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Applicants: Joseph Edward Shultz and Roger Hart

Serial No.: 12/822,990 Group Art Unit No.: 1645

Filed: June 24, 2010 Examiner: Brian J. Gangle

For: CAPTURE PURIFICATION PROCESSES FOR PROTEINS EXPRESSED IN A NON-MAMMALIAN SYSTEM

Docket No.: A-1441-US-NP

Mail Stop RCE
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

ATTN: Examiner Brian J. Gangle

AMENDMENT RESPONSE

In response to the Final Office Action having a mailing date of September 9, 2013, Applicants respectfully submit a Request for Continued Examination, the following Response and a Request for a one-month Extension of Time.

Amendments to the Claims begin on page 2.
Remarks begin on page 7.

CERTIFICATE OF EFS TRANSMISSION

I hereby certify that this correspondence and any referenced attachments are being filed with the United States Patent and Trademark Office, addressed to Mail Stop RCE, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date appearing below.

January 9, 2014 /Camilla Edwards/

Date Signature

Amendments to the Claims

The instant claim set shall replace all other prior filed claim listings.

What is claimed is:

1. (Previously presented) A method of purifying a protein expressed in a non-native soluble form in a non-mammalian expression system comprising:

(a) lysing a non-mammalian cell in which the protein is expressed in a non-native soluble form to generate a cell lysate;

(b) contacting the cell lysate with a separation matrix under conditions suitable for the protein to associate with the separation matrix;

(c) washing the separation matrix; and

(d) eluting the protein from the separation matrix, wherein the separation matrix is an affinity resin selected from the group consisting of Protein A, Protein G and a synthetic mimetic affinity resin.

2. (Original) The method of claim 1, wherein the protein is a complex protein.

3. (Original) The method of claim 2, wherein the complex protein is selected from the group consisting of a multimeric protein, an antibody and an Fc fusion protein.

4. (Original) The method of claim 1, wherein the non-mammalian expression system comprises bacteria or yeast cells.

5. (Canceled)

6. (Canceled)

7. (Original) The method of claim 1, wherein the cell lysate is filtered before it is contacted with the separation matrix.

8. (Original) The method of claim 1, further comprising refolding the protein to its native form after it is eluted.

9. (Currently amended) A method of purifying a protein expressed in a non-native limited solubility form in a non-mammalian expression system comprising:

(a) expressing a protein in a non-native limited solubility form in a non-mammalian cell;

(b) lysing a non-mammalian cell;

(c) solubilizing the expressed protein in a solubilization solution comprising one or more of the following:

(i) a denaturant;

(ii) a reductant; and

(iii) a surfactant;

(d) forming a refold solution comprising the solubilization solution and a refold buffer, the refold buffer comprising one or more of the following:

(i) a denaturant;

(ii) an aggregation suppressor;

(iii) a protein stabilizer; and

(iv) a redox component;

(e) directly applying the refold solution to a separation matrix under conditions suitable for the protein to associate with the matrix;

(f) washing the separation matrix; and

(g) eluting the protein from the separation matrix, wherein the separation matrix is a non-affinity resin selected from the group consisting of ion exchange, mixed mode, and a hydrophobic interaction resin.

10. (Original) The method of claim 9, wherein the non-native limited solubility form is a component of an inclusion body.

11. (Original) The method of claim 9, wherein the protein is a complex protein.

12. (Original) The method of claim 9, wherein the complex protein is selected from the group consisting of a multimeric protein, an antibody, a peptibody, and an Fc fusion protein.

13. (Original) The method of claim 9, wherein the non-mammalian expression system is bacteria or yeast cells.

14. (Previously presented) The method of claim 9, wherein the denaturant of the solubilization solution or the refold buffer comprises one or more of urea, guanidinium salts, dimethyl urea, methylurea and ethylurea.

15. (Previously presented) The method of claim 9, wherein the reductant comprises one or more of cysteine, dithiothreitol (DTT), beta-mercaptoethanol and glutathione.

16. (Original) The method of claim 9, wherein the surfactant comprises one or more of sarcosyl and sodium dodecylsulfate.

17. (Original) The method of claim 9, wherein the aggregation suppressor is selected from the group consisting of arginine, proline, polyethylene glycols, non-ionic surfactants, ionic surfactants, polyhydric alcohols, glycerol, sucrose, sorbitol, glucose, Tris, sodium sulfate, potassium sulfate and osmolytes.

18. (Original) The method of claim 9, wherein the protein stabilizer comprises one or more of arginine, proline, polyethylene glycols, non-ionic surfactants, ionic surfactants, polyhydric alcohols, glycerol, sucrose, sorbitol, glucose, tris, sodium sulfate, potassium sulfate and osmolytes.

