

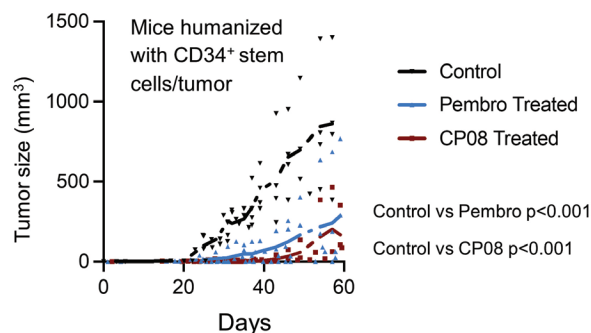


Figure 1.

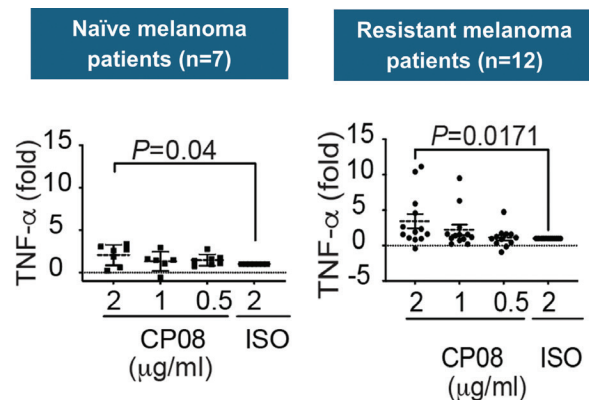


Figure 2.

Targeting Resistance: A Novel CEACAM1 Antibody to Address Immunotherapy Resistance Upstream of PD-1/PD-L1



Richard Blumberg, MD

Vice-Chair for Research, Department of Medicine;
Jerry S. Trier, MD, Endowed Chair in Gastroenterology, Brigham and Women's Hospital;
Professor of Medicine, Harvard Medical School
rblumberg@bwh.harvard.edu



While checkpoint inhibitors have transformed cancer treatment, resistance to PD-1/PD-L1 blockade remains a critical unmet need; up to 60% of patients either fail to respond or relapse after initial benefit. These treatment-resistant cancers often exploit alternative immunosuppressive pathways to evade immune detection and sustain tumor progression.

To address this challenge, we developed CP08, a high-affinity, humanized monoclonal antibody engineered to selectively bind the GFCC' interface of CEACAM1. This structural domain is essential for both homophilic (CEACAM1–CEACAM1) and heterophilic (CEACAM1–TIM-3) interactions, which are implicated in immune dysfunction and tumor invasion. By targeting this interface, CP08 blocks a previously untargeted axis of immunosuppression within the tumor microenvironment.

Preclinical studies show that CP08 restores immune surveillance and reactivates innate and adaptive immune responses in models of treatment resistance. It enhances cytokine production in patient-derived immune cells, promotes the activity of key immune cell populations such as memory-progenitor and progenitors of exhausted CD8 T cells critical to immunotherapy responses, and inhibits tumor aggressiveness. Notably, CP08 demonstrates potent monotherapy activity across several solid tumor models. Furthermore, it shows a favorable safety profile: no toxicity has been observed at clinically relevant doses in humanized mouse models.

CP08 is ready for IND-enabling toxicology studies for the treatment of melanoma, pancreatic ductal adenocarcinoma, colorectal and other solid tumors. Given the pre-clinical data package assembled, within a year, CP08 will be ready for first-in-human studies in solid tumors.

CP08 offers the potential to extend the reach of immunotherapy to patients who currently lack effective options, positioning it as a differentiated therapeutic in a high-value segment of the oncology market. This platform offers the potential to transform treatment of cancers resistant to checkpoint inhibitors. We are seeking partners to help bring this technology to the clinic.