Division of Surgical Research
Annual Report 2015
Department of Surgery
University Hospital Zurich
Switzerland
Dear Colleagues

It is my pleasure to present the Annual Report 2015 of the Division of Surgical Research at the University Hospital Zurich.

In 2015, the purchase of major laboratory equipment included an Imager for Western Blot, an autosampler for a MicroCT, an ultra-low temperature freezer, a cell counter and three pressure sensors for the Bose bioreactor. Furthermore, we had to replace some defective equipment and acquired an X-Ray tube for the MicroCT and a mobile autoclave.

For teaching activities several courses were offered. A basic course in microsurgery was offered as well as the annual Advanced Course in Experimental Microsurgery (ACEM). Our weekly research seminar is a platform to present ongoing research projects for members of the nine surgical research divisions. In the bi-weekly Journal Club a research member presents an article of general interest published by an external research group. These activities were regularly attended by the members of our Division and other researchers. Furthermore, our monthly Newsletter is presenting an article published by one of the nine surgical research divisions.

It is my great pleasure to thank all members of our Division as well as our research partners from the University, University Hospital and the Swiss Federal Institute of Technology for last year’s excellent contributions and fruitful collaborations.

Yours sincerely

Gregor Zünd, Prof. Dr. med.
Head Division of Surgical Research
1. Organisation

1.1 Position of the Division of Surgical Research within the Department of Surgery
1.2 Structural Organisation of the Division of Surgical Research

Division of Surgical Research

- Cardiovascular Surgery Research
- Visceral & Transpl. Surgery Research
- Trauma Surgery Research
- Plastic-Hand & Reconstr. Surgery Research
- Thoracic Surgery Research
- Urology Research
- Cranio-Maxillofacial Surgery Research
- Surgical Intensive Care Research
- Services
2.5 Thoracic Surgery Research

2.5.1 Transplantation Immunology

CD26 co-stimulatory blockade improves lung allograft rejection and is associated with enhanced interleukin-10 expression


The aim of the study is to target CD26 co-stimulatory activity for the attenuation of the allo-reactive Th-17 cell response during acute rejection after mouse lung transplantation. Lung transplantation between BALB/c (donor) and C57BL/6 (recipient) mice was performed including controls, CD26-inhibited (CD26-I, daily administration of Vildagliptin, 10 mg/kg sc.), and CD26 KO mice (CD26KO). Then, CD26-I treated and CD26KO mice showed significantly preserved macroscopic and histological characteristics (p<0.01), a higher PaO2/FiO2 ratio (p≤0.05), less IL-17+ cells, more levels of IL-10, less infiltrating CD3+-T cells (p<0.01), but more CD206+ alternately activated M2 macrophages (p<0.01), compared to control. We concluded that CD26 co-stimulatory blockade promotes lung allograft acceptance via reduced T cell infiltration, less expression of IL-17 and increased expression of IL-10, likely to be derived from alternatively activated macrophages.

Legend: the control group (CTRL) shows robust acute rejection of allograft (arrow) in macroscopic appearance, stronger cell infiltrations in peribronchial areas in H&E staining, and more CD3+ T cells and less CD206+ M2 macrophages in immunohistochemistry, compared to CD26/DPP4-inhibited mice (CD26-I) and CD26 knock-out mice (CD26KO).
Inhibition of tumor growth by CD26/DPP4 inhibitor

The transmembrane molecule CD26/DPP4 has been associated with various malignancies including breast cancer, lymphoma, and colorectal cancer. Recently, we found an anti-tumor effect by treatment with the CD26/DPP4 inhibitor Vildagliptin in colorectal cancer lung metastasis models in mice.

Fig.: Anti-tumor effect of CD26/DPP4 inhibitor, Vildagliptin, in colorectal cancer lung metastasis model in mouse. EMT markers were significantly modulated by Vildagliptin in vitro (A). Imbalance between autophagy and apoptosis by Vildagliptin treatment in tumor in vivo. The autophagy markers LC3, p62, and ATF4 were significantly decreased in the tumors of lungs and subcutaneous tumors also (B). Apoptotic cell death (TUNEL) was induced by Vildagliptin treatment in tumor (C).

In our ongoing research, we found that the treatment with the CD26/DPP4 inhibitor treatment had also an effect on primary lung cancer growth through means of enhanced macrophages but also by recruiting and activating NK cells into the tumor. Here, tumors decreased in size in vivo in both models, in lung tumors as well as in subcutaneously injected tumors.

Based on these data, we can conclude that the inhibition of CD26/DPP4 effectively reduces tumor in mouse models of secondary and primary lung tumors.

