Poster # 697

Preclinical characterization of AB154, a humanized α-TIGIT antibody, for use in combination therapies

Anderson AE, Udyavar A, Becker A, Seitz L, Singh H, Zhao X, Walker NPC, Walters MJ, Tan JBL

Arcus Biosciences, Inc.; 3928 Point Eden Way, Hayward, CA 94545

AB154 Binding to Human TIGIT Blocks Interaction with CD155

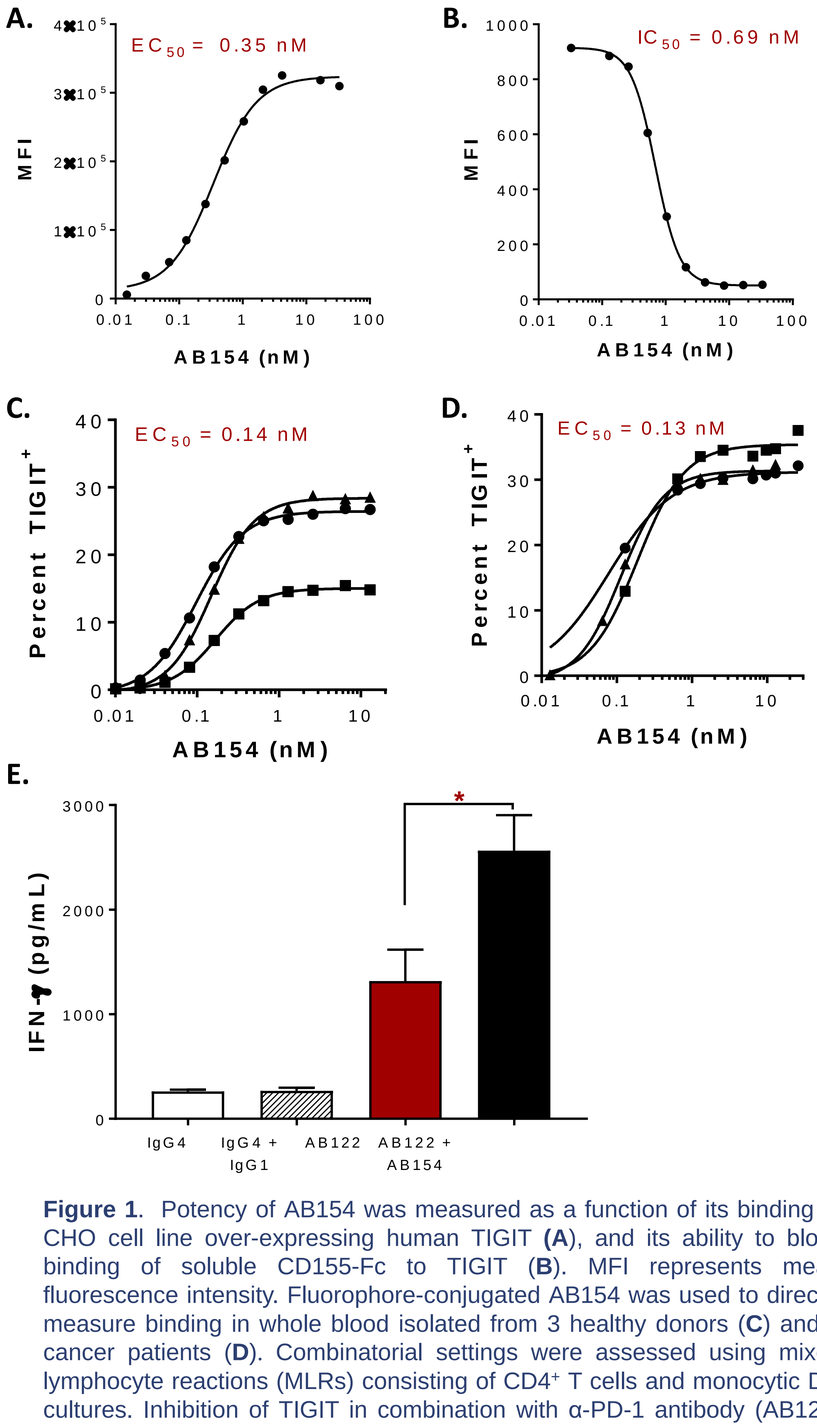


Figure 1. Potency of AB154 was measured as a function of its binding to CHO cell line over-expressing human TIGIT **(A)**, and its ability to block binding of soluble CD155-Fc to TIGIT (**B**). MFI represents mean fluorescence intensity. Fluorophore-conjugated AB154 was used to directly measure binding in whole blood isolated from 3 healthy donors (**C**) and 3 cancer patients (**D**). Combinatorial settings were assessed using mixed lymphocyte reactions (MLRs) consisting of $CD4^+$ T cells and monocytic DC cultures. Inhibition of TIGIT in combination with α-PD-1 antibody (AB122) resulted in increased IFN-γ production relative to monotherapy (**E**). *p ≤ 0.05. Predicted Human Pharmacokinetic Parameters of AB154

