What we claim is:

1.) A recombinant nucleic acid molecule comprising:

(a) a 5' and a 3' transposon-specific inverted terminal repeat (ITR),

(b) at least one nucleic acid sequence encoding a transgene expression processing (TEP) protein or a TEP functional RNA, located between the 5' and 3' ITRs and which is under the control of a promoter, and

(c) optionally at least one transgene also located between the 5' and 3' ITRs and which is under the control of a transgene promoter, wherein said nucleic acid molecule is optionally part of a vector.

2.) The recombinant nucleic acid molecule of claim 1 further comprising at least one epigenetic regulatory element, in particular at least one MAR (matrix attachment region) element.

3.) The recombinant acid molecule of claim 2, wherein the MAR element is located between the 5' and a 3' ITRs and wherein optionally a transgene such as an antibiotic resistance gene or a gene encoding an immunoglobulin, optionally under the control of a further promoter, is located between the 5' and a 3' ITR such as between the 5' ITR and the MAR.

4.) The recombinant nucleic acid molecule of any one of the preceding claims, wherein the TEP protein or TEP functional RNA is a protein or a functional RNA that is, directly or indirectly, involved in integration of nucleic acid sequences into a genome, processing or translation of the transgene RNA product or is involved in ER translocation, secretion, processing, folding, ER-Golgy-plasma membrane transport, glycosylation and/or another post-translational modification of proteins such as transgene expression products.

5.) The recombinant nucleic acid molecule of any one of the preceding claims, wherein the TEP protein is a protein of the protein secretion pathway, a protein of the recombination pathway, a protein processing or metabolic protein including chaperones such as BiP, or a combination thereof.

6.) The recombinant nucleic acid molecule of claim 5, wherein the TEP protein is one or more of the following proteins of the protein secretion pathway: hSRP14, hSec61α1, hSec61β, hSec61γ, hSRP54, hSRP9, hSRPRα, hSRPβ, and hCANX.

The TEP protein may also correspond to one or more of the following amino acid sequences of proteins of the protein secretion pathway: hSRP14 having SEQ ID NO: 13, hSec61α1 having SEQ ID NO: 15, hSec61β having SEQ ID NO: 17, hSec61γ having SEQ ID NO: 19, hSRP54 having SEQ ID NO: 21, hSRP9 having SEQ ID NO: 23, hSRPRα having SEQ ID NO: 25, hSRPβ having SEQ ID NO: 27, and hCANX having SEQ ID NO: 29 and amino acid sequences having more than 80%, 90%, 95% or 98% sequence identity with the specified sequences.

7.) The recombinant nucleic acid molecule of claims 1-5, wherein the TEP protein is one or more of the following protein processing or metabolic proteins: hUCP4, hCMPSAT, rST6Gal1, hCOMSC, hT-Synthase, hP4HA1, hP4HB, hGILZ, hCyPB, hNRF2, hHK1, hPDI, hPIN1, hSEPW1, hCALR, hDDOST, hHSP40, hATP5A1, hSERCA2, hPDIA4, hHSC70 /HSPA8, hHYOU1, hCMP-SAS, hBeclin-1, hERdj3, CHO-AGE ~~hAGE~~, hWip1, hRTP4, hREEP2, hDPM1 and hDRiP78.

8.) The recombinant nucleic acid molecule of claims 1-5, wherein the TEP protein is a chaperone, in particular, a BiP protein, more in particular, a synthetic BIP protein derivative (DroBiP) having 80%, 90%, 95% or100% sequence identity with the SEQ ID NO.: 60.

9.) The recombinant nucleic acid molecule according to any one of the preceding claims, wherein said MAR element is selected from SEQ ID NOs: 1 (MAR 1-68), 2 (MAR 1_6), 3 (MAR X_S29), 4 (MAR S4), 5 (chicken lysozyme MAR), is a engineered, in particular rearranged counterpart and/or has at least 80%, 90%, 95%, 98%, 99% or 100% sequence identity with any one of SEQ ID NOs: 1 to 5.

10.) The recombinant nucleic acid molecule according to any one of the preceding claims, wherein the TEP functional RNA within said cell comprises/consists of nucleic acid sequences encoding a functional RNA, preferably a miRNA or a shRNA, that interferes with the expression of at least one protein of a recombination pathway,

such as, but not limited to, Rad51, Rad51B, Rad51C, Rad51D, Xrcc2, Xrcc3, Rad52, Rad54, Brca1, Brca2, Cyclin D1, Ercc, MDC1, Bard1, Ligase 1, Mre 11 and/or 53BP1.

