In one example, there is disclosed a method for the production of a protein of interest in a mammalian producer cell, comprising the process steps a) providing a mammalian producer cell, b) increasing the concentration of at least one miR selected from the group consisting of miR-15, miR-16 and miR-34 in the mammalian producer cell provided in step a) so as to obtain a pro-tein production engineered mammalian producer cell, c) cultivating the protein production engineered mammalian producer cell under conditions suitable for the production of the protein of interest, and d) recovering the protein of interest produced in step c). In another example, there is disclosed a method for the preparation of a protein production engineered mammalian producer cell capable of expressing a protein of interest, comprising the process steps x) providing a mammalian producer cell, y) increasing the concentration of at least one miR selected from the group consisting of miR-15, miR-16 and miR-34 in the mammalian producer cell provided in step x) so as to obtain a protein production engineered mammalian producer cell, z) recovering the protein production engineered mammalian producer cell produced in step y). In yet another aspect, the present invention refers to a protein production engineered mammalian producer cell produced according to anyone of the methods as disclosed herein. In a further example, there is disclosed a protein production engineered mammalian producer cell comprising at least one transgenic nucleic acid sequence encoding at least one miR, which transgenic nucleic acid sequence is transiently or stably incorporated into the genome of that cell under control of at least one regulatory element allowing the over-expression of said at least one miR, wherein the at least one miR is selected from the group consisting of miR-15, miR-16 and miR-34. In yet another example,

there is disclosed a kit for the production of a protein of interest in a mammalian producer cell, comprising at least one mammalian producer cell, at least one vector containing a nucleotide sequence encoding at least one miR under control of at least one regulatory element allowing the over-expression of the at least one miR, wherein the miR is selected from the group consisting of miR-15, miR-16, miR-34 and means for transfecting the at least one cell with the at least one vector.

In one aspect, the present invention refers to a method for the production of a protein of interest in a mammalian producer cell, comprising the process steps a) providing a mammalian producer cell, b) increasing the concentration of one or more miRs selected from the group consisting of miR-15, miR-16, miR-15+miR-34, and miR-16+miR-34 in the mammalian producer cell provided in step a) by transfecting the mammalian producer cell with one or more miRs selected from the group consisting of miR-15, miR-16 , miR-15+miR-34, and miR-16+miR-34 or with at least one vector containing a nucleotide sequence encoding one or more miRs under control of at least one regulatory element allowing the over-expression of the one or more miRs, wherein the one or more miRs is selected from the group consisting of miR-15, miR-16, miR-15+miR-34, and miR-16+miR-34 so as to obtain a protein production engineered mammalian producer cell, c) cultivating the protein production engineered mammalian producer cell under conditions suitable for the production of the protein of interest, and d) recovering the protein of interest produced in step c), wherein the mammalian producer cell is a CHO cell. In another aspect, the present invention refers to a method for the preparation of a protein production engineered mammalian producer cell capable of expressing a protein of interest, comprising the pro-cess steps x) providing a mammalian producer cell, y) increasing the concentration of one or more miRs selected from the group consisting of miR-15, miR-16, miR-15+miR-34, and miR-16+miR-34 in the mammalian

producer cell provided in step x) by transfecting the mammalian producer cell with one or more miRs selected from the group consisting of miR-15, miR-16, miR-15+miR-34, and miR-16+miR-34 or with at least one vector containing a nucleotide sequence encoding one or more miRs under control of at least one regulatory element allowing the over-expression of the one or more miRs, wherein the one or more miRs is/are selected from the group consisting of miR-15, miR-16, miR-15+miR-34, and miR-16+miR-34 so as to obtain a protein production engineered mammalian producer cell, z) recovering the protein production engineered mammalian producer cell produced in step y), wherein the mammalian producer cell is a CHO cell. In yet another aspect, the present invention refers to a protein production engineered mammalian producer cell comprising at least one transgenic nucleic acid sequence encoding one or more miRs, which transgenic nucleic acid sequence is transiently or stably incorporated into the genome of that cell under control of at least one regulatory element allowing the over-expression of said one or more miRs, wherein the one or more miRs is/are selected from the group consisting of miR-15, miR-16, miR-15+miR-34, and miR-16+miR-34, and wherein the mammalian producer cell is a CHO cell. In a further aspect, the present invention refers to a kit for the production of a protein of interest in a mammalian producer cell, comprising at least one mammalian producer cell, at least one vector contain-ing a nucleotide sequence encoding one or more miRs under control of at least one regulatory element allowing the over-expression of the one or more miRs, wherein the one or more miRs is/are selected from the group consisting of miR-15, miR-16, miR-15+miR-34 and miR-16+miR-34, and means for transfecting the at least one mammalian producer cell with the at least one vector, wherein the mammalian producer cell is a CHO cell.

