Patent Claims

1. Method for the production of an immunoglobulin comprising

a) cultivating a eukaryotic cell comprising a nucleic acid encoding the immunoglobulin in a cultivation medium wherein the ratio of the current specific glucose consumption rate of a single cell in a cultivation medium to the maximum known specific glucose consumption rate of the kind of cell is kept constant, and

b) recovering the immunoglobulin from the culture.

2. Method according to claim 1, characterized in that the ratio is of from 0.8 to 0.2.

3. Method according to claim 2, characterized in that the ratio is of from 0.6 to 0.4.

4. Method for the production of an immunoglobulin comprising

a) cultivating a eukaryotic cell comprising a nucleic acid encoding the immunoglobulin in a cultivation medium wherein the amount of glucose available in the cultivation medium per time unit is kept constant and limited to a constant value of less than 80 % of the amount that could maximally be utilized by the cells in the cultivation medium per time unit, and

b) recovering the immunoglobulin from the culture.

5. Method according to claim 4, characterized in that the constant value is less than 80 % and more than 20 %.

6. Method according to any one of the preceding claims, characterized in that the cultivating is a fed-batch cultivating.

7. Method according to claim 6, characterized in that the cultivating is a fed-batch cultivating wherein the feeding is started at day 2 or day 3 of the cultivating.

8. Method according to any one of the preceding claims, characterized in that the cultivating is at a pH value of from pH 6.5 to 7.5.

~~9. Method according to claim 8, characterized in that the cultivating is at a pH value of from pH 6.9 to 7.3.~~

~~10. Method according to claim 9, characterized in that the cultivating is at a pH value of from pH 6.95 to pH 7.05 or at a pH value of from pH 7.15 to pH 7.25.~~

~~11. Method according to any one of the preceding claims, characterized in that the immunoglobulin is an immunoglobulin of class G or class E.~~

~~12. Method according to any one of the preceding claims, characterized in that the eukaryotic host cell is selected from the group comprising CHO cells, NS0 cells, HEK cells, BHK cells, hybridoma cells, PER.C6® cells, insect cells, and Sp2/0 cells.~~

~~13. Method according to claim 12, characterized in that the eukaryotic cell is a Chinese Hamster Ovary (CHO) cell.~~

~~14. Method according to any one of the preceding claims, characterized in that cultivating the host cell is performed for six to twenty days.~~

~~15. Method according to any one of the preceding claims, characterized in that the immunoglobulin is an anti-IL-6R antibody.~~

Patent Claims

~~16~~1. Use of a method ~~according to any one of claims 1 to 15~~comprising

(a) cultivating a eukaryotic cell comprising a nucleic acid encoding the immunoglobulin in a cultivation medium wherein the ratio of the current specific glucose consumption rate of a single cell in a cultivation medium to the maximum known specific glucose consumption rate of the kind of cell is kept constant, and

(b) recovering the immunoglobulin from the culture,

for decreasing the amount of an immunoglobulin with a mannose-5 glycostructure in an immunoglobulin preparation.

2. The use according to claim 1, characterized in that ratio is of from 0.8 to 0.2.

3. The use according to claim 2, characterized in that ratio is from 0.6 to 0.4.

4. Use of a method comprising

(a) cultivating a eukaryotic cell comprising a nucleic acid encoding the immunoglobulin in a cultivation medium wherein the amount of glucose available in the cultivation medium per time unit is kept constant and limited to a constant value of less than 80% of the amount that could maximally be utilized by the cells in the cultivation medium per time unit, and

(b) recovering the immunoglobulin from the culture,

for decreasing the amount of an immunoglobulin with a mannose-5 glycostructure in an immunoglobulin preparation.

5. The use according to claim 4, characterized in that the constant value is less than 80% and more than 20%.

6. The use according to any one of the preceding claims, characterized in that the cultivating is a fed-batch cultivating.

7. The use according to claim 6, characterized in that the cultivating is a fed-batch cultivating wherein the feeding is started at day 2 or day 3 of the cultivating.

8. The use according to any one of the preceding claims, characterized in that the cultivating is at a pH value of from pH 6.5 to 7.5.

9. The use according to claim 8, characterized in that the cultivating is at a pH value from pH 6.9 to 7.3.

10. The use according to claim 9, characterized in that the cultivating is at a pH value of from pH 6.95 to pH 7.05 or at a pH value of from pH 7.15 to pH 7.25.

11. The use according to any one of the preceding claims, characterized in that the immunoglobulin is an immunoglobulin of class G or class E.

12. The use according to any one the preceding claims, characterized in that the eukaryotic cell is selected from the group comprising CHO cells, NS0 cells, HEK cells, BHK cells, hybridoma cells, PER.C6® cells, insect cells, and Sp2/0 cells.

13. The use according to claim 12, characterized in that the eukaryotic cell is a Chinese Hamster Ovary (CHO) cell.

14. The use according to any one of the preceding claims, characterized in that cultivating the host cell is performed for six to twenty days.

15. The use according to any one of the preceding claims, characterized in that the immunoglobulin is an anti-IL-6R antibody.

17. Composition comprising an immunoglobulin, characterized in that the composition has been prepared with a method according to any one of claims 1 to 15.

18. The composition according to claim 17, characterized in that the immunoglobulin is an anti-IL-6R antibody.

19. The composition according to claim 17, characterized in that the anti-IL-6R antibody comprises Tocilizumab.

20. The composition according to any one of claims 17 to 19, characterized in that the mannose-5 glycostructure attached to the anti-IL-6R antibody is 8 % or less.

21. The composition according to claim 20, characterized in that the mannose-5 glycostructure is 6 % or less.

22. The composition according to claim 21, characterized in that the mannose-5 glycostructure is 4 % or less.

23. The composition according to any one of claims 18 to 22, characterized in that the G(0) glycostructure attached to the anti-IL-6R antibody is in the range from 40 % to 46 % and the G(2) glycostructure attached to the anti-IL-6R antibody is in the range from 9 % to 11 %.