GS3-2 Enhancement of ADCC activity by tandem Fc multimerization

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Monoclonal antibodies have increasingly been used as therapeutics since the first antibody therapeutic appeared in 1986. Antibodies have various functions such as neutralizing, antagonistic and cytotoxic effects. Antibody-dependent cellular cytotoxicity(ADCC) is known as one of the main mechanisms of rituximab and trastuzumab. Many kinds of antibody modifications have been examined and indicated that Fc receptors are important in ADCC activity. Those experiments also demonstrated that the affinity differences between antibodies and Fc receptors cause the variations of ADCC activity. Affinity is the strength of the binding to a single site and is distinguished from avidity which is the overall strength of the binding to multivalent sites. As multivalent binding can significantly increase avidity, we generated tandemly repeated Fc anti-CD20 antibodies and evaluated their binding activities to CD20 and Fc receptors and then ADCC activity. As a result, Fc multimerization decreased the CD20 binding but significantly augmented the binding to Fc receptors, thereby resulting in enhanced ADCC activity. As the binding of tandemly repeated antibodies to all the low-affinity Fc receptors were reinforced, it is expected that Fc multimerization will achieve the improvement of other functions such as phagocytosis and half-life.