

The research activities are well integrated on a national and international level, including the Swiss IBD cohort study. In our experimental work we can rely on facilities available at our institute, e.g. Laser Capture Microdissection, confocal microscopy, Cell-IQ® continuous live cell imaging and analysis system and a Nanostring® Platform for multiplexed assays for gene expression and mutation analysis, but also on core facilities, provided by the Dept. of Biomedical Research, including the FACS (cytometry) core facility, and the genomics core facility (with access to an Ion Torrent® instrument).

Those two core facilities are conveniently located in the building of the Institute of Pathology. In addition, access to the microscopy center (MIC), with its instruments for confocal microscopy (including live cell imaging-, and 2-photon microscopy), and to the proteomic core facility of the Medical Faculty is available. We are also part of the Interfaculty Bioinformatics Unit and are granted unrestricted access to the Next Generation Sequencing platform of the University of Bern (equipped with a illumina HiSeq3000 and a illumina MiSeq instrument). Several of our research groups also use the central mouse facility, and germ-free and gnotobiotic mouse facility (Clean Mouse Facility) at the Medical Faculty. In addition to these facilities, through collaborative efforts we also have access to other state-of-the-art facilities, including the metabolomics facilities at the Institute of Molecular Systems Biology, ETH Zurich (Group of Professor Uwe Sauer).

The spectrum of available and well-established technologies in the Division of Experimental Pathology includes confocal microscopy, fluorescent in situ hybridization (FISH), laser capture microdissection of FFPE and frozen tissue sections (including immunostained FFPE tissue sections), live-cell metabolic assays on a Seahorse XF Analyzer, 3D- cell cultures, but also the entire spectrum of FACS-based techniques in cell sorting and multi-color analysis. Highly sophisticated methodologies are established for the identification of miR's and their target sequences in normal, and diseased tissues, the assessment of autophagy, and several distinct transfection systems, including lentivirus-based transduction systems, and mRNA expression profiling from small numbers of cells and microdissected tissues are available. Furthermore, several of our research groups have a longstanding expertise in isolating and culturing primary cells, such as immune cells, primary AML blast cells, mesenchymal stromal cells, including liver sinusoidal endothelial cells, and epithelial cells from patient material, but also experimental animals. Experimental protocols for determining the functional capacities of these cell subsets ex vivo and in vitro are established and optimized.

Forschungsgruppe Stefan Freigang (Research group Stefan Freigang).

Group of Stefan Freigang, MD

Johanna Baumgartner, MSc, PhD student
Thi Thuy Hang Bui, MSc, PhD student
Svenja Ewert, research technician
Olivier Friedli, MSc, PhD student
Marleen Hanelt, MSc, PhD student
Nadia Oehninger, master student medicine
Tiina Partanen, research technician

Summary of research activities

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

Research Activities

Project 1: Molecular mechanisms of lipid-induced inflammation

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

Project 2: Immune regulation by oxidized lipids

Another major interest of the group are products of lipid peroxidation and their immuno-regulatory properties. The exposure of cellular membranes to reactive oxygen species creates a broad range of distinct oxidized phospholipid (OxPL) species that actively modulate cellular signaling processes and influence the resulting immune response (Freigang 2016). We have previously characterized a pro-resolving activity of OxPLs that can be attributed to cyclopentenone-containing OxPLs and their respective isoprostanes (Bretscher 2015). These compounds are highly bioactive and represent promising therapeutic agents for the treatment of inflammatory diseases (Friedli 2017).

Project 3: Lipid-sensing by innate-like Natural Killer T cells

Natural Killer T (NKT) cells are a subset of innate-like T lymphocytes that recognize lipid antigens presented via CD1d. Because of their potent immunoregulatory properties, NKT cells have emerged as a promising target for cancer immunotherapy (Keller 2017a). We found that deletion of the essential autophagy gene Atg5 in antigen presenting cells augments CD1d antigen presentation in vivo (Keller 2017b). These effects led to an enhanced NKT cell cytokine production upon antigen recognition and lower bacterial loads

during infection with Sphingomonas paucimobilis. We could demonstrate that loss of Atg5 in APCs impaired the clathrin-dependent internalization of CD1d molecules via the adaptor protein complex 2 (AP2) and thereby increased the surface expression of stimulatory CD1d:glycolipid complexes. Our findings indicate that the autophagic machinery assists in the recruitment of AP2 to CD1d molecules resulting in attenuated NKT cell activation.

Internal collaborations

- Yara Banz, MD-PhD
- Christoph Mueller, PhD

External collaborations

National

- Marc Donath, MD, University of Basel, Switzerland
- Olivier Guenat, PhD, University of Bern, Switzerland
- Martin Hersberger, PhD, University Children's Hospital Zurich, Switzerland
- Jan Lünemann, MD, University of Zurich, Switzerland
- Olivier Pertz, PhD, University of Bern, Switzerland
- Philippe Renaud, PhD, University of Bern, Switzerland

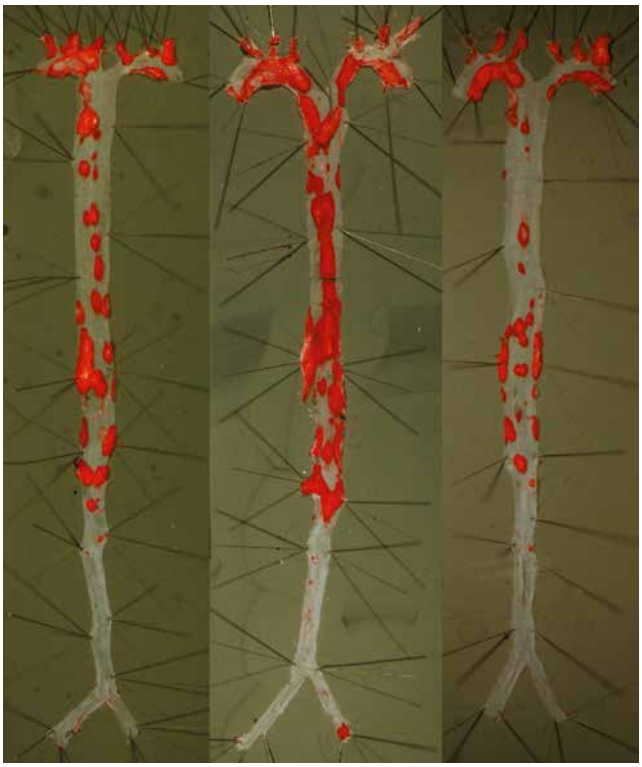
International

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

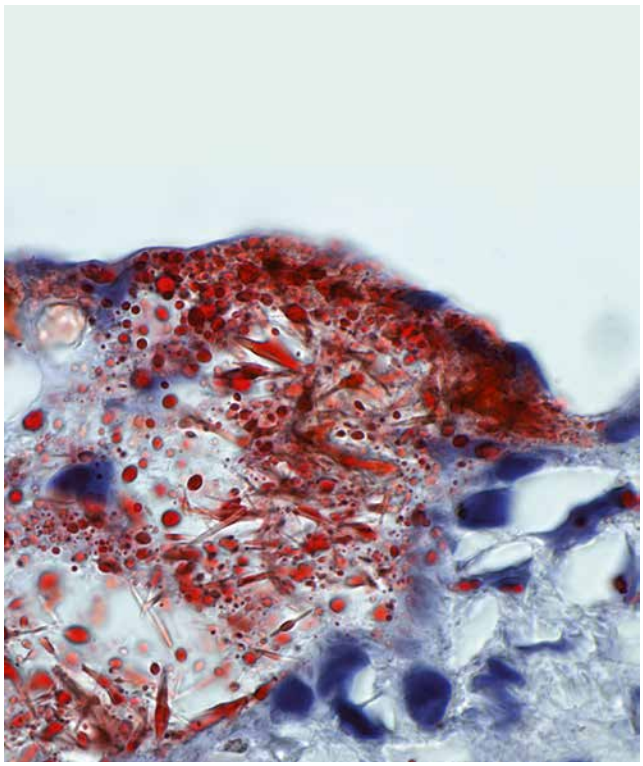
Grant support

- SNF 310030_152872, S. Freigang, (2015–2017), CHF 510'000
- SNF 316030_157702, S. Freigang, (2014–2016), CHF 240'000
- Vontobel-Stiftung, S. Freigang, (2014–2017), CHF 120'000
- UniBE Research Foundation, S. Freigang, (2014–2017), CHF 15'000
- Fondation J. Dürmüller-Bol, S. Freigang, (2014–2017), CHF 27'000
- UniBE-ID Grant, S. Freigang, (2016–2018), CHF 150'000
- 3R Research Foundation, S. Freigang (Co-PI), O.Guenat (PI), (2016-2017), *CHF 138'000
- Swiss Lung Liga, S. Freigang (PI), O.Guenat (Co-PI), (2017–2019), *CHF 162'000
- UniBE-ID Grant, S. Freigang (PI), (2018–2019), CHF 150'000
- UniBE2021 PhD fellowship, J. Baumgartner, (2017–2020), CHF 90'000

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



Atherosclerosis in the aortae of mice fed a high-fat cholesterol diet. Staining with Oil Red O reveals the lipid deposits within the atherosclerotic lesions.



Cholesterol crystals: atherosclerotic lesion in the mouse heart. Needle-shaped, transparent cholesterol crystals are visible, deposits of neutral lipids are revealed by Oil Red O staining.

Forschungsgruppe Philippe Krebs (Research group Philippe Krebs).

Group of Philippe Krebs, PhD

Ludmila Cardoso Alves, MSc, PhD student (PhD since Sep 2017)
Nick Kirschke, technician
Ioannis Kritikos, BSc, MSc student
Lukas Mager, MD, PhD, Postdoctoral fellow (until Apr 2017)
Petra Polakova, BSc, MSc student (until Feb 2017)
Regula Stuber Roos, technician, 90%
Lester Thoo Sin Lang, MSc, PhD student
Marie-Hélène Wasmer, MSc, PhD student

Summary of Research Activities

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

Research activities

Project 1: Role of cytokine signaling for myeloproliferative disease

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

Project 2: Role of cytokine signaling for colorectal cancer

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

Project 3: Cross-talk between innate and adaptive immunity

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

Internal collaborations

- Christoph Mueller, PhD
- Mario Noti, PhD
- Inti Zlobec, PhD
- Alessandro Lugli, MD
- Yara Banz, MD, PhD

External collaborations

National

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

International

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

Grant support

- Marie Curie Career Integration Grants (CIG) , Philippe Krebs, (2012–2017), €100'000
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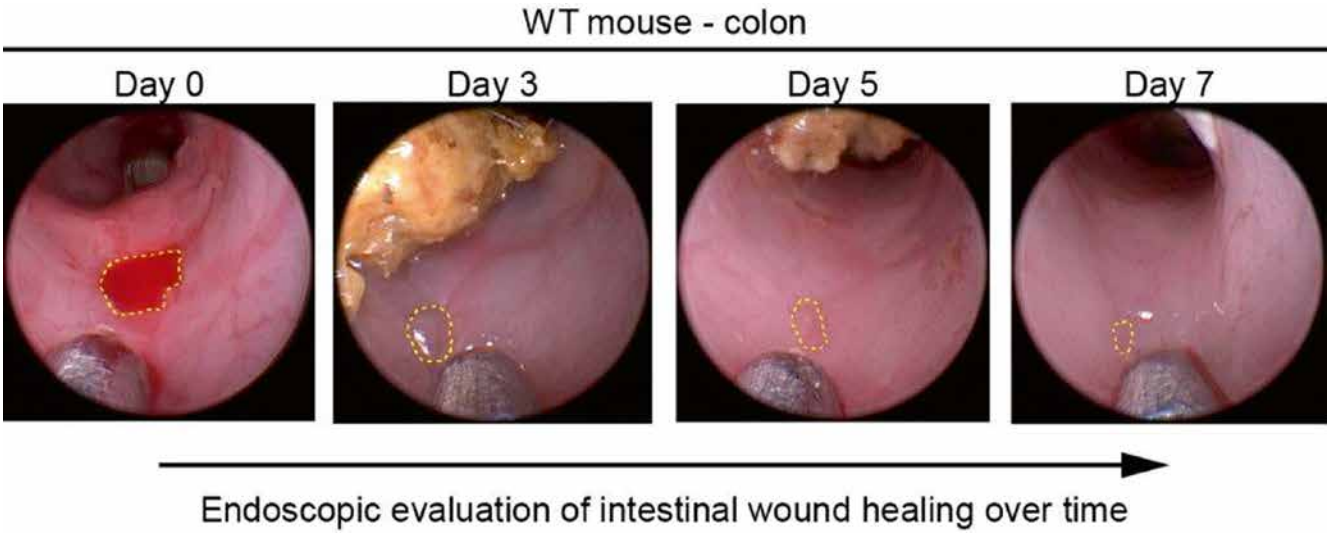
- SNSF 163086, Philippe Krebs, (2016–2019), CHF 525'000
- Vontobel Foundation, Philippe Krebs, (2015–2017), CHF 130'000
- Fondazione San Salvatore, Philippe Krebs, (2016–2017), CHF 120'000
- Gertrud-Hagmann-Stiftung, Lukas Mager, (2015–2017), CHF 241'566
- Swiss Life / Jubiläumsstiftung, Philippe Krebs, (2017–2018), CHF 30'000

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



Assessment of mucosal healing in the murine intestine. A miniature forceps was used to induce injuries in the colonic mucosa of anesthetized wild-type (WT) mice. Wound-healing was then monitored by colonoscopy at the indicated time points. Lesion size was determined by normalizing the wound area (depicted by a yellow dotted line) to the diameter of the forceps (visible on the pictures).

Group of Christoph Mueller, PhD

Nadia Corazza, PhD, staff scientist/co-PI, 60%
Martin Faderl, PhD student
Kwong Chung Cheong Kwet Choy, PhD, post-doc
Silvia Rihs, technician, 90%
Leslie Saurer, PhD, staff scientist/co-PI, 60% (till 8/2017)
Alexandra Suter, technician, 60% (SIBDCS biobank)
Diego von Werdt, PhD student
Daniel Zysset, PhD, post-doc (75%) (from May 1, 2017)

Short Summary

The main research interests of our group include:
– The molecular and cellular events operative during induction and resolution of chronic intestinal inflammation
– The functional plasticity of tissue resident T cell subsets, particularly, in the intestinal mucosa
– The participation of distinct monocyte / macrophage subsets in immunosurveillance of tumors, but also in the induction of chronic inflammatory disorders such as atherosclerosis or inflammatory bowel diseases.

Experimental mouse models of disease are generally used to test our hypotheses. These experimental findings are subsequently validated in appropriate biosamples from patients using state-of-the-art technologies.

Research activities

Our group has a longstanding interest in the complex immunoregulatory mechanisms that are operative in the intestinal mucosa during homeostatic conditions and the potential predispositions or events which can lead to disruption of tissue homeostasis during inflammatory conditions as in the case of inflammatory bowel diseases (Crohn's disease, ulcerative colitis). The importance of the intestinal microflora in shaping the functional differentiation of the local immune system, but also the reciprocal effects of local immune responses on the composition of the intestinal microflora is now well established. In our projects we aim to link the molecular and cellular characterization of distinct immune cell subsets in the intestinal mucosa and their phenotypical and functional alterations during intestinal inflammation with concurrent analyses of the intestinal microflora and any associated metabolic changes. The molecular and cellular events that regulate the maintenance of remission vs. induction of relapse in inflammatory bowel diseases is currently one of our main research topics. Here, we primarily focus on the generation of resident memory T cells, and how their generation and maintenance is influenced, e.g. by a different diet, or a distinct intestinal microbiota.

Since microbial-driven immune responses can predispose for development of tumors or even cardiovascular diseases, we have recently extended our research to other chronic inflammatory disorders (colorectal tumors and atherosclerosis). While we often use experimental mouse models to test our hypotheses, whenever possible, we validate these experimental findings using state-of-the-art technologies with patient materials, mostly archived tissue samples or biosamples obtained from the SIBDCS biobank.

Specific projects

Project 1: Molecular and cellular events that are operative during induction and resolution of chronic intestinal inflammation (Daniel Zysset, PhD, Kwong Chung Cheong Kwet Choy, PhD, Martin Faderl, MSc, Silvia Rihs)
We recently established a reversible mouse model of colitis that allows for a timed and deliberate induction of remission. Indeed, shortly after remission induction in colitic mice a rapid clinical recovery can be observed that is followed by mucosal healing on a molecular and cellular level within a few days (Brasseit et al., 2016). This allows us to characterize the molecular and cellular events that are operative in the affected colonic mucosa following a timed induction of remission.

The monitoring of immune parameters and associated changes in the metabolite profiles, generated by the intestinal microbiota, but also the host, complement these studies.

Taking advantage of gnotobiotic mice with a defined microbiota, we further investigate the critical effects mediated by the pathobiont *Helicobacter typhlonius* on the (intestinal) immune system leading to an accelerated onset of colitis. Intriguingly, in the presence of a gnotobiotic flora consisting of 12 commensal bacteria species (Brugiroux et al., Nature Microbiol 2016), *H. typhlonius* mediates an accelerated onset of colitis, although *H. typhlonius* – monoassociated mice fail to develop CD4 T cell mediated colitis.

Project 2: Functional plasticity of tissue-resident T cell subsets, notably in the intestinal mucosa (William Kwong, PhD, Diego von Werdt, MSc, Nadia Corazza, PhD, Silvia Rihs)
Our group has a longstanding interest in the functions exerted by conventional and unconventional intraepithelial T lymphocytes (IEL) in the intestine. Currently, we investigate the molecular mechanisms that regulate their tissue-resident phenotype and determine how functional activities of these cell subsets may differ under homeostatic versus inflammatory conditions. In particular, we are specifically looking at the role of the regulator of G protein signaling (RGS) proteins in governing tissue resident CD4 and CD8$\alpha\alpha$/CD8$\alpha\beta$ T cell functions in the intestinal epithelium and lamina propria during homeostasis, infections and immunopathologies.

Tissue resident memory (TRM) cells highly express RGS1 which likely contributes to their non-circulating, tissue-resident memory phenotype. We are interested how the intestinal milieu shapes expression of the Rgs1 gene and how intestinal

inflammation, but also distinct commensal bacteria and pathobionts may potentially affect Rgs1 expression leading to altered TRM cell responses.