11.) The recombinant nucleic acid molecule according to any one of the preceding claims, wherein said nucleic acid molecule is at least 5000, 6000, 7000, 8000, 90000 or 10000 bps long.

12.) The recombinant nucleic acid molecule according to any one of the preceding claims, wherein the 5' and a 3' ITRs are 5' and 3' ITRs of the Sleeping Beauty or preferably PiggyBac Transposon.

13.) The recombinant nucleic acid molecule according to any one of the preceding claims, wherein upon a first transfection of said recombinant nucleic acid molecule and a second, subsequent, transfection of a further recombinant nucleic acid molecule containing a transgene into a mammalian cell, transgene integration and/or expression is increased in said cell relative to a cell not subject to said first transfection.

14.) The recombinant nucleic acid molecule according to any one of the preceding claims, wherein the recombinant nucleic acid molecule is part of a vector.

15.) The recombinant nucleic acid molecule according to claim 15, wherein the vector comprises a singular MAR element, two or more MAR elements, wherein said element(s) are located between the 5' and 3' ITRs.

16.) The recombinant nucleic acid according to claim 14, wherein the vector comprises two MAR elements, wherein a first MAR element is positioned upstream of the TEP or TEP functional RNA and a second MAR element is positioned downstream of the TEP or TEP functional RNA, wherein the first MAR element comprises a MAR 1_6 element and/or an element that has at least 80%, 90%, 95%, 98%, 99% or 100% sequence identity with SEQ ID NO. 2, in particular a rearranged MARs based on MAR 1-6, more in particular elements that have at least 80%, 90%, 95%, 98%, 99% or 100% sequence identity with SEQ ID NO: 8 (MARs 1_6R2) and

the second MAR element comprises a MAR 1-68 element and/or an element that has at least 80%, 90%, 95%, 98%, 99% or 100% sequence identity with SEQ ID NO. 1.

17.) The recombinant nucleic acid molecule according to claim 14, wherein the vector comprises the singular MAR element, wherein the singular MAR element is positioned downstream of the TEP or TEP functional RNA, wherein the singular MAR element is a MAR 1-68 or a MAR X-29 element and/or an element that has at least 80%, 90%, 95%, 98%, 99% or 100% sequence identity with SEQ ID NOs. 1 or 3, in particular a rearranged MAR based on MAR 1-68 or a MAR X-29, in particular an element that has at least 80%, 90%, 95%, 98%, 99% or 100% sequence identity with SEQ ID NOs: 6, 7 or 10 (MARs 1_68R, 1_68R2 or X_29R3) or 9, and is preferably a MAR X-29 element and/or an element that has at least 80%, 90%, 95%, 98%, 99% or 100% sequence identity with SEQ ID NO. 3.

18.) The recombinant nucleic acid molecule according to claim 14 to 17, wherein the TEP or TEP functional RNA is under the control of an EF1 alpha promoter and is optionally followed by a BGH polyA signal.

19.) The recombinant nucleic acid molecule according to nucleic acid according to any one of claims 14 to 18, wherein the vector comprises promoter(s) and/or enhancer(s) or fusions thereof such as GAPDH, CGAPDH, SV40p, CMVp, CHO Ef1 alpha, CHO Actb and/or CHO Hspa5.

20.) A method for expressing a TEP or TEP functional RNA comprising: providing a recombinant mammalian cell comprising a transgene , and the vector is a vector according of any one of claims 14 to 19 which expresses the TEP or TEP functional RNA, wherein the TEP or TEP functional RNA expressed via said vector optionally increases an expression of a transgene in said mammalian cell by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60% or at least 70%.

21.) The method of claim 20, wherein the vector comprises a singular MAR X-29 element and/or a nucleic acid sequence having at least 80%, 90%, 95%, 98%, 99% or 100% sequence identity with SEQ ID NO. 3 and wherein, after more than 4, 5, 6, 7, 8, 9, 10, 11, 12, 13 or 14 weeks of cultivation, the TEP or TEP functional RNA

expressed via said vector increases an expression of a gene of interest by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60% or at least 70%.

22.) A recombinant mammalian cell comprising not more than 20, 15, 10 or 5 of the recombinant nucleic acid molecule of claims 1-14, preferably integrated into the genome of the cell as single copies.

23.) The recombinant mammalian cell of claim 22, wherein said nucleic acid sequence(s) encoding a TEP protein within said cell comprise(s)/consist(s) of nucleic acid sequences encoding the proteins of claims 6, 7 and/or 8.