19. (Original) The method of claim 9, wherein the redox component comprises one or more of glutathione-reduced, glutathione-oxidized, cysteine, cystine, cysteamine, cystamine and beta-mercaptoethanol.

20. (Canceled)

21. (Canceled)

22. (Currently amended) The method of claims 1 or 9, further comprising the step of ~~(a)~~ washing the separation matrix with a regeneration reagent.

23. (Original) The method of claim 22, wherein the regeneration reagent is one of a strong base or a strong acid.

24. (Original) The method of claim 23, wherein the strong acid is phosphoric acid.

25. (Original) The method of claim 23, wherein the strong base is sodium hydroxide.

26. (Original) The method of claim 22, wherein the regenerating comprises washing the separation matrix with a solution comprising one or both of a chaotrope present at a concentration of 4-6 M and a reductant.

27. (Original) The method of claim 26, wherein the chaotrope is one of urea, dimethyl urea, methylurea, ethylurea, and guanidinium.

28. (Previously presented) The method of claim 26, wherein the reductant is one of cysteine, dithiothreitol (DTT), beta-mercaptoethanol and glutathione.

29. (Previously presented) The method of claim 22, wherein the regenerating comprises washing the separation matrix with a solution comprising 50mM Tris, 10mM citrate, 6M urea, 50mM dithiothreitol (DTT) at pH 7.4.

REMARKS

Claims 1-4, 7-19 and 22-29 are currently pending. Claim 9 is herein amended to recite "directly" in step (e). Support for the amendment is found on page 23, line 4 of the specification. Claim 22 is herein amended to remove a paragraph notation.

Claim Rejections/Objections Withdrawn and New Claim Objections

Applicants acknowledge and appreciate withdrawal of the claim objections and rejections as indicated in the office action of September 9, 2013. Claims 8, 24, and 26-29 were newly objected to but would be allowable if rewritten in independent form.

Double Patenting

Claims 1-4 and 7 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-22 of copending Application No. 12/820,087. Claims 1-4, 7, 9-19, and 22 were rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-22 of copending Application No. 12/820,087 in view of Fischer et al. Applicants wish to defer a substantive response on the merits until such time as allowable subject matter is indicated.

35 USC §102

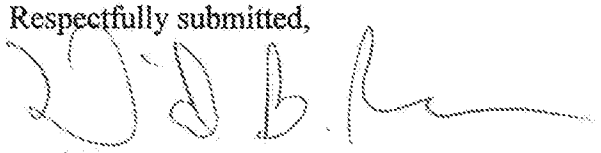
Claims 9-15 and 17-19 were rejected as being anticipated by Oliner et al. (US Pat. No. 7,138,370). Applicants have amended independent claim 9 from which claims 10-15 and 17-19 depend. Claim 9 as amended recites at step (e) "directly applying the refold solution to a separation matrix." (emphasis added). As stated on page 23 of the specification, "'[i]t is noted that when performing the method, the refold solution comprising the refolded protein of interested is applied directly to the separation matrix, without the need for diluting or removing the components of the solution required for refolding the protein. This is an advantage of the disclosed method." Lines 3-6. Oliner et al., in contrast, discloses that the solution comprising the refolded protein is subject to dialysis, precipitation, and centrifugation before being pH adjusted and loaded on the column. Therefore, Oliner et al. fails to teach each element of the claimed invention. Withdrawal of this ground of rejection is therefore courteously requested.

35 USC §103

Claims 9-19 were rejected as being obvious over Oliner et al. (US Pat. No. 7,138,370) in view of Fischer et al. Claims 9-15, 17-19, 22-23 and 25 were rejected as being obvious over Oliner et al. in view of Amersham Biosciences. Claim 9 has been amended to recite "directly" applying the refold solution to a separation matrix. As stated previously, Oliner et al. does not teach applying the solution comprising the refolded protein without the need for diluting or removing components of the solution required for refolding the protein. Rather, Oliner et al. discloses that the solution comprising the refolded protein is subject to dialysis, precipitation, and centrifugation before being pH adjusted and loaded on the column. Thus, the claimed invention provides for a more direct and efficient means of purifying a protein which provides clear advantages over the prior art. The references of Fischer et al. and Amersham Biosciences et al. do not, either alone or in combination with Oliner et al., teach or in any way suggest the unexpected advantages of the claimed method. Consequently, Applicants respectfully request withdrawal of this ground of rejection.

The Commissioner is hereby authorized to charge any fees which may be required by the accompanying papers, or credit any overpayment to Deposit Account No. 01-0519.

Respectfully submitted,



David B. Ran
Registration No. 38,589
Attorney for Applicants
Telephone: (206) 265-7309
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CUSTOMER NO: 37500

Amgen Inc.
Law Department
M/S AW2 D-4262
1201 Amgen Court West
Seattle, WA 98119-3105