Conclusions In sum, we have established a new model suitable for intravital imaging that will help identify limitations of CAR-T cells activity in the context of a solid tumor.

B. Arnaud: None. **M. Ruggiu:** None. **Z. Garcia:** None. **F. Lemaître:** None. **C. Grandjean:** None. **P. Bousso:** None.

P09.07 DETERMINING POTENCY, ACTIVATION AND EXPANSION OF ANTIGEN SPECIFIC T CELLS

B Hansen*, J Jørgensen, L Brix. *RandD Department, Immudex Aps, Virum, Denmark*

10.1136/jitc-2024-ITOC10.51

Background CAR/T Cell therapy relies on Cells with engineeredreceptors that bind tumour cells, then transduces a stimulatory signal meant toactivate the engineered Cell to kill the tumour cell. Clinical experience hasindicated that activating T-cells through its TCR alone isn't going to besufficient to mount and maintain an effective anti-tumour response. Addingadditional strength to the T cells by providing a 2nd or 3rd engineeredco-stimulatory signal are currently pursued strategies within Celltherapy. In vitro assays are needed to evaluate the effect of theadded co-stimulatory signals and to evaluate the potency of engineered T cells. Most current assays are based on cell-cell interaction which makes them hard tostandardize. We have exploredDextramer technology as an artificial antigen-presenting scaffolds able tostimulate and activate specific T cells. Dextramer displaying MHCp complexesand anti-CD28 antibody (MHC/a-CD28 Dextramer) were used to stimulate PBMCs oran TCR engineered T cell line.

Materials and Methods Healthy donor PBMCs compricing virus-specificCD8+ T cells or TCR engineered T cell lines were incubated with MHC/a-CD28 Dextramer in culture medium for6 hours to 14 days. Antigen specific T cells were following analyzed for i)activation by upregulation of CD69 and CD137, ii) cytokine production (IFN-gamma,TNF-alpha) and iii) proliferation.

Results MHC/a-CD28 Dextramer couldstimulate an activate specific T cells in PBMC sample: i) an upregulation of earlyactivation markers, CD69 and CD137 was observed, ii) increase in cytokineproduction, INF-gamma and TNF-alpha could be measured intracellular, and iii) a15 fold expansion of T cells specific for the MHCp complex of the Dextramer wasmeasured, all proliferating cells were expressing Ki-67.Nostimulation or activation of T cells were observed when incubating cellssamples with MHC/a-CD28 Dextramer displaying negative control MHCp.Similar results wereobtained when stimulating engineered T cell line.

Conclusions We have shown a simple technology to explore effectof engineered co-stimulatory signals, and evaluate potency ofengineered T cells. MHC/a-CD28 Dextramer were able to stimulate, activate andexpand specific T cells. The activation was highly antigen (i.e.MHCp) specific and CD28 co-immobilization dependent.

B. Hansen: A. Employment (full or part-time); Modest; Immudex Aps. **J. Jørgensen:** A. Employment (full or part-time); Modest; Immudex Aps. **L. Brix:** A. Employment (full or part-time); Modest; Immudex Aps..

10. Cell therapy in haematologic diseases

P10.01 NUTRITIONAL AND IMMUNOMETABOLIC MEASURES FOR RISK ASSESSMENT IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

[1,2,3]H Thurisch*, [4]K Althoff, [4]S Leitzke, [4]U Holtick, [4]C Scheid, [1,2,3]S Oganesian, [1,2,3]M Funk, [1,2]D Cordas dos Santos, [1]M von Bergwelt-Baildon, [1,2,3]S Theurich. *[1]Depatment of Medicine III, University Hospital, LMU Munich, Munich, Germany; [2]LMU Gene Center, Munich, Germany; [3]German Cancer Consortium (DKTK/DKFZ), Munich, Germany; [4]Department I of Internal Medicine, University Hospital of Cologne, University of Cologne, Cologne, Germany*

10.1136/jitc-2024-ITOC10.52

Background The hematopoietic transplant comorbidity index (HTC-CI) has been developed to determine treatment-related morbidity following allogeneic hematopoietic stem cell transplantation (alloHSCT) and includes obesity and diabetes as risk factors. On the other hand, chronic low-grade inflammation which is regularly associated with obesity and represents a mechanism of insulin resistance might mediate beneficial immune effects as demonstrated in the context of immune-check point inhibition cancer treatment. Literature on the role of a high body mass index (BMI) prior to alloHSCT remains controversial likely due to the complexity of the involved mechanisms that also comprise of increased catabolic rates and the immunonutritional status. In this study, we evaluated clinical outcomes in a large cohort of consecutive patients who underwent alloHSCT. Specifically, we analyzed pre-transplant BMI and immunonutritional scores as well as their dynamic changes in the early post-transplant phase with regard to survival and toxicities.

