

Division of Surgical Research Annual Report 2016

Department of Surgery
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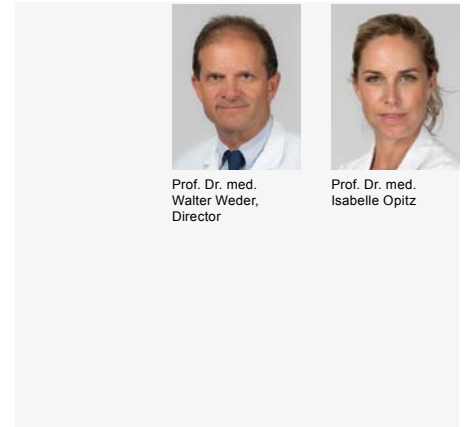
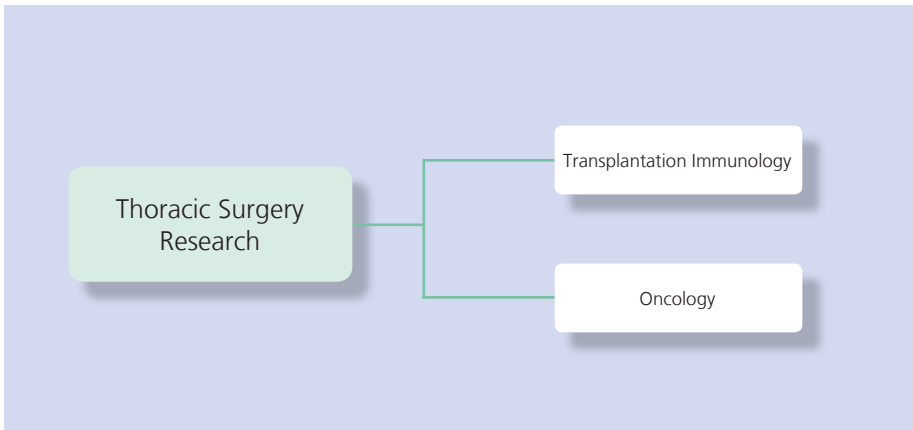


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Thoracic Surgery Research



Research in thoracic surgery focuses on different areas, such as oncology and transplantation.

Mesothelioma

One of the topics in cancer research is the development of therapeutic strategies for malignant pleural mesothelioma (MPM), an incurable thoracic malignancy related to asbestos exposure. After several years of preclinical and early clinical trials, we currently apply intracavitarily cisplatin/fibrin after macroscopic complete resection in a phase II trial to prevent local tumor recurrence (NCT01644994) (Figure 1). Various tumor biomarkers that can be useful for the prediction of disease aggressiveness and response to treatment are assessed in translational studies. In addition to protein expression and mutation profiles, we are evaluating microRNAs for their potential utility as prognostic and predictive biomarkers for the selection of patients for multimodality treatment. Besides, we are exploring novel targets for the treatment of MPM using *in vitro* cell models and pre-clinical animal models. Furthermore, we also assess the frequency germline mutation of BAP1 that predispose individuals to MPM.

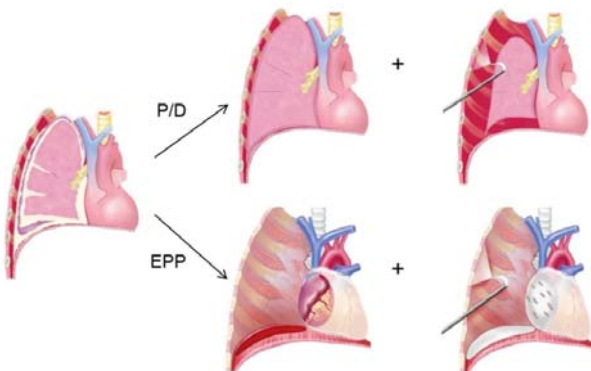


Figure 1: Macroscopic complete resection (MCR) of malignant pleural mesothelioma through P/D or EPP, followed by intracavitary chemotherapy with cisplatin/fibrin (INFLuenCe-Meso).

Chronic thromboembolic pulmonary hypertension

On the topic of chronic thromboembolic pulmonary hypertension we are interested in implementing modern imaging techniques to better diagnose patients and to estimate the operability.