24.) The recombinant mammalian cell of claim 23, wherein said nucleic acid sequence(s) encoding the TEP functional RNA within said cell comprise(s)/consist(s) of nucleic acid sequence(s) encoding a functional RNA, preferably a miRNA or a shRNA, that interferes with the expression of at least one recombination protein, preferably an HR gene, such as, but not limited to, Rad51, Rad51B, Rad51C, Rad51D, Xrcc2, Xrcc3, Rad52, Rad54, Brca1, Brca2, Cyclin D1, Ercc1, MDC1, Bard1, Ligase 1, Mre 11 and/or 53BP1.

25.) The recombinant mammalian cell of any one of claims 22 to 24, wherein the cell is a primary stem cell, a hamster, e.g., CHO (Chinese hamster ovary), cell or a human, e.g., HEK293 cell.

26.) A recombinant mammalian cell comprising:

a.) at least one TEP functional RNA and/or at least one recombinant nucleic acid sequence encoding a TEP protein or encoding TEP functional RNA ,

and

b) a recombinant nucleic acid molecule comprising:

(i) at least one transgene of interest, and

(ii) optionally, a MAR element.

27.) The recombinant mammalian cell of claim 26, wherein the TEP protein is at least one TEP of claims 6, 7 or 8.

28.) The recombinant mammalian cell of claim 26 or 27, wherein the functional RNA is a transiently transfected siRNA or an shRNA which is transcribed from said at least one isolated nucleic acid sequence, wherein the siRNA or the processed shRNA is a 20, 21, 22, 23, 24 or 25 base pairs long antisense RNA which is fully complimentary to 20, 21, 22, 23, 24 or 25 consecutive nucleotides of a mRNA of at least one target gene that is part of the NHEJ (non-homologous end-joining), HR (homologous recombination), MMEJ (Microhomolgoy mediated end joining) recombinant pathway or is a DNA repair protein such as MDC1 (mediator of DNA-damage checkpoint 1).

29.) The recombinant mammalian cell of claim 28, wherein the at least one target gene that is part of:

- the NHEJ is 53BP1 (Tumor suppressor p53-binding protein 1),

-the HR is
Rad51 (DNA repair protein RAD51), Rad51B (DNA repair protein RAD51 homolog 2), Rad51C (DNA repair protein RAD51 homolog 3), Rad51D (DNA repair protein RAD51 homolog 4), Rad52 (DNA repair protein RAD52), Rad54 (DNA repair and recombination protein RAD54) , Xrcc2 (X-ray repair complementing defective repair in Chinese hamster cells 2),
Xrcc3 (X-ray repair complementing defective repair in Chinese hamster cells 3),
Brca1 (breast cancer 1, early onset),
Brca2 (breast cancer 2, early onset),
Bard1 (BRCA1 associated RING domain 1),
- the MMEJ is
Ercc1 (excision repair cross-complementing rodent repair deficiency, complementation group 1),
Mre11 (meiotic recombination 11)
Ligase1 (DNA ligase 1),
and/or
Is the DNA repair protein MDC1.

30.) The recombinant mammalian cell of any one of any one of claims 26 to 29, wherein the at least one transgene expresses a therapeutic protein such as an immunoglobulin, a hormone such as erythropoietin, or a growth factor and wherein, optionally, in the recombinant mammalian cell transgene integration and/or expression is increased relative to a cell not comprising said recombinant nucleic acid molecule(s).

31.) The recombinant mammalian cell of any one of claims 26 to 30, wherein the cell comprises at least two TEP functional RNAs, wherein one or both of the TEP RNAs are transiently transfected siRNA, or are expressed by said isolated nucleic acid sequence(s) encoding a TEP functional RNA.

32.) The recombinant mammalian cell of any one of claims 26 to 31, wherein the recombinant mammalian cell comprises a MAR element.

33.) A method for transfecting mammalian cells, in particular hamster cells, comprising:
transfecting, optionally in a first transfection, said mammalian cells with

(i) at least one, at least two, at least three or at least four of said recombinant nucleic acids molecules of any one of claims 1 to 13 and/or

(ii) at least one , at least two, at least three or at least four isolated TEP functional RNA and at least one transgene which is, optionally, part of a recombinant nucleic acid molecule which is optionally transfected in a second, subsequent transfection, optionally together with an isolated nucleic acid or mRNA expressing a transposase which recognizes the 5' and the 3' ITR .

34.) The method of claim 33, wherein the cell is transfected with more than one, including at least two, at least three or at least four of said recombinant nucleic acid molecules encoding one, two or three of the TEP proteins specified in claim 6.

35.)The method of claims 33 or 34 , wherein each of said nucleic acid molecules is part of a vector and the vectors are co-transfected.