Project 3: Monocyte / macrophage subsets in immunosurveillance versus inflammatory disorders: TREM-1 as an amplifier of acute and chronic inflammation (Daniel Zysset, PhD; Leslie Saurer, PhD; Silvia Rihs)

TREM-1 (Triggering Receptor Expressed on Myeloid Cells-1) is an activating innate immune receptor expressed on neutrophils and subsets of monocytes / macrophages. We recently described a critical pathogenic role for TREM-1 not only in acute inflammation, but also during chronic inflammation such as in inflammatory bowel diseases (Schenk et al., 2005, 2007). We further generated and characterized a Trem1 deficient mouse line (Weber et al., 2014) and defined the contribution of TREM-1 mediated-signaling to the development and progression atherosclerosis (Zysset et al., 2016) and colitis-associated colorectal carcinoma (Saurer, Zysset et al, 2017). Additional studies on the impact of TREM-1 in the immune mediated disorders are ongoing.

Internal collaborations

- Stefan Freigang, MD
- Vera Genitsch, MD
- Philippe Krebs, PhD
- Mario Noti, PhD
- Mirjam Schenk PhD
- Inti Zlobec, PhD
- Alessandro Lugli, MD

External collaborations

National

- Andrew Macpherson, MD, Department of Clinical Research, University of Bern (Sinergia)
- Wolf Hardt, PhD, Institute of Microbiology, ETH Zurich (Sinergia)
- Uwe Sauer, PhD, Institute of Molecular Systems Biology, ETH Zurich (Sinergia)
- Walter Reith, PhD, Department of Pathology and Immunology, University of Geneva
- Gerhard Rogler, MD PhD, Division of Gastroenterology & Hepatology, University Hospital Zurich

International

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

Grant support

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- SNF 33CS30_134274 / 1, (SIBDCS; Co-PI), (2016–2018), CHF 200'000*
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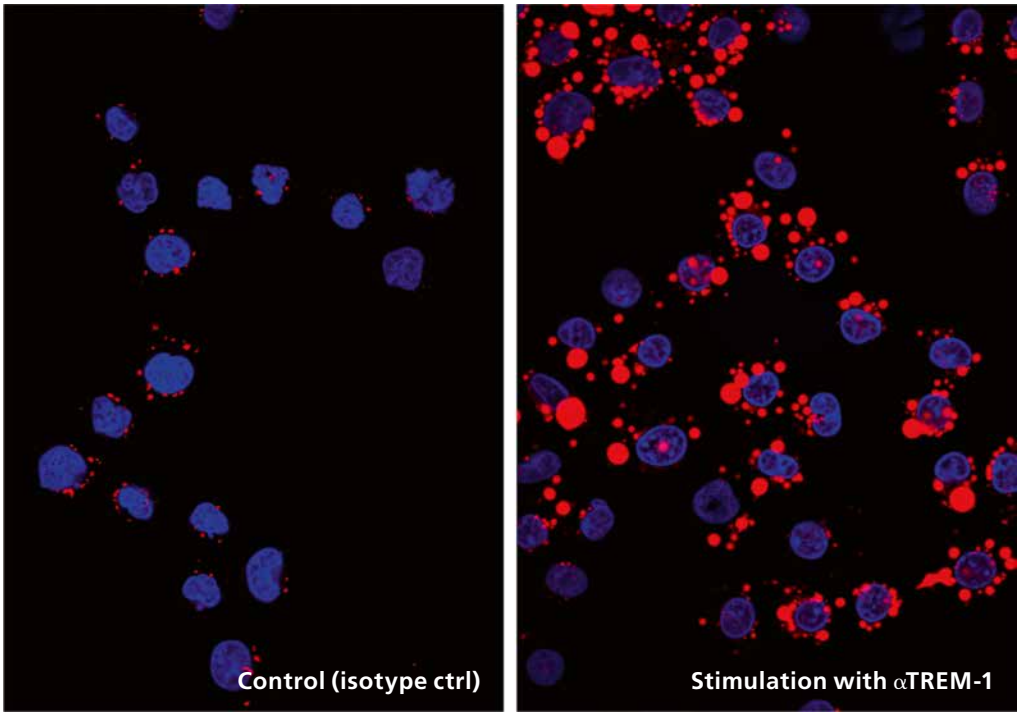
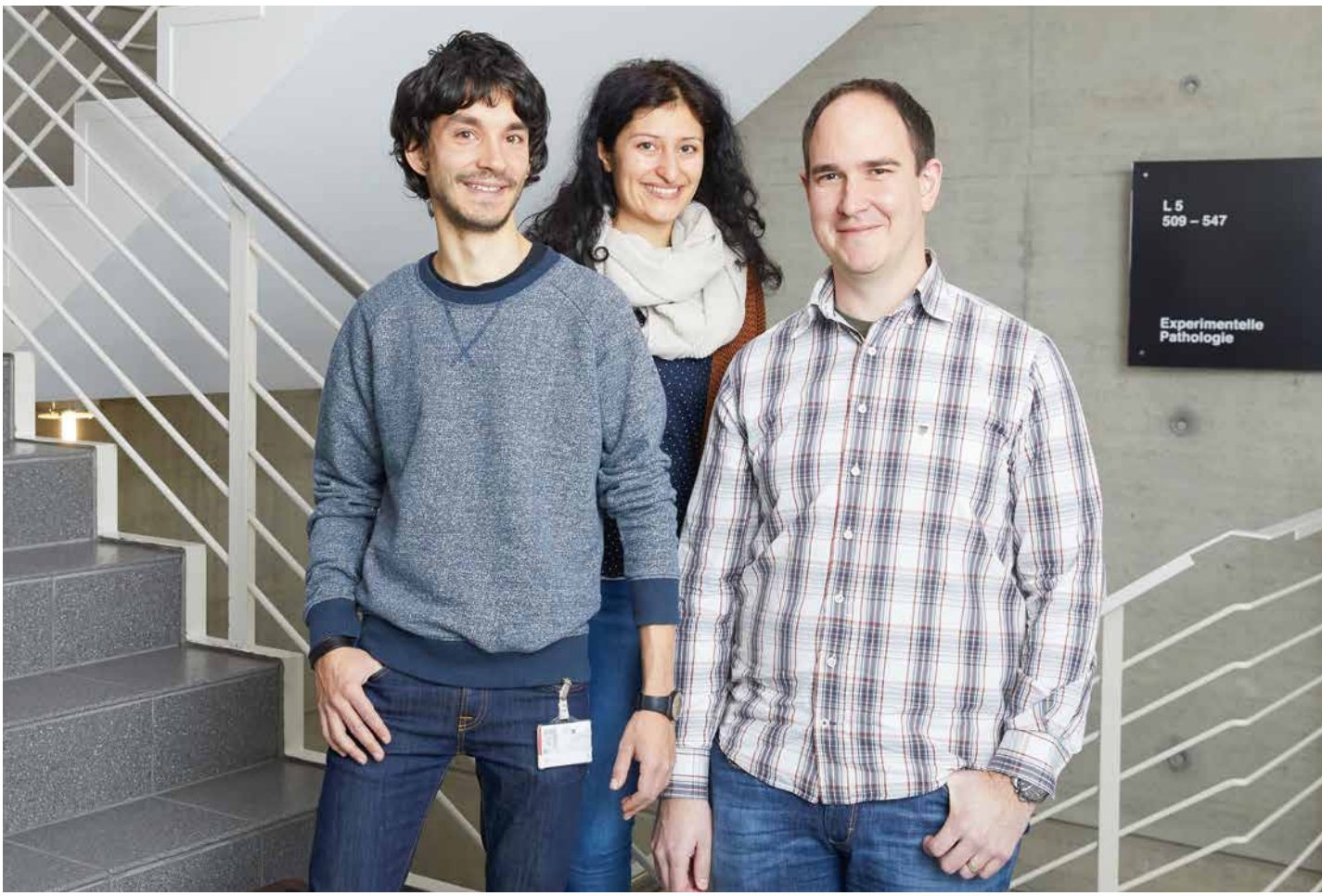
(*own share)



Monocytes cultured in dyslipidemic serum-containing medium differentiate into foam cells when TREM1 is activated.
(ORO staining; Zysset et al., Nature Comms 2016)



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

Group of Mario Noti, PhD

Maryam Hussain, MSc, PhD student
Maria Pena Rodriguez, MSc, Technician (40%, till January 2017)
Lukas Bäriswyl (50%, from February 2017)

Short Summary

Employing models of acute and chronic inflammation, microbial colonization and/or manipulation, current research focuses on how mammalian host genetics, diet and signals derived from commensal microbial communities regulate the structure, development and function of the immune system in health and disease. State-of-the-art *in vivo, ex vivo* and *in vitro* cellular and molecular approaches are used together with translational approaches to address our research questions.

Research activities

Project 1: What role play basophils in the pathogenesis of food allergies?

Food allergies have reached pandemic proportions, with an estimated 4–8% of children and adults in westernized countries living with the daily concern that exposure to certain foods may trigger a life-threatening allergic reaction. As the public health and economic burden of food allergies continues to grow, there is an urgent need to develop new intervention strategies to prevent and treat this disease. While the effector functions mediating food allergies are well described, little is known about the early immunological events that initiate these responses. In recent studies, we demonstrated that epicutaneous sensitization to food allergens on an atopic dermatitis-like skin lesion is associated with the infiltration of thymic stromal lymphopoietin (TSLP)-elicited basophils that are both necessary and sufficient for the development of food allergies (Noti et al, Nat.Med 2013; Noti et al. JACI, 2014). Employing *in vitro* and *in vivo* model systems, current research is investigating what basophil intrinsic factors promote the pathogenesis of IgE-mediated food allergies.

Project 2: Role of the Gut Microbiota in Food Allergy

The skyrocketing increase in allergies in the past decades has focused attention to disease contributing factors, most notably the gut microbiota. The microbiota plays a critical role in the induction of oral tolerance, while perturbations in this sophisticated host-microbial handshake may cause uncontrolled immune responses fostering the development of allergic

inflammation. We employ protocols to colonize axenic mice with microbial consortia derived from food allergic humans or mice to assess a potential causality of altered commensal community structures for disease development and progression. A better understanding of the role of the microbiota in food allergy may help to establish novel preventive and therapeutic intervention strategies to stem the rising tide of the food allergy epidemic.

Project 3: Aging – A reversible biological process?
For many people, extended lifetime goes along with poor general health associated with common inflammatory, neurodegenerative and metabolic disorders ultimately leading to a progressive decline in organ function and death. Therefore, elucidating the complex pathways controlling the rate of aging is of significant clinical importance in order to improve health and maintaining wellbeing throughout the life-course. In a series of new studies, we are currently investigating how changes in plasma factors associated with aging alter immune cell function at different tissue sites and whether targeted manipulation of such age-related changes have rejuvenating potential on the aging organism.

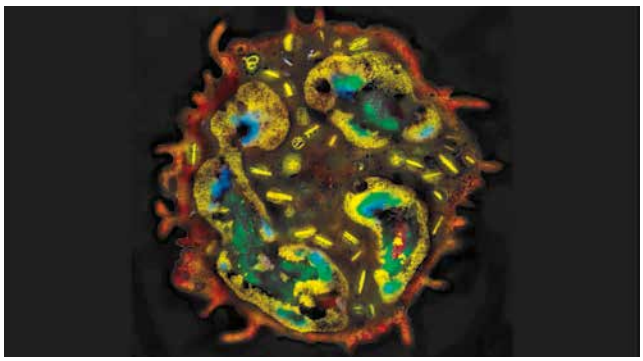
Internal collaborations
- Christoph Mueller, PhD
- Nadia Corazza, PhD
- Philippe Krebs, PhD

External collaborations
National
- Alexander Eggel, PhD, Institute of Rheumatology and Immunology, University of Bern.
- Carsten Riether, PhD, DBMR, University of Bern
- Andrew Macpherson, MD, PhD, DBMR, University of Bern
- Johan Auwerx, PhD, EPFL Lausanne
- Philipp Engel, PhD, University of Lausanne

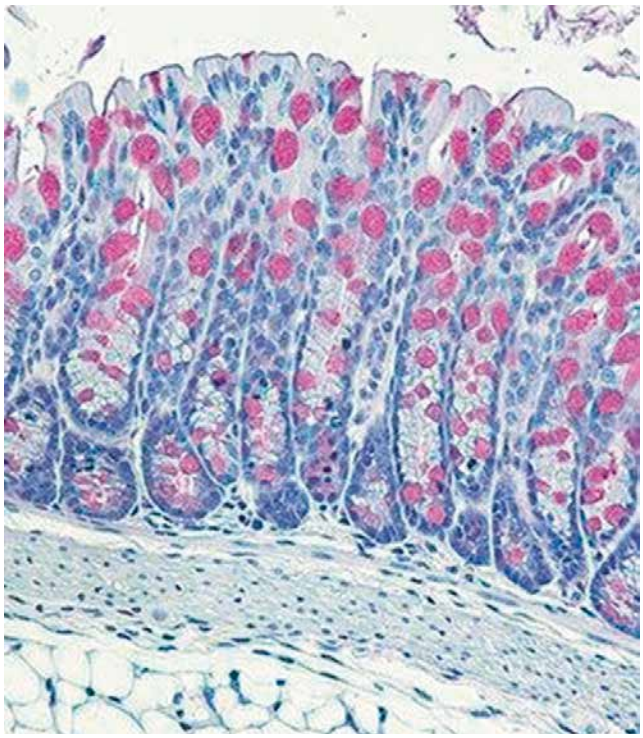
International
- David Artis, PhD, Weill Cornell University, USA
- Jonathan Spergel, MD, PhD, Childrens Hospital of Philadelphia, USA
- Brian S. Kim, MD, PhD Washington University, USA
- Thomas Brunner, PhD, Universität Konstanz, Germany
- Sven Pettersson, Lee Kong Chian School of Medicine, Nanyang, Singapore

Grant Support

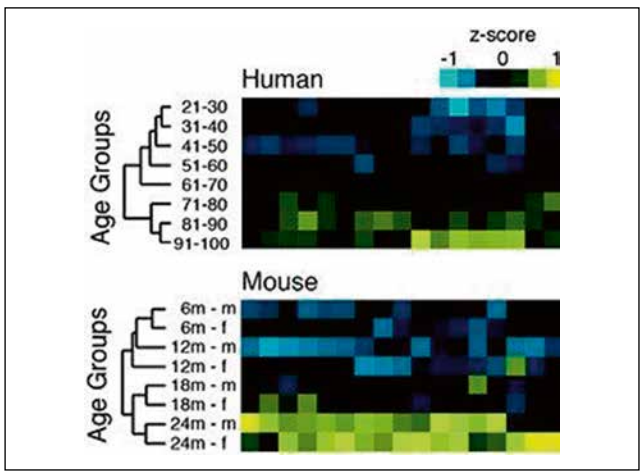
- SNF, PZ00P3_154777/1, Mario Noti, (2014–2017), CHF 599'156
- Novartis FreeNovation, Mario Noti, (2016–2018), CHF 180'000
- Novartis Foundation, Mario Noti, (2015–2017), CHF 60'000



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



H+E staining of mouse colon. Despite the physical separation of luminal bacteria and the mucosal immune system by a single layer of epithelial cells, the proper maturation of mucosal immune cells critically depends on microbial derived signals.



Age-related changes of immune factors in the plasma proteome of humans and mice.

Group of Mirjam Schenk, PhD

Thomas Gruber, PhD student
Hassan Sadozai, PhD

Short Summary

Cancer shows a steadily increasing incidence and provides a major public health problem in many parts of the world. A key player in preventing and controlling this malignant disease is the immune system. Unfortunately, in many cancer patients the anti-tumor immunity is diminished. This malfunction can be caused by improper maturation of dendritic cells (DC), which thus cannot prime and activate $CD8^+$ T lymphocytes. Cytotoxic $CD8^+$ T lymphocytes (CTL) however are essential for killing tumor cells. Using tumor-immunotherapy we aim to enhance the function of the immune system to battle tumors. 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: Generation of potent cross-presenting DC for tumor immunotherapy

Only a specific subset of DC is 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-DC will be tested in adoptive transfer as prophylactic and therapeutic treatment to established melanoma. Together, these data should identify ways to promote frequency and function of cross-presenting DC and to contribute to antitumor response in melanoma.

Project 2: Dendritic cells and their co-stimulatory properties for cytotoxic T cells in melanoma

The activation of an effective adaptive antitumor response relies mainly on presentation of tumor antigens and stimulation by DC. Despite extensive research, phenotype and function of tumor-infiltrating DC remains largely elusive and cross-presentation of tumor antigen is not well understood. We are investigating phenotype and function of TIDC and how to manipulate them 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.

Internal collaborations

- Christoph Mueller, PhD
- Inti Zlobec, PhD
- Evanthia Karamitopoulou Diamantis, MD

External collaborations

National

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

International

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

Grant Support

- Stiftung experimentelle Biomedizin, (2016–2019), CHF 763’000
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- Helmut Horten, (2017–2020), CHF 180’000
- SNF, (2018–2022), CHF 566'109

Research group Mario P. Tschan.

Group of Mario P. Tschan, PhD

Olivia Adams, PhD student (Co-supervision, Prof. R. Langer)
Magali Humbert, PhD postdoc
Félice Janser, PhD student (Co-supervision, Prof. R. Langer)
Céline Krähenbühl, Master student (BMA)
Sophie Milesi, Master student (BIO)
Severin Mosimann, Master student (BIO)
Nicolas Niklaus, PhD student
Sarah Parejo, MSc, 80%
Julia Parts, PhD student
Anna Schläfli (-Bill), PhD, postdoc, 70%
Deborah Shan, technician, 80%
Igor Tokarchuk, MD-PhD student
Kristin Uth, PhD student (Co-Supervision Prof. I. Zlobec)

Summary of Research Activities

Regulation and function of autophagy networks in tumor pathology and therapy resistance

Short Summary

My team focuses on characterizing the regulation and function of different autophagy pathways in acute myeloid leukemias, breast, esophageal and lung cancer pathology. In close collaboration with clinical pathologists, we decipher the molecular pathways of the autophagy recycling pathway frequently attenuated in these tumor types and in resistance mechanisms towards chemo- or targeted therapies.

Research Activities

Project 1: PU.1 functions in cellular fitness of acute myeloid leukemia (AML) cells (Project Leader: Mario Tschan)
The ETS-transcription factor PU.1 is needed throughout hematopoietic differentiation particularly by orchestrating terminal differentiation of macrophages and neutrophils. Low PU.1 levels can lead to the transformation of myeloid progenitor cells to AML. Since the role of PU.1 in hematopoietic development is well characterized and is not fully explaining the function of PU.1 in AML cellular fitness, we are currently investigating how PU.1 affects autophagy and alternative splicing of genes involved in apoptosis regulation.

Project 2: Non-canonical macroautophagy and chaperone-mediated autophagy (CMA) in acute myeloid leukemia (AML) (Project Leader: Magali Humbert)
Great progress has been made in the classification of AML, but less in terms of treatment. In 1985, the introduction of all-trans retinoic acid (ATRA) to therapy turned the deadliest form of AML, acute promyelocytic leukemia (APL) into a curable disease. Unfortunately, most non-APL patients only weakly respond to ATRA. This project aims at elucidating the involvement of macroautophagy and CMA in ATRA responses and how the interplay between leukemia blast cells and their niche affects both pathways. Autophagy modulation may support current differentiation therapies.

