CLAIMS

WHAT IS CLAIMED:

1. A method of recombinant production of an antibody comprising:
    a) providing a cell-free protein expression system containing a target protein exhibiting an antibody epitope;
    b) modifying the cell-free system by introducing one or more agents that block the antibody epitope on the target protein but do not eliminate the activity of the target protein in the cell-free system;
    c) introducing one or more nucleic acids encoding an antibody that binds to the antibody epitope to the cell free system; and,
    d) initiating transcription and translation of the antibody in the cell-free system under conditions so that the antibody is produced.

2. The method of claim 1, wherein the agent that blocks the antibody epitope is a peptide or a small molecule.

3. The method of claim 1, wherein the agent does not affect the activity of the target protein as compared to the target protein activity in the absence of the agent or wherein the target protein activity is reduced about 10% or about 50% as compared to the target protein activity in the cell-free system in the absence of the agent.

4. A method of recombinant production of an antibody comprising
    a) providing a cell-free protein expression system containing a target protein exhibiting an antibody epitope;
    b) modifying the cell-free system by introducing one or more agents that block an antibody paratope that binds to the antibody epitope on the target protein;
    c) introducing one or more nucleic acids encoding an antibody comprising the antibody paratope to the cell free system; and,
    d) initiating transcription and translation of the antibody in the cell-free system under conditions so that the antibody is produced.

5. The method of claim 1 or 4, wherein the antibody is a monoclonal antibody and the cell-free protein expression system is a mammalian cell-free protein expression system.

6. The method of claim 4, further comprising removing the agent that binds the antibody paratope following production of the antibody, optionally wherein the antibody is isolated prior to removal of the agent from the antibody.

7. The method of claim 1 or 4, wherein the cell-free system comprises a cell lysate, in particular a cell lysate selected from the group consisting of wheat germ lysates, insect cell lysates, reticulocyte lysates, keratinocyte lysates, cell extracts from CHO cells, HeLa cells, myeloma cells, hybridoma cells and cultivated lymphoma cells.

8. The method of claim 4, wherein the agent is introduced to the cell-free system prior to initiating transcription and translation of the antibody.

9. The method of claim 4, wherein the agent that blocks the antibody paratope is a peptide.

10. A method of recombinant production of an antibody, the method comprising:
    a) introducing an agent that selectively binds to a target epitope on an intracellular protein to cells to create a modified cell line;
    b) creating a cell-free antibody production system from the modified cell line;
    c) introducing a nucleic acid template to the cell-free antibody production system, wherein the nucleic acid template encodes an antibody that selectively binds to the target epitope on the intracellular protein; and,
    d) initiating transcription and translation from the nucleic acid template to produce the antibody in the cell-free antibody production system.

11. The method of claim 1, 4 or10, further comprising e) isolating the antibody from the cell-free system.

12. The method of claim 1, 4 or10, wherein the target protein is selected from an intracellular protein in the secretory pathway of the cell line, a stress protein and a cell signaling protein.

13. The method of claim 10, wherein the target protein is expressed on an organelle of the cell line, in particular the endoplasmic reticulum or the Golgi apparatus.

14. The method of claim 13, wherein the target protein is an endoplasmic reticulum chaperone, in particular a calreticulin, a heat shock protein or an isomerase, or the target protein is glucose-regulated protein 78 (GRP78), HSP47, PDI, calreticulin or GP94 or wherein the target protein is a Golgi complex protein, in particular selected from GOLPH2, GOLPH3, GM130, ATP6V1A, ATP6V1E1, ATP6VOA2, TMEM165, GOLGB1, SCYL1BP1, TRAPPC11, TRAPPC2 and TRIP11.

15. The method of claim 10, wherein the cell line is a mammalian cell line and, optionally the target protein that is natively expressed is an intracellular protein in the secretory pathway of the mammalian cell line.