Lung cancer

With regard to lung cancer research, we are developing a new mass spectrometry protocol for the quantitation of serine hydrolases enzymatic activities in lung adenocarcinoma surgical resection specimens. The application of this new methodology will allow us to validate the biomarkers previously discovered in our last study. (Figure 2)

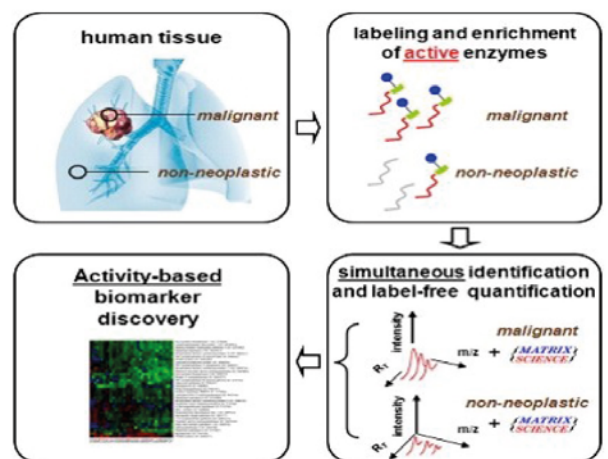


Figure 2: We screen lung resection specimens with activity based biomarker discovery and mass spectrometry and search for a) the modulation of enzyme activities caused by posttranslational events occurring during lung cancer progression, and b) new enzymatic targets to develop novel anti-lung cancer therapies

Lung transplantation

Another focus of our research is lung transplantation. Currently lung transplantation is the accepted treatment option for patients in end-stage lung disease. Waiting list mortality is continuing to be an issue among lung transplant candidates even after three decades of success stories in the field. Novel strategies have been implemented to overcome this shortage, such as application of extended criteria (marginal) donor lungs, donation after cardiac death donors, living donor lobar lung transplantation, and *ex vivo* lung perfusion for re-evaluation of injured donor lungs. **Ex vivo lung perfusion (EVLP)** provides future potential for the re-evaluation, treatment, and repair of injured donor lungs for transplantation by using alternative approaches.

Recently, we are interested in using cytokine filters during EVLP. The results are encouraging and this strategy will be tested in future in a large animal transplant model.

Immunological interfaces: Another research interest focusses on **immunological interfaces** in experimental lung cancer and lung transplantation. Our previous research showed

that the inhibition of CD26/DPP4 by Vildagliptin resulted in a reduction of incidence and growth of lung metastasis from colorectal cancer *in vivo*. In our ongoing work, we show that upon CD26/DPP4-inhibition, antitumoral macrophages and NK cells enrich within lung tumors and enhance their activity and cytotoxicity against the tumor thus leading to a significant reduction of lung tumor burden. Ongoing work in our experimental lung transplantation research explores the role of IL-2 stimulated and enhanced regulatory T cells, which leads to viable long term engraftment in a fully MHC-mismatched mouse lung transplantation model.

Further clinical research focuses on refinement of existing programs such as our PEA and LVRS programs.

Lung volume reduction surgery (LVRS) for emphysema: In the field of lung volume reduction surgery focus is on outcome research. Additionally, patient selection criteria and pre-operative imaging is the focus in several studies.

Awards:

Opitz Isabelle, Friess Martina, Meerang Mayura, Kirschner Michaela, Bérard Karima, Olivia Lauk, Weder Walter
Poster Prize at the Joint Meeting of the German, Austrian and Swiss Societies for Surgery, Freiburg, Germany
"Factors associated with long term freedom from recurrence after induction chemotherapy and extrapleural pneumonectomy in mesothelioma patient"

Kathrin Oehl

Best poster prize of the Swiss Biotech Network at the Retreat of the MTB graduate school «Tracking the Clonal Origin and Chemotherapy Resistance of Malignant Pleural Mesothelioma» (Co-Author)

Kathrin Oehl

Prize for the best oral free paper presentation at the 3rd Joint Annual Meeting of the Swiss and Austrian Societies of Pathology in Vienna, Austria, «Tracking the Clonal Origin and Chemotherapy Resistance of Malignant Pleural Mesothelioma» (Co-author)

Claudio Caviezel

"ESTS-AME-Prize Observership Attachment in China 2016" at the annual ESTS meeting in Naples

Ilker Iskender, Tugba Cosgun, Stephan Arni, Michael Trinkwitz, Stefan Fehlings, Nikola Cesarovic, Thomas Frauenfelder, Walter Weder, Ilhan Inci

SGC Best Poster Prize 2016 "Cytokine Filtration Modulates Pulmonary Metabolism and Edema Formation During *Ex Vivo* Lung Perfusion"

Wolfgang Jungraithmayr

Chair Position at Medical University Brandenburg

1st placed-listed W3-Professorship and offer for the Chair position at the Medical University Brandenburg (Lehrstuhl), Department of Thoracic Surgery, Germany.

