

CLAIMS

1. A method for treatment of a cell culture medium, the method comprising: holding a cell culture medium in a vessel under conditions suitable for inoculation of the medium with a eukaryotic cell that has been engineered to recombinantly express an exogenous protein, characterized in that the medium comprises the following nutrients
 - one or more of cystine, cysteine and a cysteine derivative; and
 - one or more redox active trace metalsand in that the medium comprising the nutrients is held under said conditions suitable for inoculation for a period of at least 10 hours in the absence of cells prior to inoculation.
2. The method according to claim 1 wherein the medium is supplemented with both of (1) one or more of cystine, cysteine and a cysteine derivative; and (2) a redox active trace metal:
 - (i) before addition of the medium to the vessel;
 - (ii) at the same time as addition of the medium to the vessel;
 - (iii) after addition of the medium to the vessel and before the vessel is under conditions suitable for inoculation of the medium with the eukaryotic cell; or
 - (iv) in the vessel, when the vessel is under conditions suitable for inoculation of the medium with the eukaryotic cell.
3. The method according to claim 1 or 2 wherein the medium is held under the conditions suitable for inoculation for a period of at least about 24 hours, at least about 48 hours, at least about 72 hours or at least about 96 hours.
4. The method according to any one of claims 1 to 3, wherein said supplementation takes place before addition of the medium to the vessel.
5. The method according to any one of claims 1 to 3, wherein said supplementation takes place after addition of the medium to the vessel.
6. The method according to any one of claims 1 to 5, wherein the vessel is a bioreactor.
7. The method according to any one of claims 1 to 6, wherein the supplemented medium is in a bioreactor at or prior to inoculation thereof.

8. The method according to any one of claims 1 to 7 wherein the cysteine derivative is selected from the group consisting of: S-sulfocysteine, S-sulfocysteinylglycine, N-acetyl cysteine (NAC), cysteine S-linked N-acetyl glucosamine (GlcNAC-cys), homocysteine, L-cysteine mixed disulphides or various peptides, S-alkylated cysteine with a thiol-protecting group, cysteine with a thiol-protecting group, reduced glutathione (GSH), oxidized GSH, S-sulfoglutathione, γ - glutamylcysteine, cysteinylglycine, N-butanoyl α -glutamyl-cysteinylglycine, S-acyl-GSH and S-carboxy-L-cysteine,.
9. The method according to any one of claims 1 to 8 wherein the medium comprises about 0.5 mM to about 16 mM of one or more of cystine, cysteine and a cysteine derivative for at least about 10 hours at conditions suitable for inoculation.
10. The method according to any one of claims 1 to 9, wherein the redox active trace metal is one or more selected from the group consisting of iron, copper, chromium, cobalt, selenium, manganese, vanadium and molybdenum.
11. The method according to claim 10, wherein the one or more of iron, copper, chromium, cobalt, selenium, manganese, vanadium and molybdenum is added to the medium as a Trace Element Solution at a cumulative concentration of about 6 μ M to about 350 μ M.
12. The method according to any one of claims 1 to 11 wherein conditions suitable for inoculation are: a pH of about pH 6.0 to about pH 8.0, a temperature of about 20°C to about 39°C; and a % O₂ of about 10 to about 80%.
13. The method according to any one of claims 1 to 12 wherein the eukaryotic cell is a mammalian cell, a yeast cell or an insect cell.
14. A cell culture medium obtainable by the method of any one of claims 1 to 13.
15. Use of the medium of claim 14 in a eukaryotic cell fermentation process for production of recombinant protein.
16. A method for producing a recombinant protein by recombinant expression from a eukaryotic cell, the method comprising:

- subjecting a cell culture medium suitable for cultivating said eukaryotic cell to the method according to any one of claims 1 to 13,
- inoculating the treated cell culture medium with a eukaryotic cell engineered to recombinantly express an exogenous protein to form a cell culture,
- cultivating the cell culture so that the recombinant protein is produced.

17. The method of claim 16, wherein the recombinant protein is an antibody.

18. The method according to claim 16 or 17, further comprising a step of recovering the recombinant protein from the cell culture.