Response to the reviewers' comments

We thank the editor and reviewers for considering our study and we appreciate the time and care taken to provide us with valuable suggestions to improve the manuscript. We have addressed the specific concerns of the reviewers as indicated below and have revised our manuscript accordingly. We hope that our revised paper now meets the criteria for publication in *Antibodies*.

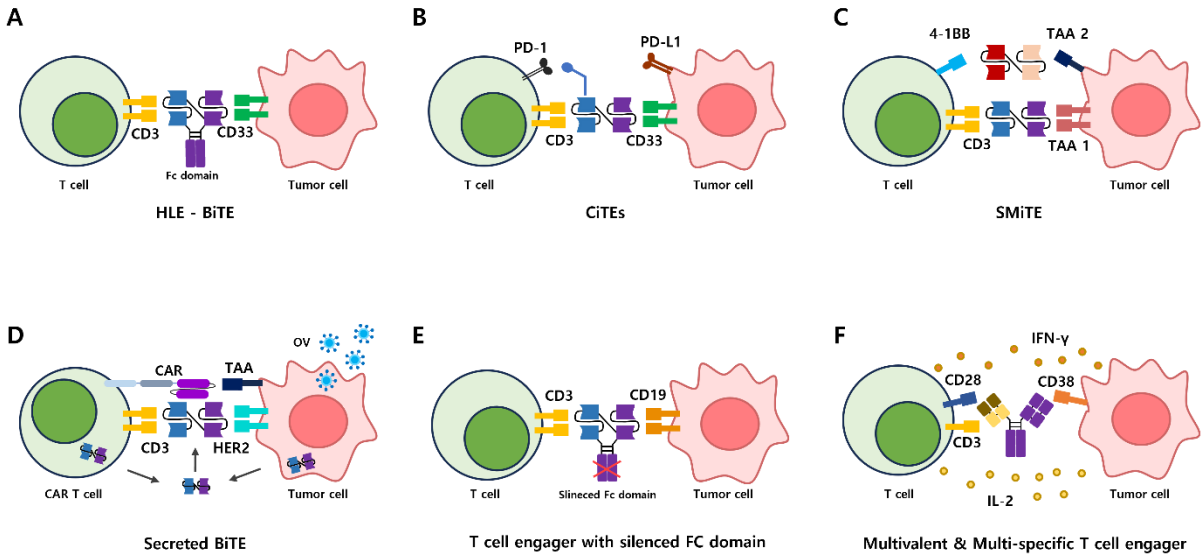
Reviewer 2

This manuscript is well-written and provides a thorough overview of ICEs, including their classifications, mechanisms of action, and emerging research trends. However, it can be further improved by addressing the following concerns:

1. Figure 3 - Triple-Specific TCEs:

The depiction of triple-specific TCEs targeting CD3, CD28, and CD38 in the treatment of myeloma is inaccurate. While activated T cells do express CD38, the design of these TCEs aims to bring T cells into proximity with myeloma cells, which express CD38. Please revise the figure to reflect this mechanism accurately. For reference, see the explanation provided here: Cancer.gov - Anti-CD38-CD28xCD3 Tri-Specific Monoclonal Antibody SAR442257.

→ We appreciate the reviewer's suggestions. we have modified Figure 3 as shown below.



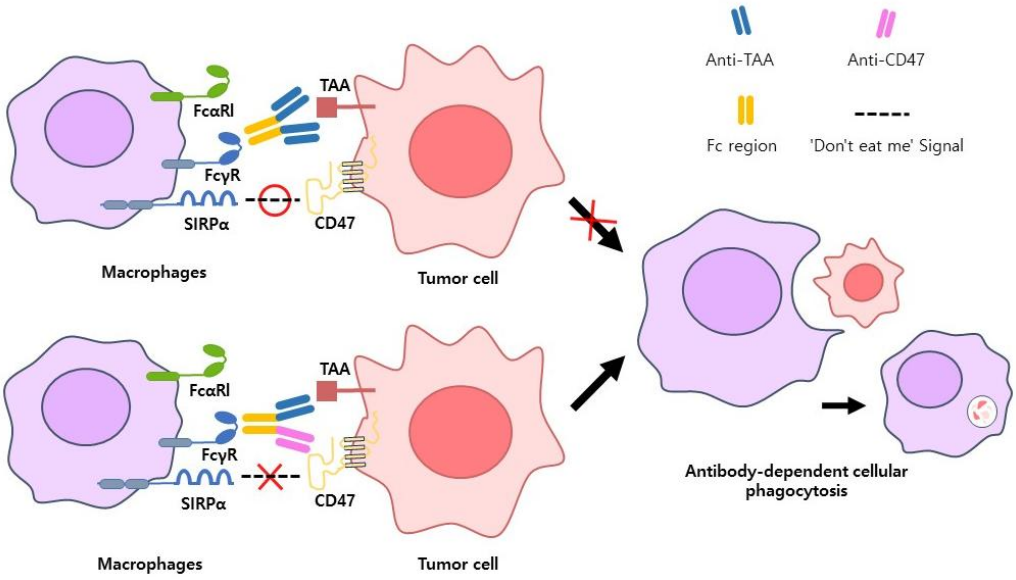
(F) Multispecific and Multivalent T-cell Engagers: These engage multiple target antigens (CD38, TAA) and T-cell markers (CD3, CD28), inducing stronger and more comprehensive immune responses. This process triggers the secretion of IFN-γ and IL-2, boosting T cell activation and cytotoxicity.

2. Figure 8 - Diagram Clarifications:

• In the upper right panel, consider adding legends or annotations to clarify that the blue antibody recognizes the tumor-associated antigen (TAA).

• In the lower left panel, distinguish the roles of each component for clarity: the red part of the scFv recognizes the TAA, the blue scFv targets CD47, and the Fc region (use a distinct color) binds to Fc receptors on macrophages. This will enhance reader understanding of the mechanism.

→ In accordance with your suggestion, we have replaced figure 8 as shown below.


Anti-TAA
Anti-CD47
Fc region
'Don't eat me' Signal
TAA
FcαRI
FcγR
SIRPα
CD47
Macrophages
Tumor cell
TAA
FcαRI
FcγR
SIRPα
CD47
Macrophages
Tumor cell
Antibody-dependent cellular phagocytosis