Figure 3: Anti-tumor effect of Vildagliptin in various tumor models. Vildagliptin reduced tumor size in the subcutaneous cell line injection model (A). A human lung cancer cell line (H460) was injected onto nude mice. NK cell markers (Nkp46, NkI.1) and cytokines produced by NK cells (IFN-γ, TNF-α, IL-10) were analyzed by RT-PCR in the tumor developed by subcutaneous LLC injection (B). Vildagliptin treatment increased the tumor NK cell population.
The impact of preconditioning by Sevoflurane in experimental mouse lung transplantation

The aim of this study is to evaluate if preconditioning by sevoflurane could potentially protect from primary graft dysfunction (PGD) or acute rejection (AR) after lung transplantation (Tx). We performed mouse lung transplantations in various combinations 18 hours after preconditioning of donor by Sevoflurane for 2 hours. Allogeneic grafts with Sevoflurane preconditioning showed attenuation of acute rejection pathology on day 3, with upregulation of anti-inflammatory macrophage (M2), and syngeneic grafts with the treatment also yielded higher levels of TNF-α and IL-6 and lower level of IL-10, compared to the non-treated control. We concluded that sevoflurane preconditioning showed protective effects on lung transplants in PGD and AR.

Experimental chronic lung allograft rejection – which mouse model is reliable?

The aim of this study was to investigate an appropriate experimental protocol for chronic rejection after mouse lung transplantation. We performed single mouse lung transplantation in various protocols. Chronic rejection lesions were most prominently induced in the MHC major mismatch combination with suboptimal dose of immunosuppressant on the 8th week, compared to the minor mismatch combination. We concluded that this protocol is the most reliable CR model.

Collaborations:
- Institut klinische Biochemie der Universität Antwerpen, Belgien
- Diagnostische Radiologie des USZ Zürich, CH
- 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)
Ex vivo administration of trimetazidine improves post-transplant lung function in a pig model

Ex vivo lung perfusion (EVLP) is an establish method to reassess marginal donor lungs. It is also a platform to deliver therapeutics outside the body. Previously we have shown the beneficial effects of trimetazidine (TMZ) on ischemia reperfusion injury in a rat model. This study evaluated the effect of ex vivo delivered TMZ in a pig lung transplant model.

Pig lungs were retrieved and stored 24h at 4°C followed by 4h of EVLP according to the Toronto protocol on randomly allocated two groups (n=5,each): control (CON) and treatment (TMZ). TMZ (5mg/kg) was added in the prime solution prior to EVLP. Left lungs were then transplanted and recipients were observed for 4h. Lung function and mechanics were recorded hourly throughout reperfusion. At the end of 4h of reperfusion, the right pulmonary artery was occluded for 5 minutes to assess isolated allograft function. Bronchoalveolar lavage (BAL) and tissue samples were harvest- ed for biochemical assessments.

TMZ group showed a significantly better oxygenation throughout the 4-h reperfusion period (p=0.04) and after isolation of the allograft (p=0.04). During EVLP, TMZ group showed a trend toward higher oxygenation (p=0.06). Dynamic compliance and pulmonary vascular resistance were comparable between the two groups during EVLP. Tissue thiobarbituric acid level, myeloperoxidase activity and total protein concentration in BAL were significantly lower in the TMZ group at the end of EVLP. Detailed EVLP and transplantation findings are shown in Table 1.

Ex vivo administration of TMZ improved pulmonary gas exchange after reperfusion. Protective effect of TMZ was attributed to inhibition of lipid peroxidation and neutrophil infiltration during EVLP. Further studies are warranted to elucidate mechanisms of the beneficial effect of TMZ in this setting.

Cytokine filtration modulates pulmonary metabolism and edema formation during ex vivo lung perfusion

Ex vivo lung perfusion (EVLP) improved the algorithm in donor lung management. Cytokine accumulation has been shown in both the clinical and experimental EVLP settings, which may be harmful for pneumocytes especially during extended EVLP. Our objective was to test the safety and efficacy of continuous cytokine filtration during prolonged EVLP in a pig model.

Donor lungs were retrieved from randomly allocated female pigs and stored for 24h at 4°C. EVLP was performed during 12h according to the Toronto protocol. In the treatment group, the perfusate was continuously filtered with an absorbent device (CytoSorb®) via a venovenous shunt after the reservoir, whereas we did not implement the additional filter in the control group (n=5/each) (Figure 1).

