Abstract 606 Figure 3  Correlation between IFN-γ and CXCL10 expression stratified by EGF expression. A. Cutaneous squamous cell carcinoma cell lines (GSE87676, n=44). B. Cutaneous squamous and basal cell carcinoma tumor samples (GSE125285, n=35).

role of EGF in modulating inflammation, and to understand this process in the pathogenesis of EGF receptor inhibitor-induced cutaneous toxicities and skin cancers.

Acknowledgements Emory Integrated Genomics Core

REFERENCES

607  TJ210 (MOR210), A DIFFERENTIATED ANTI-CSAR ANTIBODY FOR ANTI-CANCER THERAPY

Jane Meng*, Zhengyi Wang, Wei Cao, Chan Chen, Joan Huaqiong Shen, Christian Aupfinger, Julia Neugebauer, Stefan Haertle, Mab Bypharma, Beijing, China; MorphoSys AG, Munich, Germany

Background  Extensive investigations into the tumor microenvironment (TME) have uncovered molecular mechanisms linking aberrant complement activation and cancer progression. Specifically, C5a, as a highly potent chemoattractant, recruits immune suppressive myeloid derived suppressive cells (MDSCs), neutrophils and M2 macrophages into the tumor site and accelerates tumor progression. Blockade of C5a/C5aR (CD88) pathway has been identified as a promising target to control MDSCs and restore tumor-killing ability of T and NK cells. TJ210, in licensed from MorphoSys as MOR210, is a differentiated anti-C5aR monoclonal antibody with a unique binding epitope.

Methods  Interaction of TJ210 with C5aR was assessed through binding of the recombinant antigen, Flp-In CHO cells expressing C5aR and primary neutrophils. In vitro blockade of C5a/C5aR pathway was tested by inhibition of CD11b upregulation on granulocytes and monocytes induced by C5a, as well as neutrophil migration towards C5a. The in vitro synergistic effect of TJ210 with anti-PD-1 antibody was assessed in a T cell and differentiated MDSC co-culture system. The in vivo anti-tumor effect was tested in the MC38 syngeneic mouse model, in which mice were treated with a TJ210 mouse surrogate antibody either alone or in combination with an anti-PD-1 antibody.

Results  TJ210 bound to C5aR with high affinity and did not cross-react with other GPCR members including C5L2, ChemR23, FPR1 and C3aR. Unlike the reference antibody, TJ210 specifically interacted with the N-terminus of C5aR but not extracellular loops. TJ210 effectively inhibited CD11b upregulation on granulocytes and monocytes as well as neutrophil migration mediated by C5a. When compared with the reference antibody, TJ210 maintained potent antagonism at high ligand concentrations and over longer duration, properties that might translate into beneficial in vivo effects at pathophysiological conditions. In the in vitro co-culture system, presence of TJ210 and anti-PD-1 antibody enhanced IFN-γ release compared to either single agent, indicating a synergistic effect on T cells. In the in vivo syngeneic mouse model, combination treatment effectively inhibited tumor growth. Immune cell population analysis revealed significant elevation of CD8+ T cells and M1 macrophages compared to mono-treatment.

Conclusions  This series of in vitro and in vivo data demonstrate that TJ210 is a differentiated anti-C5aR antibody with unique binding epitope exhibiting superior anti-tumor potential especially in combination with an anti-PD-1 antibody. These data support further clinical studies of TJ210 in patients with solid tumors.

John Flickinger*, Jagmohan Singh, Yanki Yarman, Robert Carlson, Scott Waldman, Adam Snook, Thomas Jefferson University, Philadelphia, PA, USA

Background  The Gram-positive bacterium Listeria monocytogenes (Lm) is a promising vector for cancer immunotherapy due to its ability to directly infect antigen-presenting cells, induce potent CD8+ T-cell immunity, and remodel immuno-suppressive tumor microenvironments. Recent clinical trials have demonstrated safety and immunogenicity of Lm-based cancer vaccines in lung, cervical, pancreatic, and other cancers. In colorectal cancer, the transmembrane receptor guanylyl cyclase C (GUCY2C) is an emerging target for immunotherapy. Here, we examined the immunogenicity of a recombinant strain of Listeria monocytogenes secreting GUCY2C (Lm-GUCY2C). Surprisingly, Lm-GUCY2C vaccination induced...