36.)The method of claim 35, wherein said co-transfection, preferably a co-transfection of recombinant nucleic acid molecules encoding proteins SRP14, SRP9 and SRP54-increases transgene integration and/or expression in said cell relative to a cell not subject to such co-transfection.

37.)The method of claim 33 or any subsequent claim, wherein a number of said mammalian cells that stably express said TEP protein or TEP functional RNA is obtained to obtain recombinant mammalian cells and wherein said number of recombinant mammalian cells is independent from the presence of said MAR element.

38.) The method of claim 33 or any subsequent claim, wherein said mammalian cells are transfected a second time.

39.) The method of claim 33, wherein at least 30%, 40% or 45% of said mammalian cells become recombinant mammalian cells and express said transgene.

40.) The method of claim 33, wherein said mammalian cell is transfected with said at least one isolated TEP functional RNA and a vector comprising said at least one transgene and optionally a 3' ITR and 5' ITR flanking said at least one transgene, optionally together with an isolated nucleic acid or mRNA expressing a transposase with recognizes the 5' and the 3' ITR.

41.) The method of claim ~~33~~ 28 or any subsequent claim, wherein said transgene is a therapeutic protein such as an immunoglobulin, hormone, cytokine or growth factor.

42.) The method of claim 33 ~~28~~ or any subsequent claim, wherein said recombinant nucleic acid molecule comprises optionally a selection marker and wherein the at least one transgene is expressed

(a) without selection for said marker, or

(b) with selection for said marker, e.g. via a selection agent contained in a culture medium, and

(c) in absence of transposase, or

(d) in presence of transposase.

43.) The method of claim 33, wherein said TEP functional RNA is encoded by a recombinant nucleic acid sequences encoding a shRNA or comprises/consists of a siRNA that interferes with the expression of at least one HR gene, such as, but not limited to, Rad51, Rad51B, Rad51C, Rad51D, Xrcc2, Xrcc3, Rad52, Rad54, Brca1, Brca2, Cyclin D1, Ercc1, MDC1, Bard1, Ligase 1, Mre 11 and/or 53BP1.

43.) The method of claim 33 rr any subsequent claim, wherein transgene integration and/or expression is increased in such a cell relative to a cell not transfected with said isolated nucleic acid molecules and/or said at least one of said isolated TEP functional RNAs.

44.) A kit comprising in one container at least one vector comprising the any one of the recombinant nucleic acid molecules according to claims 1 to 13 and, in a second optional container a vector encoding a compatible transposase and in a further container instruction of how to use the vector or vectors.

45.) The kit of claim 44, wherein more than one vector is provided in one or more containers and wherein the TEP proteins are at least two of the following: a chaperone, SRP14, SRP9, or SRP54.

46) The kit of claim 44 , wherein the TEP functional RNA(s) within said vector(s) comprise(s)/consist(s) of nucleic acid sequences encoding a miRNA, siRNA or a shRNA that interferes with the expression of at least one HR gene, such as, but not limited to, Rad51, Rad51B, Rad51C, Rad51D, Xrcc2, Xrcc3, Rad52, Rad54, Brca1, Brca2-Cyclin D1, Ercc1, MDC1, Bard1, Ligase 1, Mre 11 and/or 53BP1, and optionally in a further container siRNA(s) that interferes with the expression of at least one HR gene, such as, but not limited to, Rad51, Rad51B, Rad51C, Rad51D, Xrcc2, Xrcc3, Rad52, Rad54, Brca1, Brca2, Cyclin D1, Ercc1, MDC1, Bard1, Ligase 1, Mre 11 and/or 53BP1.

47) Use of the recombinant nucleic acids of claims 1-13 and/or the recombinant mammalian cells of claim 22 to 31, preferably for increasing transgene integration and/or expression.

48.) An expression vector comprising:

(a) a transgene which is flanked, upstream by a promoter and downstream by a polyadenylation signal,

(b) a singular MAR element downstream of the polyadenylation signal, or

(c) a first MAR element upstream of the transgene of interest and a second MAR element downstream of said transgene integration site.

49.) The expression vector of claim 48, wherein the singular or first and second MAR elements are selected from MAR elements 1_68, 1_6, 1_6R2, 1_68R, 1_68R2, X_29R3 or X_29 or elements that have at least 80%, 90%, 95%, 98%, 99% or 100% sequence identity with SEQ ID NOs: 1, 2, 3, 6, 7, 8, 9 or 10.

