P06.06.B. STANDARDIZATION OF THERAPY AND MANUFACTURING USING TUMOR-ASSOCIATED ANTIGEN-STIMULATED AUTOLOGOUS DENDRITIC CELLS CO-CULTURED WITH CYTOKINE-INDUCED KILLER CELLS IN CANCER IMMUNOTHERAPY
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BACKGROUND: The application of DC-CIK in the field of cancer immunotherapy has been shown to be an effective treatment. However, the cost of DC-CIK treatment is prohibitive for many patients, and the lack of standard manufacturing processes and treatment strategies are the main limitations. MATERIAl AND METHODS: Our experiments used tumor-lysate instead of tumor cell line as tumor-associated antigen source with DCs co-culture. We provide the most efficient method for obtaining autologous DC-CIK cells from peripheral blood. Flow cytometry was used to evaluate DCs activation, CBA assay was used to quantify cytokines secreted by CIK cells, and the antitumor activity of DC-CIK was evaluated in vitro by K562 cell line. RESULTS: We demonstrate that the manufacturing process of employing frozen Peripheral Blood Mononuclear Cells (PBMCs) can balance patient’s comfort and economic benefits. DC-CIK can effectively upgrade the immunological specificity of CIK cells to tumors in the presence of tumor-associated antigen. In vitro experiments showed that when the number of DC: CIK cells was co-cultured in 1:20 ratio on the 14th day, the antibody-bound cytotoxicity secreted by CIK cells was the largest, and the antitumor immune effect was the most potent. When the number of CIK: K562 cells was in 23:1 ratio, the cytotoxic activity of CIK on K562 cells was the highest. CONCLUSION: We developed an efficient activated fashion of DC-CIK, established the optimal ratio of DC: CIK, and the immunogenic activity and the best cytotoxic model of CIK to K562 cells.

P06.07.A. NATURAL KILLER CELLS LYSE GLOILOBLASTOMA STEM CELLS AND INCREASE THEIR SENSITIVITY TO CHEMOTHERAPY
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BACKGROUND: Glioblastoma is the most common and lethal brain tumor in the adult population and immunotherapy is playing increasingly a central role in the treatment of many cancers. Nevertheless, the search for effective immunotherapeutic approaches for glioblastoma patients continues. In this study, we aimed to explore the therapeutic potential of allogeneic highly activated super-charged natural killer (NK) cells in glioblastoma. MATERIAL AND METHODS: Chromosome release- and calcine release-based cytotoxicity assays, ELISA, ELISPOT, and multiplex cytokine assays were used to measure the cytotoxicity of NK cell culture against glioblastoma stem cells (GSCs) and secretion of cytokines. Cell surface marker expression using flow cytometry and cell growth in vitro and in vivo were measured to determine GSC phenotype. NK cell killing and penetration in 3D were measured using confocal microscopy (the Stupp protocol). RESULTS: NK cells efficiently lysed patient-derived GSCs in 2D and 3D models potentially reversing the immunosuppression observed in patients. NK cells secreted IFN-γ, upregulated GSC surface expression of CD54 and MHC class I and increased sensitivity of GSCs to chemotherapeutic drugs. Co-localization of NK cells with GBM cells in perivascular niches in glioblastoma tissues and their direct contact with GSCs in tumorspheres suggests their ability to infiltrate glioblastoma tumors and target GSCs. CONCLUSION: Allogeneic super-charged NK cells appear to be a potential therapeutic approach for glioblastoma by selectively killing therapy-resistant cancer stem cell population, increasing their immune-related surface markers and enhancing their sensitivity to chemotherapy. Due to GSC heterogeneity and plasticity personalized immunotherapeutic strategies should be developed to effectively target glioblastomas.