The present invention solves its technical problem by the provision of the teaching of the independent claims.

CLAIMS

1. A method for the production of a protein of interest in a mammalian producer cell, comprising the process steps

a) providing a mammalian producer cell,

b) increasing the concentration of one or more miRs selected from the group consisting of miR-15, miR-16, miR-15+miR-34 and miR-16+miR-34 in the mammalian producer cell provided in step a) by transfecting the mammalian producer cell with one or more miRs selected from the group consisting of miR-15, miR-16, miR-15+miR-34 and miR-16+miR-34 or with at least one vector containing a nucleotide sequence encoding one or more miRs under control of at least one regulatory element allowing the over-expression of the one or more miRs, wherein the one or more miRs is/are selected from the group consisting of miR-15, miR-16, miR-15+miR-34 and miR-16+miR-34 so as to obtain a protein production engineered mammalian producer cell,

c) cultivating the protein production engineered mammalian producer cell under conditions suitable for the production of the protein of interest, and

d) recovering the protein of interest produced in step c),

wherein the mammalian producer cell is a CHO cell.

2. A method for the preparation of a protein production engineered mammalian producer cell capable of expressing a protein of interest, comprising the process steps

x) providing a mammalian producer cell,

y) increasing the concentration of one or more miRs selected from the group consisting of miR-15, miR-16, miR-15+miR-34 and miR-16+miR-34 in the mammalian producer cell provided in step x) by transfecting the mammalian producer cell with one or more miRs selected from the group consisting of miR-15, miR-16, miR-15+miR-34 and miR-16+miR-34 or with at least one vector contain-

ing a nucleotide sequence encoding one or more miRs under control of at least one regulatory element allowing the over-expression of the one or more miRs, wherein the one or more miRs is/are selected from the group consisting of miR-15, miR-16, miR-15+miR-34 and miR-16+miR-34 so as to obtain a protein production engineered mammalian producer cell,

z) recovering the protein production engineered mammalian producer cell produced in step y),

wherein the mammalian producer cell is a CHO cell.

3. The method according to claim 1 or 2, wherein the miR-15 is miR-15a or miR-15b.

4. The method according to any one of the preceding claims, wherein the miR-34 is miR-34a, miR-34b or miR-34c.

5. The method according to any one of the preceding claims, wherein two of the miRs or two of the nucleotide sequences encoding said two of the miRs are transfected.

6. The method according to any one of the preceding claims, wherein the miR is a mature miR, a precursor miR or a primary miR.

7. The method according to any one of the preceding claims, wherein the at least one vector encoding the one or more miRs in step b) or y) is transiently or stably transfected.

8. The method according to any one of the preceding claims, wherein the mammalian producer cell is transfected with a nucleotide sequence encoding the protein of interest prior to step a) or x) or during step b) or y).

9. The method according to any one of claims 1 to 7, wherein the protein production engineered mammalian producer cell obtained after step b) or y) is transfected with a nucleotide sequence encoding the protein of interest.

10. The method according to any one of the preceding claims, wherein the CHO cell is selected from the group consisting of a CHO-K1 cell, a CHO-K1SV cell, a DG44 CHO cell, a DUXB11 CHO cell, a CHO GS knock-out cell and a CHO FUT8 GS knock-out cell.

11. The method according to any one of the preceding claims, wherein the regulatory element allowing the over-expression of the one or more miRs is a promoter.

12. The method according to any one of the preceding claims, wherein the protein production engineered mammalian producer cell is a cell exhibiting an increased specific production rate or an increased time integral of viable cell concentration or both.

13. A protein production engineered mammalian producer cell produced according to anyone of the methods of claims 2 to 12.

14. A protein production engineered mammalian producer cell comprising at least one transgenic nucleic acid sequence encoding one or more miRs, which transgenic nucleic acid sequence is transiently or stably incorporated into the genome of that cell under control of at least one regulatory element allowing the over-expression of said one or more miRs, wherein the one or more miRs is/are selected from the group consisting of miR-15, miR-16, miR-15+miR-34 and miR-16+miR-34, and wherein the mammalian producer cell is a CHO cell.

15. A kit for the production of a protein of interest in a mammalian producer cell, comprising at least one mammalian producer cell, at least one vector containing a nucleotide sequence encoding one or more miRs under control of at least one regulatory element allowing the over-expression of the one or more miRs, wherein the one or more miRs is/are selected from the group consisting of miR-15, miR-16, miR15+miR-34 and miR-16+miR-34, and means for transfecting the at least one mammalian producer cell with the at least one vector, wherein the mammalian producer cell is a CHO cell.