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(54) Title: ANTIBODIES COMPRISING MODIFIED HEAVY CONSTANT REGIONS

(57) Abstract: Provided herein are heavy chain constant regions (referred to as "modified heavy chain constant regions"), or functionally equivalent fragments thereof, that enhance biological properties of antibodies relative to the same antibodies in unmodified form. An exemplary modified heavy chain constant region includes an IgG2 hinge and three constant domains (i.e., CH1, CH2, and CH3 domains), wherein one or more of the constant region domains are of a non-IgG2 isotype (e.g., IgG1, IgG3 or IgG4). The heavy chain constant region may comprise wildtype human IgG domain sequences, or variants of these sequences. Also provided herein are methods for enhancing certain biological properties of antibodies that comprise a non-IgG2 hinge, such as internalization, agonism and antagonism, wherein the method comprises replacing the non-IgG2 hinge of the antibody with an IgG2 hinge.



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