Table 1: EVLP: Ex Vivo Lung Perfusion, TBARS: Thiobarbituric Acid Reactive Substances, MPO: Myeloperoxidase activity, BAL: Bronchoalveolar lavage, *: 5 minutes after occlusion of the right pulmonary artery, kPa: kilo Pascal. All values presented as mean±SD

![Figure 1. EVLP system combined with cytokine filtration](image-url)
EVLP physiology, perfusate gases and biochemistry were monitored hourly, along with lung X-ray studies at the end of perfusion. Perfusate samples were analyzed with a multiplexed cytokine assay at 1h, 3h, 6h, and 12h time points. Cytokine filtration significantly improved dynamic compliance during the 12h perfusion period (Fig 2A). In the filter group, we characterized a decrease in both glucose consumption (Fig 2B) and lactate production, along with reduced amount of hydrogen, potassium, and calcium ions. Lung X-rays taken at the end of perfusion showed increased consolidation in the control group (Fig 2C). Interleukin (IL)-1α, IL-1β, IL-6, IL-8 (Fig 2D, shown as example), IL-10, IL-12, IL-18, and TNF-α levels were significantly reduced in the filter group.

Continuous perfusate filtration through sorbent beads is effective and safe during prolonged EVLP. Cytokine removal decreased the development of pulmonary edema and suppressed anaerobic glycolysis in this setting. Further studies are needed to test the beneficial effect of cytokine filtration on post-transplant lung function.

Collaborations:
- 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

2.5.2 Oncology

2.5.2.1 Lung cancer

Activity-based proteomics: biomarker identification in human lung adenocarcinoma

S. Arni, S. Hillinger

In Switzerland, lung adenocarcinoma is a major cause of cancer related deaths. We previously characterized with the activity based proteomics (ABP) methodology several biomarkers in order to improve the risk stratification provided by conventional staging algorithm. We plan to now validate our biomarkers and are developing a new SWATH MS protocol for ABP of the serine hydrolase superfamily, combining both high throughput and high reproducibility.

Collaborations:
- Dr. Tatjana Sajic and Prof. Ruedi Aebersold, Department of Biology, Institute of Molecular Systems Biology (IMSB), ETH Zurich, Switzerland
2.5.2.2 Malignant pleural mesothelioma

Localized intracavitary therapy for MPM – from bench to bedside:
Phase I dose-escalation monocentric open trial for the evaluation of the safety of Intracavitary cisplatin-Fibrin Localized Chemotherapy after pleurectomy/decortication or extrapleural pneumonectomy for the treatment of patients with malignant pleural Meso(thelioma (INFLuenCe – Meso I)


Safety and tolerability of intracavitary chemotherapy with cisplatin-fibrin were assessed in a Phase I-dose-escalation trial that enrolled 12 mesothelioma patients. Four dose levels of Cisplatin (11, 22, 33 and 44 mg/m² BSA; n=3 per group) mixed with fibrin gel was sprayed to the chest wall and the surface of the lungs after macroscopic complete resection of tumors.

We demonstrated that the administration of intracavitary cisplatin-fibrin as high as 44 mg/m² BSA is safe. We detected no dose limiting toxicity. The median serum cisplatin AUC₀₋₂₄ of all dosages are still below the suggested renal toxicity risk level, 25 h*μg/g (figure 1a), while local tissue cisplatin concentration was high above cytotoxic limit (figure 1b).

We are currently conducting a Phase II trial for the confirmation of safety and tolerability of this treatment approach (Phase II Monocentric Open Trial for the Evaluation of the Safety of Intracavitary Cisplatin-Fibrin Localized Chemotherapy after Pleurectomy/Decortication or Extrapleural Pneumonectomy for the Treatment of Patients with Malignant Pleural Meso(thelioma (INFLuenCe – Meso II)). In this trial, additional 20 patients will be enrolled.

Until end of 2015, 2 patients were treated.

MicroRNAs as prognostic and predictive tumour markers assisting the selection of patients with malignant pleural mesothelioma for multimodality treatment

In this project, we are investigating the prognostic value of microRNAs, i.e. the six microRNA signature miR-Score, which has been shown to be associated with survival outcomes with high prognostic accuracy (Kirschner et al, Mol Oncol 2015). In addition, associations between microRNA expression and response to standard chemotherapy regimens are also being investigated.

