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Antibody production with site-specific non-natural amino acid incorporation for generation of antibody drug conjugates

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ANTIBODY PRODUCTION WITH SITE-SPECIFIC NON-NATURAL AMINO ACID INCORPORATION FOR GENERATION OF ANTIBODY DRUG CONJUGATES

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Ambrx's mammalian expression platform (EuCODE) enables site-specific incorporation of non-natural amino acids into antibodies. This EuCODE technology provides a means for stable payload linkages at defined sites and with a defined DAR of 2 for antibody drug conjugate (ADC) generation. While the ability to control the DAR and payload site can provide an advantage to an ADC, the incorporation of the non-natural amino acid into the antibody heavy chain introduces a unique challenge for antibody production.

To achieve high production of monoclonal antibodies (mAbs) containing non-natural amino acids, we engineered a CHO-K1 cell line which stably contains Ambrx's patented tRNA and RNA synthetase system components. Then this engineered CHO-K1 cell line was transfected with the gene of interest to generate stable cell lines producing mAbs containing Ambrx's non-natural amino acid at selected sites. Methodology for vector design (single vector containing both the heavy chain and light chain versus two separate vectors) was investigated for high producing clone generation.

In order to achieve manufacturability of the technology, a fed batch process was developed to achieve high titer. Basal media, feed, and feeding strategy of feed supplements and the non-natural amino acid were studied. Furthermore, we investigated how media components affect the efficiency of non-natural amino acid incorporation in mAbs.