related to mesenchymal transition in GBM such as NF-kB and CEBPB were accessible from normal to tumor-associated microglia. On the other hand, tissue-associated macrophages exhibited enhanced calcium-regulated NFAT TF accessibility. Tumor-associated IWP and IWR myeloid cells also showed a gain of DGE of apoptosis and a reduction of proliferation-related genes.

Conclusions Our studies demonstrate that in addition to the previous dogma of myeloid mediated immune suppression that contributes to tumor immune escape, epigenomic reprogramming in the brain TIME leads to unexpected activation of transcriptional pathways that can trigger transdifferentiation and cell death of myeloid cells further promoting tumor progression. In summary, we provide an unparalleled epigenomic landscape of glioma-associated myeloid cells that may have translational implications.

Acknowledgements This study in Krishna Bhat's laboratory was supported by the generous philanthropic contributions to The University of Texas (UT) MD Anderson Cancer Center (MDACC) Moon Shots Program™, Marnie Rose Foundation, NIH grants: R21 CA222992 and R01CA225963. This study was partly supported by the UT MDACC start-up research fund to Linghua Wang and CPRIT Single-Core grant RP180684 to Nicholas Navin.

Trial Registration NA

Ethics Approval The brain tumor/tissue samples were collected as per MD Anderson internal review board (IRB)-approved protocol numbers LAB03-0687 and, LAB04-0001. One non-tumor brain tissue sample was collected from a patient undergoing neurosurgery for epilepsy as per Baylor College of Medicine IRB-approved protocol number H-13798. All experiments were compliant with the review board of MD Anderson Cancer Center, USA.

Consent Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0833

834 CRISPR-MEDIATED IN SITU EDITING OF LIVER RESIDENT MACROPHAGES FOR TREATING LIVER CANCERS

Zhutian Zeng*, Wei Liu. *University of Science and Technology of China, Hefei, China*

Background Liver cancer is one of the leading cause of cancer death worldwide with limited treatment options. The liver accommodates the largest population of tissue resident macrophages in the body, namely Kupffer cells. Immune deviation of hepatic immune responses from anti-tumor towards pro-tumor is crucial for cancer progression. This process is closely correlated with the functional polarization of these macrophages. In situ genome editing of liver resident macrophage with intention to shift macrophage function to stimulate anti-tumor immune responses is promising in treating liver cancers.

Methods We have previously shown that Kupffer cells quickly capture and phagocytose circulating bacteria, making bacteria as a potential liver macrophage-specific deliver vector. Taking advantages of the clustered regularly interspaced short palindromic repeats (CRISPR)-Cas9 technology, we have established a bacteria mediated genome editing methods for liver resident macrophages in vivo.

Results We used a non-pathogenic Escherichia coli (E. coli) strain as a deliver vector for the CRISPR-Cas9 plasmids, essentially all liver resident macrophages but neither liver sinusoids endothelial cells nor hepatocytes were shown to taken up the bacteria, indicating the robustness and specificity of E. coli-mediated plasmid delivery. To test the genome editing efficiency, we chose VSIG4, Tim-4 and F4/80 that were highly expressed by Kupffer cells and validated the gene knockout/knockdown effects using intravital imaging. Expression of these receptors by Kupffer cells diminished by more than 90%. Simultaneously editing of multiple genes was also achieved with a slightly decreased efficiency when compared to single gene editing. The acute inflammatory responses and the hepatotoxity caused by bacteria were ameliorated by pre-immunization with the same E. coli strain, and can be further minimized by using a mutant E. coli strain that processed a modified LPS structure, which dramatically decreased the TLR-4 mediated inflammatory signaling and improved the safety of this method. Moreover, we have shown that not only embryonically-derived Kupffer cell but also monocyte-derived liver macrophages could be edited. The applications of this approach in treating primary liver cancers and liver metastasis are under investigation.

Conclusions Taken together, we have established a rapid, efficient and convenient method to achieve in situ genome editing of liver resident macrophages in vivo. By targeting essential genes that instruct macrophage polarization, this method could be used as immunotherapy for liver diseases, including cancers.

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0834

Immune cell types

835 STRUCTURAL DIFFERENCE CAUSED BY MUTATED RESIDUES IS CORRELATED WITH IMMUNOGENICITY OF NEOANTIGENS AND SPECIFICITY OF REACTIVE T CELLS

Tomoyo Shinkawa*, Serina Tokita, Takayuki Kanaseki, Toshihiko Torigoe. *Sapporo Medical University, Sapporo, Japan*

Background Host T-cell response is limited to only a small fraction of nonsynonymous mutations; however, the molecular properties of those immunogenic neoantigens remain elusive.

Methods Here, we interrogated the HLA class I ligandome of a microsatellite instability (MSI)-type cancer cell line using a proteogenomic approach, and found an immunogenic 9-mer neoantigen, AKF9. The AKF9 was a non-anchor type neoantigen that harbored a single amino-acid substitution (Asn > Lys) at position 8, which did not affect the HLA-binding affinity.

Results In order to assess a determinant of the immunogenicity, we prepared a panel of AKF9 variants with substitutions at position 8, and found that CD8+ T-cell responses were biased toward residues with structural difference from the wild-type. Interestingly, a substitution with moderate structural change (Asp) also induced reactive T cells; however, in contrast to the others, induced T cells frequently cross-reacted to the wild type HLA ligand. To validate these findings, we used in silico prediction of accessible surface areas and scored the difference between neoantigens and wild types (ΔASA). Evaluation of reported clinical datasets demonstrated that patient T-