Collaborations:

- Institut klinische Biochemie der Universität Antwerpen, Belgien
- Eidgenössische Technische Hochschule (ETH) Zürich, CH
- Klinik für Pneumologie, Universität Leuven, Belgien
- Institute of Physiology, Perelman University Pennsylvania, Philadelphia, USA
- Institut für Molekularbiologie, Universitätsspital Zürich, Universität Zürich, CH
- Klinik für Immunologie, Universitätsspital Zürich, CH
- Centre Hospitalier, Department of Thoracic Surgery, Strasbourg, France (Gilbert Massard)
- Dr. Shampa Chatterjee, Associate Professor, Institute for Environmental Medicine University of Pennsylvania
- Gilles Willemin, Mouse Metabolic Evaluation Facility (MEF), Center for Integrative Genomics, University of Lausanne
- Dr. Serena Di Palma, Functional Genomics Center Zurich, ETH Zurich/University of Zurich
- Dr. Keke Yu, Department of Pathology, Shanghai Chest Hospital, Shanghai, China
- Dr. Tatjana Sajic and Prof. Ruedi Aebersold, Department of Biology, Institute of Molecular Systems Biology (IMSB), ETH Zurich, Switzerland
- Dr. S. Gray, Translational Cancer Research Group, Trinity Center for Health Sciences, Institute of Molecular Medicine, St. James's Hospital, Dublin, Ireland
- Prof. Dr. H. Moch, PD Dr. A. Soltermann, Dr. B. Vrugt, Institut für klinische Pathologie, UniversitätsSpital Zürich
- Prof. Dr. M. de Perrot, Dr. G. Allo, Dr. M. Tsao, Dr. Licun Wu, Division of Thoracic Surgery, Toronto General Hospital and Princess Margaret Hospital, University of Toronto, Toronto, Canada
- Dr. V. Serre Beinier, Département de chirurgie, Université de Genève
- Prof. Dr. W. Klepetko, Dr. M. Hoda, Division of Thoracic Surgery, Medical University Vienna
- Prof. Dr. R. Bueno, Department of Surgery, Brigham and Women's Hospital, Boston
- Dr. A. Jetter, Institut für Pharmakologie und Toxikologie, UniversitätsSpital Zürich
- Prof. Dr. D. Günther, Labor für organische Chemie, ETH Zürich
- Prof. Dr. B. Seifert, Department of Biostatistics, Epidemiology, Biostatistics and Prevention Institute, University of Zürich
- PD Dr. T. Frauenfelder, Dr. D. Nguyen-Kim, PD Dr. A. Boss, Institut für diagnostische und interventionelle Radiologie, UniversitätsSpital Zürich
- Prof. Dr. M. Pruschy, Dr. A. Brogkini-Tenzer, Institut für molekulare Radiologie, UniversitätsSpital Zürich
- Prof. Dr. M. Carbone, Prof. Dr. H. Yang, Prof. Dr. G. Gaudino, University of Hawai'i, Cancer Center, Honolulu
- Prof. Dr. G Reid, Prof. Dr. N. van Zandwijk, Asbestos Diseases Research Institute, Sydney, Australia
- Dr. Alessandra Curioni, Prof. Rolf Stahel, Clinic of Oncology, Zurich University Hospital
- Dr. Bart Vrugt, Institute for Surgical Pathology, Zurich University Hospital
- Dr. Hubert Rehrauer, Functional Genomic Center, University of Zurich
- Prof. Lorenza Penengo, IMCR, University of Zurich
- Prof. Beat Schwaller, Department of Medicine, University of Fribourg
- Prof. Egbert Smit, NKI, Amsterdam
- Dr. Victor Van Beusechem, Department of Medical Oncology VUmc, Amsterdam