P06.08.B. RADIATION THERAPY ENHANCES ANTI-TUMOR ACTIVITY OF MET CAR T-BASED IMMUNOTHERAPY FOR GLOILOBLASTOMA
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BACKGROUND: Glioblastoma is the most frequent primary brain tumor with dismal prognosis after standard treatment with surgery, and chemoradiation (the Stupp protocol). After a decade of failed clinical trials, tumor-treating fields have been first to show the added benefit of improved overall survival compared to the Stupp protocol (20.9 months vs 16.0 months). However, GBM remains a devastating disease, with almost inevitable recurrence, and limited options for second-line therapy. Radiation therapy (RT), is a standard therapy option for GBM, and it is used in most GBM cases affecting tumor through induction of DNA damage. Recently, RT has been investigated as a mediator of T-cell based therapies in the context of immunosuppressive GBM microenvironment. The findings have shown promise in combination of T cell-based therapies, such as chimeric antigen receptor (CAR) T cell therapies, in improving the tumor infiltrating and penetrative immunity. MET is a relevant oncogene in the context of GBM, being involved in stem-like properties, radiation response and resistance. Hence, MET appeared to be a plausible target for combination with RT. In our research, we use MET-targeting CAR T cells (MET-CAR T cells) combined with radiation, and hypothesize synergistic interaction in GBM treatment. MATERIAl AND METHODS: We used adherent (2D) and stem-like (3D) human GBM cell lines with different levels of MET expression. For MET-CAR T cell generation we did retrovirus-mediated transduction of activated human T cells and sorted the CAR-positive cells. We co-cultured MET-CAR T cells with GBM cells with or without RT, and assessed the killing and cytokine production in CAR T cells. RESULTS: Our results indicated that 3 Gy radiation combined with MET-CAR T cells increases their potential in tumor cell killing. We observed increased CAR T cells effect at lower CAR T to target cells ratios when combined with radiation, even when radiation treatment did not lead to a significant decrease in viability. This phenomenon was similar across different types of cell lines (adherent, stem-like), different levels of MET expression, and different sensitivity to CAR T cells. We investigated the underlying mechanisms via intracellular cytokine measurement. We observed the most prominent response in TNF-α-expression. We also observed an increase in Granzyme B expression in co-culture with RT in some of the cell lines, especially in CD8+ subpopulation of CAR T cells. IFN-gamma expression increased in some adherent glioma cell lines but not in stem-like cell lines. CONCLUSION: In conclusion, our data demonstrates the potency of MET-CAR T cells against GBM, and increased effectiveness when combined with radia-

P07 ADVANCED NEUROSURGICAL TECHNIQUES

P07.01.A. TOPICAL FLUORESCENT PROBE FOR VISUALIZATION OF GLOILOBLASTOMA
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BACKGROUND: Glioblastoma (GBM) is the most aggressive form of cancer that originates within the central nervous system (CNS). GBM represents 15% of all primary brain tumors, but the cause is unclear, and there is no clear way to prevent it. At the moment, various sophisticated and specific surgical procedures are being used, but there are relatively simple methods. In this study, we use a turn-on-type fluorescent probe that can sense cytokine (Cys) amino acid in the GBM site, and developed a topological treatment methods for image-guided surgery (IGS). RESULTS: The probe can distinguish the GBM cells and disease sites. Besides, the probe has no short or long-term toxicity and immune response. CONCLUSION: The present findings hold promise for the appli-

P07.02.B. NEURO-ONCOLOGICAL AUGMENTED REALITY PLANNING (NOAP)
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BACKGROUND: When preparing for the resection of an intracranial lesion, neuronavigation with a tracked pointer is most often used to delineate lesion borders and the optimal approach. This can sometimes prove challenging, especially for deep-seated lesions. Augmented Reality (AR), directly displaying the lesion on the patient’s skin, can simplify and improve this step. MATERIAl AND METHODS: We developed a system for inside-out infrared tracking that does not require an external tracking camera or external computer and allows for heads-up displaying an AR scene on the Microsoft HoloLens II. Twenty patients planned for the resection of an