ESTS Biology Club Fellowship 2024

Centre: Medical University of Vienna, Austria

1. Drug distribution in isolated perfused human lobes with non-small cell lung cancer

Supervisor: Clemens Aigner

The intratumoral distribution of systemic therapies for non-small cell lung cancer remains poorly understood, resulting in divergent response rates. Platinum compounds represent the backbone of systemic treatment. Therefore, we will assess the tissue distribution patterns of different approved and experimental Pt-based drugs in near-physiological conditions using an isolated lung perfusion model (ILP) of surgically resected human lung lobes (Sci Rep 2019, doi: 10.1038/s41598-019-48719-8). This ILP model, combined with LA-ICP-MS (Laser Ablation Inductively Coupled Plasma Mass Spectrometry), offers a unique potential to evaluate intratumoral (including stromal)- and peritumoral distribution of Pt (Br J Clin Pharmacol 2023, doi: 10.1111/bcp.15813). Pt distributions and levels will be correlated with histo- and molecular pathological features of the tumors and also with clinical data. The resulting correlations might represent a step forward in understanding NSCLC tissue Pt penetration and might, therefore, lead to the development of optimized treatment protocols.

2. Personalizing mechanical ventilation during prolonged EVLP to protect alveolar structure and prevent ventilation-induced lung injury

Supervisor: Alberto Benazzo

Currently, the ventilation strategy during ex vivo lung perfusion (EVLP) is standardized and follows the one size fits all principle. However, there is increasing evidence that certain ventilation settings have the potential to damage marginal grafts. The lung stress index (SI) is a parameter derived from the shape of the pressure-time curve measured at constant inspiratory flow. It can indicate tidal overdistension, alveolar de-recruitment or non-damaging ventilation. Several studies have already shown the clinical benefit of personalized mechanical ventilation (MV) based on SI to prevent ventilator-induced lung injury (VILI) in ARDS patients. The current study will investigate the feasibility and biological impact of using SI to guide MV during EVLP. This is a prospective pilot study with donor organs that were discarded at the time of retrieval. Included organs will be studied under acellular normothermic EVLP and ventilation settings will be continuously adjusted based on real-time measurements of SI to avoid VILI. In parallel, circulating cytokine concentrations and cell apoptosis will be measured at fixed time points. Both functional and biological data will be compared with clinical EVLP lungs. This study has the potential to provide a measurable and reliable parameter to personalize MV during EVLP and reduce VILI.

3. Translational research on thymic epithelial tumors

Supervisor: Bernhard Moser

The research fellow will be engaged in experimental basic science research on biomarkers of the tumor microenvironment (e.g. fibroblast populations) in thymic epithelial tumors based on previously acquired bioinformatics and high throughput immunohistochemical analysis. Furthermore the fellow will work on internationally establishing the beta version of the Thymic database in ESTS centers participating to provide detailed high quality data on thymic epithelial tumor treatment and will work on the international roll out of several ESTS thymic working group projects that are currently underway such as "Minimally-invasive (VATS, RATS) vs. open (thoracotomy, sternotomy) thymectomy in stage I and II patients." 'The involvement in all clinical aspects of patients with thymic epithelial tumor treatment: diagnosis, tumor board, robotic thymectomy and open surgery, follow-up and their database documentation will part of the experience.

Contact:

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