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.

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

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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.

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10. Cell therapy in haematologic diseases

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

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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).