50.) The expression vector according to claim 48, wherein the singular or first and second MAR(s) is/ are selected from rearranged MAR elements 1_6R2, 1_68R, 1_68R2 or X_29R3 or elements that have at least 80%, 90%, 95%, 98%, 99% or 100% sequence identity with SEQ ID NOs: : 6, 7, 8, or 10, wherein, optionally, the MAR element(s) increase an expression of the transgene of interest by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60% or at least 70% relative to their non-rearranged counterparts.

51.) The expression vector according to claim 48 to 50, wherein the promoter is an EF1 alpha promoter and the polyadenylation signal is a BGH polyA signal.

52.) The expression vector according to claim 48 to 51, wherein the vector comprises promoter(s) and/or enhancer(s) or fusions thereof such as GAPDH, CGAPDH, CSV40p, CMVp, CHO Ef1alpha, CHO Actb or CHO Hspa5.

53.) The expression vector of claim 52, wherein said promoter is GAPDH promoter and comprises a CMV enhancer.

54.) The expression vector according to claims 48 to 53, wherein said one or first and second MAR, enhancer, promoter, transgene of interest and polyadenylation signal are located between a 5' and 3' ITR.

55.) The expression vector according to claims 48 to 54, comprising

(a) a singular MAR element downstream of the polyadenylation signal, wherein said singular MAR element is preferably a MAR 1-68 or a MARX-29 element and/or an element that has at least 80%, 90%, 95%, 98%, 99% or 100% sequence identity with SEQ ID NOs. 1 or 3, in particular a rearranged MAR based on MAR 1-68 or a MAR X-29, in particular an element that has at least 80%, 90%, 95%, 98%, 99% or 100% sequence identity with SEQ ID Nos : 6, 7 OR 10 (MARs 1_68R, 1_68R2 or X_29R3) or SEQ ID NO: 9, and is preferably a MAR X-29 element and/or has at least 80%, 90%, 95%, 98%, 99% or 100% sequence identity with SEQ ID NO. 3, or

(b) a first MAR element upstream of the transgene of interest and a second MAR element downstream of said transgene of interest wherein the first MAR element, preferably comprises a 1_6 element and/or has at least 80%, 90%, 95%, 98%, 99% or 100% sequence identity with SEQ ID NO. 2, in particular with rearranged MARs based on MAR 1-6, in particular elements that have at least 80%, 90%, 95%, 98%, 99% or 100% sequence identity with SEQ ID NO: 8 (MAR 1_6R2) and the second MAR element that preferably comprises a MAR 1-68 element and/or has at least 80%, 90%, 95%, 98%, 99% or 100% sequence identity with SEQ ID NO.1.

56.) The expression vector according to 55, comprising the singular MAR element, wherein the singular MAR element is positioned downstream of the polyadenylation site and is a MAR 1-68 or a MAR X-29 and/or has at least 80%, 90%, 95%, 98%, 99% or 100% sequence identity with SEQ ID NOs. 1 or 3, in particular rearranged MARs based on MAR 1-68 or a MAR X-29, in particular elements at least 80%, 90%, 95%, 98%, 99% or 100% sequence identity with SEQ ID Nos : 6, 7 or 10 (MARs 1_68R, 1_68R2 or X_29R3) or 9, and is preferably a MAR X-29-derived element and/or has at least 80%, 90%, 95%, 98%, 99% or 100% sequence identity with SEQ ID NO. 3.

57.) The expression vector according to 55, comprising a first MAR element upstream of the transgene and a second MAR element downstream of said transgene of interest, wherein the first MAR element comprises a MAR 1_6 element and/or has at least 80%, 90%, 95%, 98%, 99% or 100% sequence identity with SEQ ID NO 2 and the second MAR element comprises a MAR 1_68 element and/or has at least 80%, 90%, 95%, 98%, 99% or 100% sequence identity with SEQ ID NO. 1.

58.) A method for expressing a transgene comprising:
providing a recombinant mammalian cell comprising one of the vectors of claims 48 to 57 comprising said transgene and expressing the transgene, wherein said MAR elements(s) increase an expression of the transgene preferably by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60% or at least 70%.

59.) The method of claim 58, wherein the vector comprises a singular MAR X_29 element and/or a nucleic acid that has at least 80%, 90%, 95%, 98%, 99% or 100% sequence identity with SEQ ID NO. 3 and wherein, after more than 4, 5, 6, 7, 8, 9, 10, 11, 12, 13 or 14 weeks of culture, the MAR element increase an expression of the transgene of interest by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60% or at least 70%.