Project 3: Retinoic acid therapy and autophagy in breast cancer treatment (Project Leader: Anna Schläfli-Bill)
One of the challenges in (breast) cancer treatment are cancer stem-cells since they often sustain anti-cancer therapy. Interestingly, there is evidence that activation of the epithelial-mesenchymal-transition (EMT) program enhances stemness. Reversing EMT by differentiation therapy holds therefore great potential. We found that the differentiation-inducing agent all-trans retinoic acid (ATRA) induces autophagy in some breast cancer cells. Importantly, autophagy supports the acquisition of epithelial traits of normal and cancer cells. We are therefore interested to understand the role of autophagy during EMT and the therapy-induced reversion of EMT.

Internal collaborations

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

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

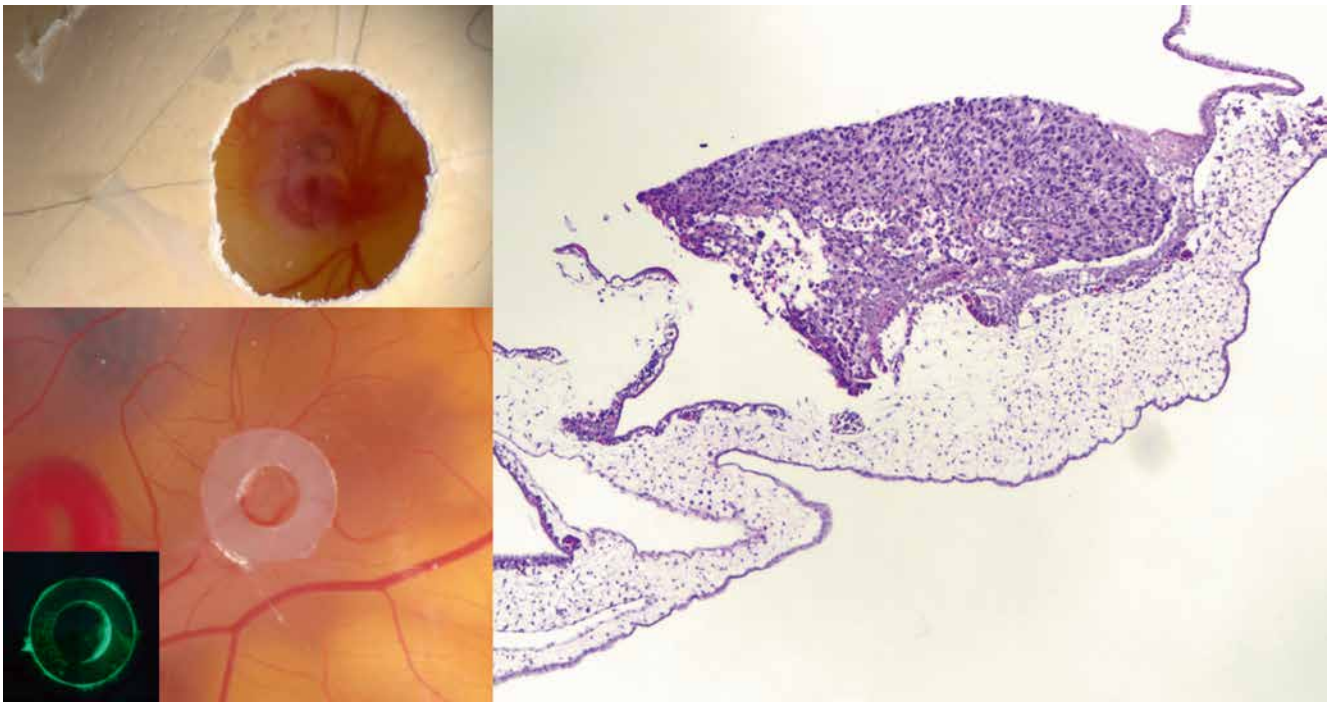
International

- Bruce E. Torbett, PhD, TSRI, La Jolla, CA, USA
- Tassula Proikas-Cezanne, Dpt. of Molecular Biology, University of Tuebingen, Germany
- Enrico Garattini, MD, Istituto di Ricerche Farmacologiche Mario Negri, Milano, Italy
- Mojgan Djavaheri-Mergny, PhD, INSERM U916 VINCO, Bordeaux Cedex, France
- Thomas Brunner, PhD, Dpt. of Biology, University of Konstanz, Germany

Grant Support

- SNSF_31003A_173219, Mario Tschan, (2017–2021), CHF 693'600
- SNSF MD-PhD 03/17, Kristina Seiler, Mario Tschan, (2018–2020), CHF 180'000
- UniBE international 2021, I.Tokarchuk, Mario Tschan, (2018–2020), CHF 90'000
- BKL , Magali Humbert, (2017–2018), CHF 85'000
- UniBE Initiator Grants, Magali Humbert, (2017–2018), CHF 16’500
- KFS, KFS-3409-02-2014, Mario Tschan, (2014–2018), CHF 390'000
- Claudia von Schilling Foundation for Breast Cancer Research, R. Langer, Co-PI Mario Tschan, (2018), *CHF 30’000
- SNSF31003A_166578, Inti Zlobec, Co-PI Mario Tschan, (2016–2019), *CHF 305'000
- KFS-3700-08-2015, Rupert Langer, Co-PI Mario Tschan, (2015–2017), *CHF 214'000
- UniBE Initiator Grants, Anna (Schläfli) Bill, (2016–2017), CHF 16’150
- BKL, Anna (Schläfli) Bill, (2016–2017), CHF 80'000

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



Chick Chorioallantoic Membrane (CAM) Xenograft Assay for Esophageal Cancer (SK-GT-4) Cells. Top left: assessing the CAM and incubation with SK-GT-4 cells. Bottom left: growing SK-GT-4 cells on the CAM. Cells were seeded into a plastic ring for better handling. Because SK-GT-4 cells were labeled with GFP, they could also be visualized by fluorescence. Right: CAM tissues with growing SK-GT-4 cells stained with hematoxylin eosin.

Group of Erik Vassella, Dr. pharm.

Ulrich Baumgartner, PhD student
Fabienne Chantal Berger, Master student (BIO) (bis 28.2.17)
Alexander Zulliger, Master student (BIO) (bis 28.2.17)
Jaison Phour, technician (ab 1.10.17)
Cornelia Schlup, technician, 90%

Short summary

My research team is aiming at identifying microRNAs that are implicated in resistance to chemo- and targeted therapy of non-small cell lung cancer and gliomas.

Project 1: MicroRNAs implicated in EGFR signaling of NSCLS
A global understanding of microRNA function in signaling pathways may provide insights into improving the management of cancer patients treated with targeted therapy. We currently investigate miRNAs that are regulated by major branches of EGFR signaling for their role in proliferation, migration, apoptosis and resistance to tyrosine kinase inhibitors in non-small cell lung cancer.

Project 2: Screening for microRNAs conferring temozolomide resistance in glioblastoma cell lines
We follow an unbiased approach for the identification of microRNAs that are most efficient at conferring temozolomide resistance in glioblastoma cells by screening a lentiviral microRNA library.

Research Activities

microRNAs are short regulatory RNAs at the post-transcriptional level that are implicated in a wide variety of basic biological processes as well as in cancer. A global understanding of microRNA function in signaling pathways may provide insights into improving the management of cancer patients treated with targeted therapy. To identify microRNAs implicated in EGFR signaling in NSCLC, we transduced bronchial epithelial BEAS-2B cells with retroviral vectors expressing KRAS(G12V) and monitored miRNA expression patterns by microarray analysis. Through this approach, we defined miR-29b as an important target for upregulation by mutant KRAS in non-small cell lung cancer. miR-29b conferred apoptosis resistance by targeting TNFAIP3/A20, a negative regulator of NF-κB signaling. Surprisingly, miR-29b could confer sensitivity to intrinsic apoptosis triggered by exposure to cisplatin, a drug used widely in lung cancer treatment. Thus, miR-29b expression may tilt cells from extrinsic to intrinsic mechanisms of apoptosis. miR-19b was identified as an important target for upregulation by another major branch of EGFR signaling, the PI3K/AKT pathway. This miRNA is an important mediator of EGFR signaling for proliferation, apoptosis and migration and confers resistance to TKI inhibitors. Interestingly, the same microRNA was also identified in a lentiviral screen for miRNAs conferring resistance to the alkylating agent temozolomide in another tumour system, glioblastoma. We are currently investigating molecular mechanisms of temozolomide resistance elicited by this miRNA. Finally, we follow a translational approach for the identification of acquired mutations and alterations in gene expression of recurrent temozolomid-resistant glioblastoma. In conclusion, our research may unravel novel resistance mechanisms in cancer.

Internal Collaborations

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

External Collaborations

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

Grant Support

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

Team Translational Research Unit (TRU).

1.2 Translational Research Unit (TRU)

Head: Inti Zlobec, PhD

Overview

The Translational Research Unit (TRU) is a core facility of the Institute of Pathology, University of Bern. Our aim is to share our expertise with and provide services in tissue-based methods for internal co-workers, researchers from the University and Insel Hospital as well as external groups from Switzerland and abroad. Our main areas of interest are in tissue biobanking, histology, tissue microarraying, tissue visualisation, digital pathology and image analysis.

TRU has 151 clients and has handled approximately 600 requests this year stemming from 139 different projects (excluding Tissue Biobanking). Collaborative projects with external research groups comprise one-third of the projects in TRU.

Approximately 77% of all of TRU's services in 2017 were funded by 3rd party money, while the remaining 23% are generously sponsored by the Institute of Pathology. This institutional funding aims to cover predominantly start-up projects for our pathologists and researchers.

Histology

Our lab has expertise in histological techniques and tries to personalize each research project. Sections are cut for many purposes: laser capture microdissection, DNA/RNA extraction, immunohistochemistry and other special downstream techniques (e.g. MALDI). Histology is the basis of all the work performed in TRU. This year, we have re-embedded 2618 blocks, and cut thousands of slides for H&E or special stains (n=2246 slides), immunohistochemistry, TUNEL or ISH (n=4563), for laser capture microdissection (n=14), or slides requiring special DNAse/RNAse-free conditions (n=54).

Tissue visualisation

Each year a large number of antibodies is established in TRU. This year again, 71 different markers were newly set up not only for human tissues or cell lines but also for mouse, horse and pig tissue, in collaboration with the comparative pathology platform, COMPATH (collaboration with the Institute for Animal Pathology).

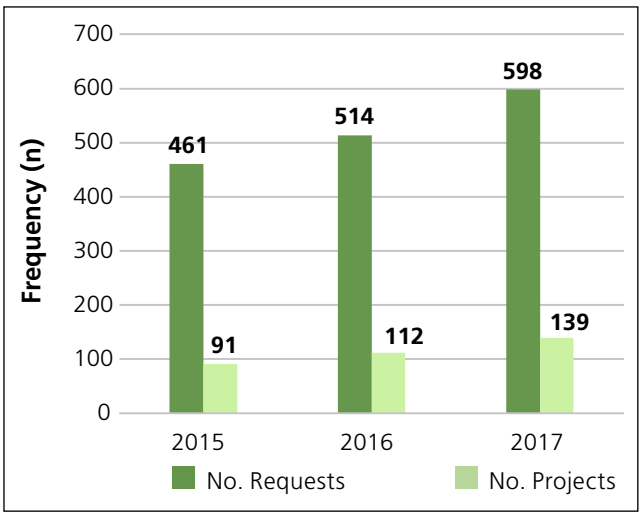
In 2017, 220 different antibodies were used for various research projects. We routinely perform mRNA in situ hybridisation (ISH) using automated immunostainers and can now additionally offer TUNEL assays for human and mouse. Briefly, 4563 slides were stained in our lab this year, including 22% in the frame of collaborations between our institute and external groups.

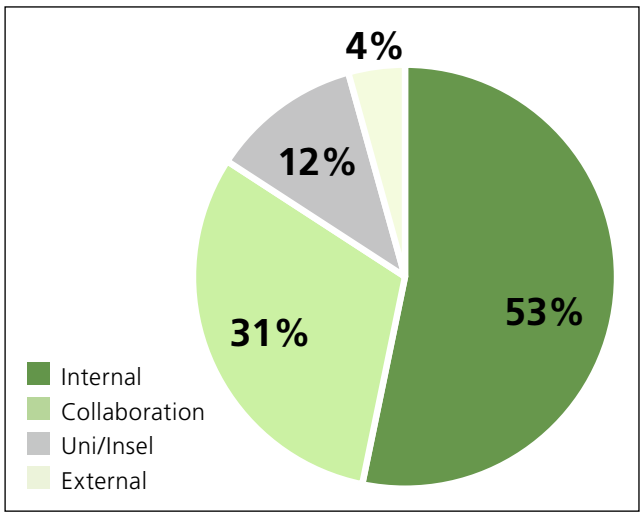
Digital pathology

Modern pathology goes hand-in-hand with digitisation. TRU has been working on digital pathology on four fronts this year: slide scanning, next-generation Tissue Microarrays (ngTMA), purchase of a new database for research and digital slide management, and digital image analysis.

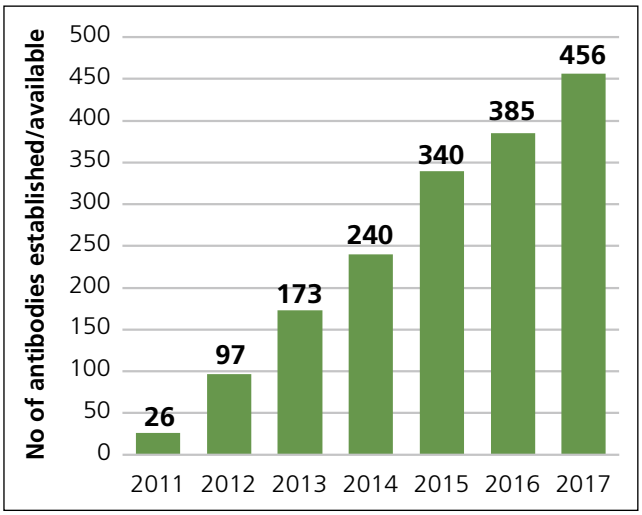
1. Slide scanning

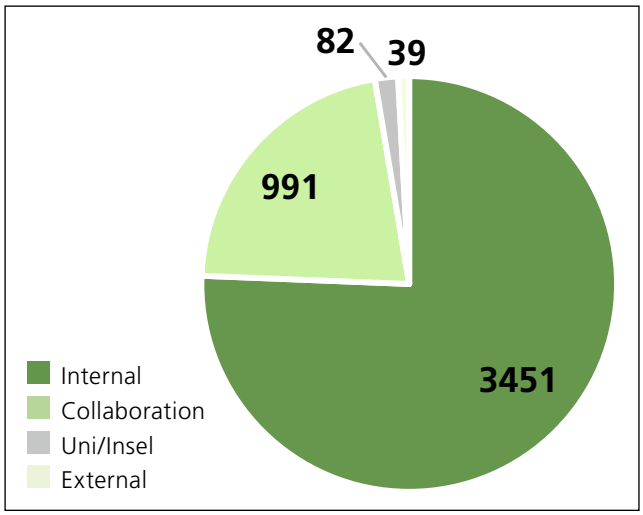
The requests for slide scanning in TRU are either for publication, education or research purposes. Downstream work includes histomorphological evaluation of tissue slides after H&E staining, immunohistochemistry, or other stains/hybridisation using





Overview





Tissue visualisation

manual or digital image analysis solutions and for further use in tissue microarray construction.

Our slides are saved locally on a NAS with more than 50 TB of storage space, and on an external Case Center accessible via the web. Currently 100 users have access to Case Center for slide viewing, sharing and annotation-creation. This platform is also being used for diagnostic slide sharing by the medical doctors of the Clinical Pathology laboratory. The success of our digital pathology platform is also owed to the strong collaboration with our informatics team. Led by Mr. Oliver Jochum, the IT department at the Institute of Pathology is fundamental to most aspects of TRU's daily business.

2. Next-generation Tissue Microarrays (ngTMA®)

a. Statistics:

Interest in the construction of ngTMAs for research questions continues to rise. Since the inception of ngTMA in 2012 (www.ngtma.com), just under 600 ngTMA blocks have been made in TRU. This year, 21 different ngTMA projects (resulting in 130 different ngTMA blocks) were constructed which is consistent with previous years, however the size and complexity of the project has risen as well.

Immunohistochemistry double-staining with pan-cytokeratin and CD8 on a large ngTMA.

In total, we estimate that more than 12'000 patients are included onto ngTMAs, many of whom are annotated with detailed clinical information including follow-up. Ten-percent of all ngTMAs made are collaborations with the Inselspital/University. In addition to constructing TMAs, annotations on digital slides can also be used as a basis for coring out material into tubes for downstream molecular analysis.

b. ngTMA network:

One of TRU's major projects this year is carried out in collaboration with the Cancer Registry of Geneva and University Hospital (HUG) on a Swiss National Science Foundation project to investigate mismatch repair proteins on 6000 colorectal cancer patients. Aim of the project is to obtain a better estimate of the number of possible familial colorectal cancer cases in the Canton. This project is an exceptional example of pathology informatics, facilitating collaboration between different Universities; slides are scanned and stored on servers at the HUG, whereas the ngTMAs are constructed in Bern.

3. Research database

TRU set out to evaluate database/slide management systems for research with the aim of handling digital scans, patient-related data and managing prognostic cohorts including TMAs. After a Request for Information (RFI) in 2016, a public call for tender was organized in August 2017. Two companies participated. The company Telemis has been selected and a major strategic aim for 2018 includes the customization of the database with integration of scans and specific focus on a Human Research Act compliant workflow.

4. Digital image analysis

The TRU is testing various commercially-available and open image analysis software. These software are being compared using a set of pre-defined criteria with the aim of selecting one for the institute, first for research and eventually for translation into diagnostic practice.

Image analysis projects are becoming increasingly popular and TRU not only collaborates, but also trains students and researchers to handle image analysis using different software. This year, we have been involved with 19 different digital image analysis projects. Experiences in machine-learning are being made, in collaboration with ARTORG at the University of Bern and it is an aim of TRU to increase expertise in this area in 2018.

5. ngTMA® and digital pathology speaking engagements

In 2017, members of TRU have been invited to speak about ngTMA and work in digital pathology at numerous events including the Biomedical Transporters Conference, the American Association for Cancer research (AACR), University of Helsinki, St. Andrew's University, Sysmex's Cancer Management Symposium and the 4rd Digital Pathology Congress. Digital pathology has also been included into the teaching curriculum at the EUROPOLA course on lab animals given by the Institute of Animal Pathology, as well as in courses for the Biomedical, Cell Biology and Bioinformatics students of the University of Bern.

