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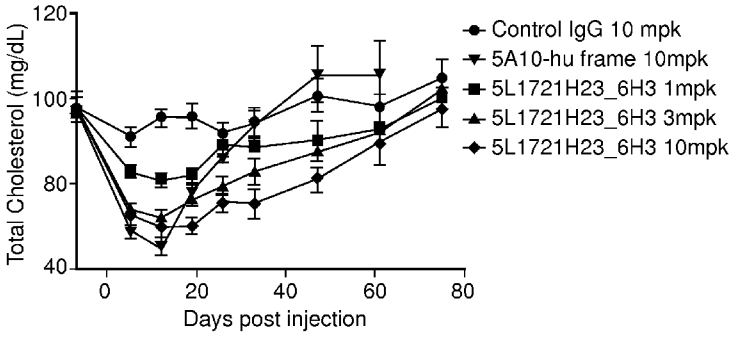
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[Continued on next page]

(54) Title: ANTIBODIES WITH pH DEPENDENT ANTIGEN BINDING

FIGURE 7B



(57) Abstract: The present invention relates to antibodies with pH dependent binding to its antigen such that the affinity for antigen binding at physiological pH (i.e., pH 7.4) is greater than at endosomal pH (i.e., pH 6.0 or 5.5). In other words, the K_D or k_{off} ratio at pH 5.5/ pH 7.4 or at pH 6.0/ pH 7.4 is more than, or ranges between, 2, 3, 4, 8, 10, 16, 20, 30, 40, or 100 or more. Such pH dependent antibodies preferentially dissociate from the antigen in the endosome. This can increase antibody half life, as compared to antibodies with equivalent K_DS at pH 7.4 but with no pH dependent binding, when the antigen is one that undergoes antigen-mediated clearance (e.g., PCSK9). Antibodies with pH dependent binding can decrease total antigen half life when the antigen undergoes reduced clearance when bound to antibody (e.g., IL6). Antibodies with pH dependent binding can also prolong the decrease in antigen which is not antibody-bound. This can be important when antagonizing a target antigen typically present at high levels (e.g., IgE, DKK1, C5 and SOST). In addition, such antibodies can increase antigen half life when the antigen is a receptor and the receptor has increased clearance when bound to antibody (e.g, GMCSF receptor).

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