

CLAIMS:

1. A transgenic non-human animal having a genome comprising a transgene
5 comprising a first insulator element, a response element, a promoter, a
bioluminescent reporter, a functional element and a second insular element.
2. The transgenic non-human animal of claim 1, wherein the first insulator element is
selected from the group consisting of matrix attachment regions (MAR), DNase
10 I-hypersensitive site (HS4) and inverted terminal repeats (ITR).
3. The transgenic non-human animal of claim 1, wherein the second insulator
element is selected from the group consisting of matrix attachment element
(MAR), HS4 and ITR.
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4. The transgenic non-human animal of claim 1, wherein the first insulator element is
the same as the second insulator element.
5. The transgenic non-human animal of claim 1, wherein the response element is
20 selected from the group consisting of cAMP response element (CRE), activator
protein 1 (ASP1), glucocorticoid response element (GRE), heat shock response
element (HSE), serum response element (SRE), thyroid response element
(TRE) and estrogen response element (ERE).
- 25 6. The transgenic non-human animal of claim 5, wherein the response element is
repeated in tandem two to twenty-four times.
7. The transgenic non-human animal of claim 6, wherein the response element is
repeated in tandem six times.
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8. The transgenic non-human animal of claim 7, wherein the response element is
CRE.

9. The transgenic non-human animal of claim 1, wherein the promoter is herpes simplex virus thymidine kinase minimal (HSV TK min).
10. The transgenic non-human animal of claim 1, wherein the bioluminescent reporter is selected from the group consisting of luciferase, chloramphenicol acetyltransferase (CAT), beta-galactosidase, secreted alkaline phosphatase (SEAP), human growth hormone (hGH) and green fluorescent protein (GFP).
11. The transgenic non-human animal of claim 1, wherein the functional element is human growth hormone (hGH) gene.
12. The transgenic non-human animal of claim 1, wherein the transgene comprises SEQ ID NO: 18.
13. The transgenic non-human animal of claim 11, wherein the transgene comprises SEQ ID NO: 19.
14. A cell isolated from the transgenic non-human animal of claim 1.
15. A tissue slice isolated from the transgenic non-human animal of claim 1.
16. A method of identifying a G protein-coupled receptor (GPCR) ligand, the method comprising:
- (a) measuring an amount of bioluminescence in the transgenic non-human animal of claim 1;
 - (b) administering a test agent to the transgenic non-human animal;
 - (c) measuring an amount of bioluminescence of the transgenic non-human animal at one or more time points following administration of the test agent; and
 - (d) comparing the amount of bioluminescence measured in (a) to the amount of bioluminescence measured in (c)
- wherein a difference in the amount of bioluminescence in (a) compared to (c) identifies the test agent as a GPCR ligand.

17. A method of identifying a G protein-coupled receptor (GPCR) ligand, the method comprising:

- (a) preparing a tissue slice from the transgenic non-human animal of claim 1;
- 5 (b) measuring an amount of bioluminescence in the tissue slice;
- (c) administering a test agent to the tissue slice;
- (d) measuring an amount of bioluminescence of the tissue slice at one or more time points following administration of the test agent; and
- (e) comparing the amount of bioluminescence measured in (b) to the amount
- 10 of bioluminescence measured in (d)

wherein a difference in the amount of bioluminescence in (b) compared to (d) identifies the test agent as a GPCR ligand.

18. A method of identifying a G protein-coupled receptor (GPCR) ligand, the method comprising:

- (a) preparing a cell isolated from the transgenic non-human animal of claim 1;
- (b) measuring an amount of bioluminescence in the cell;
- (c) administering a test agent to the cell;
- (d) measuring an amount of bioluminescence in the cell at one or more time
- 20 points following administration of the test agent; and
- (e) comparing the amount of bioluminescence measured in (b) to the amount of bioluminescence measured in (d)

wherein a difference in the amount of bioluminescence in (b) compared to (d) identifies the test agent as a GPCR ligand.

19. A method of monitoring GPCR function in a non-human animal, the method comprising:

- (a) transgenically modifying a non-human animal to express a transgene comprising a first insulator element, a response element, a promoter, a
- 30 bioluminescent reporter, a functional element and a second insular element;
- (b) monitoring bioluminescence from the non-human animal; and
- (c) correlating said bioluminescence to GPCR function.