(A) Kaplan-Meier analysis after stratification by miR-Score (HR for score-negative patients = 4.12, P=0.00009). (B) ROC curve analysis of the miR-Score resulted in an AUC of 0.867 (95% CI:0.76-0.96). Figure adapted from Kirschner et al, Mol Oncol 2015
**Prognostic and predictive biomarkers for malignant pleural mesothelioma**


Malignant Pleural Mesothelioma (MPM) is an aggressive and heterogeneous tumor, thus biomarkers predicting outcomes and treatment effectiveness are needed. We employed tissue microarrays as a tool to investigate prognostic significance of proteins and pathways known to be frequently altered in MPM.

Figure. Low Merlin expression and high Survivin labeling index is associated with poor outcomes of MPM. Kaplan-Meier survival curves according to dichotomized expression of cytoplasmic Merlin in pre-CTX samples (A: OS, B: PFS) and Survivin labeling indices in pre- and post-CTX tissues (C: pre-CTX, D: post-CTX). CI, confidence interval; CTX, chemotherapy; OS, overall survival; PFS, progression free survival.

(A) median OS (months) (95% CI) low (n=55): 11 (8-14) vs high (n=49): 23 (20-26)
(B) median PFS (months) (95% CI) low (n=55): 11 (8-13) vs high (n=49): 15 (12-18)
(C) median PFS (months) (95% CI) low (n=52): 17 (12-21) vs high (n=46): 10 (8-13)
(D) median PFS (months) (95% CI) low (n=67): 15 (10-19) vs high (n=61): 13 (10-15)

In the recent study, we found that the expression of two proteins frequently altered in MPM, Merlin and Survivin, was associated with survival outcomes (figure). These results were confirmed using 2 independent cohorts of MPM patients.

A new prognostic score supporting treatment allocation for multimodality therapy for malignant pleural mesothelioma - an update


A prognostic score was defined considering tumor volume, histology, CRP and response to chemotherapy and identified patient groups not benefitting from multimodality treatment in a cohort of patients receiving cisplatin-based induction chemotherapy followed by extrapleural pneumonectomy (EPP) at the University Hospital Zurich.

The MMPS was tested in 63 patients undergoing induction chemotherapy followed by EPP between 1999 and 2015. Patients with score 0 survived significantly longer than patients with score 3 or higher (Figure).

Figure. Kaplan-Meier curve of overall survival (OS) in months of patients undergoing induction chemotherapy followed by EPP with the different MMPS (including 4 variables: volumetry pre CTX > 500ml, CRP pre CTX > 30mg/l, non-epithelioid histology in pre CTX biopsy, PD according to modified RECIST criteria).
Sarcomatoid differentiation during progression of malignant pleural mesothelioma

Malignant pleural mesothelioma presents in the three histological subtypes epithelioid, biphasic and sarcomatoid, of which epithelioid is the most common and the subtype associated with the best prognosis. Investigating histopathological characteristics of mesothelioma cases during disease progression in a series of 36 patients, we observed in 28% of patients with epithelioid or biphasic subtype in the pre-treatment biopsy, a transition towards biphasic or sarcomatoid subtype during disease progression. This sarcomatoid differentiation was associated with a significantly shorter median overall survival (OS) compared to those patients with stable histology (19 months; 95% CI: 17-21 vs 34 months; 95% CI: 23-46; p=0.04).

Investigation of genetic alterations underlying chemotherapy resistance and novel drug targets for malignant pleural mesothelioma by next generation sequencing

We employ next generation sequencing to investigate the fundamental mechanisms of malignant pleural mesothelioma (MPM) development and treatment resistance and to find predictive biomarkers and new drug targets.

The objectives of this study are (i) to investigate the intra-tumor heterogeneity and to track the clonal origin and treatment resistant clones at different time points during treatment; ii) to identify genetic alterations that are associated with the response to chemotherapy and (iii) to systematically investigate MPM samples using the Oncomine Focus Assay that enables simultaneous detection of thousands of variants across 52 genes targetable by available oncology drugs.

Figure. Example of an MPM patient, with the initial diagnosis of an epithelioid MPM, undergoing multimodal treatment with cisplatin/pemetrexed induction chemotherapy followed by surgery. MPM tissue samples were taken at the initial treatment-naive biopsy (referred to as phase 1), at extrapleural pneumonectomy after combined induction chemotherapy (phase 2) and at relapse (phase 3). DNA was isolated from punches taken from two areas in phase 1, six areas in phase 2 and three areas in phase 3, followed by ultra-deep amplicon resequencing. Subsequently, based on a systematic literature review, a custom-designed MPM-specific sequencing panel was established, targeting the coding sequence of the 30 most frequently mutated genes in MPM.
Genetic and genealogic studies evaluating the Swiss origin of a specific BAP1 cancer syndrome

The presence of germline mutations in the gene encoding the BRCA1-associated protein (BAP1) has been identified as a common heritable factor predisposing to a number of cancers, including malignant pleural mesothelioma (MPM). Genetic and genealogic studies of one specific BAP1 mutation found in four US-families, have recently suggested the origin of this mutation to be in Switzerland. In this project we are further screening possible descendants of the supposed founder family in order to formally confirm the origin of the rare BAP1 germline mutation in Switzerland.