CLAIMS

1. A recombinant nucleic acid molecule comprising:

(a) a 5' and a 3' transposon-specific inverted terminal repeat (ITR),

(b) at least one nucleic acid sequence encoding a transgene expression processing (TEP) protein or a TEP functional RNA, located between the 5' and 3' ITRs and which is under the control of a promoter, and

(c) at least one MAR (matrix attachment region) element.

2. A recombinant nucleic acid molecule according to Claim 1, in which there is provided at least one transgene also located between the 5' and 3' ITRs and which is under the control of a transgene promoter.

3. A recombinant nucleic acid molecule according to Claim 1 or 2, in which the MAR element is located between the 5' and a 3' ITRs.

4. A recombinant nucleic acid molecule according to Claim 2 or 3, in which the transgene is an antibiotic resistance gene or a gene encoding an immunoglobulin.

5. A recombinant nucleic acid molecule according to any preceding claim, in which the TEP protein or TEP functional RNA is a protein or a functional RNA that is, directly or indirectly, involved in integration of nucleic acid sequences into a genome, processing or translation of the transgene RNA product or is involved in ER translocation, secretion, processing, folding, ER-Golgy-plasma membrane transport, glycosylation and/or another post-translational modification of proteins such as transgene expression products.

6. A recombinant nucleic acid molecule according to any preceding claim, in which the TEP protein is a protein of the protein secretion pathway, a protein of the recombination pathway, a protein processing or metabolic protein including chaperones such as BiP, or a combination thereof.

7. A recombinant nucleic acid molecule according to any preceding claim, in which the TEP protein is one or more of the following proteins of the protein secretion pathway:

(a) one or more of the following proteins of the protein secretion pathway: hSRP14, hSec61α1, hSec61β, hSec61γ, hSRP54, hSRP9, hSRPRα, hSRPβ, and hCANX; or

(b) one or more of the following amino acid sequences of proteins of the protein secretion pathway: hSRP14 having SEQ ID NO: 13, hSec61α1 having SEQ ID NO: 15, hSec61β having SEQ ID NO: 17, hSec61γ having SEQ ID NO: 19, hSRP54 having SEQ ID NO: 21, hSRP9 having SEQ ID NO: 23, hSRPRα having SEQ ID NO: 25, hSRPβ having SEQ ID NO: 27, and hCANX having SEQ ID NO: 29 and amino acid sequences having more than 80%, 90%, 95% or 98% sequence identity with the specified sequences.

8. A recombinant nucleic acid molecule according to any preceding claim, in which the TEP protein is one or more of the following protein processing or metabolic proteins: hUCP4, hCMPSAT, rST6Gal1, hCOMSC, hT-Synthase, hP4HA1, hP4HB, hGILZ, hCyPB, hNRF2, hHK1, hPDI, hPIN1, hSEPW1, hCALR, hDDOST, hHSP40, hATP5A1, hSERCA2, hPDIA4, hHSC70 /HSPA8, hHYOU1, hCMP-SAS, hBeclin-1, hERdj3, CHO-AGE, hWip1, hRTP4, hREEP2, hDPM1 and hDRiP78.

9. A recombinant nucleic acid molecule according to any preceding claim, in which the TEP protein is a synthetic BIP protein derivative (DroBiP) having 80%, 90%, 95% or100% sequence identity with the SEQ ID NO.: 60.

10. A recombinant nucleic acid molecule according to any preceding claim, in which the MAR element is selected from SEQ ID NOs: 1 (MAR 1-68), 2 (MAR 1_6), 3 (MAR X_S29), 4 (MAR S4), 5 (chicken lysozyme MAR), is a engineered, in particular rearranged counterpart and/or has at least 80%, 90%, 95%, 98%, 99% or 100% sequence identity with any of SEQ ID NOs: 1 to 5.

11. A recombinant nucleic acid molecule according to any preceding claim, in which the TEP functional RNA within the cell comprises/consists of nucleic acid sequences encoding a functional RNA, preferably a miRNA or a shRNA, that interferes with the expression of at least one protein of a recombination pathway, such as, but not limited to, Rad51, Rad51B, Rad51C, Rad51D, Xrcc2, Xrcc3, Rad52, Rad54, Brca1, Brca2, Cyclin D1, Ercc, MDC1, Bard1, Ligase 1, Mre 11 and/or 53BP1.

12. A recombinant nucleic acid molecule according to any preceding claim, in which the nucleic acid molecule is at least 5000, 6000, 7000, 8000, 90000 or 10000 bps long.

13. A recombinant nucleic acid molecule according to any preceding claim, in which the 5' and a 3' ITRs are 5' and 3' ITRs of the Sleeping Beauty or preferably PiggyBac Transposon.

