

IMMUNE ACTIVATING MULTISPECIFIC ANTIGEN-BINDING MOLECULES AND USES THEREOF

Abstract

An antigen-binding molecule comprising a first antigen-binding moiety that is capable of binding to CD3 and CD137 (4-1BB), but does not bind to CD3 and CD137 at the same time (i.e. dual-binding to CD3 and CD137 but not simultaneously); and a second antigen-binding moiety capable of binding to a molecule specifically expressed in a cancer tissue, specifically Glypican-3 (GPC3) is provided. Due to the dual binding to CD3 and CD137 but not simultaneously and with fine-tuned binding kinetics, and the binding to GPC3, the multispecific antigen-binding molecule express strong cytotoxic activity for cancer cells with reduced adverse effects. Further, by adapting antibody engineering technologies and a molecular format design (including charged mutations in the framework region and/or constant region, VH/VL exchanged, and Fc region selection), the multispecific antigen-binding molecule with favorable stability, manufacturability/produceability and structural homogeneity is provided.

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