Prof. Dr. med.
Walter Weder,
Director



Prof. Dr. med.
Isabelle Opitz



PD Dr. med.
Sven Hillinger



Prof. Dr. med.
Ilhan Inci



Prof. Dr. med.
Dr. sc.nat.
Wolfgang
Jungraithmayr



Dr. med.
Claudio Caviezel



Dr. med.
Olivia Lauk



PD Emanuela
Felley-Bosco,
PhD



Stephan Arni,
PhD



Mayura Meerang,
PhD,
Postdoctoral
Fellow



Michaela Kirschner,
PhD,
Postdoctoral
Fellow



Jae Hwi Jang,
PhD,
Research Fellow



Dr. med.
Yoshito Yamada,
PhD,
Research Fellow



Dr. med.
Tatsuo Maeyashiki,
PhD,
Research Fellow



Christine Opelz,
Lab. Technician



Vanessa Orlowski,
Lab Technician



Manuel Ronner,
Lab Technician



Dr. med. vet.
Martina Friess,
Data Manager



Cordelia Bommeli,
Study Coordinator



Chloé Spichiger,
PhD,
Scientific
Administration



5. Grants

Thoracic Surgery Research:		
Zürcher Krebsliga	Prognostic Marker for MPM	I. Opitz
SNF Overhead		I. Opitz
Stiftung Becon	Gewebe- und Datenbank für das MPM – ein paneuropäisches Projekt	I. Opitz
Vontobel Stiftung	MikroRNAs als prognostische und prädiktive Tumormarker für die multimodale Behandlung des malignen Pleuramesothelioms	I. Opitz
Lunge Zürich	MicroRNAs as prognostic and predictive tumour markers assisting the selection of patients with malignant pleural mesothelioma for multimodality treatment	I. Opitz
SNF Professorship	MPM – an integral approach for better outcome	I. Opitz
Krebsforschung Schweiz	Mesoscape 001-pS6: Construction of a multi-institutional European Tissuebank	I. Opitz
Polianthes Foundation	Comprehensive Investigation of Predictive Biomarkers for Chemotherapy Response and Novel Drug Targets in Patients with MPM by Next Generation Sequencing	I. Opitz
SAKF Foundation	Multi-omics profiling for identification of novel circulating biomarkers for malignant pleural mesothelioma	I. Opitz
Swiss National Science Foundation Sinergia grant	From asbestos exposure to cancer: a systemic approach to detect loss of homeostatic control in the mesothelial environment	E. Felley-Bosco
Walter Bruckerhoff Stiftung	Targeting epigenetic deregulation	E. Felley-Bosco
Polianthes Foundation	Mechanisms underlying development of resistance and progression to mesenchymal phenotype in mesothelioma	E. Felley-Bosco
Innovationspool	Implementierung der „Synapse 3D“ Software von Fujifilm zur Planung und Simulation von (minimal-invasiven) anatomischen Lungenresektionen, Lungenvolumenreduktionschirurgie und minimal-invasiven Zugängen	C. Caviezel
Hartmann Müller Stiftung	The role of cytokine filtration during <i>ex vivo</i> lung perfusion	I. Inci
Hermann Klaus Stiftung	<i>Ex vivo</i> reconditioning of donor lungs with Trimetazidine after prolonged cold ischemia	I. Inci
Lungen Liga Zurich	The effect of lung volume reduction surgery on outcome after lung transplantation in patients with emphysema	I. Inci
Innovationspool	Assessment and reconditioning of donor lungs with <i>ex vivo</i> lung perfusion system	I. Inci
Schweizerischer Nationalfonds	Suppression of lung tumor growth by CD26 /DPP4-inhibition	W. Jungraithmayr
Helene Bieber Fonds	The CD26-costimulatory pathway is critical for Th17-mediated lung transplant improvement	W. Jungraithmayr
Hartmann-Müller Stiftung	The protective effect of local anesthetics on primary graft dysfunction after experimental lung transplantation	W. Jungraithmayr
Kurt und Senta Herrmann-Stiftung	Blockade of CD26/DPP4 - co-stimulation to improve lung transplant survival	W. Jungraithmayr
Stiftung für wissenschaftliche Forschung	Ein neues Therapiekonzept zur Bekämpfung des Lungenkarzinoms durch Hemmung der CD26/DPP4	W. Jungraithmayr
Forschungskredit, University Zurich	The protective role of CD26/DPP4-inhibition in lung transplantation – a preclinical study	W. Jungraithmayr
Assistant Professorship, University Zurich	Lungentransplantation	W. Jungraithmayr
Development program “Filling the Gap”	The protective role of CD26/DPP4-inhibition in lung transplantation – a preclinical study	W. Jungraithmayr

Hermann Klaus-Stiftung, University Zurich	A new therapeutic concept against lung cancer through inhibition of CD26/ DPP4	W. Jungraithmayr
Stiftung für Krebsbekämpfung, University Zurich	Ein neues Therapiekonzept zur Bekämpfung des Lungenkarzinoms durch Hemmung der CD26/DPP4	W. Jungraithmayr
SAKF Foundation	Biomarkers with enzymatic activities for improved risk stratification of lung cancer patients	S. Hillinger

6. Publications 2016

1. Abegg K, Corteville C, Bueter M, and Lutz TA. Alterations in energy expenditure in Roux-en-Y gastric bypass rats persist at thermoneutrality. *International Journal of Obesity* 40: 1215-1221, 2016.
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13. Bhattacharya I, Ghayor C, and Weber FE. The Use of Adipose Tissue-Derived Progenitors in Bone Tissue Engineering - a Review. *Transfusion Medicine and Hemotherapy* 43: 336-343, 2016.
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