Co-expression of PD-1 and TIGIT in Multiple Tumor Types

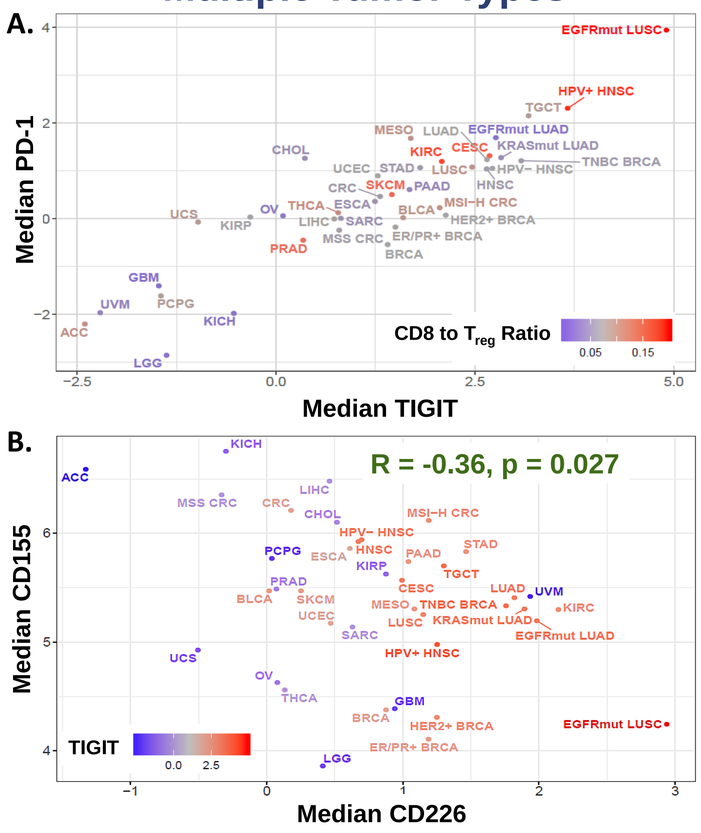


Figure 2. Median TIGIT and PD-1 expression derived from The Cancer Genome Atlas (TCGA) database is shown (**A**). Red indicates high CD8-to-T_{reg} ratio and blue indicates low CD8-to-T_{reg} ratio. Axis numbers indicate log2 transformed expression of counts per million. (**B**) CD226 negatively correlates with CD155. TIGIT expression in each tumor type is shown as a low (blue) to high (red) gradient. Distribution of TIGIT and PD-1 in T_{reg} and $CD8^+$ T cells isolated from lung (black), colorectal (red), and renal (blue) tumors are shown (**C**). TIGIT mean fluorescence intensity (MFI) in each subset is shown in (**D**).