20. A method of making a non-human transgenic animal for use in monitoring GPCR function, the method comprising:

- 5 (a) transgenically modifying a non-human animal to express a transgene comprising a first insulator element, a response element, a promoter, a bioluminescent reporter, a functional element and a second insular element;
- (b) measuring an amount of bioluminescence in the transgenic non-human animal of (a);
- 10 (c) administering a GPCR ligand to the transgenic non-human animal;
- (d) measuring an amount of bioluminescence of the transgenic non-human animal at one or more time points following administration of the GPCR ligand; and
- 15 (e) comparing the amount of bioluminescence measured in (b) to the amount of bioluminescence measured in (d)
- wherein a difference in the amount of bioluminescence in (b) compared to (d) identifies the non-human transgenic animal for use in monitoring GPCR function.

CLAIMS

1. A transgenic non-human animal having a genome comprising:
a transgene construct comprising, in the 5' to 3' direction, a first insulator element, a response element, a promoter, a bioluminescent reporter, a human growth hormone (hGH) functional element, and a second insulator element, wherein the first insulator element and the second insulator element are different, and
wherein the response element is a cyclic AMP response element (CRE) comprising the nucleic acid sequence of either SEQ ID NO: 6 or 11.
2. The transgenic non-human animal of claim 1, wherein the first insulator element is selected from the group consisting of a matrix attachment region (MAR), a DNase I-hypersensitive site (HS4), and an inverted terminal repeat (ITR).
3. The transgenic non-human animal of claim 1, wherein the second insulator element is selected from the group consisting of a matrix attachment region (MAR), a DNase I-hypersensitive site (HS4), and an inverted terminal repeat (ITR).
4. The transgenic non-human animal of claim 1, wherein the promoter is a herpes simplex virus thymidine kinase minimal promoter (HSV TK min).
5. The transgenic non-human animal of claim 1, wherein the bioluminescent reporter is selected from the group consisting of luciferase, chloramphenicol acetyltransferase (CAT), beta-galactosidase, secreted alkaline phosphatase (SEAP), human growth hormone (HGH), and green fluorescent protein (GFP).
6. The transgenic non-human animal of claim 1, wherein the transgene construct comprises the nucleic acid sequence of SEQ ID NO: 18.

7. The transgenic non-human animal of claim 1, wherein the transgene construct comprises the nucleic acid sequence of SEQ ID NO: 19.
8. A cell isolated from the transgenic non-human animal of claim 1.
9. A tissue slice isolated from the transgenic non-human animal of claim 1.
10. A transgenic non-human animal having a genome comprising:
a transgene construct comprising, in the 5' to 3' direction, a first insulator element, a response element, a promoter, a bioluminescent reporter, a human growth hormone (hGH) functional element, and a second insulator element,
wherein the first insulator element is a matrix attachment region (MAR), the response element is a cAMP response element (CRE) that is repeated six times, the promoter is a herpes simplex virus thymidine kinase minimal promoter (HSV TK min), the bioluminescent reporter is luciferase, the human growth hormone (hGH) functional element is a hGH gene with a poly A tail, and the second insulator element is a matrix attachment region (MAR) that is different from the first insulator element.
11. The transgenic non-human animal of claim 10, wherein the response element is a cyclic AMP response element (CRE) comprising the nucleic acid sequence of SEQ ID NO: 11.
12. A transgenic non-human animal having a genome comprising a transgene construct comprising the nucleic acid sequence of either SEQ ID NO: 18 or 19.
13. The transgenic non-human animal of claim 12, wherein the transgene construct comprises the nucleic acid sequence of SEQ ID NO: 18.
14. The transgenic non-human animal of claim 12, wherein the transgene construct comprises the nucleic acid sequence of SEQ ID NO: 19.

15. A transgenic non-human animal having a genome comprising a transgene construct comprising the nucleic acid sequence of either SEQ ID NO: 6 or 11.
16. The transgenic non-human animal of claim 12, wherein the transgene construct comprises the nucleic acid sequence of SEQ ID NO: 6.
17. The transgenic non-human animal of claim 12, wherein the transgene construct comprises the nucleic acid sequence of SEQ ID NO: 11.