6. References 2017

ngTMA has been referenced in several publications this year.

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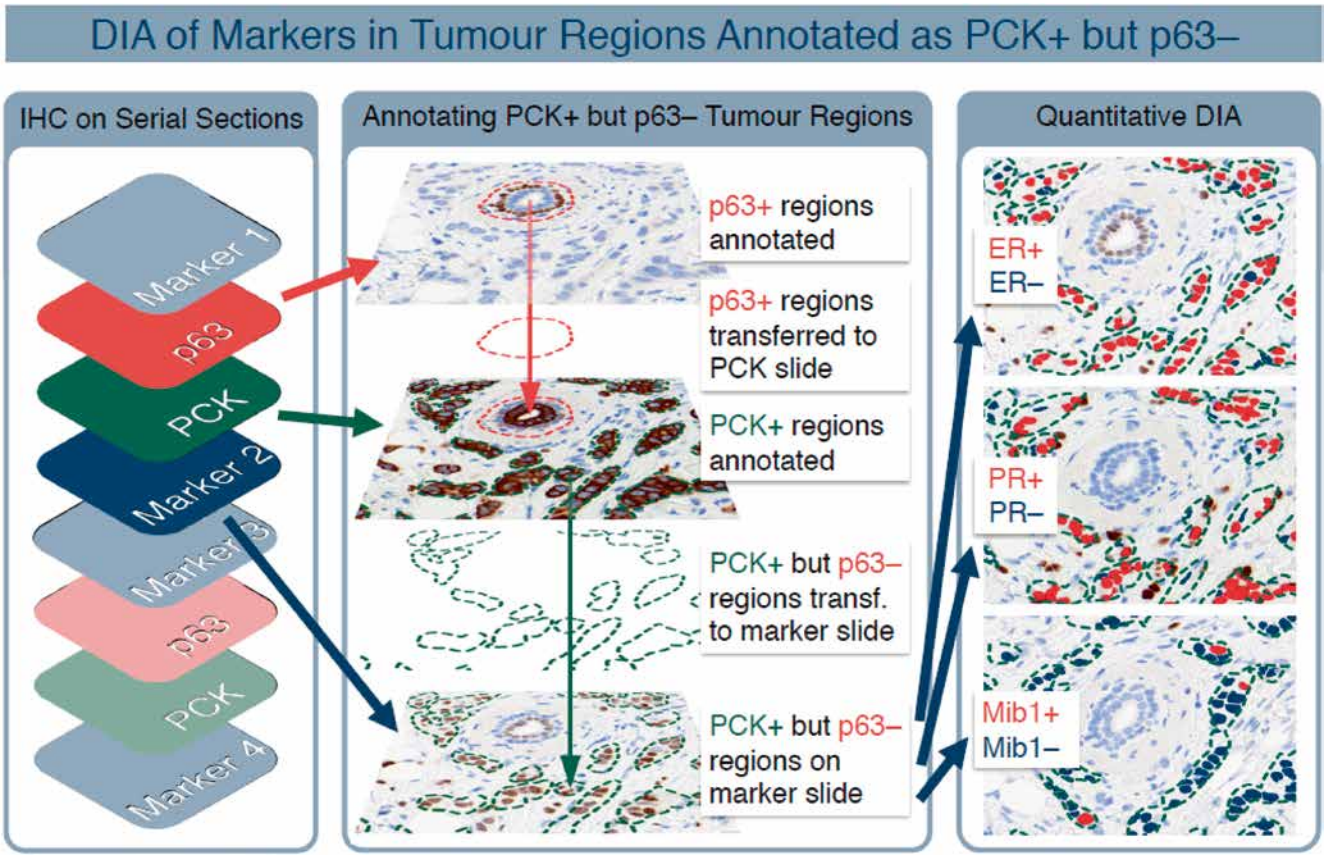

Digital image analysis of breast biopsies by M. Eichmann and T. Rau.

Tissue Bank Bern (TBB)

Director: Prof. Aurel Perren

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

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

1. Statistics

In 2017, the TBB markedly expanded its tissue collection to 1859 patients and more than 5000 different samples, bringing the total number of fresh-frozen stored samples to > 37'000. The last years have witnessed a rise in the number of patient samples included into the TBB due to the intensified collaboration between clinical departments of the Insel Hospital, our own doctors and technical staff. The Women's Clinic (Frauenklinik), Departments for Neurosurgery, Visceral Surgery and Internal Medicine as well as urology and thoracic surgery contribute the largest number of specimens to TBB.

2. Biobank Bern (Liquid and Tissue)

The year 2017 saw the bridging of TBB with the Liquid Biobank (LBB) of the Insel Hospital: a shared commission is in place to oversee both biobanks, a common website (www.biobank.ch) has been published and the Reglement of both TBB and LBB have been harmonized.

3. Projects

The number of TBB projects continues to rise. In comparison to last year's 23 projects/queries, TBB received 30 different requests for tissue. Moreover, 30% of these requests come from the Insel Hospital or University/DBMR research groups.

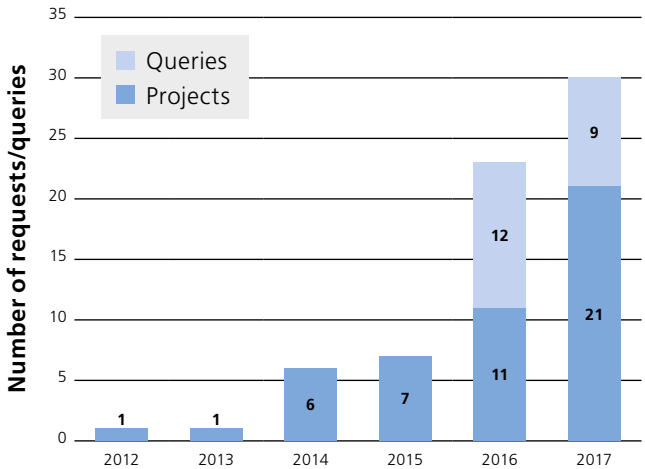

Figure 2 shows the number and type of different tissues provided to researchers from the TBB either as frozen samples or as fresh material. RNALater stored samples are also available for a majority of samples collected until now. Moreover, a trend toward the collection of fresh material for primary cell cultures could be appreciated this year. Samples of pNET, lung, breast, colorectum and ovary tissues are collected prospectively, thus leading to new challenges with regard to logistics and pre-analytics.

4. TBB networks

TBB works together with the Swiss Biobanking Platform (SBP) to help standardize and harmonize biobanking procedures across Switzerland with the final aim of being able to search and exchange samples between the different University Hospitals. To this end, a recent Swiss National Science Foundation project called PathoLink was funded, in which each of the five University Institutes of Pathology participates. The aim is to be able to deliver standardized tissue-related data (by means of synoptic reporting and coding, as well as minimal datasets for pre-analytical variables and tissue handling) across each of five major tumor entities to a central biobank repository managed by the SBP.

5. TBB speaking engagements and visits

T. Rau, Symposium of the BRoTHER project.
Regenbsurg 4–5.12.2017
«Structured Data in Biobanking. Benefits for internal use and multi-lingual situations.»

Visits to TBB and TRU are organised on a regular basis, often in conjunction with tours of the Liquid Biobank (LBB).

6. References

The TBB has been referenced in numerous articles this year.

1. Trippel M, Imboden S, Papadia A, Mueller MD, Mertineit N, Härmä K, Nicolae A, Vassella E, Rau TT. Intestinal differentiated mucinous adenocarcinoma of the endometrium with sporadic MSI high status: a case report. Diagn Pathol. 2017 May 12;12(1):39. doi: 10.1186/s13000-017-0629-0. PubMed PMID: 28494767; PubMed Central PMCID: PMC5427532.

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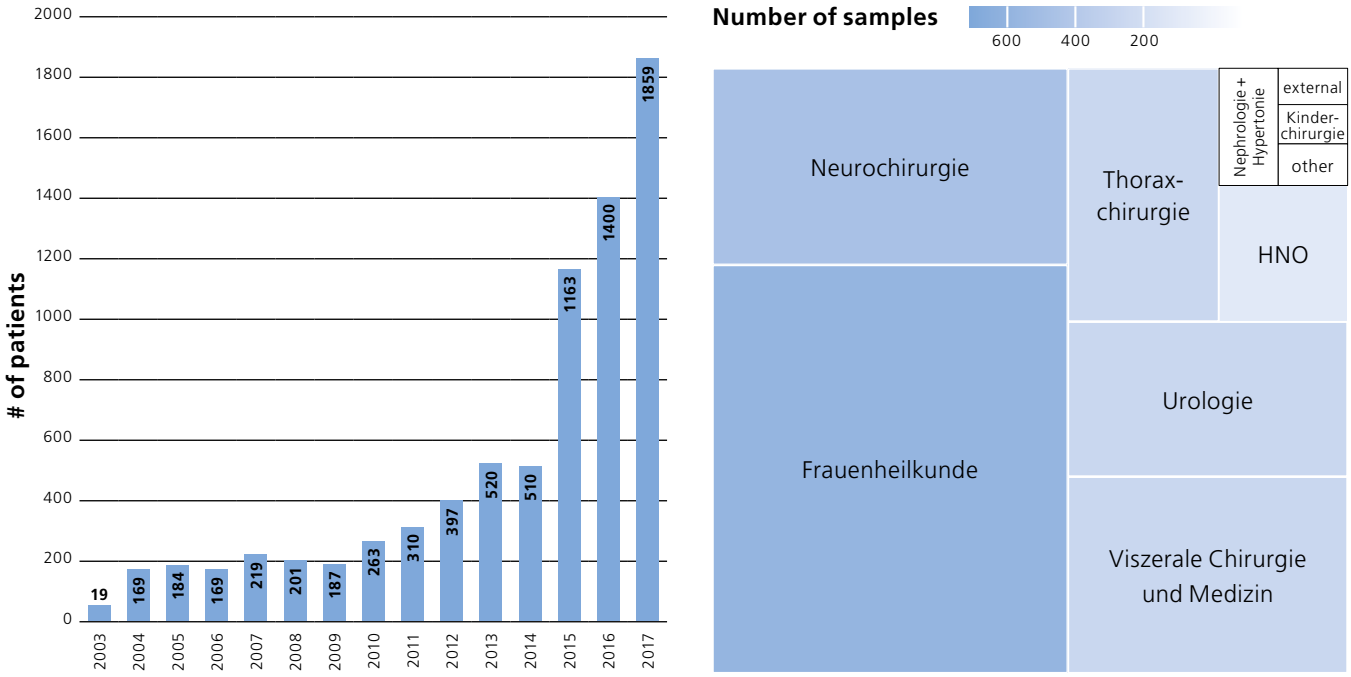

Figure 1: Statistics

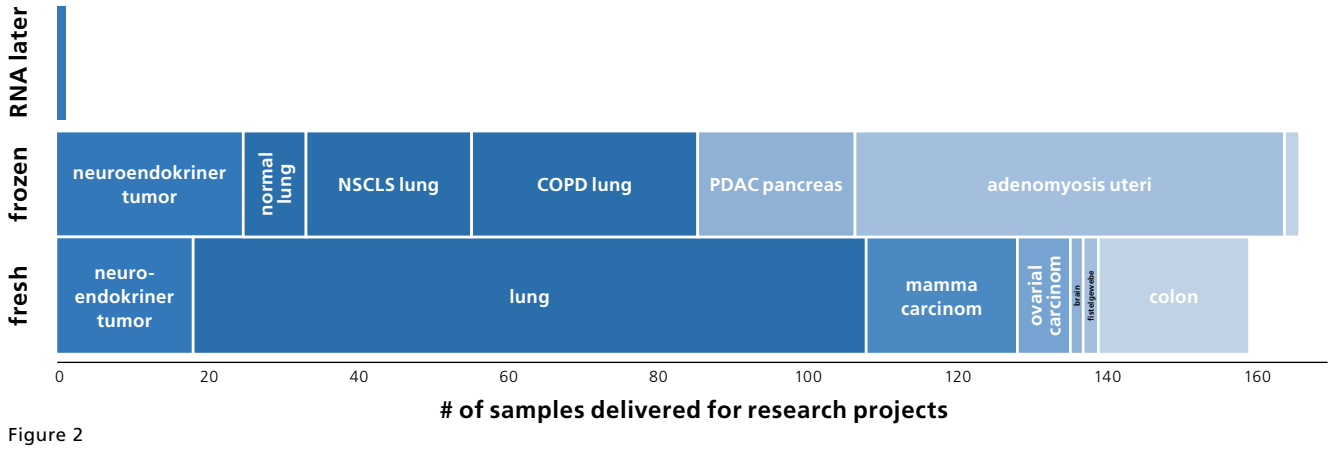

Figure 2

4. Laedrach C, Salhia B, Cihoric N, Zlobec I, Tapia C. Immunophenotypic profile of tumor buds in breast cancer. Pathol Res Pract. 2017 Dec 5. pii: S0344-0338(17)30846-4. doi: 10.1016/j.prp.2017.11.023. [Epub ahead of print] PubMed PMID: 29254793.

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Group of Yara Banz, MD PhD

Rahel Friedli, medical student
Martina Rentsch, medical student
Olivia Steinsiepe, medical student
Simone Zwicky, medical student
Westerhuis, Mira, medical student

Short Summary

An aberrant activity and altered levels of interleukins play an important role in the tumorigenesis of solid tumors as well as hematological neoplasms. Interleukin-33 (IL-33) appears to play an important role in some malignancies as well as diseases associated with fibrosis. Recently, a collaborative effort from the Institute demonstrated an important role for IL-33 in the development myeloproliferative neoplasms (MPN). Ongoing preclinical as well as clinical work is investigating the role of IL-33 in MPN initiation as well as progression. Furthermore parallel studies aim to look at its potential role in lymphomagenesis, where its function is essentially unknown.

Research Activities

Project 1

Investigation of the role of interleukin-33 in hematological neoplasms: The project focuses on IL-33 in the initiation and progression of myeloproliferative neoplasms as well as ist role in malignant lymphomas. This will occur using basic animal models of MPN-like diseases (s. investigational work of Philippe Krebs), in vitro experiments, in a retrospective manner by investigating archived bone marrow and lymphoma samples (tissue microarray, cohort of lymphoma patients) and in a prospective manner in a clinical study (MPN patients).

Kurzzusammenfassung

Eine aberrante Aktivität und veränderte Interleukin Werte spielen eine wichtige Rolle in der Entwicklung von soliden Tumoren sowie von hämatologischen Neoplasien. Interleukin-33 (IL-33) spielt eine wichtige Rolle in einigen malignen Neoplasien und auch in fibrosierenden Erkrankungen. Eine kollaborative Arbeit aus dem Institut hat eine wichtige Rolle für IL-33 in der Entstehung myeloproliferativer Neoplasien (MPN) aufgezeigt. Laufende präklinische und klinische Studien erforschen die Rolle von IL-33 sowohl in der Krankheitsentstehung als auch in der Krankheitsprogression. Zusätzliche Studien sollen zudem die Rolle von IL-33 in der Entstehung maligner Lymphome untersuchen, wo bislang keine Daten existieren.

Forschungsinteressen

Projekt 1

Untersuchung der Rolle von Interleukin-33 in hämatologischen Neoplasien: Das Projekt fokussiert einerseits auf die Initiation andererseits die auf die Progression myeloproliferativer Neoplasien sowie auf die Funktion von IL-33 in malignen Lymphomen. Die Forschung beinhaltert Tierstudien von MPN-ähnlichen Erkrankungen (s. experimentelle Arbeit von Philippe Krebs), in vitro Experimente, retrospektive Analysen von archivierten Knochenmakrsbiopsien sowie Lymphomproben (tissue microarry, Kohorte von Lymphompatienten) sowie prospektiver Natur in einer klinischen Studie (MPN Patienten).

Internal collaborations

- Philippe Krebs, MD

External collaborations

National

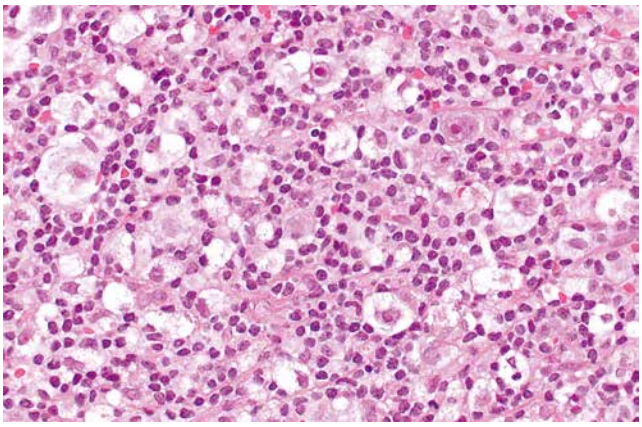
- Ulrike Bacher, MD, Department of Hematology, University Hospital, Inselspital, Bern
- Urban Novak, MD, Department of Oncology, University Hospital, Inselspital, Bern
- Thomas Pabst, MD, Department of Oncology, University Hospital, Inselspital, Bern
- Robert Rieben, PhD, Department for Biomedical Research, University of Bern
- Alexandre Theocharides, MD, Department of Hematology, University Hospital Zürich

International

- Christian Schürch, MD PhD, Stanford University, USA

Grant Support

- Bernische Krebs Liga, Yara Banz and Philippe Krebs, 2017–2018, 65'000 CHF



Hochauflösendes Bild eines malignen Lymphoms (Merkmale zwischen einem klassischen Hodgkin-Lymphom und einem diffusen grosszelligen B-Zell-Lymphom.
High-resolution image of a malignant lymphoma (with features intermediate between a classical Hodgkin Lymphoma and a diffuse large B-cell Lymphoma).

Group of Sabina Berezowska, MD

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

Short Summary

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

Research activities

Project 1: Lung cancer remains the leading cause of cancer death worldwide.

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

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

Project 2:

Lung cancer has been surprisingly shown to be amenable to immunotherapeutic approaches. Several PD-1 and PD-L1 immune checkpoint inhibitors have been approved for the treatment of patients with advanced NSCLC or are in advanced clinical studies. PD-L1 expression and tumor infiltrating lymphocytes are in the focus of many investigators. Mostly primary tumors are studies. Because 20–40% of all NSCLC patients develop brain metastases, with an associated drop in prognosis, we are interested in the characterization of cerebral metastases of lung cancer in comparison to the primary site. We conduct tissue-based research using next generation tissue micro arrays and immunohistochemistry. Hereby, one project focuses on the immunohistochemical expression of immune checkpoint marker expression and tumor infiltrating lymphocytes.

