IMST-55. LYMPH NODE AND URINE METABOLOMICS: A NON-INVASIVE STRATEGY TO PREDICT EFFICACY OF DENDRITIC CELL VACCINE IMMUNOTHERAPY
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INTRODUCTION: We recently demonstrated that robust migration of DC to the draining lymph nodes and leukocytes in vaccinated lymph nodes can be used to predict the outcome of DC based immunotherapy. METH- ODS: DCs were generated from the bone marrow of adult mice. DCs were harvested, electroporated with OVA mRNA and used to vaccinate mice that received OT-1 splenocytes. After vaccination, the animals underwent lymph node harvest and were subjected to flow cytometry (FC) and analyzed with ANOVA and student's T-test. RESULTS: PD1+PolyIC treatment of mice resulted in 80% long-term survival of mice and improved survival compared to control group and PD1 or Poly IC groups alone (p<0.0001). When the tumor infiltrating immune cells were analyzed with FC, we found significantly increased effector T-cells and decreased naive T-cells in PD1+PolyIC group. Interestingly, memory T-cells increased in deep cervical lymph nodes and in the spleen. Activated DCs and macrophages were increased in the spleen with PD1+PolyIC treatment. Also, in the PD1+PolyIC group migratory DGs were decreased in the brain and increased in the lymph node and spleen. CONCLUSION: Poly IC causes increased ingestion and enhances antigen presentation of myeloid cells in GBM to potentiate anti-PD1 mediated anti-tumor immune response.

IMST-56. TUMOR LYSATE-PULSED DC VACCINATION INDUCES NEOANTIGEN-SPECIFIC T CELL RESPONSES
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Dendritic cell (DC) vaccines currently in phase III trials for glioblastoma use autologous tumor lysate (ATL) as an antigen source to induce a lympho- cytic infiltration but it remains unclear what epitopes this immune response is specifically directed against. We hypothesized that the most immunologi- cally relevant target antigens in the ATL are neoantigens arising from tumor-specific mutations. To test this, we identified non-synonymous coding mutations in the GL261 murine glioma cell line and human GBM samples using whole exome seq, RNAseq, and bioinformatics software to predict the mutated sequences which result in enhanced peptide-MHC binding. Nine candidate neoantigens were identified from the GL261 glioma line. Mice bearing intracranial GL261 gliomas were vaccinated with control, ATL, or neoantigen-pulsed DC vaccination. Tumor-infiltrating lympho- cytes (TILs) were isolated and co-cultured with DCs pulsed with peptides containing the neoantigen sequences for flow cytometry. 5x10^3 -2x10^5 TILs were recovered from vaccine-treated animals, whereas <10^3 were recovered from controls, indicating a enhanced T cell infiltration due to the vaccine.Ex vivo restimulation induced CD69 upregulation in 0, 21, and 26% of TILs in control, ATL, and neoantigen-pulsed DC vaccinated groups, respectively. Survival was significantly extended similarly in both ATL and neoantigen- pulsed DC vaccinated groups compared with control treatment (p<0.01). In human GBM patients, we identified an average of 15 strong binding and 9 weak binding neoantigens per tumor from 8 patients treated with ATL DC vaccination. TCR sequencing from the original tumor and TIL cultures revealed common high-frequency TCR clonotypes. Together, these studies indicate that tumor lysate DC vaccines are capable of priming CD8+ T cell responses directed at tumor-specific mutations in mice. Further studies are underway to characterize the immune responses to these candidate neoanti- gens in human patients following ATL-pulsed DC Therapy.

IMST-57. THERAPEUTIC POTENTIAL OF THE NATURAL HUMAN IgG1K ANTIBODY PRITUMUMAB
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Pritumumab is a natural human IgG1 kappa antibody derived from a regional draining lymph node of a patient with cerebral carcinoma. The rec- ognized antigen is an altered form of vimentin, called eeto-domain vimentin (EDV), expressed on the cell surface of epithelial tumor cells. A recombinant version of the mAb was made using the GPE® system in CHO cells. In a series of comparable studies in CO mice, GPE® mAb was compared with a CHO mAb. Binding specificity with both flow cytometry and immunohis- tochemical analysis, Western blot analysis, and Antibody-Dependent Cell- Mediated Cytotoxicity (ADCC) activity confirms the comparability of the two mAbs. Studies include both establishing a xenograft model in immunodeficient strain and athymic nude mice in which pritumumab was effective in preventing tumor growth in nude mice but not in SCID mice. Analysis of a blood brain barrier model suggests pritumumab shows minimal distribution in normal brain tissue and significant binding in tumor areas of brain tumors in vitro. The mAbs cross the tumor brain barrier. Overall, these data together suggest pritumumab is suitable for development as an anti-tumor therapeutic.

IMST-58. MODULATING THE MYELOID COMPARTMENT TO POTENTIATE ANTI-PD1 MEDIATED IMMUNOTHERAPY AGAINST Glioblastoma
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INTRODUCTION: Combinatorial immunotherapy targeting multiple immune compartments to treat glioblastoma (GBM) is an attractive tool due to the complex immune microenvironment. Activation of toll-like receptor 3 (TLR3) is known to stimulate antigen presenting cells (APC) and dendritic cells (DC) and secretion of inflammatory cytokines (interferon gamma, IL-6, and TNF-alpha). Through augmentation of antigen presentation with PD1 blocker and Poly IC, we sought to enhance the anti-tumor immune response in vitro using a novel model. METHODS: Under ACUAP approval, C57Bl/6 mice underwent implantation of GL261 cells in the left striatum stereotactically. The presence of tumor was confirmed by bioluminescence at day 7. Mice were ran- domized to 4 groups: Control, PD1, Poly IC, and PD1+Poly IC treatment. Survival was assessed using log-rank analysis and described using Kaplan- Meier curves. Immune response at the tumor site and systemically was assessed with flow cytometry (FC) and analyzed with ANOVA and student's T-test. RESULTS: PD1+PolyIC treatment of mice resulted in 80% long-term sur-

survival of mice and improved survival compared to control group and PD1 or PolyIC groups alone(p<0.0001). When the tumor infiltrating immune cells were analyzed with FC we found significantly increased effector T-cells and decreased naive T-cells in PD1+PolyIC group. Interestingly, memory T-cells increased in deep cervical lymph nodes and in the spleen. Activated DCs and macrophages were increased in the spleen with PD1+PolyIC treatment. Also, in the PD1+PolyIC group migratory DGs were decreased in the brain and increased in the lymph node and spleen. CONCLUSION: Poly IC causes increased ingestion and enhances antigen presentation of myeloid cells in GBM to potentiate anti-PD1 mediated anti-tumor immune response.

IMST-59. MODULATING GLIOMA-MEDIATED MYELOID-DERIVED SUPPRESSOR CELL DEVELOPMENT WITH SULPHARFACE
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INTRODUCTION: Glioblastoma is the most common primary tumor of the brain and has terrible long-term survival. Local and systemic immu-