14. A recombinant nucleic acid molecule according to any preceding claim, in which the recombinant nucleic acid molecule is part of a vector.

15. A recombinant nucleic acid molecule according to Claim 14, in which the vector comprises a singular MAR element, two or more MAR elements, in which the element(s) are located between the 5' and 3' ITRs.

16. A recombinant nucleic acid according to Claim 14, in which the vector comprises two MAR elements, in which a first MAR element is positioned upstream of the TEP or TEP functional RNA and a second MAR element is positioned downstream of the TEP or TEP functional RNA, in which the first MAR element comprises a MAR 1_6 element and/or an element that has at least 80%, 90%, 95%, 98%, 99% or 100% sequence identity with SEQ ID NO. 2, in particular a rearranged MARs based on MAR 1-6, more in particular elements that have at least 80%, 90%, 95%, 98%, 99% or 100% sequence identity with SEQ ID NO. 8 (MARs 1_6R2) and the second MAR element comprises a MAR 1-68 element and/or an element that has at least 80%, 90%, 95%, 98%, 99% or 100% sequence identity with SEQ ID NO. 1.

17. A recombinant nucleic acid molecule according to Claim 14, in which the vector comprises the singular MAR element, in which the singular MAR element is positioned downstream of the TEP or TEP functional RNA, in which the singular MAR element is a MAR 1-68 or a MAR X-29 element and/or an element that has at least 80%, 90%, 95%, 98%, 99% or 100% sequence identity with SEQ ID NOs. 1 or 3, in particular a rearranged MAR based on MAR 1-68 or a MAR X-29, in particular an element that has at least 80%, 90%, 95%, 98%, 99% or 100% sequence identity with SEQ ID NOs: 6, 7 or 10 (MARs 1_68R, 1_68R2 or X_29R3) or 9, and is preferably a MAR X-29 element and/or an element that has at least 80%, 90%, 95%, 98%, 99% or 100% sequence identity with SEQ ID NO. 3.

18. A recombinant nucleic acid molecule according to any of Claims 14 to 17, in which the TEP or TEP functional RNA is under the control of an EF1 alpha promoter and is optionally followed by a BGH polyA signal.

19. A recombinant nucleic acid molecule according to any of Claims 14 to 18, in which the vector comprises promoter(s) and/or enhancer(s) or fusions thereof such as GAPDH, CGAPDH, SV40p, CMVp, CHO Ef1 alpha, CHO Actb and/or CHO Hspa5.

20. A method for expressing a TEP or TEP functional RNA comprising providing a recombinant mammalian cell comprising a transgene, and the vector is a vector according to any of Claims 14 to 19 which expresses the TEP or TEP functional RNA, in which the TEP or TEP functional RNA expressed via the vector optionally increases an expression of a transgene in the mammalian cell by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60% or at least 70%.

21. A method according to Claim 20, in which the vector comprises a singular MAR X-29 element and/or a nucleic acid sequence having at least 80%, 90%, 95%, 98%, 99% or 100% sequence identity with SEQ ID NO. 3 and in which, after more than 4, 5, 6, 7, 8, 9, 10, 11, 12, 13 or 14 weeks of cultivation, the TEP or TEP functional RNA expressed via the vector increases an expression of a gene of interest by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60% or at least 70%.

22. A recombinant mammalian cell comprising not more than 20, 15, 10 or 5 copies of a recombinant nucleic acid molecule according to any of Claims 1 to 19.

23. A recombinant mammalian cell according to Claim 22 in which recombinant nucleic acid molecule is integrated into the genome of the cell as single copies.

24. A recombinant mammalian cell according to Claim 22 or 23, in which the nucleic acid sequence(s) encoding a TEP protein within the cell comprise(s)/consist(s) of nucleic acid sequences encoding one or more of the proteins according to any of Claims 7, 8 and/or 9.

25. A recombinant mammalian cell according to Claim 24, in which the nucleic acid sequence(s) encoding the TEP functional RNA within the cell comprise(s)/consist(s) of nucleic acid sequence(s) encoding a functional RNA, preferably a miRNA or a shRNA, that

interferes with the expression of at least one recombination protein, preferably an HR gene, such as, but not limited to, Rad51, Rad51B, Rad51C, Rad51D, Xrcc2, Xrcc3, Rad52, Rad54, Brca1, Brca2, Cyclin D1, Ercc1, MDC1, Bard1, Ligase 1, Mre 11 and/or 53BP1.

26. A recombinant mammalian cell according to any of Claims 22 to 25, in which the cell is a primary stem cell, a hamster, a CHO (Chinese hamster ovary) cell, a human cell, or HEK293 cell.

