Acne inversa, also known as hidradenitis suppurativa (HS), is a neglected, prevalent, chronic, painful, recurrent abscesses that drain malodorous fluid and lead to disfiguring scars that can stigmatize, and debilitating inflammatory skin disease. HS patients suffer from deep, mucous membrane pemphigoid (MMP). BP-IgG targeting the non-collagenous NC16A (NC16A) domain of BP180 is thought to be a pathogenic antibody that induces skin fragility in mice and the depletion of BP180 in keratinocytes. In this study, stimulation with mAbs against NC16A in combination with Fc-binding proteins, such as protein G and the anti-IgG Fc antibody, was found to enhance BP180 depletion. Although mAbs against the C-terminus of BP180 show pathogenicity neither in vivo nor in vitro, the treatment of mAbs targeting the C-terminus with Fc-binding proteins, such as protein G and the anti-IgG Fc antibody, was found to clearly induce skin fragility in mice and BP180 depletion in keratinocytes. The BP180 depletion was observed under stimulation with mAbs and Fc-binding proteins and the anti-IgG Fc antibody, suggesting that Fc-binding proteins may enhance the pathogenicity of autoantibodies in pemphigoid diseases.