Internal collaborations

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

External collaborations

National

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

International

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

Grant support

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

Group of Eva Diamantis-Karamitopoulou, MD

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

Summary of Research Activities Short Summary

The main interest of the group is the study of the tumor microenvironment of the ductal pancreatic adenocarcinoma (PDAC). This includes the characterization of the tumor cells with special focus on the Epithelial-Mesenchymal Transition (EMT)-like tumor budding cells at the invasive front of PDAC, as well as the stromal cells and the immune cells surrounding them. Our aim is the identification of genetic and epigenetic changes of the different cell populations that promote the aggressive (EMT)-like tumor budding phenotype in PDAC.

Research Activities

Targeted therapies and immunotherapy have improved treatment options of many solid tumors, except pancreatic ductal adenocarcinoma (PDAC) which remains one of the most difficult-to-treat malignancies. With its increasing incidence and up to date no major progress, PDAC represents an urgent medical need. Despite our increasing knowledge regarding the molecular background of PDAC, this has so far not been translated into clinically relevant information.

Tumor microenvironment is of critical importance, both for the better understanding of the mechanisms involved in the initiation and progression of carcinogenesis as well as for improving diagnostic and therapeutic approaches. It includes invasive cancer cells, immune cells and stromal cells, which provide a communication network via secretion of growth factors and chemokines. Moreover, understanding the interaction between tumor- and immune cells will increase our knowledge of the mechanisms of cancer progression, since specific immune expression signatures may render the tumor microenvironment permissible for single cancer cell invasion.

Aggressive PDACs are characterized by increased numbers of dissociative growing tumor cells at the invasive front with epithelial-mesenchymal transition (EMT)-like features, coined tumor buds, shown to represent an independent adverse prognostic factor in many gastrointestinal cancers including PDAC. The microenvironment associated with tumor budding is therefore especially interesting, since it probably has a distinguished role in supporting tumor budding cells, promoting their migration, angioinvasion, stem cell features and metastatic potential. We could recently show that the tumor microenvironment of the invasive front of PDAC displays a significant heterogeneity concerning the balance between tumor- and host-associated factors depending on the molecular changes, the differential gene expression, as well as the microRNA dysregulation. During our studies we have observed that aggressive PDACs display a tumor-favoring immune-cell composition, especially in the immediate environment of the tumor buds, that protects budding cells, preventing their elimination by the host immune response and indicating a close interaction of the immune response with the EMT-process.

However, although this interaction guarantees the survival of tumor cells, it is of itself not sufficient. There is strong evidence that also other cells of the tumor microenvironment, like stromal cells are involved in pancreatic cancer progression by interacting with tumor cells. Our findings suggest that this may involve the regulation of the EMT-like tumor budding phenotype in PDAC. Furthermore, in a recent project we investigated the molecular background behind the phenotypic diversity and the differential balance between tumor- and host-associated factors in the TME of the invasive front of pancreatic cancer and could describe distinct immunphenotypes with prognostic/predictive significance. The general objective of our research projects is to provide information on the mechanisms behind the different microenvironmental patterns in PDAC and their impact on the EMT-process and the neoplastic progression.

Project 1: Integrative molecular and microenvironmental analysis of pancreatic ductal adenocarcinoma to identify distinct prognostic subgroups with different therapeutic opportunities

Despite our increasing knowledge regarding the molecular background of pancreatic ductal adenocarcinoma, this has so far not been translated into clinically relevant information. Integrative analysis of molecular and morphological data will allow the correlation of pathways and transcriptional networks that are active in the tumor microenvironment (TME) with specific morphological and immunophenotypic features. This will lead to the recognition of specific microenvironmental signatures (TME-signatures) that will be used in the clinical routine for more accurate risk assessment and patient selection towards a personalized therapy approach.

Project 2: Characterization of the tumor microenvironment to reveal differences in the tumor-host interaction between the short-, long- and mid-term survivors of pancreatic cancer

This project will investigate the balance between tumor- and host-related factors in the tumor microenvironment of the invasive front of pancreatic cancer and will address whether specific phenotypes, immune cell compositions, stromal cell subtypes and EMT- marker expression patterns are correlated with the molecular subgroups and with outcome of the patients.

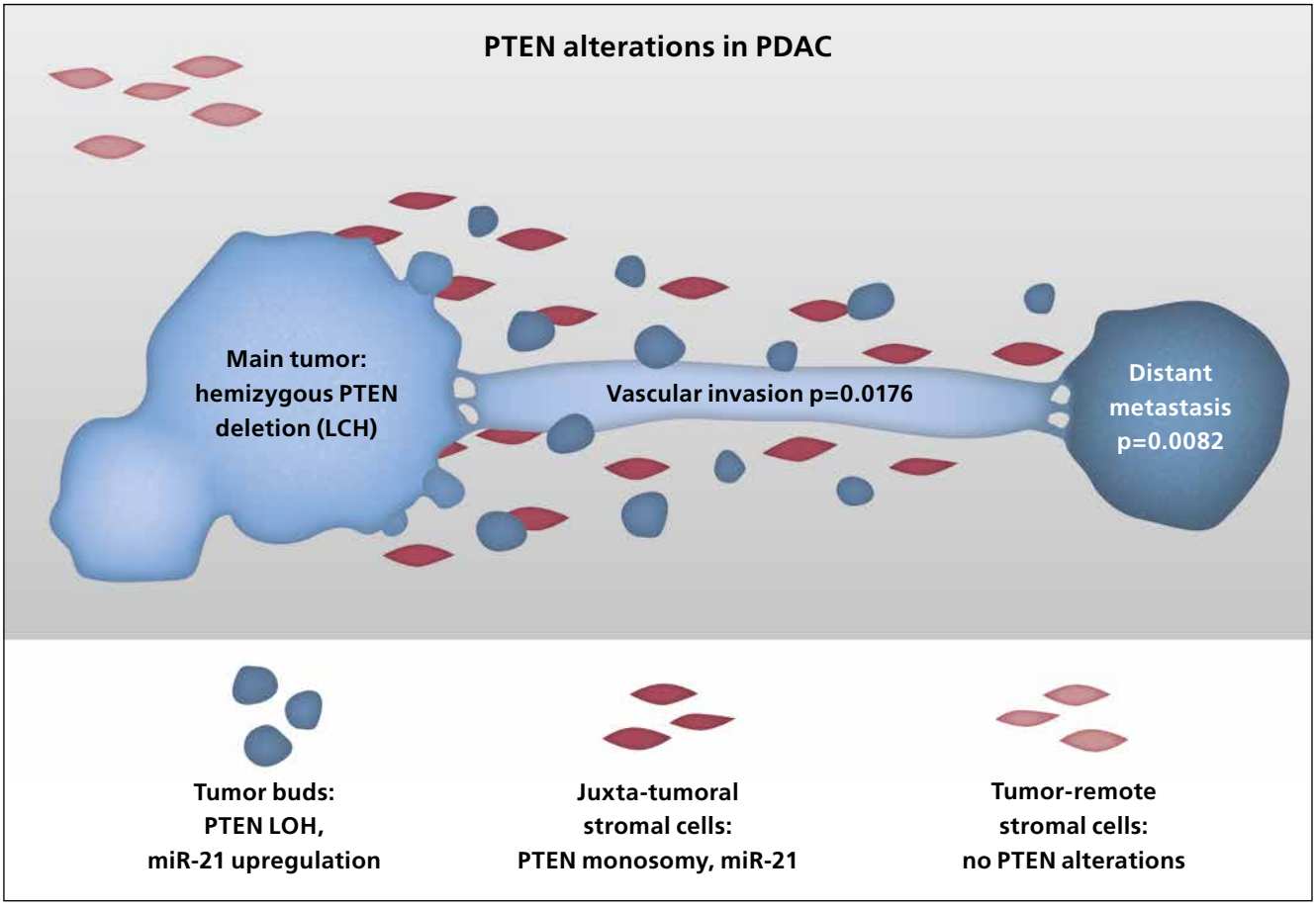
Internal collaborations
- Erik Vassella, PhD
- Inti Zlobec, PhD
- Irene Centeno, PhD
- José Galván, PhD

External collaborations

National
- Beat Gloor, MD, Department of Visceral Surgery, Insel University Hospital, Bern
- Mathias Worni, MD, Department of Visceral Surgery, Insel University Hospital, Bern
- Luigi Terracciano, MD, Institute of Pathology, University of Basel
- Christine Sempoux, MD, Institute of Pathology, University of Lausanne

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

Grant support
- Werner und Hedy Berger-Janser Stiftung zur Erforschung der Krebskrankheiten, Eva Diamantis, (2015–2017), CHF 33'410
- Stiftung für klinisch-experimentelle Tumorforschung, Eva Diamantis, (2016–2017), CHF 60'000



Group of Rupert Langer, MD

Bastian Dislich, MD, PhD
Olivia Adams, PhD Student (Co-supervision Mario Tschan, until July 2017)
Ariane Janser, PhD Student (Co-supervision Mario Tschan)
José Galvàn, PhD (20%)

Master students / dissertation candidates:
Monique Niklaus, Simon Nobs, Alexandra Stein, Laura Noser, Domink Arnold, Nicola Blaser, Julia Wiprechtiger, Matea Sunic, Lisa Alfare, Sandra Reschke, Mafalda Trippel, Ronan Gabriel, Andreas Schmid, Claudia Jaccard

Short Summary

We are investigating histomorphological and molecular characteristics of upper gastrointestinal tract tumors, especially esophageal carcinomas, in correlation with biological and clinical factors, treatment response (e.g. neoadjuvant chemotherapy and targeted therapy) and patient prognosis. A special focus of our molecular studies lies on the impact of cellular stress reactions and death mechanisms including autophagy on tumor behavior and resistance to conventional radio/chemotherapy and targeted treatment. Morphologically we are concentrating on the assessment of response to cytotoxic treatment based on histology and on the investigation of morphological features of tumors with potentially prognostic impact such as tumor budding, inflammation and tumor microenvironment.

Research Activities

Project 1: We are investigating the impact of cellular stress reactions and death mechanisms on tumor behavior and chemotherapy and resistance. In this field we are closely collaborating with Mario Tschan's group of the experimental pathology department. One focus lies on the investigation of autophagy, a cellular degradation process that has been described to play an important role not only for the maintaninance of normal cellular homeostasis but also for cancer. However, the role in malignant diseases is not completely understood, since it may promote tumor death on the one hand and be benefitial for cell survival on the other hand. We are analyzing the expression of autophagy related proteins in human biopsy and resection samples and correlate the expression patterns with clinical and pathological parameters, including tumor regression after neoadjuvant chemotherapy. The tissue analyses are complemented by functional cell line experiments that mirror the clinical scenario (i.e. treatment with conventional chemotherapeutics, but also with targeting drugs). Another interesting group of molecules are the so-called heat shock proteins (HSPs) that also play a role in cellular stress response. We are investigating a link between these two mechanisms, in specific relation to response to chemo- and targeted therapy. Here, we are focusing on Her2 targeting treatment which represents powerful therapeutic option in breast cancer and potentially also in upper gastrointestinal malignancies. We aim at elucidating potential mechanisms for resistance to this therapy, thereby also comparing breast cancer and gastroesophageal adenocarcinomas which both show overexpression of Her2 in a substantial number of cases.

Project 2: A second focus of our work is the assessment of response to cytoxotic treatment based on histology and the identification of general morphological and molecular characteristics that are associated with response to neoadjvant treatment. We have shown that tumor regression is a reliable prognostic factor after neoadjuvant therapy in adenocarcinomas of the upper gastrointestinal tract, and that grading of tumor regression based on histology can be considered as highly reproducible and feasible. Future studies will also encompass the histopathologic analysis of the effect of targeted treatment. We are also working on a comprehensive histological and molecular characterization of esophageal cancer cases that were included in the large clinical SAKK trial 75/08 where the impact of additional EGFR targeted treatment in a neoadjuvant therapy concept was investigated.

Project 3: Moreover, we are investigating features of the tumor-host interaction with potentially prognostic impact and impact on biology such as tumor budding, inflammation (i.e. specific and non-specific host reaction), and the role of the tumor microenvironment, in particular tumor associated stromal cells (fibroblasts) using several immunohistochemical markers for a more comprehensive characterization of esophageal and gastric adenocarcinomas.

Internal collaborations

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

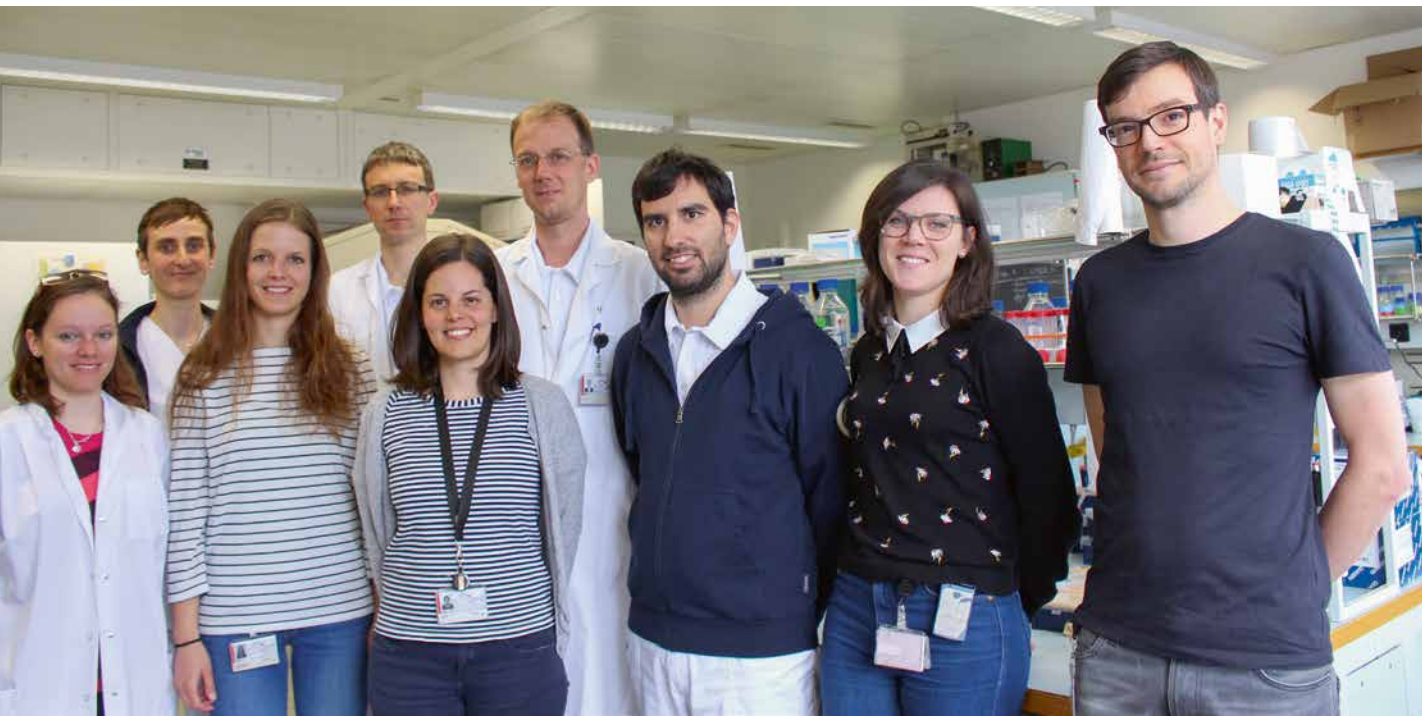
External collaborations

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

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

Grant support

- Schweizerische Krebsliga KFS-3700-08-2015, Rupert Langer (PI), Mario Tschan (Co-I), (2016–2018) *CHF 214'000
- SAKK 75/08, Rupert Langer (PI), Erik Vassella (Co-PI), (2018), CHF 130'000
- Krebsstiftung Schweiz, (2017–18), CHF 15'000, Rupert Langer and José Gàlvan
- Hans-Altschüler-Stiftung, Rupert Langer and José Gàlvan, (2018), CHF 9'700
- Claudia von Schilling Stiftung , Rupert Langer, (2018), CHF 30'000



Forschungsgruppe Aurel Perren.

Group of Aurel Perren, MD

Ilaria Marinoni, PhD, Junior PI, 80%
Anja Schmitt, MD, Attending Pathologist, 80%
Matthias Dettmer, MD Attending Pathologist
Tabea Wiedmer, MSc, Post-Doc
Annunziata Di Domenico, MSc, PhD-student
Charalampos Saganas, MD, Resident
Renaud Maire, MSc, Technician, 90%
Clémence Mooser, BSc master Student (BMS)
Avanee Ketkar, BSc master Student (Bio)
Mirjam Franzelli, cand. med.
Janine Straub, cand. med.

Short Summary

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

Dissection of the role of DAXX and ATRX in PanNET: DAXX and ATRX expression is lost in 40% of sporadic PanNETs. DAXX and ATRX are involved in epigenetic regulation. We have shown that DAXX/ATRX loss predicts reduced survival and that DAXX/ATRX loss precedes ALT (Alternative Lengthening telomeres) activation and CIN (Chromosomal instability) along tumor progression. We found that DAXX/ATRX negative tumors showed DNA hypomethylation suggesting that epigenetic changes are involved in PanNET progression upon DAXX/ATRX loss. We focus on understanding epigenetic dysregulation in PanNETs and its impact on tumor progression and therapy response.