Exploring novel treatment for malignant pleural mesothelioma: Effects of hedgehog antagonist in an orthotopic malignant pleural mesothelioma rat model

An autocrine driven upregulation of the Hedgehog (Hh) signaling pathway has been described in malignant pleural mesothelioma (MPM) tumors. However, our investigation revealed that the Hh pathway is activated in both tumor and stroma of MPM tumor specimens and an orthotopic immunocompetent rat MPM model (Figure; Meerang et. al, Mol Cancer Ther 2016). The rat MPM model receiving daily treatment with a Hh antagonist, vismodegib, showed a significant reduction of tumor volume, and tumor growth delay. We detected reduced levels of Hh target genes namely Glioma associated oncogene 1 (GLI1) and Hedgehog Interacting Protein (HHIP) only in stromal part of vismodegib treated tumors. Our study provides a novel data regarding paracrine Hh activation in MPM and emphasized the role of Hh signaling as a treatment target for MPM.
Prevalence of BRCA-1 associated protein 1 germline mutation in sporadic malignant pleural mesothelioma cases
A. Rusch, G. Ziltener, K. Nackaerts, W. Weder, R. A. Stahel, E. Felley-Bosco

A large proportion of mesothelioma tumor specimens have a mutation in the BRCA1-associated protein 1 (BAP1) gene and germline BAP1 mutations predispose to malignant pleural mesothelioma (MPM). Our aim was to investigate germline BAP1 mutations in sporadic MPM patients.

One out of 78 patients showed a germline synonymous mutation in exon 11. In all other patients wild-type sequence without any single-nucleotide polymorphisms was detected. Taking into account previous similar screenings, the prevalence of germline BAP1 mutations in sporadic MPM patients can be estimated around 1-2%, suggesting a minor role of germline BAP1 mutation in the pathogenesis of sporadic MPM.

Preclinical malignant pleural mesothelioma models to accelerate clinical research on targeted therapies
N. Echeverry, G. Ziltener, D. Barbone, W. Weder, R. A. Stahel, C. Broaddus, E. Felley-Bosco

Given the limited effect of chemotherapy in malignant pleural mesothelioma (MPM), a big effort is being made to find new treatment options. The PI3K/mTOR pathway was reported to be upregulated in MPM. We tested the cell growth inhibition properties of two dual PI3K/mTOR inhibitors NVP-BEZ235 and GDC-0980 on 19 MPM cell lines. We could identify resistant and sensitive lines; however there was no correlation to the down-regulation of PI3K/mTOR activity markers. As a result of mTOR inhibition both drugs efficiently induced long-term autophagy but not cell death. Autophagy blockade by chloroquine in combination with the dual PI3K/mTOR inhibitors significantly induced caspase-independent cell death involving RIP1 in the sensitive cell line SPC212. Cell death in the resistant cell line Mero-82 was less pronounced and it was not induced via RIP1 dependent mechanism, suggesting the involvement of RIP1 downstream effectors. Based on these results, we identify autophagy as one of the main mechanisms of cell death resistance against dual PI3K/mTOR inhibitors in MPM. As PI3K/mTOR inhibitors are under investigation in clinical trials, these results may help interpreting their outcome, and suggest ways for intervention (Figure next page).
Figure. Inhibition of autophagy with chloroquine combined with inhibition of PI3K/mTOR signaling induces spheroid cell death.
(a) Representative light micrographs of SPC212 and Mero-82 spheroids treated as indicated with 1 μM NVP-BEZ235, 1 μM GDC-0980 and 20 μM CQ for 6 days.
(b) Fold increase volume (growth) of spheroids shown in (a).
(c) Viability is presented as percentage of ATP content SPC212 and Mero-82 spheroids treated as described in (a).
Data are presented as means +/- SD from ≥3 independent experiments. Significance was determined by Anova test (**p<0.005, *p<0.01 and *p<0.05; n.s.: not significant).