Materials and Methods Clinical records of 664 consecutive patients undergoing alloHSCT between 2012 and 2017 at the Department of Medicine I, University Hospital of Cologne, Germany, were retrospectively analyzed. Patients were categorized into four BMI classes and three immunometabolic risk groups according to the modified Glasgow Prognostic Score (mGPS) measured pre-transplant and on day 30 post-transplant. Overall survival (OS), non-relapse mortality (NRM) and the development of a clinically relevant acute graft-versus-host disease (GvHD) $\geq$2 grade were compared using Kaplan-Meier survival analysis. Additional analyses stratified for sex and focused on a disease and transplant setting homogenized cohort.

Results Median BMI of the cohort was 24.6 (15.1-50.4) kg/m^2. OS and NRM differed significantly between BMI classes (OS p = 0.02; NRM p = 0.05), with a significant survival benefit of overweight (median OS: 21 and 22 months in normal weight and obese, > 50% alive after 60 months in overweight). In contrast to the male cohort, in females also obesity had a favourable impact (p = 0.50; median OS: 16 months in normal weight; 35 months in overweight and >50% alive after 60 months in obese). mGPS classes, both determined pre-transplant and on day 30, experienced significantly different OS and NRM (OS p < 0.001; NRM p < 0.002), in which hypoalbuminemia combined with elevated C-reactive protein (mGPS 2) correlated with worst OS, NRM and a tendency of higher GvHD incidence. The extend of mGPS increase from day 0 to 30 impacted all outcomes significantly (OS p = 0.02; NRM p = 0.05; GvHD p = 0.01).

Especially an increase to an mGPS of 2 was associated with significantly worse OS, NRM and higher GvHD incidence (median OS: 13 and 7 months in mGPS 0->2 and 1->2, respectively; 49 months in mGPS 0->1).

Conclusions Our data suggest a more complex role of metabolic pathologies as currently reflected by obesity and diabetes categories within the HTC-CI. Therefore, future prospective studies that include body composition as well as sensitive measures of disturbed glucose tolerance and metabolic rates are warranted to determine immunometabolic risk factors for alloHSCT outcomes.

H. Thurisch: None. **K. Althoff:** None. **S. Leitzke:** None. **U. Holtick:** None. **C. Scheid:** None. **S. Oganesian:** None. **M. Funk:** None. **D. Cordas dos Santos:** None. **M. von Bergwelt-Baildon:** None. **S. Theurich:** None.

11. Combination Therapy

P11.01 ONCOLOGICAL OUTCOMES OF LAPAROSCOPIC VERSUS OPEN RADICAL TOTAL GASTRECTOMY FOR UPPER-MIDDLE GASTRIC CANCER AFTER NEOADJUVANT CHEMOTHERAPY

S Li-LI*, G You-xin, Z Zhi-wei. *Fujian Medical University Union Hospital,Department of Gastric Surgery, Fuzhou, China*

10.1136/jitc-2024-ITOC10.53

Background Laparoscopic technique has been increasingly used in gastrectomy, but the safety and feasibility of the laparoscopic total gastrectomy (LTG) for advanced proximal gastric cancer (PGC) after neoadjuvant chemotherapy (NAC) is unclear.

Materials and Methods A retrospective analysis of 146 patients who received NAC followed by radical total gastrectomy at Fujian Medical University Union Hospital from January 2008 to December 2018 was performed. The primary endpoints were long-term outcomes.

