CLAIMS

1. An isolated eukaryotic host cell for recombinant production of a product of interest, wherein the effect of the expression product of gene C12orf35 is impaired in said cell because functional expression of gene C12orf35 is reduced or eliminated by gene knock-out, gene mutation, gene deletion, gene silencing or a combination of any of the foregoing, wherein the C12orf35 gene is a gene encoding a protein that shares at least 70% identity with one or more of the amino acid sequences shown in SEQ ID NO: 1 to 7 or the protein encoded by SEQ ID NO: 8, and wherein the cell comprises at least one heterologous polynucleotide encoding the product of interest, wherein the product of interest is a polypeptide.

2. The isolated eukaryotic host cell according to claim 1, wherein the eukaryotic host cell has one or more of the following characteristics:

a) the C12orf35 gene comprises as gene mutation one or more mutations in the C12orf35 gene which provide a non- or less functional expression product;
b) at least one or all copies of gene C12orf35 is deleted or functionally inactivated in the genome of the eukaryotic cell;
c) a portion of a chromosome is deleted, wherein the deleted portion comprises gene C12orf35.

3. The isolated eukaryotic host cell according to claim 1 or 2, wherein the eukaryotic cell has one or more of the following characteristics:

a) the eukaryotic cell is a metazoan cell;
b) the eukaryotic cell is a vertebrate cell;
c) the eukaryotic cell is a mammalian cell;
d) the eukaryotic cell is a rodent cell;
e) the eukaryotic cell is a hamster cell;
f) the eukaryotic cell is a CHO cell;
g) the eukaryotic cell is provided as cell clone or cell line;
h) the eukaryotic cell expresses endogenously DHFR and a folate receptor.

4. The isolated eukaryotic host cell according to claim 2, wherein a portion of a chromosome is deleted, wherein the deleted portion comprises gene C12orf35, and wherein:

a) the eukaryotic cell is a hamster cell and at least a portion of the telomeric region of chromosome 8 is deleted, wherein said deleted portion comprises gene C12orf35; or
b) the eukaryotic cell is a mouse cell and at least a portion of the telomeric region of chromosome 6 is deleted, wherein said deleted portion comprises gene C12orf35.

5. The isolated eukaryotic host cell according to claim 4, wherein the isolated eukaryotic cell has one or more of the following characteristics:

a) the deleted telomeric region comprises gene C12orf35 and comprises one or more genes selected from the group consisting of Bicd1, Amn1, methyltransferase-like protein 20, Dennd5b, FAM60A, Caprin2, Ipo8 and RPS4Y2;
b) the deletion is induced by chromosome breakage and the breakpoint is located centromeric of the Ipo8 gene;
c) the deletion is induced by chromosome breakage and the breakpoint is located centromeric of the Ipo8 gene within the Tmtc1 gene;
d) at least a portion of the telomeric region is deleted in both chromosomes of the respective chromosome pair, wherein the deleted portions comprise gene C12orf35.

6. The isolated eukaryotic host cell according to one or more of claims 1 to 5, wherein the C12orf35 gene is a gene encoding a protein that shares at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identity with one or more of the amino acid sequences shown in SEQ ID NO: 1 to 7 or the protein encoded by SEQ ID NO: 8, and/or wherein additionally the effect of protein FAM60A is impaired in said cell, wherein the FAM60A protein shares at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identity with one or more of the amino acid sequences shown in SEQ ID NO: 11 to 18.

7. The isolated eukaryotic host cell according to one or more of claims 1 to 6, wherein:

a) the functional expression of gene C12orf35 is reduced or eliminated in said cell and wherein the reduction or elimination results in an increase in the volumetric production of a recombinant product of interest compared to a corresponding cell wherein the functional expression of gene C12orf35 is not reduced or eliminated; and/or
b) the genome of the eukaryotic cell is altered to impair the effect of the expression product of gene C12orf35 in said cell.

8. The isolated eukaryotic host cell according to one or more of claim 1 to 7, wherein the heterologous polynucleotide encoding the product of interest is comprised in an expression cassette that is integrated into the genome of the eukaryotic cell.

9. The isolated eukaryotic host cell according to one or more of claims 1 to 8, having one or more of the following characteristics:

a) the eukaryotic cell comprises integrated into its genome at least one heterologous polynucleotide encoding the product of interest and at least one heterologous

polynucleotide encoding a selectable marker or reporter polypeptide and wherein said heterologous polynucleotides are located on the same or different expression vectors;

b) the eukaryotic cell comprises a heterologous polynucleotide encoding a folate receptor as selectable marker and/or comprises a heterologous polynucleotide encoding a dihydrofolate reductase (DHFR) as selectable marker;

c) the eukaryotic cell secretes said polypeptide of interest into the cell culture medium; and/or

d) the product of interest is a polypeptide selected from a therapeutic polypeptide and a diagnostic polypeptide.