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

Autophagy and lysosomal permeability in PanNET biology and treatment: Autophagy plays a major role in mediating metastasis formation as well as therapy response and resistance. PanNET patients often display primary or secondary resistance to the approved treatments. We investigate *in vitro* and *in vivo* the role of auto-phagy in PanNET development and in mediating therapy response and resistance. The

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

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

Internal collaborations

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

External collaborations

National

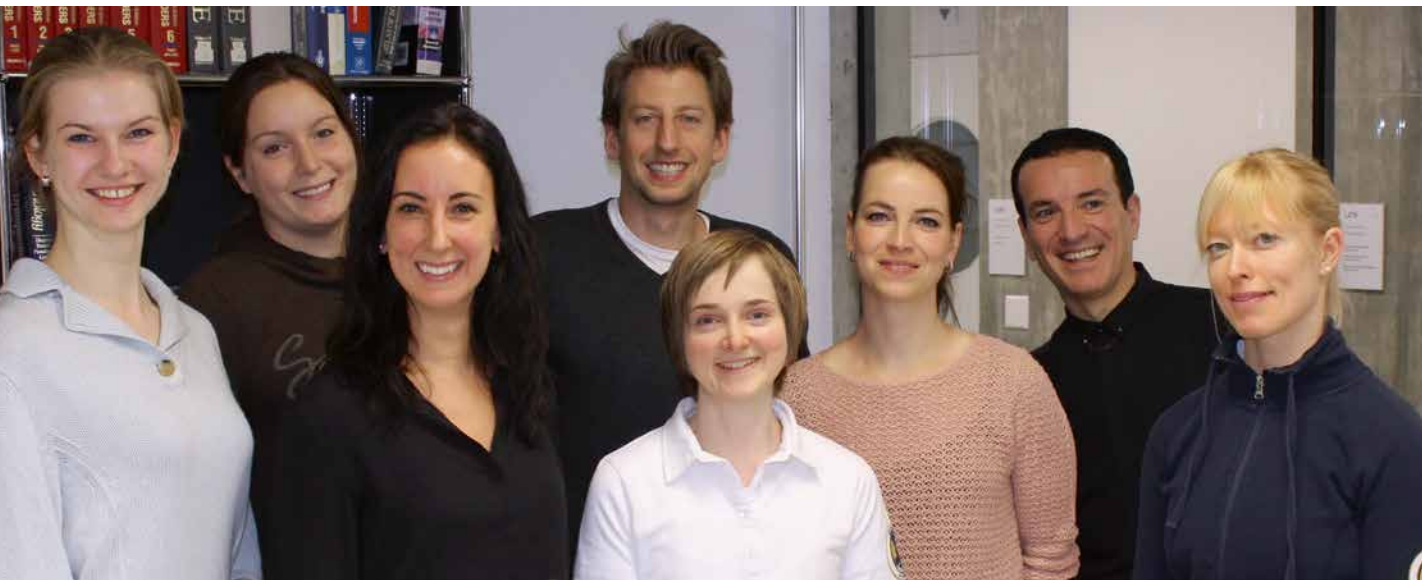
- Prof. Martin Walter, Dept. Of nuclear medicine, University of Geneva
- Prof. Roche-Philippe Charles, Institut für Biochemie, University of Bern

International

- Dr. Chrissie Thirlwell, Department of Cancer Biology, Clinical Lecturer Medical Oncology University College London, United Kingdom
- Prof. Marja Jäättelä, Head of Research Cell Death and Metabolism, Danish Cancer Society Research Center Copenhagen, Denmark
- Prof. Anne Couvelard and Dr. Jérôm Cros, Department of Pathology, Hospital Beaujon, Clichy, France
- Prof. Marianne Pavel head of the Neuro-Endocrine Tumor Unit, Charité Berlin, Germany
- Prof. Massimo Falconi, Surgery Departement, San Raffaele, Milan, Italy
- Dr. Christopher Heaphy, John Hopkins University School of Medicine, US
- Prof. Luca Mastracci, Department of Surgical Science and Integrated Diagnostics (DISC), University of Genoa, Italy
- Prof. Dr. Yuri Nikiforov, University of Pittsburgh medical center, Pittsburgh, Pennsylvania
- Prof. Dr. Marina Nikiforova, University of Pittsburgh medical center, Pittsburgh, Pennsylvania, USA, USA

Grant support

- KLS 3360-02-2014 (Aurel Perren and Ilaria Marinoni (Co-Applicant)), (2014–2017), CHF 286'900
- Tumor Forschung Bern (Ilaria Marinoni), (2015–2018), CHF 90'000
- SNF Marie Heim-Vögtlin (Ilaria Marinoni), (2016–2018), CHF 206'000
- Desirée and Niels Yde Foundation Ilaria Marinoni, (2016–2019), CHF 54'000
- Berner Krebsliga (Matthias Dettmer PI), (2017–2019), CHF 70`000



Team Translational Research Unit (TRU).

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

Alessandro Lugli, MD, Head of Clinical Pathology
Inti Zlobec, PhD, Head of TRU
Annika Blank, MD, staff pathologist
Heather Dawson, MD, staff pathologist
Lena Sokol, PhD, post-doctoral fellow
Kristin Uth-Gottardi, MSc, PhD student
Stefan Zahnd, MSc, PhD student

MD Thesis and Dissertation students:
Sandra Burren, MD
Lucine Christe, MD
Elia Fischer, MD
Janina Graule, MD
Claudia Jaccard, MD
Claudia Läderach, MD
Christian Lambert
David Marx, MD
Sara Meyer
Katharina Reche
Lynn Richmond, MD
Carla Schenker
Julia Unternaehrer

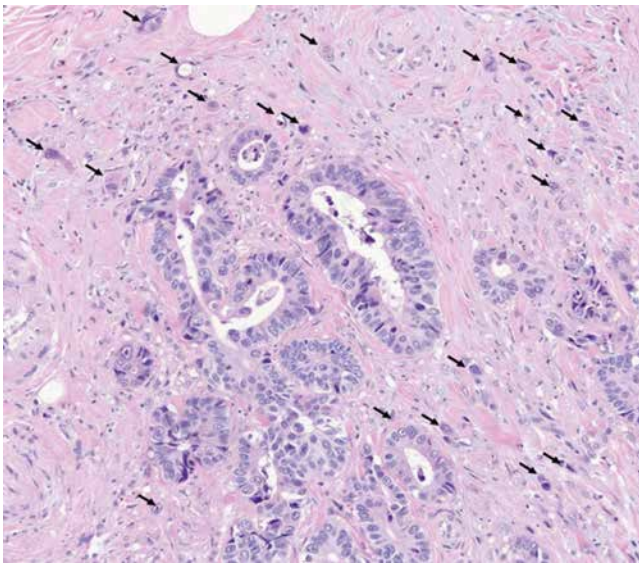
Short Summary

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

Research Activities

Project 1:

Tumor budding is an important prognostic feature in colorectal cancer. As detached single cells or small clusters, tumor buds correlate with aggressive tumor behavior. We aim to standardize the diagnostic reporting of tumor budding. To this end, we organized the 1st International Tumor Budding Consensus Congress (ITBCC) 2016, where reporting recommendations were successfully set. Our work concentrates on answering open questions concerning the nature of buds, relation to epithelial-mesenchymal transition (EMT) and impact of the microenvironment in both colorectal cancers and liver metastases. The ultimate aim is to find targets that could be exploited in the destruction of these cells.



H&E staining of tumor budding in colorectal cancer.

Project 2:
The CDX2 protein, a marker of intestinal differentiation, is decreased/lost in up to 20% of colorectal cancers. CDX2 loss is associated with microsatellite instability, high-level CpG island methylation and BRAF mutation, features of the serrated pathway. Our recent studies show that CDX2 promoter hypermethylation is a reason for this loss that can be recovered upon DNMTi treatment. Moreover, work with HDACi suggests the involvement of specific HDACs in CDX2 regulation. Together with Prof. M. Tschan, we investigate genetic/epigenetic modifications of CDX2 using CRISPR/Cas9 technology. This interesting story is on-going work by PhD student Kristin Uth-Gottardi.

Project 3:
In this project, we aim to identify novel prognostic protein biomarkers in patients with stage II and III colorectal cancers by selectively isolating tumor epithelial cells from formalin-fixed paraffin-embedded tissue. This is performed by using digital scans of the H&E slides from each patient, annotating these scans in specific histological areas which can then be aligned to the tissue block and cored out. Protein is extracted and a shotgun-proteomics based mass spectrometric analysis is performed. This laboratory/bioinformatics project is the work of PhD student Stefan Zahnd and a collaboration with Manfred Heller, Proteomics Facility, DBMR.

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

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

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

Grant Support

- Dutch Cancer Society (Consortia grant), 10602, Prof. Iris Nagtegaal, I.Zlobec, A. Lugli, Consortia, 2017–2020, CHF 100'000
- Swiss Cancer League, KFS-3966-08-2016 , Prof. M. Hediger, I.Zlobec, 2017–2020, CHF 50'000
- Swiss National Science Foundation, 31003A_166578, I.Zlobec, M. Tschan, 2016–2019, CHF 305'040
- Swiss National Science Foundation, 320030_163342, S. Benhamou, I.Zlobec, 2015–2018, CHF 191'117
- Swiss Cancer League, KFS 4108-02-2017, A. Lugli, H. Dawson, 2017–2019, CHF 139'450

2 Akademische Grade

2.1 Akademische Grade intern

Alexander Zulliger, MSc
MicroRNA miR-125b mediates chemoresistance in glioma cell lines by inducing autophagy
Supervisor: Eric Vassella

Alexandra Kündig, MMed
Komplettierung der klinisch-pathologischen Charakteristika und Überlebensdaten eines Kollektivs von zerebral metastasierten Lungenkarzinomen
Supervisor: Sabina Berezowska, Rupert Langer

Alexandra Stein, Dr. med.
High intratumoural but not peritumoural inflammatory host response is associated with better prognosis in primary resected oesophageal adenocarcinomas
Supervisor: Rupert Langer

Anna Steinert, PhD
Regulation and Function of the Interleukin 19 in Intestinal Immunity
Supervisor: Hendrik Niess

Carla Alicia Ruckstuhl, PhD
Regulation of «stemness» in immune cells and leukemia stem cells
Supervisor: Adrian Ochsenbein

Christian Schafroth, MD
BRAF VE1 analysis in colorectal cancer
Supervisor: Inti Zlobec

Clemence Mooser, MSc
nti-tumoral treatment of 3D pancreatic neuroendocrine tumor cell culture
Supervisor: Aurel Perren

Elena Blanc, PhD
(Université Claude Bernard Lyon, France)
L'interleukine-33 : de son expression dans le cancer du sein à l'activation des cellules NK
Supervisor: Nathalie Bendriss Vermare;
External reviewer: Philipp Krebs

Elsa Sartori, MD
Low co-expression of epidermal growth factor receptor and its chaperone heat shock protein 90 is associated with worse prognosis in primary glioblastoma, IDH-wildtype
Supervisor: Sabina Berezowska, Inti Zlobec

Fabienne Chantal Berger, MSc
miR-19b is a mediator of EGFR signaling in non-small cell lung cancer
Supervisor: Eric Vassella

Fiorenza Fumagalli, PhD
Unraveling the molecular pathways controlling recovery from a transient ER stress in mammalian cells
Supervisor: Maurizio Molinari

Jens Brönnimann, Dr. med.
Role of SMADs in epithelial mesenchymal transition in pancreatic cancer
Supervisor: Eva Diamantis

Julia Parts, PhD
Exploring metabolic pathways in acute myeloid leukemia
Supervisor: Mario P. Tschan

Karina Bauer, Dr. med.
(Technische Universität München)
Expression Analysis of Heat Shock Proteins in Gastrointestinal Carcinomas
Supervisor: Ch. Mueller

Luc Xavier Marie Lebon, PhD
(EPFL, Lausanne, Switzerland)
The microbiota provides colonisation resistance against intestinal helminths by regulating intestinal physiology
Supervisor: Nicola Harris

Ludmila Cardoso Alves, PhD
Regulation of CD8+ T cell response during infectious and sterile inflammation
Supervisor: Philipp Krebs

Manuel Keller, MMed
Komplettierung der klinisch-pathologischen Charakteristika und Überlebensdaten eines Kollektivs von Plattenepithelkarzinomen der Lunge
Supervisor: Sabina Berezowska, Rupert Langer

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

Miriam Flury, MD
DNA extraction from tumor buds in colorectal cancer
Supervisor: Inti Zlobec

Monique Niklaus, Dr. med.
Expression analysis of LC3B and p62 indicates intact activated autophagy is associated with an unfavorable prognosis in colon cancer
Supervisor: Maurizio Molinari

Myriam Franzelli, Masterarbeit
Frequency of PD-L1 expression and the Role of Tumor-associated Macrophages (TAM) in Pancreatic Neuroendocrine Neoplasms
Supervisor: Annika Blank

Nadia Oehninger, MSc
The regulation of the inflammatory response by oxidized lipids
Supervisor: Stefan Freigang

Nicolas Niklaus, MSc
The role of DMTF1 isoforms during cisplatin resistance, migration, and autophagy in breast cancer cells
Supervisor: Mario P. Tschan

Nicolas Pierre Desbaillets, PhD
(EPFL, Lausanne, Switzerland)
Targeting cancer stem cell by T cell engineering
Supervisor: Joerg Huelsken

Nina Tremp, BSc
Construction of a vector for inducible DAXX recombination in vitro in murine pancreatic neuro endocrine tumor cells
Supervisor: Aurel Perren

Olivia Adams, PhD
The role of autophagy in the biology of esophageal adenocarcinomas, including the impact on chemo- and HER2 targeted therapeutic response
Supervisor: Rupert Langer and Mario Tschan

Pascal Fischer, Masterarbeit
Construction of a next-generation tissue microarray (ngTMA) of thyroid cancer
Supervisor: Matthias Dettmer

Petra Polakova , MSc
Role of purinergic signaling for chronic virus infection
Supervisor: Philippe Krebs

Philipp Zens, MMed
Zusammenstellung eines Kollektivs neoadjuvant behandelter Lungenkarzinome und einer Kontrollgruppe primär resezierter Tumore
Supervisor: Sabina Berezowska, Rupert Langer

Poorya Amini, PhD
Optical atrophy 1 (OPA1) is essential for NET formation and antibacterial functions in neutrophils
Supervisor: Hans-Uwe Simon

Rahel Thomi, PhD
Interleukin-32, interleukin-35 and LL-37 in the pathogenesis of hidradenitis suppurativa
Supervisor: Robert Hunger

Ramona Reinhart, PhD
The importance of BCL-2 family members in cell survival and cell death regulation of basophils
Supervisor: Thomas Kaufmann

Robin van Brummelen, BSc
Lipid-induced inflammatory responses of macrophage-derived foam cell
Supervisor: Stefan Freigang

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

Sarah Parejo, MSc
Role of FOXO3 and ATG16L1 in ATRA-mediated autophagy in breast cancer cells
Supervisor: Mario P. Tschan

Shunqing Liang, PhD
Targeting chemoresistance in non-small cell lung cancer
Supervisor: Ren-Wang Peng

PhD Tabea Wiedmer, PhD
(Graduate school Bern)
Autophagy inhibition improves current pancreatic neuroendocrine tumor therapy via a lysosome-dependent mechanism
Supervisor: Aurel Perren

Ulrich Baumgartner, PhD
microRNAs as modulators of cell signalling and their role in chemoresistance in solid cancer
Supervisor: Eric Vassella

Viviane Brönnimann, BSc
(Biological Sciences Faculty)
Assessment of factors regulating Rgs1 expression – in vitro exposure of CD8+ T cells to different cytokines
Supervisor: Ch. Mueller

3 Publikationen

Artikel in Sammelband

- Couvelard A, Hammel P, Komminoth P, Mete O, Pacak K, Perren A, Stratakis C
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4 Vorträge

Banz Yara
- 15.06.17: GCA – exploring the diagnosis landscape
  EULAR Symposium, Madrid, Spain
- 30.11.17: Sjögren – das Syndrom – die Histologie
  Berner Immunologietagung, Bern, Schweiz

Berezowska Sabina
- 14.01.17: PD-L1 Clone SP142
  organized by Roche
- 02.02.17: PD-L1 Clone SP142 – Scoring Seminar
  organized by Roche
- 20.03.17: Immuncheckpoint-Inhibition bei soliden Tumoren –
  die Sicht des Pathologen
  Onco-Lunch Basel
- 05.04.17: PD-L1 Testing – from the biopsy to the report –
  the view of a Pathologist
  MSD, invited talk
- 24.04.17: Molekularpathologische Untersuchungen
  beim Lungenkarzinom
  Fortbildungsveranstaltung der Thoraxchirurgie und Pneumologie
  01.09.17: Identifikation von Kandidaten für Immuntherapie –
  was bietet die Pathologie
  Orphan Malignancies Seminar
- 10.11.17: Moderation of the poster session
  the annual meeting of the Swiss Society of Pathology
  (SGPAth/SSPath)

Diamantis-Karamitopoulou Eva
- 25.01.17: Adenocarcinoma of thePancreas, the Perihilar
  and Distal Extrahepatic Bile Ducts, the Gallbladder and the
  Ampulla of Vater
  Internal Education Rounds Department of Gastroenterology
  and Visceral Surgery, Inselspital Bern
- 05.05.17: Erkrankungen der Bauchspeicheldrüse
  SHT Symposium 2017
- 18.06.17: Tumor microenvironment of pancreatic cancer
  Internal Education Rounds Institute of Pathology, University of
  Lausanne
- 04.09.17: Chair: Best Poster Session Digestive Diseases Pathology:
  Liver and Pancreas, BPS-06
  29th European Congress of Pathology
- 04.09.17: Chair: Poster Session Digestive Diseases Pathology:
  Liver and Pancreas, PS-07
  29th European Congress of Pathology

Dislich Bastian
- 2.–5.9.17:
  Talk: What is the role of EBV in esophageal cancer? – what is the
  impact of EBV in the major types and in rare subtypes of esophageal
  cancer and is there any prognostic or therapeutic relevance?
  Talk: Can the role of adaptive immune system in esophageal
  cancer be specified?
  World Congress OESO, Geneva

Freigang Stefan
- 17.08.17: Linking macrophages, fats and inflammation – immune
  mechanisms in atherosclerosis
  Cardiovascular Colloquium, Inselsital Bern

Genitsch Vera
- 07.12.17: What's new about histopathological Oxford classification?
  Annual Meeting of the Swiss Society of Nephrology,
  Invited talk, IgA Nephropathy

Humbert Magali
- 04.05.17: Autophagy pathways active during APL therapy –
  identification of key autophagic networks
  Annual Swiss Hematology Meeting, Lausanne

Krebs Philippe
- 01.03.17: IL-33 signaling contributes to the pathogenesis of
  myeloproliferative neoplasms & The ESRP1-GPR137 axis contributes
  to intestinal pathogenesis
  University Hospital Regensburg, Germany
- 07.04.17: IL-33/ST2 signaling in cancer und immunopathology
  University Hospital Bern, Switzerland
- 12.04.17: NK cell-mediated regulation of adaptive immunity
  University Hospital Bern, Switzerland
- 25.04.17: Alternative mRNA splicing and intestinal pathogenesis
  EPFL, Lausanne, Switzerland
- 14.09.17: Transcriptional and post-transcriptional regulation
  of immunopathology
  University of Geneva, Switzerland

Langer Rupert
- 17.03.17: Autopsie im 21. Jahrhundert
  Universität Bern – Seniorenuniversität
- 2.–5.9.17: Chair: Oral presentations – Basic science
  World Congress OESO, Geneva
- 2.–5.9.17:
  Talk: What is the natural course of Lymphocytic Esophagitis
  Talk: What is the role of EBV in esophageal cancer? –
  what is the biological background of EBV associated gastro-
  intestinal cancer?
  Talk: Is there a role for the immunoscore in esophageal cancer?
  World Congress OESO, Geneva

