CLAIMS

~~1. A DNA construct for inserting a heterologous gene~~ sequence into a host genome comprising the sequence: Replaced by new claims

5' X-A-P-B-Q-C-Y 3'

in which

X and Y	are substantially homologous with respective portions of the host genome
P	is an internal ribosome entry site (IRES),
Q	is the heterologous gene sequence,
A, B and C	are, separately, optional linker sequences.

2. A DNA construct according to Claim 1 in which X and Y are of sufficient length to undergo homologous recombination with the host genome so as to insert the A-P-B-Q-C sequence into the host genome.

3. A DNA construct according to Claim 2 in which X and Y are each at least 1000 base pairs in length.

4. A DNA construct according to Claim 1, 2 or 3 in which X and Y are both homologous with a part of an endogenous host gene.

5. A DNA construct according to Claim 4 in which X and Y comprise the host elements regulating expression of the endogenous gene.

6. A DNA construct according to any preceding claim in which all of the linker sequences A, B, and C are absent.

7. A DNA construct according to any preceding claim ~~additionally comprising a polyadenylation signal at the 3'~~

~~(downstream) end of the heterologous gene.~~

Replaced by new claims

8. A DNA construct according to any preceding claim additionally comprising a splice acceptor, for example the rabbit b-globin splice acceptor, 5'(upstream) of the heterologous gene.

9. A DNA construct according to claim 8 in which the splice acceptor permits functional integration of the heterologous gene into an intron sequence.

10. A DNA construct according to any preceding claim additionally comprising a truncation/ cleavage/ transcription terminator sequence 5'(upstream) of X.

11. A DNA construct according to claim 10 in which the truncation/ cleavage/ transcription terminator sequence includes a splice acceptor and a polyadenylation signal.

12. A DNA construct according to Claim 10 or 11 omitting the IRES.

13. A DNA construct according to Claim 10 or 11 or 12 in which the transcription terminator is the Upstream Mouse Sequence or a poly A sequence, such as the SV40 polyadenylation signal.

14. A DNA construct according to any previous claim in which the heterologous gene codes for a selectable marker, such as antibiotic resistance, to facilitate selection of cells in which the heterologous gene has inserted into the host genome.

15. A DNA construct according to any previous claim further comprising a splice acceptor 5' to the IRES.

16. Use of a DNA construct according to any previous claim ~~for inserting a heterologous gene into a host genome~~

~~17. A method of inserting a heterologous gene into a target~~ endogenous gene in a host cell genome comprising transforming the host cell with a vector comprising a DNA construct according to any of Claims 1-15.

Replaced by new claims

18. A method of expressing a heterologous gene in a host cell comprising the steps:-

1. making a DNA construct according to any of Claims 1-15,
2. allowing the construct to undergo homologous recombination with or random integration into the host cell genome.

19. A cell or an animal comprising a heterologous gene inserted using a DNA construct according to any of Claims 1-15.

20. A descendant of a cell or an animal according to Claim 19, wherein the descendant has inherited the heterologous gene.

21. A vector containing a DNA construct according to any of ~~Claims 1-15.~~

Expression of Heterologous Genes

Abstract

A DNA construct is described containing an expression unit of an internal ribosome binding site (IRES) coupled to a heterologous gene sequence; this expression unit is bounded at 5' and 3' ends by DNA sequences that enable homologous recombination or integration of the construct with the DNA of a targetted host to obtain expression of the heterologous gene in the host.

Figure 8