Collaborations:
- 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. Marc de Perrot, Dr. Licun Wu, Division of Thoracic Surgery, Toronto General Hospital
- Prof. Egbert Smit, NKI, Amsterdam
- Dr. Victor Van Beusechem, Department of Medical Oncology VUmc, Amsterdam


**Thoracic Surgery**


### Plastic, Hand and Reconstructive Surgery

<table>
<thead>
<tr>
<th>Source</th>
<th>Title of Project</th>
<th>Project Leader</th>
</tr>
</thead>
<tbody>
<tr>
<td>Swiss Life Research Grant, Zurich</td>
<td>Skin grafting and tissue engineering of skin substitutes in burn surgery - what we can learn from nature</td>
<td>N. Lindenblatt</td>
</tr>
<tr>
<td>Hartmann Müller-Stiftung für Med. Forschung</td>
<td>Effect of moderate anemia in free vascular tissue transfer</td>
<td>N. Forster</td>
</tr>
<tr>
<td>Hartmann-Müller Stiftung für Med. Forschung</td>
<td>Knochenersatzkonstrukte</td>
<td>J. Buschmann</td>
</tr>
<tr>
<td>Wolfemann-Nägeli-Stiftung</td>
<td>Sehnenreparatur mit einem reversibel expandierbaren Schlauch - Kaninchenmodell in vivo</td>
<td>J. Buschmann</td>
</tr>
<tr>
<td>EMDO Stiftung, Zürich</td>
<td>Fabrikation eines Polymerschlauches zur Sehnenreparatur</td>
<td>J. Buschmann</td>
</tr>
<tr>
<td>AbMedica, Lainate (Italy)</td>
<td>Sehnenreparatur mit einem reversibel expandierbaren Schlauch - Kaninchenmodell in vivo</td>
<td>J. Buschmann</td>
</tr>
<tr>
<td>Hartmann-Müller Stiftung</td>
<td>Sehnenreparatur unter Zuhilfenahme eines mit PDGF-BB bestückten Degrapol-Rohrs</td>
<td>J. Buschmann</td>
</tr>
</tbody>
</table>

### Thoracic Surgery

<table>
<thead>
<tr>
<th>Source</th>
<th>Title of Project</th>
<th>Project Leader</th>
</tr>
</thead>
<tbody>
<tr>
<td>Swiss National Science Foundation</td>
<td>From asbestos-exposure to cancer: a systemic approach to detect loss of homeostatic control in the mesothelial environment</td>
<td>E. Felley-Bosco</td>
</tr>
<tr>
<td>Baugarten Stiftung</td>
<td>Preclinical Malignant Pleural Mesothelioma models to accelerate clinical research on targeted therapy</td>
<td>E. Felley-Bosco</td>
</tr>
<tr>
<td>Walter Bruckerhoff Stiftung</td>
<td>Targeting epigenetic deregulation</td>
<td>E. Felley-Bosco</td>
</tr>
<tr>
<td>Polianthes Foundation</td>
<td>Overcoming development of resistance and progression to mesenchymal phenotype in mesothelioma</td>
<td>E. Felley-Bosco</td>
</tr>
<tr>
<td>Polianthes Foundation</td>
<td>Comprehensive investigation of predictive biomarkers for chemotherapy response and novel drug targets in patients with MPM by next generation sequencing</td>
<td>I. Schmitt-Opitz</td>
</tr>
<tr>
<td>Krebsforschung Schweiz</td>
<td>Mesoscapes 001-pS6: Construction of a multi-institutional European tissue bank</td>
<td>I. Schmitt-Opitz</td>
</tr>
<tr>
<td>Swiss National Science Foundation, Förderungsforschulen</td>
<td>Magnetic resonance imaging for the detection of chronic lung allograft rejection in mouse lung transplantation</td>
<td>W. Jungraithmayr</td>
</tr>
<tr>
<td>Swiss National Science Foundation, Förderungsforschulen</td>
<td>Malignant Pleural Mesothelioma - an integral approach for better outcome</td>
<td>I. Schmitt-Opitz</td>
</tr>
<tr>
<td>Forschungskredit der Universität Zürich</td>
<td>Attenuation of acute lung allograft rejection by CD26 inhibition – a preclinical model</td>
<td>W. Jungraithmayr</td>
</tr>
<tr>
<td>Stiftung für wissenschaftliche Forschung, Zürich</td>
<td>Lung tumor growth reduction by CD26 inhibition</td>
<td>W. Jungraithmayr</td>
</tr>
<tr>
<td>Assistenz-Professur an der UZH</td>
<td>Lungentransplantation</td>
<td>W. Jungraithmayr</td>
</tr>
<tr>
<td>Förderungsprogramm &quot;Filling the Gap&quot;, FTG-1617-02</td>
<td>Attenuation of acute lung allograft rejection by CD26 inhibition – a preclinical model</td>
<td>W. Jungraithmayr</td>
</tr>
<tr>
<td>Hermann Klaus-Stiftung</td>
<td>Primary lung tumor growth inhibition by CD26</td>
<td>W. Jungraithmayr</td>
</tr>
<tr>
<td>Innovationspool</td>
<td>Assessment and reconditioning of donor lungs with ex vivo lung perfusion system</td>
<td>I. Inci</td>
</tr>
<tr>
<td>Lungenliga Zürich</td>
<td>Ex vivo reconditioning of donor lungs with inhaled N-Acetyl cysteine after prolonged cold ischemia</td>
<td>I. Inci</td>
</tr>
<tr>
<td>Hermann-Klaus Stiftung</td>
<td>Ex vivo reconditioning of donor lungs with Trimetazidine after prolonged cold ischemia</td>
<td>I. Inci</td>
</tr>
</tbody>
</table>
### Thoracic Surgery