10. A method for selecting a host cell which recombinantly expresses a product of interest, wherein the product of interest is a polypeptide, comprising

(a) providing of eukaryotic cells according to one or more of claims 1 to 9 as host cells; and

(b) selecting one or more host cells expressing the product of interest.

11. The method according to claim 10, having one or more of the following characteristics

a) said host cells provided in stage (a) are mammalian cells;

b) said host cells provided in stage (a) additionally comprise at least one heterologous polynucleotide encoding a selectable marker and stage (b) comprises culturing said plurality of host cells under conditions selective for the selectable marker;

c) said host cells provided in stage (a) comprise at least two heterologous polynucleotides each encoding a selectable marker wherein the first selectable marker is a folate receptor and wherein the second selectable marker is a DHFR and wherein stage (b) comprises culturing said plurality of host cells in a selective culture medium which comprises folate in a limiting concentration and a DHFR inhibitor

d) heterologous polynucleotides are introduced into the eukaryotic cells by transfecting one or more expression vectors;

e) stage (b) comprises multiple selection steps;

f) stage (b) comprises performing a flow cytometry based selection;

g) the selected host cells recombinantly express an immunoglobulin molecule.

12. A method for recombinantly producing a product of interest, comprising utilizing a eukaryotic host cell according to one or more of claims 1 to 9 as host cell for recombinant expression of the product of interest and comprising

(a) culturing the host cells under conditions that allow for the expression of the product of interest;

(b) isolating the product of interest from the cell culture medium and/or from said host cells; and
(c) optionally processing the isolated product of interest.

13. A method for producing a eukaryotic cell according to one or more of claims 1 to 9, comprising impairing the effect of the expression product of an gene C12orf35 in said cell, wherein the C12orf35 gene is a gene encoding a protein that shares at least 70% identity with one or more of the amino acid sequences shown in SEQ ID NO: 1 to 7 or the protein encoded by SEQ ID NO: 8.

14. A method comprising analyzing eukaryotic cells for their suitability as host cells for recombinant expression of a product of interest by analyzing directly or indirectly whether the effect of the expression product of endogenous gene C12orf35 is impaired in said cells, wherein the C12orf35 gene is a gene encoding a protein that shares at least 70% homology or identity with one or more of the amino acid sequences shown in SEQ ID NO: 1 to 7 or the protein encoded by SEQ ID NO: 8,
wherein the method further comprises selecting at least one cell wherein the functional expression of C12orf35 is impaired because functional expression of gene C12orf35 is reduced or eliminated by gene knock-out, gene mutation, gene deletion, gene silencing or a combination of any the foregoing, for recombinant expression of the product of interest.

15. The method according to claim 14, comprising one or more of the following features:

a) directly analyzing comprises analyzing whether the functional expression of gene C12orf35 is reduced or eliminated in said cells;
b) prior to analysis, the eukaryotic cells are treated with an agent that induces chromosome breakage and wherein the analysis comprises analyzing whether treatment with said agent resulted in a deletion of a portion of a chromosome which includes gene C12orf35;
c) prior to analysis, the eukaryotic cells are transfected with a heterologous polynucleotide encoding a product of interest and a heterologous polynucleotide encoding a selectable marker, and wherein prior to analysis at least one selection step is performed to identify successfully transfected host cells;
d) the method comprising additionally analyzing directly or indirectly whether the effect of FAM60A is impaired in said cells, wherein the FAM60A protein shares at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identity with one or more of the amino acid sequences shown in SEQ ID NO: 11 to 18;
e) the eukaryotic cells are hamster cells and the method comprises analyzing whether expression of one or more genes located in the telomeric region of chromosome 8 and being selected from the group consisting of the Tmtc1 gene and genes located telomeric of the Tmtc1 gene is eliminated or reduced thereby

analyzing whether the expression of gene C12orf35 is reduced or eliminated in said cells;

f) a plurality of cell clones is analyzed for discriminating between stable and unstable and/or between high and low producing cell clones and wherein one or more cell clones are selected as production clone wherein the expression of gene C12orf35 and optionally FAM60A is reduced or eliminated, wherein the FAM60A protein shares at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identity with one or more of the amino acid sequences shown in SEQ ID NO: 11 to 18.