regulated (Barron et al. 2011 Journal of Biotechnology 151:204–211). The successful exogenous over-expression of miR-7 resulted in a blocking of cell proliferation and increased normalised (per cell) recombinant protein production at 37 °C but the yield was still lower than from cells at reduced temperature.

The impact of miR manipulation is often investigated using reporter genes and 'sponge vectors' (Ebert et al. 2007 Nature Methods 4:721-726). In order to demonstrate the influence of miRs on industrially-relevant phenotypes it is necessary to validate this by either reducing or increasing expression of the miR in question. Jadhav et al. (Jadhav et al. 2012 Biotechnology and Bioengineering 109:1376-1385) recently reported that the functional analysis of miRs in CHO cells can be successfully demonstrated using a recombinant EPO-FC-producing CHO cell line and transient transfection over a four day period.

Commercial recombinant protein production often requires large-scale manufacturing processes. Despite recent advances in industrial processes, recombinant protein production remains a challenging task. Therefore there is still the need to provide further improved means and methods for the production of proteins in a more efficient and optimised way.

The present invention is inter alia based on the technical problem to provide improved or further means and methods for the industrial scale production of proteins.

Summary

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 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 pro-tein of interest, and d) recovering the protein of interest produced in step c). 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 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 aspect, the present invention refers to 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 aspect, the present in-

vention 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 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.

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