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(54) Title: EGFR x CD28 MULTISPECIFIC ANTIBODIES

(57) Abstract: The present invention provides multispecific antibodies that bind to EGFR and CD28 (EGFRxCD28) as well as anti-EGFR antibodies. Such antibodies may be combined with a further therapeutic agent such as an anti-PD1 antibody. Methods for treating cancers (e.g., EGFR-expressing cancer) by administering the antibodies (e.g., and combinations thereof with anti-PD1) are also provided. The EGFRxCD28 antibodies of the present invention embody a tumor-targeted immunotherapeutic modality combined with PD-1 inhibition. These bispecific antibodies bind a tumor-specific antigen (TSA) (EGFR) with one arm and the co-stimulatory receptor, CD28, on T-cells with the other arm. Combination therapy with PD-1 inhibitors specifically potentiated intra-tumoral T cell activation, promoting an effector memory-like T cell phenotype without systemic cytokine secretion in a variety of syngeneic and human tumor xenograft models. Combining this class of CD28-co-stimulatory bispecific antibodies with the clinically validated anti-PD-1 treatment provides a well-tolerated antibody therapy with markedly enhanced anti-tumor efficacy.



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