

In one aspect, the present disclosure provides a method for producing an antibody of the human IgG1 subclass by cultivating a CHO cell that has been transfected with one or more expression cassettes comprising the nucleic acids encoding the heavy and the light chains of the antibody,

5 wherein the nucleic acids encoding the antibody heavy and light chains are codon usage optimized with the codon usage of human cells and/or the codon usage of CHO cells,

wherein in the part of the nucleic acid encoding the heavy chain variable domain at least one non-paired donor splice site is removed,

10 wherein the removal of the non-paired splice sites is by introducing an amino acid silent mutation in the nucleotide sequence NGGTA(G)AG (SEQ ID NO: 01) in the codon NGG or the codon GGT or the codon GTA(G),

wherein the nucleic acids encoding the heavy chain of the antibody are genomically organized DNA.

15 In another aspect, the present disclosure provides a method for producing an antibody of the human IgG1 subclass by cultivating a CHO cell comprising one or more nucleic acids encoding the heavy and the light chains of the antibody,

wherein in the nucleic acid encoding the heavy chain variable domain non-paired donor splice sites are removed by introducing amino acid sequence silent nucleotide
20 changes in the non-paired donor splice site consensus sequence NGGTA(G)AG (SEQ ID NO: 01) in the codon NGG or the codon GGT or the codon GTA(G),

wherein non-paired donor splice sites according to the sequence of SEQ ID NO: 01 are not removed in the nucleic acid encoding the heavy chain constant region,

25 wherein the one or more nucleic acids encoding the antibody heavy chain are genomically organized DNA.

In one example the antibody is an antibody of the human IgG1 subclass. In one example the antibody is a humanized antibody of the human IgG1 subclass. In one example the constant region of the antibody comprises mutations suitable to induce heterodimerization or modify Fc-receptor binding.

The present disclosure provides the use of the removal of non-paired donor splice sites only in a part of a human or hamster codon-usage optimized nucleic acid sequence encoding an antibody for reducing mis-splicing or/and increasing antibody expression yield when said nucleic acid is used to produce the antibody in CHO cells, whereby the part is the part that encodes the heavy chain variable domain. In another aspect, the present disclosure provides the use of the removal of non-paired donor splice sites in a part of a human or hamster codon-usage optimized nucleic acid sequence encoding an antibody, whereby the part is the part that encodes the heavy chain variable domain, for reducing mis-splicing or/and increasing antibody expression yield when said nucleic acid is used to produce the antibody in CHO cells, wherein the removal of the non-paired splice sites is by introducing an amino acid silent mutation in the nucleotide sequence NGGTA(G)AG (SEQ ID NO: 01) in the codon NGG or the codon GGT or the codon GTA(G), wherein the one or more nucleic acids encoding the antibody heavy chain are genomically organized DNA.