Lugli Alessandro
- 28.04.17: Change of culture is not a mission impossible in Pathology
  University of Padova, Italy
- 03.09.17: Tumor budding in GI carcinomas
  Annual Meeting of the European Society of Pathology,
  Amsterdam, Netherlands
- 04.10.17: International Tumor Budding Consensus (ITBCC) 2016
  Dianapath, Pathology Centre, Geneva, Switzerland
- 08.11.17: International Tumor Budding Consensus (ITBCC) 2016
  und Update in der Pathologie der kolorektalen Polypen
  Institute of Pathology, München North, Germany
- 18.11.17: LEAN Management: Leadership, Development and Vision
  Sakura Symposium, Vienna, Austria

Mueller Christoph
- 24.05.17: TREM1 links dyslipidemia with inflammation and
  lipid deposition in atherosclerosis
  Seminaire RIA, Bern
- 06.07.17: Inflammation amplifiers: new players and unexpected roles
  European Research Group of Oral Biology Meeting (ERGOB) Prangins

Noti Mario
- 08.02.17: Type-2 immune cells in allergic inflammation and beyond
  Institute of Physiology, University of Zurich, Switzerland
- 16.03.17: Basophil-derived IL-4 promotes food allergic inflammation,
  Chair: Poster session, Immunology and Allergy
  XI World Immune Regulation Meeting, Davos, Switzerland
- 07.04.17: Animal Models of Anaphylaxis
  EAACI Task Force, Vienna, Austria

Noti Mario
- 12.05.17: Epithelial-derived cytokines license type-2 immunity
  University of Konstanz, Germany
- 04.09.17: Type-2 immune cells in allergic inflammation and beyond
  Novartis Institutes for Biomedical Research Basel, Switzerland

Perren Aurel
- 31.01.17: pNET Epigenetis
  San Raffaele Hospital, Milano
- 09.02.17: SwissNET and the European NET Community
  NET nurse day, Bern
- 08.03.17: Pathology overview & new advances to aid therapy
  7th Annual ENETS Postgraduate Course
- 09.03.17: Talk Classification of NEN G3: News and challenges
  7th Annual ENETS Postgraduate Course
- 12.03.17: Endokrine Organe Schnittsemina: Digitale Lehrserie 284
  53. Symposium IAP Schilddrüsenseminar, Bonn
- 23.03.17: NET Pathology: Current standards and new trends
  Post-ENETS, Advanced training seminar, Zürich
- 21.04.17: Pankreatische Neuroendokrine Tumoren: Neuigkeiten in Klassifikation und biologischem Verständnis
  Freitagskolloquium Institut für Pathologie und Molekular-pathologie, USZ, Zürich
- 18.08.17: Pathologie der neuroendokrinen Tumore: «Relevanz im klinischen Alltag»
  Onkolunch Kantonsspital St. Gallen
- 29.06.17: Pathological classification of NET
  ESMO Barcelona
- 03.09.17: Endocrine Pathology: Morphology meets molecular pathology in GEP neuroendocrine tumours
  ESP Amsterdam
- 24.10.17: Pancreatic NETs, morphological and molecular progression
  RNSH Liver Meeting, Royal North Shore Hospital, Sidney, Australia
- 07.12.17: New aspects in the classification of G3 neuroendocrine neoplasms
  The Kinghorn Center Gastrointestinal Cancer meeting, TKKC, Sidney, Australia

Rau Tilman
- 22.02.17 «Organisation Biobanken» VETsuisse Fakultät
  VETsuisse Fakultät, Bern
- 4.–5. 12.2017: Structured Data in Biobanking. Benefits for internal use and multi-lingual situations
  Symposium of the BROTHER-project, Regensburg

Schenk Mirjam
- 12.04.17: Current topics in Pharmacology and Theranostics, invited talk
  Institute of Pharmacology
- 29.11.17: invited talk
  BIC, Bern Immunology Club
- 18.12.17: Symposium Stiftung Experimentelle Biomedizin

Tschan Mario
- 07.03.17: Assessing Autophagy in Primary Human Tumor Tissue
  COST Action «Transautophagy», Working Group 2 Meeting, Tuebingen, Germany
- 28.11.17: Inverse regulation of Chaperone-Mediated Autophagy and non-canonical macroautophagy during retinoic acid therapy of acute myeloid leukemia cells
  7th Autophagy Scientific Days organized by CFATG, Paris

Zlobec Inti
- 09.08.17: Biomarkers in cancer research: combining next-generation tissue microarrays (ngTMA) and digital image analysis (DIA)
  Biomedical Transporters Conference, Lausanne,Switzerland
- 03.04.17: Trends in tissue microarraying: from the pre- to the post-digital era
  American Association for Cancer Research Congress, Washington DC, USA
- 27.03.17: ngTMA
  Department of Pathology, University of Helsinki, Helsinki, Finland
- 25.03.17: The ITBCC- consequences for the practicing pathologist
  Swiss Association of Gastrointestinal Pathology (SAGIP), Bern, Switzerland
- 24./25. 2.2017: TMA User Group Meeting: Trends in tissue microarraying: grom the pre- to the post-digital era
  Sysmex Cancer Management Symposium, Hamburg, Germany
- 24./25.02.2017: Application of ngTMA to the tumor microenvironment in colorectal cancer
  Sysmex Cancer Management Symposium, Hamburg, Germany
- 24./25.02.2017: Chair of session «Digital Pathology»
  Sysmex Cancer Management Symposium, Hamburg, Germany
- 17.02.17: Biomarkers in the digital era
  EUROPOLA course, Bern Switzerland
- 07.02.17: Biomarkers in the digital era
  Departmental seminar, School of Medicine, St. Andrews University, Scotland
- 19.01.17: Biomarkers and digital pathology
  MEL-PLEX Workshop Quantitative biophotonics for translational systems biology, Copenhagen, Denmark

5 Drittmittel

Banz Yara/Krebs Philippe
- Bernische Krebs Liga, 2017–2018, CHF 65'000

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

S. Benhamou (PI), Zlobec Inti (Co-PI)
- Swiss National Science Foundation, 2015–2018, CHF 525'000

Berezowska Sabina
- Fondation J. Dürmüller-Bol, 2017–2018, CHF 9'500

Dettmer Matthias
- Berner Krebsliga, 2017–2019, CHF 70'000

Diamantis Eva
- Werner und Hedy Berger-Janser Stiftung, 2015–2017, CHF 33'410
- Stiftung für klinisch-experimentelle Tumorforschung, 2016–2017, CHF 60'000

Freigang Stefan
- SNF 310030_152872, 2015–2017, CHF 510'000
- SNF 316030_157702, 2014–2016, CHF 240'000
- Vontobel-Stiftung, 2014–2017, CHF 120'000
- UniBE Research Foundation, 2014–2017, CHF 15'000
- Fondation J. Dürmüller-Bol, 2014–2017, CHF 27'000
- UniBE-ID Grant, 2016–2017, CHF 150'000
- UniBE-ID Grant, 2018–2019, CHF 150'000

Freigang Stefan (Co-PI), O. Guenat (PI)
- 3R Research Foundation, 2016–2017, CHF 138'000
- Swiss Lung Liga, 2017–2019, CHF 162'000

Hediger M. (PI) Zlobec Inti (Co-PI)
- Swiss Cancer League, 2017–2020, CHF 196'500

Krebs Philipp
- Marie Curie Career Integration Grants (CIG), 2015–2017, € 1000'000
- SNSF, 163086, 2016–2019, CHF 525'000
- Vontobel Foundation, 2015–2017, CHF 130'000
- Fondazione San Salvatore, 2016–2017, CHF 120'000
- Swiss Life / Jubiläumsstiftung, 2017–2018, CHF 30'000

Krebs Philipp/Yara Banz
- Swiss Cancer League, KLS-3408-02-2014, 2016–2019, CHF 124'000

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

Langer R., Co-PI Mario Tschan
- KFS-3700-08-2015, 2015–2017, CHF 214'000

Langer Rupert/José Gàlvan
- Krebsstiftung Schweiz, 2017–2018, CHF 15'000

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

Lukas Mager
- Gertrud-Hagmann-Stiftung, 2015–2017, CHF 241'566

Magali Humbert
- BKL, 2017–2018, CHF 85'000
- UniBE Initiator Grants, 2017–2018, CHF 16'500

Marinoni Ilaria
- Tumor Forschung Bern, 2015–2018, CHF 90'000
- SNF Marie Heim-Vögtlin, 2016–2018, CHF 206'000
- Desirée and Niels Yde Foundation, 2016–2019, CHF 54'000

Mueller Christoph
- SNF 310030_170084, 2016–2019, CHF 525'000
- SNF 33CS30_134274 / 1, 2016–2018, CHF 200'000
- SNF CRSII3_136286 / 1, 2015–2017, CHF 456'531

Nagtegaal I. (PI) Zlobec Inti; Lugli Alessandro (Co-PI)
- Consortia, Dutch Cancer Society (Consortia grant), 2017–2020, € 1.6 M

Noti Mario
- SNF, PZ00P3_154777/1, 2014–2017, CHF 599'156
- Novartis FreeNovation, 2016–2018, CHF 180'000
- Novartis Foundation , 2015–2017, CHF 60'000

Perren Aurel / Marinoni Ilaria (Co-Applicant)
- KLS 3360-02-2014, 2014–2017,CHF 286'900

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

Schläfli (Bill) Anna
- UniBE Initiator Grants, 2016–2017, CHF 16'150
- BKL, 2016–2017, CHF 80'000

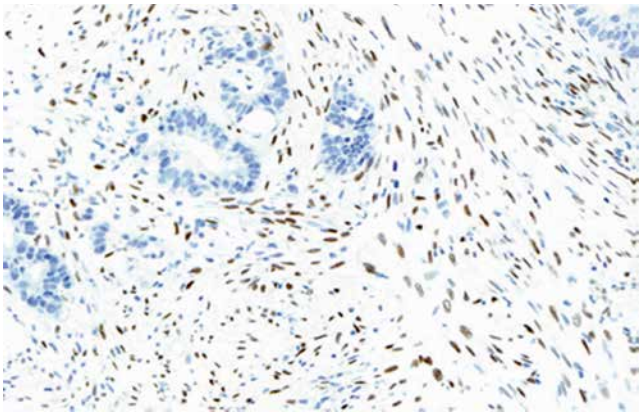
Tschan Mario
- SNSF_31003A_173219, 2017–2021, CHF 693'600

Tschan Mario
- KFS-3409-02-2014, 2014–2018, CHF 390'000

Zlobec I., Co-PI Tschan Mario
- SNSF31003A_166578, 2016–2019, CHF 305'000
- Swiss National Science Foundation, 2016–2019, CHF 305'000

6 Preise, Ernennungen, Auszeichnungen

Anlässlich des 183. Dies Academicus der Universität Bern wurde am 2.12.2017 **Dr. Daniel Zysset** der Dr. Lutz Zwillenberg-Preis verliehen. Dieser Preis soll Ansporn sein für junge Talente, die eine innovative Arbeit als Dissertation oder eine hochkarätige Publikation als Postdoktorierende vorgelegt haben.



Dr. med. Melina Helbling, unter der Betreuung von Prof. I. Zlobec, hat den 1. Fakultätspreise für die Dissertation «TWIST 1 and TWIST2 promoter methylation influences the EMT-like tumor budding phenotype in colorectal cancer» gewonnen.

Manuel Keller hat für seine Dissertationsarbeit «Adverse prognostic value of PD-L1 expression in primary resected pulmonary squamous cell carcinomas and paired mediastinal lymph node metastases» den Preis für das beste Projekt eines Medizinstudenten erhalten.
Tag der Klinischen Forschung 2017, Department for BioMedical Research (DBMR), 31.10.17, Bern.

>>> Studentische Lehre

Der Einsatz der Pathologie besteht in Vorlesungen und Kursen für die Studenten der Humanmedizin, der Zahnmedizin, des Studienganges Biomedical Sciences und der Zellbiologie (Cell Biology), wo verschiedenste Vorlesungen, Kurse und Praktika über Histologie, Allgemeinen und Speziellen Pathologie, Molekularpathologie und Tumorpathologie von Mitgliedern des Instituts für Pathologie organisiert und angeboten werden. Zudem sind Mitglieder des Instituts aktiv in der Ausbildung von PhD Studenten der Graduate School for Cellular and Biomedical Sciences (GCB) involviert.

Die Lehrveranstaltungen werden von Mitarbeitern sowohl der klinischen als auch der experimentellen Pathologie gehalten, wobei je nach Thema und Schwerpunkt des Studienganges bzw. der Veranstaltung Ärzte oder Naturwissenschaftler als Dozenten fungieren.

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

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

Im Masterstudiengang, hier zunächst im 4. Studienjahr (Einführungskurs 2) und im 5. Studienjahr (Schlusskurs 1) wird das erlangte Wissen auf die spezielle, organbezogenen Pathologie angewendet. Hierbei wird ein systematisches Curriculum durchlaufen, das alle Organsysteme und ihre wichtigsten Erkrankungen abdeckt. Es besteht aus theoretischen Vorlesungen und praktischen Kursen, in denen die Studierenden sich mittels Makroskopie und Mikroskopie vertiefende Kenntnisse aktiv erarbeiten. Ergänzend finden wöchentlichen Autopsiedemonstrationen statt, in denen anhand aktueller Fallbeispiele die aktive Erarbeitung pathophysiologischer Zusammenhänge und Sequenzen verschiedenster Krankheiten im Vordergrund steht. Zudem wird unser Institut bei den Studierenden als sehr guter Ort angesehen, um im Rahmen einer Masterarbeit ersten Kontakt mit wissenschaftlichen Arbeiten zu erhalten, und auch später wird die Möglichkeit angenommen, dieses in einer folgenden Dissertation fortzusetzen.

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

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

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

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

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

Studiengänge der Philosophisch-Naturwissenschaftliche Fakultät

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

1. Seminarreihen

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

2. Vorlesungsreihen im Fachgebiet Pathologie

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

2.1. General Pathology and Histology

Coordinator: Philippe Krebs

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

General overview of the course:

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

2.2. Selected Topics in Molecular Pathology

Coordinator: Erik Vassella

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

General overview of the course:

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

2.3. Cellular and Molecular Immunology

Coordinator: Christoph Müller

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

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

3. Weitere Lehrveranstaltungen

Dozierende der Experimentellen Pathologie unterrichten zudem in Lehrmodulen, die von anderen Instituten koordiniert werden, wie dem «Practical Course in Immunology» des Instituts für Zellbiologie (phil. nat. Fakultät), in Seminarveranstaltungen im Gebiet Tumorpathologie, in der Vorlesungsreihe «Blut und Abwehr» im 2. Studienjahr Medizin und dem dazu gehörenden Lerngruppenunterricht (PBL).

Weiterhin sind Dozierende des Instituts im Rahmen von 3–4–wöchigen experimentellen Praktika an der Ausbildung von Studierenden der Studienrichtungen «Cell Biology» (UniBE) und im Studiengang «Biomedical Sciences» beteiligt, der durch die Universitäten Fribourg und Bern angeboten wird.

>>> Weiterbildung

Ärztliche Weiterbildung im 21. Jahrhundert soll nicht nur den Nachwuchs für den Fachbereich garantieren, sondern Perspektiven schaffen, die zukunftsweisend sind. Sie soll auch dem Strukturwandel und dem jährlich steigenden Spezialisierungsdrang Rechnung tragen. Zusätzlich soll sie modern, attraktiv und motivierend, gleichzeitig aber auch bedarfsgerecht sein und die notwendigen Kompetenzen ökonomisch vermitteln. Strategisches Ziel unseres Pathologie-Weiterbildungsprogramms ist, herausragende Diagnostiker, Forscher, und für die Zukunft offene Pathologen auszubilden.

Unser Weiterbildungsprogramm stellt die klinisch orientierte Funktion der Pathologie in den Vordergrund. Es verfügt über **definierte Abschnitte (Module),** welche auch aufgrund individueller Bedürfnisse der Assistierenden unterschiedlich gestaltet werden können. So entsteht eine individuelle, zeitlich und inhaltlich flexible Struktur.

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

Weiterbildungsmodule.

Modul 1

- **1A: Autopsie 1**
- **1B: Zuschnitt 1**
- **1C: Histo 1**

- **Mini-CEX**
- **DOPS**

12 Monate

Modul 2

- **2A: Histo 2**
- **2B: Schnellschnitt**
- **2C: Zuschnitt 2**
- **2D: Autopsie 2**
- **2E: Tumorboards**
- **2F: Spezialgebiete (KM-, Nieren-, Leberbiopsien etc., fakultativ)**

- **Mini-CEX**
- **DOPS**

36 Monate

Modul 3

- **3: Zytologie**
- **nach Bedarf Zuschnitt**

- **Mini-CEX**
- **DOPS**

6 Monate

Schlussprüfung:
6 Monate vor der FMH-Prüfung

Modul 4

- **4A: Mol Path**

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

- **fakultativ**

Modul 2 mit flexiblen Untereinheiten.

Das Modul 2 stellt den Hauptkorpus der spezifischen Pathologie-Ausbildung dar und dauert 36 Monate, kann aber je nach Erfahrung und Lernkapazität verkürzt oder verlängert werden. Die Reihenfolge, der Inhalt und die Schwerpunkte können und sollen flexibel gestaltet werden. Teilnahme an klinisch-pathologischen Konferenzen und Tumorboards sind ebenfalls Inhalt dieses Moduls. Die Absolvierung der Themenblöcke setzt das Erfüllen der Mindestanforderungen der FMH voraus. Der Einblick in die Diagnostik von hoch spezialisierten Gebieten, wie die Knochenmark-, Nieren- und Leberbiopsien, ist prinzipiell möglich und wird je nach Interesse und Kapazitäten organisiert.

Es wird empfohlen, dass die Anmeldung für die Facharztprüfung erst nach Absolvierung aller obligatorischen Themenblöcke der Module 1 bis 3 erfolgt.

Das Modul 3 verkörpert die Ausbildung im Bereich Zytologie und kann mit dem Modul 4A (Molekularpathologie) kombiniert werden.

Das Modul 4A erschafft einen Einblick in die modernen diagnostischen Methoden der Molekularpathologie einschliesslich moderner NGS-Technologie, die für die Patienten Therapie-relevant sind.

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

In das Weiterbildungsprogramm sind regelmässige Zwischenevaluationen (arbeitsplatzbasierte Assessments) als Etappenkontrollen integriert. Evaluationsmethoden wie Mini-CEX und DOPS werden als essentieller Bestandteil der Weiterbildung und strukturiertes Rückmeldungsinstrument betrachtet. Aus der Zwischenbilanz erfolgt eine neue Zielvereinbarung.

Fallbesprechungsraum.

Arbeitsplatz-basiertes Assessment

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

Datum der Durchführung:

Weiterbildner/in: Ärztin/Arzt in Weiterbildung:

Unterschrift: Unterschrift:

Mini-CEX-Formular.