Results The patients were divided into two groups: 89 were in the LTG group and 57 were in the open total gastrectomy (OTG) group. The LTG group had a significantly shorter operative time (median 173 min vs. 215 min, $p < 0.001$), less intraoperative bleeding (62 ml vs. 135 ml, $p < 0.001$), higher total lymph-node (LN) dissections (36 vs 31, $p=0.043$), and higher total chemotherapy cycle completion rate ($\geq$ 8 cycles) (37.1% vs. 19.7%, $p = 0.027$) than OTG. The 3-year overall survival (OS) of the LTG group was significantly higher than that of the OTG group (60.7% vs. 35%, $p = 0.0013$). Survival with inverse probability weighting(IPW) correction for Lauren type, ypTNM stage, NAC schemes and the times at which the surgery was performed showed that there was no significant difference in OS between the two groups ($p = 0.463$). Postoperative complications (25.8% vs. 33.3%, $p = 0.215$) and recurrence-free survival (RFS) ($p = 0.561$) between the LTG and OTG groups were also comparable.

Conclusions In experienced gastric cancer surgery centers, LTG is recommended as the preferred option for such patients who performed NAC, owing to its long-term survival is not inferior to OTG, and it offers less intraoperative bleeding, better chemotherapy tolerance than conventional open surgery.

S. Li-LI: None. **G. You-xin:** None. **Z. Zhi-wei:** None.

P11.02 A COMPLEX HUMAN TUMOR ORGANOID MODEL CONSISTING OF MALIGNANT CELLS, FIBROBLASTS AND IMMUNE CELLS ENLIGHTS THE EFFECT OF CHEMOTHERAPY-INDUCED SENESCENT TUMOR CELLS ON NK-CELL ANTI-TUMOR RESPONSES

[1]D Ammon*, [1]M Fabits, [1]M Sykora, [1]J Kabiljo, [1]A Theophil, [2]V Atanasova, [2]H Dolznig, [1]M Bergmann. *[1]Division of Visceral Surgery, Department of General Surgery, Medical University of Vienna, Vienna, Austria; [2]Center of Pathobiochemistry and Genetics, Institute of Medical Genetics, Medical University of Vienna, Vienna, Austria*

10.1136/jitc-2024-ITOC10.54

Background Primary human organoids have been shown to be predictive for selectivechemotherapy and thus be a valuable model for cancer research. One of manytumor evasion strategies in response to DNA-damaging chemotherapy treatment isthe induction of senescence to acquire a state of resistance. Fortunately,natural killer (NK) cells recognize senescent tumor cells, get activated andtrigger tumor killing in assistance of T-cells, as it was shown in mice studiesand cell lines. Additionally, it has been described that activation of theSTING pathway strongly enhance NK-cell responses. Therefore, we hypothesized,that STING-activated NK-cells are superior in killing chemotherapy-inducedsenescent tumor organoids. To test this hypothesis in a primary humandisease-relevant model, we established a complex system consisting of tumor organoids,matched primary cancer-associated fibroblasts (CAFs) and immune cells.

Materials and Methods To establish complex organoid cultures, we investigated various air-liquid-interface(ALI) culture conditions of primary tumour spheroids, CAFs and peripheral bloodmononuclear cells (PBMCs). Senescence was induced by Etoposide treatment and wasverified by β-galactosidase staining. Immune cells were activated by either ionomycinand PMA, or a STING agonist ADU-S100.

Results Immune cell viability was preserved for 48 hours in the established ALI cultureconsisting of PBMCs and organoids in one phase and fibroblasts in a secondcompartment. Functional applicability of the system was evaluated through ionomycinand PMA induced immune cell activation which resulted in tumor cell death asquantified by zombie violet positive staining. Confocal microscopy further verifiedimmune cell infiltration and immune cell mediated disintegration of organoids.Senescence was inducible by DNA-damaging chemotherapy in 3Dco-culture of tumor organoids and CAFs. Moreover, a combination of senescenceinduction by DNA-damaging chemotherapy and subsequent STING-pathway activation ledto a more pronounced NK-cell activation (CD69) and degranulation (CD107a) incontrast to non-senescent controls.

Conclusions We developed a complex 3D culturesystem of tumor, stromal and immune cells to mimic the tumor microenvironment andto assess the impact of senescent organoids on STING-activated immune cells in a primary human model.

D. Ammon: None. **M. Fabits:** None. **M. Sykora:** None. **J. Kabiljo:** None. **A. Theophil:** None. **V. Atanasova:** None. **H. Dolznig:** None. **M. Bergmann:** None.