27. A method for transfecting mammalian cells, in particular hamster cells, comprising transfecting the mammalian cells with

(i) at least one, at least two, at least three or at least four of the recombinant nucleic acids molecules according to any of Claims 1 to 13 and/or

(ii) at least one, at least two, at least three or at least four isolated TEP functional RNA and at least one transgene.

28. A method according to Claim 27, in which the transgene is part of a recombinant nucleic acid molecule.

29. A method according to Claim 27 or 28, in which the transgene can be transfected in a second, subsequent transfection.

30. A method according to Claim 29, in which the second, subsequent transfection can also include transfection together with an isolated nucleic acid or mRNA expressing a transposase which recognizes the 5' and the 3' ITR.

31. A method according to any of Claims 27 to 30, in which the cell is transfected with more than one, including at least two, at least three or at least four of the recombinant nucleic acid molecules encoding one, two or three of the TEP proteins specified in Claim 7.

32. A method according to any of Claims 27 to 31, in which each of the nucleic acid molecules is part of a vector and the vectors are co-transfected.

33. A method according to Claim 32, in which the co-transfection, preferably a co-transfection of recombinant nucleic acid molecules encoding proteins SRP14, SRP9 and

SRP54 increases transgene integration and/or expression in the cell relative to a cell not subject to such co-transfection.

34. A method according to any of Claims 27 to 33, in which a number of the mammalian cells that stably express the TEP protein or TEP functional RNA is obtained to obtain recombinant mammalian cells and in which the number of recombinant mammalian cells is independent from the presence of the MAR element.

35. A method according to any of Claims 27 to 34, in which the mammalian cells are transfected a second time.

36. A method according to any of Claims 27 to 35, in which at least 30%, 40% or 45% of the mammalian cells become recombinant mammalian cells and express the transgene.

37. A method according to any of Claims 27 to 36, in which the mammalian cell is transfected with the at least one isolated TEP functional RNA and a vector comprising the at least one transgene.

38. A method according to Claim 37, in which a 3' ITR and 5' ITR flanks the at least one transgene.

39. A method according to Claim 38, in which there is also provided an isolated nucleic acid or mRNA expressing a transposase which recognizes the 5' and the 3' ITR.

40. A method according to any of Claims 27 to 39, in which the transgene is a therapeutic protein such as an immunoglobulin, hormone, cytokine or growth factor.

41. A method according to Claim 27, in which the TEP functional RNA is encoded by a recombinant nucleic acid sequences encoding a shRNA or comprises/consists of a siRNA that interferes with the expression of at least one HR gene, such as, but not limited to, Rad51, Rad51B, Rad51C, Rad51D, Xrcc2, Xrcc3, Rad52, Rad54, Brca1, Brca2, Cyclin D1, Ercc1, MDC1, Bard1, Ligase 1, Mre 11 and/or 53BP1.

42. A method according to any of Claims 27 to 43, in which transgene integration and/or expression is increased in such a cell relative to a cell not transfected with the isolated nucleic acid molecules and/or the at least one of the isolated TEP functional RNAs.

43. A kit comprising in one container at least one vector comprising a recombinant nucleic acid molecule according to any of Claims 1 to 13.

44. A kit according to Claim 43 comprising a second container comprising a vector encoding a compatible transposase and in a further container instruction of how to use the vector or vectors.

45. A kit according to Claim 43, in which more than one vector is provided in one or more containers and in which the TEP proteins are at least two of the following: a chaperone, SRP14, SRP9, or SRP54.

46. A kit according to Claim 43, in which the TEP functional RNA(s) within the vector(s) comprise(s)/consist(s) of nucleic acid sequences encoding a miRNA, siRNA or a shRNA that interferes with the expression of at least one HR gene, such as, but not limited to, Rad51, Rad51B, Rad51C, Rad51D, Xrcc2, Xrcc3, Rad52, Rad54, Brca1, Brca2 Cyclin D1, Ercc1, MDC1, Bard1, Ligase 1, Mre 11 and/or 53BP1, and optionally in a further container siRNA(s) that interferes with the expression of at least one HR gene, such as, but not limited to, Rad51, Rad51B, Rad51C, Rad51D, Xrcc2, Xrcc3, Rad52, Rad54, Brca1, Brca2, Cyclin D1, Ercc1, MDC1, Bard1, Ligase 1, Mre 11 and/or 53BP1.

47. Use of a recombinant nucleic acid according to any of Claims 1 to 13 and/or a recombinant mammalian cell according to any of Claims 22 to 25 for increasing transgene integration and/or expression.