Enhanced site specific conjugation yield of human serum albumin to GLP-1 via faster Click Chemistry

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A GLP-1 is a kind of therapeutic peptide hormone. However, GLP-1 has a limitation, rapidly degrad in the human body due to its own short amino acid sequence. But, By conjugating a protein, the half-life of GLP-1 could be dramatically increased. human serum albumin(HSA) has been used to extend the serum half-life of therapeutic proteins owing to its exceptionally long serum half-life via the neonatal Fc receptor (FcRn)-mediated recycling mechanism. In this study, it was also expected to increase the half-life by conjugating this HSA to GLP-1.

To achieve a homogeneous product and maintaining the GLP-1 effect as much as possible, it is necessary to proceed with site-specific conjugation. In a previous research, GLP-1 and HSA conjugation were performed using the SPAAC reaction, which is one of Click-Chemistry, and a HSA-GLP-1 conjugate was obtained. However, in the SPAAC method, the conjugation yield is too low. To overcome this limitation, the GLP-1 HSA conjugation was performed using other Click-Chemistry reaction. For this reaction, a non-natural amino acid (NNAA) having an appropriate reactive group was introduced into GLP-1 through DNA seq mutation and amber codon suppression.