Receptor Occupancy Assay to Measure TIGIT Engagement by AB154

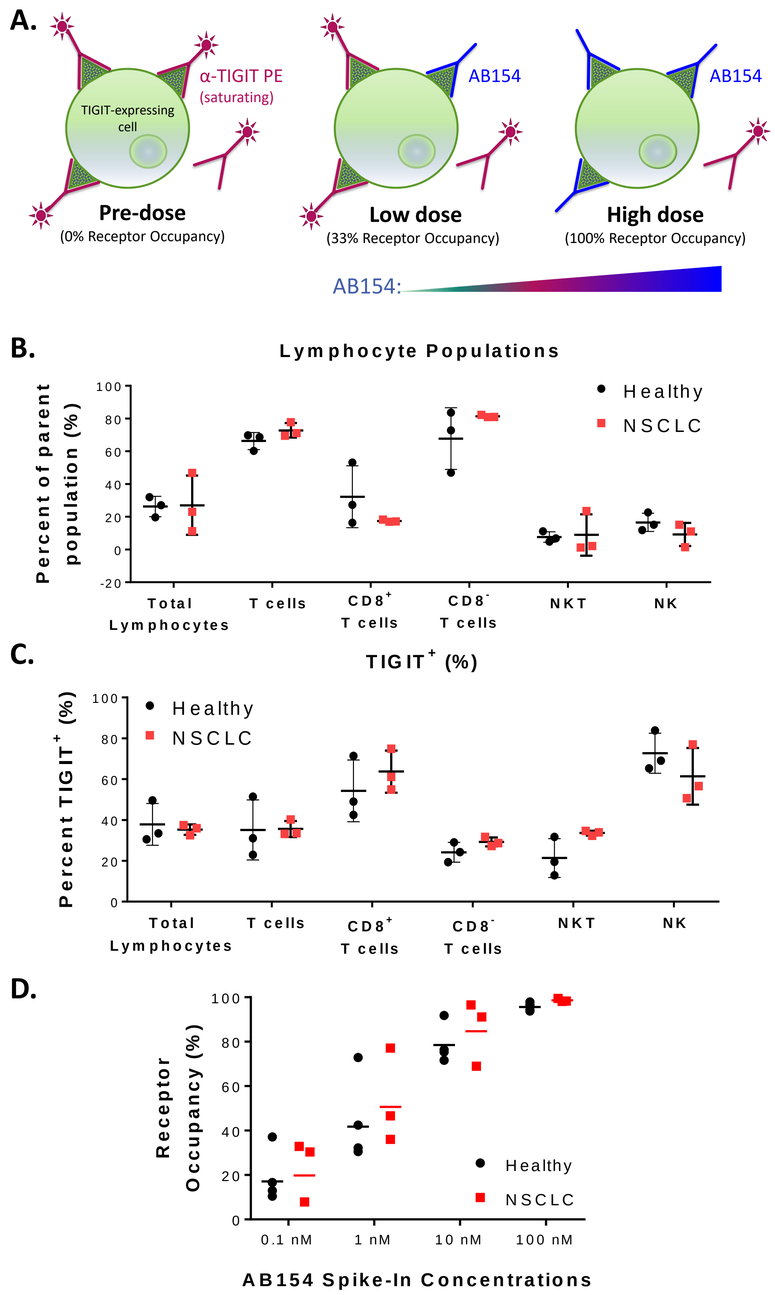
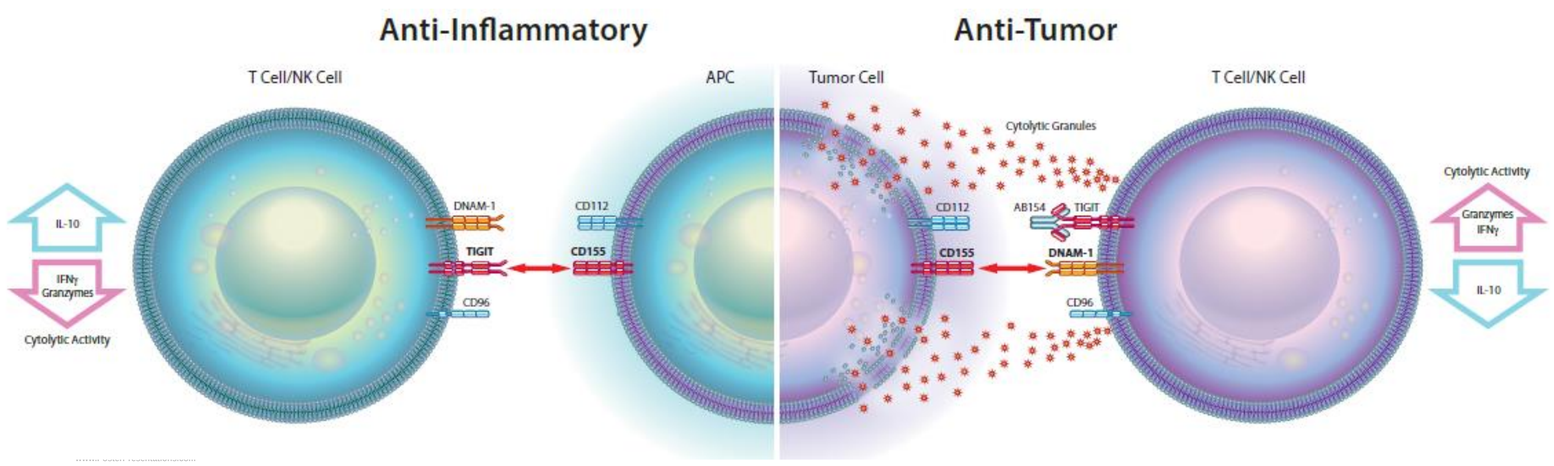


Figure 3. Receptor occupancy was determined using saturating levels (>EC_{90}) of a commercially-available α-TIGIT antibody that binds competitively with AB154 (**A**). Therefore, the apparent IC_{50}, as measured in this assay, is higher than the binding affinity of AB154 shown in Figure 1. Lymphocyte distribution (**B**), amount of TIGIT expressed (**C**) and receptor occupancy (**D**) were comparable between cancer patients and healthy donor blood samples.



Conclusion

- AB154 is a humanized α-TIGIT antagonistic antibody that blocks TIGIT/CD155 interactions at potencies < 1 nM
- Combination of AB154 with α-PD-1 (AB122) antibodies significantly increased IFN-γ secretion relative to anti-PD-1 alone
- TIGIT and PD-1 expression are correlated in many tumor types and are often co-expressed on tumor infiltrating lymphocytes (TILs).
- A robust flow cytometry based assay has been developed to monitor TIGIT receptor occupancy in clinical samples
- AB154 is currently undergoing clinical evaluation in a dose escalation study, alone and in combination with AB122