What is claimed is:

1. A host cell capable of expressing a polypeptide of interest comprising:

    a) a targeted integrated exogenous nucleic acid sequence of interest (SOI) encoding a first polypeptide of interest and a first selection marker flanked by two recombination recognition sequences (RRSs), wherein the targeted integrated exogenous SOI is integrated within a targeted locus of the genome of the host cell; and

    b) a randomly integrated exogenous nucleic acid SOI encoding a second polypeptide of interest and a second selection marker, wherein the randomly integrated SOI is integrated at least once in the genome of the host cell.

2. The host cell of claim 1, wherein the first and the second polypeptide of interest are the same.

3. The host cell of claim 1, wherein the first and the second selection marker are the same.

4. The host cell of claim 1, comprising one to ten randomly integrated exogenous nucleic acid SOIs.

5. The host cell of claim 1, wherein the targeted locus is at least ~~about~~ 90% homologous to a sequence selected from SEQ ID Nos. 1-7.

6. The host cell of claim 1, further comprising a second targeted integrated exogenous nucleic acid SOI encoding a second polypeptide of interest and a second selection marker integrated within a targeted locus of the genome of the host cell, wherein the first targeted integrated exogenous nucleic acid SOI and the first selection marker are flanked by a first and a third RRS and the second targeted exogenous SOI and second selection marker are flanked by a second and the third RRS.

7. The host cell of any of claim 1-5, wherein the polypeptides of interest are selected from the group consisting of: a single chain antibody, an antibody light chain, an antibody heavy chain, a single-chain Fv fragment (scFv), and an Fc fusion protein.

8. The host cell of any one of claims 1-5, wherein the host cell is a mammalian host cell.

9. The host cell of claim 8, wherein the host cell is a hamster host cell, a human host cell, a rat host cell, or a mouse host cell.

10. The host cell of claim 9, wherein the host cell is a CHO host cell, a CHO K1 host cell, a CHO K1SV host cell, a DG44 host cell, a DUKXB-11 host cell, a CHOK1S host cell, or a CHO K1M host cell.

11. The host cell of any one of claims 1-7, wherein the targeted integration of the SOIs and selection markers are promoted by an exogenous nuclease.

12. The host cell of 11, wherein the exogenous nuclease is selected from the group consisting of a zinc finger nuclease (ZFN), a ZFN dimer, a transcription activator-like effector nuclease (TALEN), a TAL effector domain fusion protein, an RNA-guided DNA endonuclease, an engineered meganuclease, and a clustered regularly interspaced short palindromic repeats (CRISPR)-associated (Cas) endonuclease.

13. A method of expressing a polypeptide of interest comprising:

a) providing a host cell comprising an exogenous nucleotide sequence integrated at a targeted locus of the genome of the host cell, wherein the exogenous nucleotide sequence comprises two RRSs flanking a first selection marker;

b) introducing into the cell provided in (a) a nucleic acid comprising two RRSs matching the two RRSs of the integrated exogenous nucleotide sequence and flanking a first exogenous SOI encoding a first polypeptide of interest and a second selection marker;

c) introducing a recombinase or a nucleic acid encoding a recombinase, wherein the recombinase recognizes the RRSs;

d) selecting for cells expressing the second selection marker;

e) introducing, via random integration, a second exogenous SOI encoding a second polypeptide of interest and a third selection marker into the genome of the host cell;

f) selecting for cells expressing the third selection marker; and

g) culturing the host cell under conditions sufficient to express the first and second polypeptides of interest.

14. The method of claim 13, further comprising recovering the first and second polypeptides of interest from the host cell culture.

15. The method of claim 13, wherein the first and the second polypeptides of interest are the same.

16. The method of claim 13, wherein the targeted locus is at least ~~about~~ 90% homologous to a sequence selected from SEQ ID Nos. 1-7.

17. The method of any of claims 13-16, wherein the first and second polypeptides of interest are selected from the group consisting of: a single chain antibody, an antibody light chain, an antibody heavy chain, a single-chain Fv fragment (scFv), and an Fc fusion protein.

18. The method of any one of claims 13-17, wherein the host cell is a mammalian host cell.

19. The method of claim 18, wherein the host cell is a hamster host cell, a human host cell, a rat host cell, or a mouse host cell.

20. The method of claim 19, wherein the host cell is a CHO host cell, a CHO K1 host cell, a CHO K1SV host cell, a DG44 host cell, a DUKXB-11 host cell, a CHOK1S host cell, or a CHO K1M host cell.

21. The method of any of claims 13-20, wherein the targeted integration of any of the SOIs is promoted by an exogenous nuclease.

22. The method of claim 21, wherein the exogenous nuclease is selected from the group consisting of a zinc finger nuclease (ZFN), a ZFN dimer, a transcription activator-like effector nuclease (TALEN), a TAL effector domain fusion protein, an RNA-guided DNA endonuclease, an engineered meganuclease, and a clustered regularly interspaced short palindromic repeats (CRISPR)-associated (Cas) endonuclease.

23. The method of any of claims 1-22, wherein the expression of the SOIs is controlled by a regulatable promoter.

24. The method of claim 23, wherein the regulatable promoter is selected from the group consisting of SV40 and CMV promoters.