<table>
<thead>
<tr>
<th>Source</th>
<th>Title of Project</th>
<th>Project Leader</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hartmann-Müller Stiftung</td>
<td>Ex vivo reconditioning of donor lungs with inhaled N-Acetyl cysteine after prolonged cold ischemia</td>
<td>I. Inci</td>
</tr>
<tr>
<td>Hartmann-Müller Stiftung</td>
<td>The role of cytokine filtration during ex vivo lung perfusion</td>
<td>I. Inci</td>
</tr>
<tr>
<td>Lunge Zürich</td>
<td>MicroRNAs as prognostic and predictive tumor markers assisting the selection of patients with Malignant Pleural Mesothelioma for multimodality treatment</td>
<td>I. Schmitt-Opitz, M. Kirschner</td>
</tr>
<tr>
<td>Dr. Arnold U. u. Susanne Huggenberger-Bischoff Stiftung zur Krebsforschung (Krebsstiftung)</td>
<td>In vivo study of the efficacy of a dual phosphatidylinositol-3-kinase (PI3K)/mTOR-inhibitor in the treatment of malignant pleural mesothelioma</td>
<td>W. Weder, I. Schmitt-Opitz</td>
</tr>
<tr>
<td>Krebsliga Zürich</td>
<td>Prognostic Marker for Malignant Pleural Mesothelioma</td>
<td>I. Schmitt-Opitz</td>
</tr>
<tr>
<td>BECON AG Foundation</td>
<td>Prognostische Marker für das Maligne Pleuramesotheliom</td>
<td>I. Schmitt-Opitz</td>
</tr>
<tr>
<td>Vontobel Stiftung</td>
<td>MikroRNAs als prognostische und prädiktive Tumormarker für die multimodale Behandlung des malignen Pleuramesothelioms</td>
<td>I. Schmitt-Opitz, M. Kirschner</td>
</tr>
<tr>
<td>Stiftung für angewandte Krebsforschung</td>
<td>Activity based protein profiling in human lung cancer biopsies</td>
<td>W. Weder, S. Hillinger, S. Arni</td>
</tr>
<tr>
<td>Novartis Pharma AG Basel</td>
<td>Identification and validation of drug targets and biomarkers for COPD/emphysema and other end-stage lung disease</td>
<td>W. Weder, S. Hillinger</td>
</tr>
<tr>
<td>EMDO-Stiftung, Zurich, Switzerland</td>
<td>Impact of sevoflurane anesthesia on primary graft dysfunction after experimental mouse lung transplantation</td>
<td>W. Jungraithmayr</td>
</tr>
<tr>
<td>Universität Zürich, Projektförderung (Abt. I-III)</td>
<td>Suppression of lung tumor growth by CD26/DPP4-inhibition</td>
<td>W. Jungraithmayr</td>
</tr>
<tr>
<td>Kurt und Senta Hermann-Stiftung, Liechtenstein, VADUZ</td>
<td>Blockade of CD26/DPP4-costimulation to improve lung transplant survival</td>
<td>W. Jungraithmayr</td>
</tr>
<tr>
<td>Helene Bieber-Fonds</td>
<td>The CD26-costimulatory pathway is critical for Th17-mediated lung transplant improvement</td>
<td>W. Jungraithmayr</td>
</tr>
</tbody>
</table>