Arbeitsplatz-basiertes Assessment

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

Datum der Durchführung:

Weiterbildner/in: Ärztin/Arzt in Weiterbildung:

Unterschrift: Unterschrift:

DOPS-Formular.

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

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

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

Das tägliche und wöchentliche Weiter- und Fortbildungsprogramm des IFP gibt zudem reichlich Gelegenheit für strukturierte Weiterbildung gemäss den SIWF-Anforderungen.

Interne Weiterbildungsveranstaltungen

Weiterbildung	Zeit	Ort	Ziel
Montag			
Assistenten-Fälle	08.20–08.50	L247	Übung Fallpräsentation Interessante Fälle der Vorwoche werden demonstriert und kurz das Wesentliche erwähnt
Makro-Visite	13.00–13.15	Labor	Makroskopische Beurteilung von Operationspräparaten, praktisches Vorgehen
Dienstag			
Vortrag oder Journal Club	08.20–08.50	L247	Vermittlung von theoretischem Wissen Übung an der Präsentation einer wissenschaftlichen Arbeit
Makro-Visite	13.00–13.15	Labor	Makroskopische Beurteilung von Operationspräparaten, praktisches Vorgehen
Mittwoch			
Schnitte des Tages	08.20–08.50	L247	Inhaltliche Vorbereitung zu 3 didaktischen Fällen aus einem Gebiet der täglichen Diagnostik
Makro-Visite	13.00–13.15	Labor	Makroskopische Beurteilung von Operationspräparaten, praktisches Vorgehen
Bern Teaching Round in Pathology	1x Monat 17.00–18.30	L247	Vertiefung in grösseren diagnostischen Themenblöcken (siehe separates Programm)
Donnerstag			
PMD-Teaching	08.20–08.50	Autopsie	Makroskopische Beurteilung von wichtigen Autopsie-Befunden
Makro-Visite	13.00–13.15	Labor	Makroskopische Beurteilung von Operationspräparaten, praktisches Vorgehen
Seminar	17.15–18.00	L431	Gast-Vorträge über aktuelle wissenschaftliche Themen
Freitag			
Schnitte des Tages	08.20–08.50	L247	Inhaltliche Vorbereitung zu 3 didaktischen Fällen aus einem Gebiet der täglichen Diagnostik
Makro-Visite	13.00–13.15	Labor	Makroskopische Beurteilung von Operationspräparaten, praktisches Vorgehen
Täglich			
Tumor-Boards und klinisch-pathologische Konferenzen	siehe separates Wochen-Programm		

>>> Fortbildung

Donnerstagsseminare 2017

	Titel	**Referent/-in**
16.01.	Immunomodulatory cell death	Dr. Ben Croker, Boston Children's Hospital, Harvard, Boston
09.02.	QuPath: An open source platform for digital pathology	Dr. Pete Bankhead, Philips
16.02.	Induction of differential macrophage and microglial glioblastoma phagocytosis by anti-CD47 treatment – implication of tumor subtypes	Dr. Gregor Hutter, Universitätsspital Basel
23.03.	Intravital and whole-organ imaging of immune responses	Prof. Jens Stein, Theodor Kocher Institut, Universität Bern
27.03.	Reprogramming the immune response in Alzheimer's disease	Prof. Kati Andreasson, Department of Neurology and Neurological Sciences and Stanford Neuroscience Institute, Stanford University
30.03.	Resistance mechanisms to targeted therapies in breast and lung cancer	Prof. Henrik Ditzel, Physician-in-Chief, Head, Department of Cancer and Inflammation Research, University of Southern Denmark
06.04.	Harnessing metabolic relay to educate macrophage polarization in sepsis and the tumor microenvironment	Prof. Ping-Chih Ho, Department of Fundamental Oncology, University of Lausanne Ludwig Center for Cancer Research
20.04.	Patient-derived insights into the pathogenesis of myeloproliferative neoplasms	Dr. Theocharides Alexandre, Hematology, University Hospital Zurich
25.04.	Epithelial cell communication with the microbiota and the immune system mediated by a TNF super family receptor	Prof. Mitchell Kronenberg, Ph.D. President and Chief Scientific Officer, La Jolla Institute for Allergy and Immunology, CA, USA
27.04.	Mechanisms of regulation of chronic intestinal inflammation by autophagy	Prof. Kevin Maloy, Univ of Oxford, UK
04.05.	Immunometabolic regulation of lymphocyte function	Prof. Dr. med. Christoph Hess, Department of Biomedicine, University Hospital Basel
11.05.	Using zebrafish as a tool in biomedical research	Prof. Dr. med. Claudia Lengerke, Dept Biomedizin und Klinik für Hämatologie, Universitätsspital Basel
17.05.	Workshop exp. Pathologie	
18.05.	Protective and pathologic immune surveillance in the central nervous system	Doron Merkler, Associate Professor, Department of Pathology and Immunology, University of Geneva
08.06.	Molecular subtyping of pancreatic cancer and its precursor lesions	Prof. Dr. med. I. Esposito, Director, Institute of Pathology, Heinrich-Heine-University of Duesseldorf
17.08.	Translational regulation of autophagy by eukaryotic translation initiation factor 5A (EIF5A)	Lisa Frankel, Assistant professor, Lund Group, Biotech Research & Innovation Centre, University of Copenhagen, Denmark
24.08.	Mesothelioma – histologic subtyping and differential Diagnosis	Dr. med. univ. Dr. rer. nat Luka Brcic, Institut für Pathologie, Medizinische Universität Graz
25.08.	Gastrointestinal Lymphocytoses	Dr. in med. univ. et scient. med. Iva Brcic, Institut für Pathologie, Medizinische Universität Graz

	Titel	**Referent/-in**
11.09.	Building Health Systems: Cancer and Pathology as a Paradigm in Low- and Middle-Income Countries	Dr. Danny A. Milner, Jr, MD, MSc, Chief Medical Officer, American Society for Clinical Pathology
14.09.	Genomics of Barrett's esophagus progression	Prof. Matthew Stachler, Associate Pathologist at Brigham and Women's Hospital, Harvard Medical School
12.10.	Intestinal CD4 T cell homing during inflammation and cancer – What is the impact of GPR15?	Prof. Dr. Astrid Westendorf, Medizinische Fakultät, Universitätsklinikum Essen
19.10.	Reducing the Experts Headache: Making the most of annotations for automatic biomedical image segmentation	Prof. Dr. Raphael Sznitman, ARTORG Center for Biomedical Engineering Research, University of Bern
26.10.	EBV-associated B-cell lymphoproliferative disorders – an update	Dr. med. Alina Nicolae, Hôpitaux Universitaires Henri-Mondor, Institut national de la santé et de la recherche médicale (INSERM), Créteil, France
09.11.	Targeting Cancer Stem Cells: Differentiation- and Immuno-Therapies	Prof. Joerg Huelsken, PhD, Science de la Vie, ISREC institute; EPFL Lausanne; Switzerland
16.11.	Digitale Pathologie – alles neu? Oder altes neu?	PD Dr. Gian Kayser, Institut für Klinische Pathologie, Departement für Pathologie, Universitätsklinikum Freiburg
23.11.	Cellular plasticity in cancer: driving force and therapeutic target	Prof. Thomas Brabletz, Chair Experimental Medicine I, Nikolaus-Fiebiger-Center for Molecular Medicine, University Erlangen-Nuernberg

>>> Im Fokus: Postmortale Diagnostik

PMD Raum.

In den letzten Jahrzehnten hat sich die Pathologie insbesondere im Bereich der Tumordiagnostik durch die immer umfassenderen Möglichkeiten z.B. der immunohistochemischen Diagnostik, und auch der molekularen Pathologie deutlich verändert, und wird dies z.B. im Hinblick auf neue Möglichkeiten z.B. im Zusammenhang mit der zunehmenden Digitalisierung auch weiterhin tun. Im gleichen Zeitraum konnte hingegen sowohl national, als auch international eine ebenso deutliche Abnahme der Autopsiezahlen beobachtet warden. Die Gründe hierfür sind multifaktoriell, und reichen von veränderter Perzeption der Autopsie in der medizinischen Fachwelt und der Öffentlichkeit, über verbesserten diagnostischen Möglichkeiten zu Lebzeiten der Patienten bis hin zu nicht zu unterschätzenden finanziellen Rahmenbedingungen des modernen Gesundheitswesens. Dies alles zusammen hat letztlich zu einer Situation geführt, in der diese «klassische» Subdisziplin der Pathologie, ein immer noch wertvolles Mittel der medizinischen Qualitätssicherung und der medizinischen Aus- und Weiterbildung in seiner Existenz bedroht ist.

Vor diesem Hintergrund wurde nach mehrjähriger Vorbereitungszeit im Jahr 2016 das Projekt «Einführung der Postmortalen Diagnostik (PMD) im Institut für Pathologie der Universität Bern» gestartet. Ziel dieses Unternehmens war es, die Autopsie als «Postmortale Diagnostik» sowohl technisch als auch inhaltlich in einen zeitgemässen Zustand zu bringen. Das Projekt wurde als Studie von der Kantonalen Ethikkommission bewilligt, und ist im Sommer 2017 abgeschlossen worden. Im Rahmen des Unternehmens wurden eine Reihe von Massnahmen ergriffen, von denen einige wichtige im Folgenden näher dargestellt werden sollen:

Implementierung von Prinzipien des LEAN Management Systems

Am Institut für Pathologie der Universität Bern hat in den letzten Jahren durch die Implementierung des LEAN Management System eine kontinuierliche Arbeitsprozessoptimierung stattgefunden, die neben einer verbesserten Nutzung von personellen und räumlichen Ressourcen auch zu einer deutlichen Reduktion der Durchlaufzeiten für Biopsie- und Operationspräparate geführt hat. Auch in der Abteilung der Postmortalen Diagnostik konnte durch Komprimierung des administrativen Teils der im Rahmen eines Falles der postmortalen Diagnostik anfällt Zeit und Ressourcen eingespart werden. Ebenso wurden

die Räumlichkeiten den aktuellen Bedürfnissen angepasst und vom Raumkonzept nach LEAN Massstäben gestaltet: aus vier Autopsieräumen entstanden ein grosser Raum für postmortale Diagnostik, ein Präsentations- und Teaching Raum, ein Raum für die klassische Autopsie und ein separates Büro für die Präparatoren. Das ursprünglich gemeinsame Büro für Ärzte und Präparatoren wurde zu einem Diagnostikraum, analog zu den Räumlichkeiten in der Klinischen Pathologie.

Modernisierung der Einrichtung

Dieser Diagnostikraum verfügt neben zwei voll ausgestatteten ärztlichen Arbeitsplätzen nun auch über die Möglichkeit, digital zu fotografieren, sowie einen Projektionsbildschirm für Fallbesprechungen. Weiterhin wurde die Möglichkeiten der makroskopischen Fotodokumentation modernisiert, und zwar mit einem Prototyp des Spot Imaging™ Dokumentationssystems. Wir verfügen nun über eine fest installierte Fotostation mit der Möglichkeit, nicht nur hochauflösende makroskopische Bilder anzufertigen, sondern auch direkt über das Kamerasystem mit Kollegen aus der Pathologie und Klinik zu kommunizieren. Zudem haben wir mit einer mobilen Kamera aus diesem System die Möglichkeit, in situ Aufnahmen und Videos anzufertigen. Weiterhin wurde auch der Zuschnittsplatz erneuert, und prototypisch für einen Ein-Personen-Betrieb ausgestattet.

Personelle Neustrukturierung des PMD Teams

Mit der Einführung der Fachgruppe Postmortale Diagnostik analog den anderen organbezogenen Fachgruppen wird die Konstanz in der Durchführung der postmortalen Eingriffe und Untersuchungen, der Befundung und Ausbildung gewährleistet. Aktuell bilden fünf Fachärzte und Fachärztinnen das Kernteam der PMD, welches ergänzt wird durch die Rotationsassistierenden und den zuständigen Facharzt für die Neuropathologie. In diesem Zusammenhang wurde auch das Befundsystem umgestellt: statt eines makroskopischen Erstberichtes wird nun analog eines Befundes der Histopathologie der PMD Befund gleich unter Berücksichtigung der relevanten histopathologischen Untersuchungen erstellt. In einem Zweitbericht sind jetzt lediglich noch Zusatzbefunde enthalten. Somit erhalten die klinischen Kollegen in der Regel innerhalb von 10 Werktagen einen in den meisten Fällen bereits definitiven Befund, anstatt zuvor innerhalb der ersten 2 Tage einen reinen makroskopischen Befund ohne Histologie, und einen definitiven Befund nach durchschnittlich 30 Tagen.

Präpariermethoden

Die Entwicklung und Implementierung moderner und zeitgemässer Präpariermethoden stellt einen wesentlichen Bestandteil des Kulturwandels im Bereich der postmortalen Diagnostik dar. Unterstützt durch die räumlichen Umbauten und Anschaffung chirurgischer Gerätschaften und Bestecke wurden wichtige Schritte in Richtung einer postmortalen «operativen» Diagnostik gemacht, die sich an chirurgischen Präparationstechniken und Zugängen orientiert. In diesem Zusammenhang war die Einführung der minimal-invasiven postmortalen Diagnostik, die unter Mithilfe von Kollegen der Klinik für Viszerale Chirurgie und Medizin des Inselspitals implementiert werden konnte, ein sehr wichtiger Punkt. Erste derartig durchgeführte Untersuchungen konnten minimal invasiv (d.h. mittels Thorakoskopie oder Laparoskopie) die gezielten Fragstellungen der klinischen Kollegen beantworten.

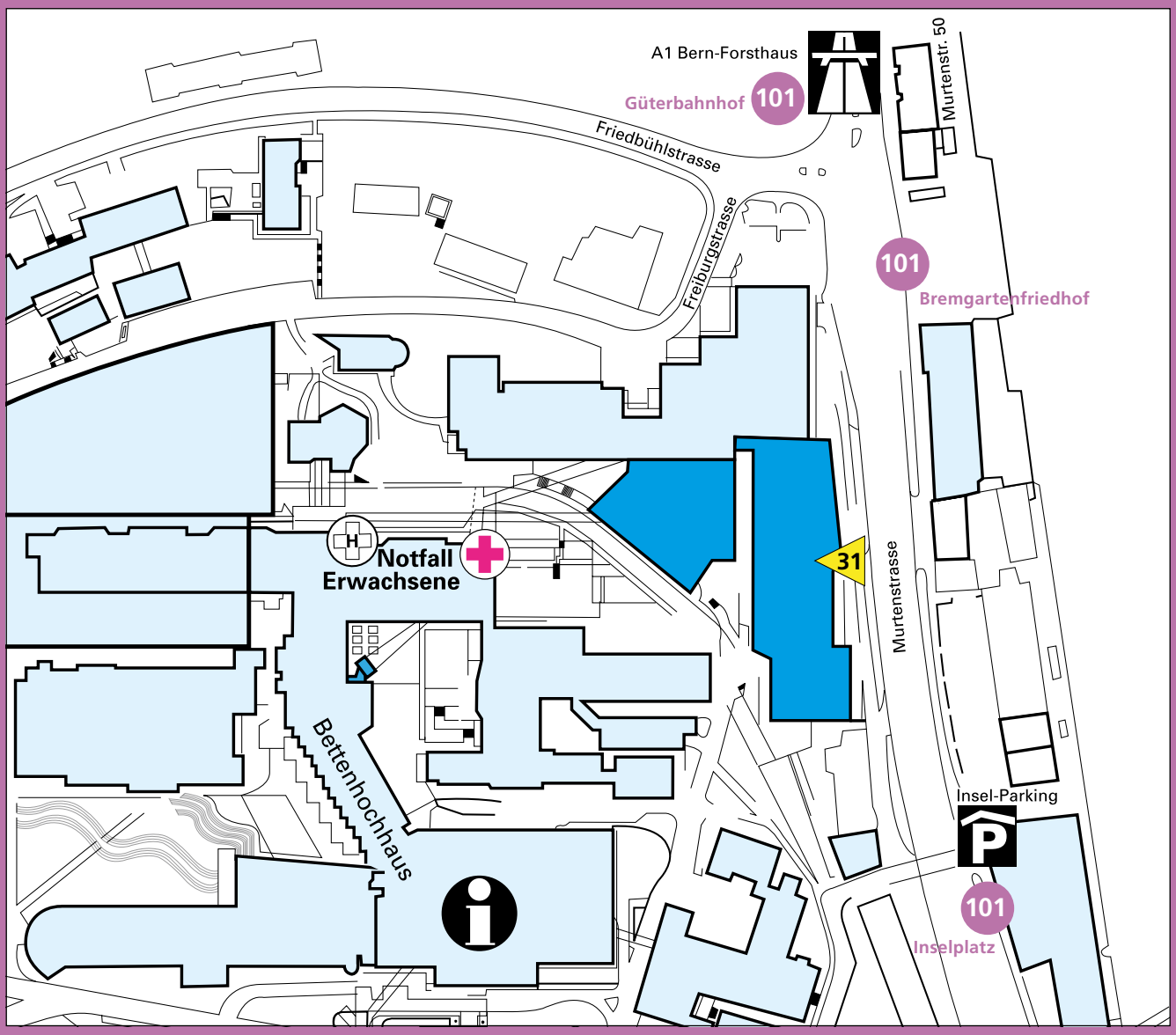
Lehre, Forschung, Aus- und Weiterbildung

Traditionell ist die Pathologie ein wichtiger Bestandteil der medizinischen Ausbildung. Im sogenannten «Makrokurs» des 4. Studienjahrs können sich die Studierenden Organpathologien an Beispielpräparaten selbst erarbeiten. Die Überarbeitung und Kartierung der Organpräparate wurde ebenfalls im Rahmen unseres PMD Projektes durchgeführt. Die Mitglieder des PMD Teams bestreiten zudem auch die bei Studierenden sehr beliebte «Autopsiedemo», ein Kurs des 4. und 5. Studienjahrs, bei dem aktuelle oder archivierte Fälle aus der PMD demonstriert und diskutiert werden. Einmal wöchentlich findet zudem im Rahmen der strukturierten Weiterbildung der Assistierenden eine spezielles PMD Teaching statt. In Masterarbeiten und Dissertationen haben Studierende zudem auch die Möglichkeit, sich wissenschaftlich mit Themen aus der postmortalen Diagnostik auseinanderzusetzen.

Wir denken, dass wir durch diese Neuerungen und Umstrukturierungen nun in der Lage sind, eine moderne postmortale pathologische Diagnostik anbieten zu können, die in zeitgemässer Weiterführung der «klassischen Autopsie» als Werkzeug der medizinischen Qualitätssicherung, als wichtiger Bestandteil der Lehre, Aus- und Weiterbildung, aber auch als Perspektive für Forschung und Weiterentwicklung dienen kann.

Postmortaler minimal invasiver Eingriff.

>>> Situationsplan



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