CLAIMS

1. An isolated eukaryotic host cell for recombinant production of a product of interest, wherein the genome of the eukaryotic cell is altered so that the effect of protein FAM60A is impaired in said cell because functional expression of gene FAM60A is reduced or eliminated by gene knock-out, gene mutation, gene deletion, gene silencing or a combination of any of the foregoing, wherein the FAM60A protein shares at least 75% identity to one or more of the amino acid sequences shown in SEQ ID NO: 1 to 8, and wherein said cell comprises integrated into its genome at least one heterologous polynucleotide encoding the product of interest comprised in an expression cassette, wherein the product of interest is a polypeptide.

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

   a) the FAM60A gene comprises as gene mutation one or more mutations in the FAM60A gene which provide a non- or less functional expression product;
   b) at least one copy of gene FAM60A 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 FAM60A.

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 FAM60A, 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 FAM60A;

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 FAM60A,

and wherein optionally, the isolated eukaryotic host cell has one or more of the following characteristics:

i) the deleted telomeric region comprises gene FAM60A and comprises one or more genes selected from Caprin2 and Ipo8;
ii) the deletion is induced by chromosome breakage and the breakpoint is located centromeric of the Ipo8 gene;
iii) the deletion is induced by chromosome breakage and the breakpoint is located centromeric of the Ipo8 gene within the Tmtc1 gene;
iv) at least a portion of the telomeric region is deleted in both chromosomes of the respective chromosome pair, wherein the deleted portions comprise gene FAM60A.

5. The isolated eukaryotic host cell according to one or more of claims 1 to 8, wherein the endogenous 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 to one or more of the amino acid sequences shown in SEQ ID NO: 1 to 8, and/or wherein in said cell additionally the effect of the expression product of gene C12orf35 is impaired, wherein the C12orf35 gene is a gene encoding a protein that shares at least 75%, 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% homology or identity to one or more of the amino acid sequences shown in SEQ ID NO: 10 to 16 or the protein encoded by SEQ ID NO: 17.

6. The isolated eukaryotic host cell according to one or more of claims 1 to 5, wherein the eukaryotic cell comprises stably 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.

7. The isolated eukaryotic host cell according to one or more of claims 1 to 6, having one or more of the following characteristics:

   a) the eukaryotic cell secretes said polypeptide of interest into the cell culture medium; and/or
   b) the product of interest is a polypeptide selected from a therapeutic polypeptide and a diagnostic polypeptide.

8. The isolated eukaryotic host cell according to one or more of claims 1 to 12, originating from a population of respective cells, wherein on average at least 40%, preferably at least 50% of the cells originating from said population of respective cells do not lose more than 30%, preferably 25%, of their expression titer (volumetric) over a time period of 8 weeks, preferably 10 weeks, more preferably over a time period of 12 weeks.

9. 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 eukaryotic cells according to one or more of claims 1 to 8 as host cells; and
   (b) selecting one or more host cells expressing the product of interest.

10. The method according to claim 9, 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.

11. The method according to claim 9 or 10, having one or more of the following characteristics

a) stage (b) comprises multiple selection steps;

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

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

12. A method for recombinantly producing a product of interest, wherein the product of interest is a polypeptide, comprising utilizing a eukaryotic host cell according to one or more of claims 1 to 8 as host cell for recombinant expression of the product of interest and comprising

(a) culturing the host cells according to one or more of claims 1 to 8 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 host cell according to one or more of claims 1 to 8, comprising altering the genome of an eukaryotic cell to impair the effect of protein FAM60A in said cell and stably transfecting into said cell at least one expression vector comprising a polynucleotide encoding a product of interest comprised in an expression cassette, wherein the product of interest is a polypeptide.

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 FAM60A is impaired in said cells, wherein the FAM60A protein shares at least 75% identity to one or more of the amino acid sequences shown in SEQ ID NO: 1 to 8,

wherein the method further comprises selecting at least one cell wherein the functional expression of FAM60A is impaired because functional expression of gene FAM60A is reduced or eliminated by gene knock-out, gene mutation, gene deletion, gene silencing or a combination of any of 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 FAM60A 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 FAM60A;

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 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 75%, 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 to one or more of the amino acid sequences shown in SEQ ID NO: 10 to 16 or the protein encoded by SEQ ID NO: 17;

e) the 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 functional expression of gene FAM60A is reduced or eliminated in said cells;

f) a plurality of cell clones is analyzed for discriminating between stable and unstable cell clones and wherein one or more cell clones wherein the functional expression of gene FAM60A is reduced or eliminated are selected as production clone;

g) a plurality of cell clones is analyzed for discriminating between stable and unstable and between high and low producing cell clones and wherein one or more cell clones wherein the functional expression of gene FAM60A is reduced or eliminated are selected as production clone.

16. Use of an isolated eukaryotic host cell for recombinantly expressing a product of interest, wherein the genome of the eukaryotic cell is altered so that the effect of protein FAM60A is impaired in said cell because functional expression of gene FAM60A is reduced or eliminated by gene knock-out, gene mutation, gene deletion, gene silencing or a combination of any of the foregoing, wherein the FAM60A protein shares at least 75% identity to one or more of the amino acid sequences shown in SEQ ID NO: 1 to 8 and wherein the product of interest is a polypeptide and the use comprises stably transfecting the eukaryotic cell with an expression vector comprising a polynucleotide encoding the polypeptide of interest.