### Urology

<table>
<thead>
<tr>
<th>Source</th>
<th>Title of Project</th>
<th>Project Leader</th>
</tr>
</thead>
<tbody>
<tr>
<td>Swiss National Science Foundation</td>
<td>Non-invasive monitoring of muscle precursor cell differentiation in vivo by magnetic resonance imaging</td>
<td>D. Eberli, Co-Applicant</td>
</tr>
<tr>
<td>Helmut Horten Stiftung</td>
<td>Cell-enriched hydrogel biomaterial with optimized release of NGF and VEGF for the improvement of innervation and functionality of bioengineered bladder tissue</td>
<td>D. Eberli</td>
</tr>
<tr>
<td>Janssen Pharamaceutica NV</td>
<td>Antitumor effect of androgen synthesis inhibitors and autophagy inhibition in prostate cancer cells</td>
<td>D. Eberli</td>
</tr>
<tr>
<td>Research Grant from &quot;Novartis Stiftung für Biologisch-Medizinische Forschung&quot;</td>
<td>Improving human muscle engineering by PGC-1alpha overexpression</td>
<td>D. Eberli</td>
</tr>
<tr>
<td>Max &amp; Hedwig Niedermayer Stiftung</td>
<td>The Role of Autophagy in the Differentiation of Adipose Derived Stem Cells for Functional Smooth Muscle Bioengineering</td>
<td>D. Eberli</td>
</tr>
<tr>
<td>Klinischer Forschungsschwerpunkt &quot;Molekular Imaging Network Zurich&quot;, Co-Applicant</td>
<td>In-vivo characterization of differentiating muscle precursor cells applying multi-modal molecular imaging</td>
<td>D. Eberli</td>
</tr>
<tr>
<td>Fonds zur Förderung des akademischen Nachwuchses (FAN) der ZUNIV</td>
<td>Antitumor effect of Abiraterone and autophagy inhibition in prostate cancer cells</td>
<td>D. Eberli</td>
</tr>
<tr>
<td>Helmut Horten Stiftung</td>
<td>Cell-enriched hydrogel biomaterial with optimized release of NGF and VEGF for the improvement of innervation and functionality of bioengineered bladder tissue</td>
<td>D. Eberli</td>
</tr>
</tbody>
</table>
7. Awards 2015

Ekaterina Kachaylo
Young Investigator Bursary to ILC
EASL, Vienna, April 2015

Magda Langiewicz
Young Investigator Bursary to ILC
EASL, Vienna, April 2015

Magda Langiewicz
Young Investigator Award – Oetliker Prize
Swiss Physiological Society, Basel, Sept. 2015

Magda Langiewicz
ZIHP Symposium Best Poster Award
Zurich Center for Integrative Human Physiology (ZIHP), Zurich, August 2015

Magda Langiewicz
Best Poster Award
14th Day of Clinical Research, Zurich, 9 April 2015

Enrica Saponara
Best Basic Research Award
Department of Visceral and Transplantation Surgery, December 2015.

Sabrina Sonda
Poster Prize
14th Day of Clinical Research, Zurich, 9 April 2015.

Wolfgang Jungraithmayr
Experimentell-wissenschaftlicher Preis 2015
“CD26 Co-stimulatory blockade improves lung allograft rejection and is associated with enhanced IL-10 expression”
UniversitätsSpital Zürich, Transplantationszentrum, Zürich, 20.11.2015.

Wolfgang Jungraithmayr
Beste experimentelle freie Mitteilung
“Lung allograft acceptance by CD26 co-stimulatory blockade is due to a balanced expression of IL17 and IL10”
Schweizerische Gesellschaft für Thoraxchirurgie, Bern, 25.11.2015.

Etienne Xavier Keller
Jahrespreis 2015 for the Dissertation:
“Antibody response to BK polyomavirus as a prognostic biomarker and potential therapeutic target in prostate cancer” (Oncotarget 2015, (6)8; 6459-6469)
Faculty of Medicine, UZH 2015

Ashkan Mortezavi
Poster Prize
“Inhibition of autophagy significantly increases the antitumor effect of Abiraterone in LnCap prostate cancer cells”
Schweizerische Gesellschaft für Urologie (SGU), St. Gallen 2015

Souzan Salemi
Poster Prize Stem Cell Research
“Synergistic effects of combining undifferentiated adult stem cells and differentiated cells for the engineering of functional bladder smooth muscle tissue”
Annual Meeting of the European Association of Urology (EAU), Madrid 2015

Christian Fankhauser
Forschungsförderungsprojekt (FFP)
Preis der med Alumni Zürich, 2015

Dr. Paulin Jirkof
IQ Consortium and AALAC International
Global 3Rs Award, 2015
Phoenix, Arizona, USA, November 2015