What is claimed:

1. An isolated polynucleotide encoding an OgLuc variant polypeptide having at least 60% amino acid sequence identity to SEQ ID NO: 1 comprising at least one amino acid substitution at a position corresponding to an amino acid in SEQ ID NO: 1 wherein the OgLuc variant polypeptide has enhanced luminescence relative to a non-*Oplophorus* luciferase.

2. The polynucleotide of claim 1, wherein the non-*Oplophorus* luciferase is a *Renilla* luciferase.

3. The polynucleotide of claim 1, wherein the non-*Oplophorus* luciferase is a firefly luciferase.

4. A polynucleotide encoding an OgLuc variant polypeptide having at least 60% amino acid sequence identity to SEQ ID NO: 1 comprising at least one amino acid substitution at a position corresponding to an amino acid in SEQ ID NO: 1 wherein the OgLuc variant polypeptide has enhanced luminescence relative to an OgLuc polypeptide of SEQ ID NO: 3 with the proviso that the polypeptide encoded by the polynucleotide is not one of those listed in Table 47.

5. A polynucleotide encoding an OgLuc variant polypeptide having at least 60% amino acid sequence identity to SEQ ID NO: 1 comprising at least one amino acid substitution at a position corresponding to an amino acid in SEQ ID NO: 1 wherein the OgLuc variant polypeptide has enhanced luminescence relative to a polypeptide of SEQ ID NO: 31 with the proviso that the polypeptide encoded by the polynucleotide is not SEQ ID NO: 3 or 15.

6. A polynucleotide encoding an OgLuc variant polypeptide having at least 60% amino acid sequence identity to SEQ ID NO: 1 comprising at least one amino acid substitution at a position corresponding to an amino acid in SEQ ID NO: 1 wherein the OgLuc variant polypeptide has enhanced luminescence relative to a polypeptide of SEQ ID NO: 29 with the proviso that the polypeptide encoded by the polynucleotide is not SEQ ID NO: 3 or 15.

7. The polynucleotide of any one of claims 1-6, wherein the polypeptide has at least 80% amino acid sequence identity to SEQ ID NO: 1.

8. The polynucleotide of any one of claims 1-7, wherein the polypeptide has at least 90% amino acid sequence identity to SEQ ID NO: 1.

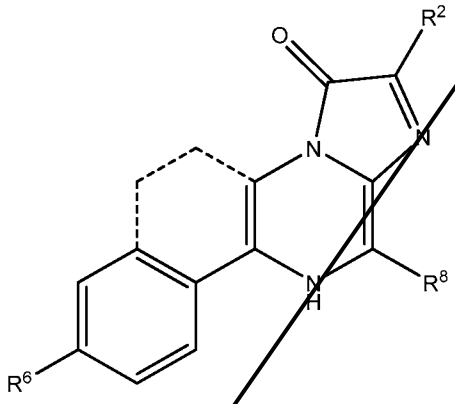
9. The polynucleotide of any one of claims 1-8, wherein the OgLuc variant polypeptide has at least one of enhanced protein stability or enhanced biocompatibility relative to the polypeptide of SEQ ID NO: 3.

10. The polynucleotide of any one of claims 1-9, wherein the OgLuc variant polypeptide has at least one of enhanced enzyme stability or enhanced biocompatibility relative to a *Renilla* luciferase.

11. The polynucleotide of any one of claims 1-10, wherein the OgLuc variant polypeptide has at least one of enhanced enzyme stability or enhanced biocompatibility relative to a firefly luciferase.

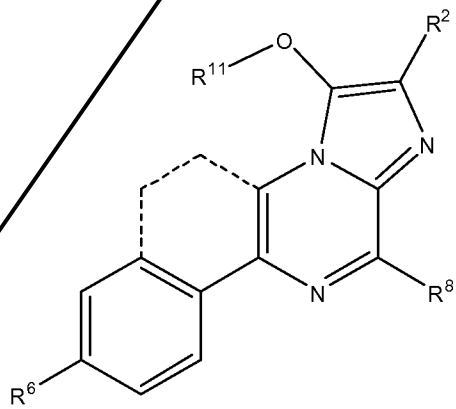
12. The polynucleotide of any one of claims 1-11, wherein the OgLuc variant polypeptide has enhanced luminescence relative to the polypeptide of SEQ ID NO: 3 in the presence of a coelenterazine.

13. The polynucleotide of any one of claims 1-12, wherein the OgLuc variant polypeptide has enhanced luminescence relative to the polypeptide of SEQ ID NO: 3 in the presence of a compound of formula (Ia) or (Ib):



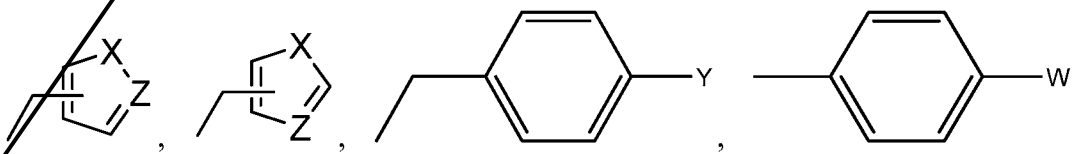
(Ia)

or



(Ib)

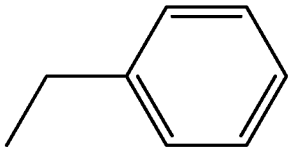
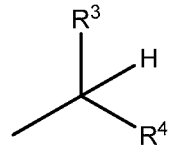
wherein R^2 is selected from the group consisting of



, , , or C_{2-5} straight chain alkyl;

R^6 is selected from the group consisting of -H, -OH, $-NH_2$, -OC(O)R or $-OCH_2OC(O)R$;

R^8 is selected from the group consisting of

, , H or lower cycloalkyl;

wherein R^3 and R^4 are both H or both C_{1-2} alkyl;

W is $-NH_2$, halo, -OH, -NHC(O)R, $-CO_2R$;

X is –S-, –O- or $–NR^{22}$-;

Y is –H, -OH, or $–OR^{11}$;

Z is –CH- or –N-;

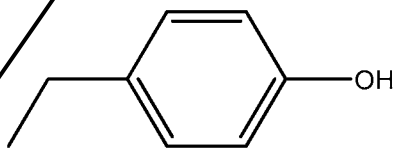
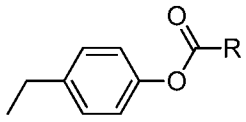
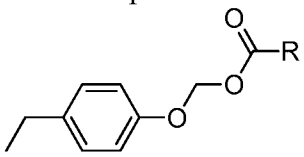
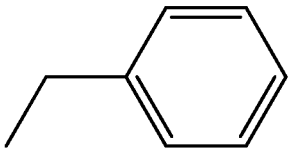
each R^{11} is independently –C(O)R'' or $–CH_2OC(O)R''$;

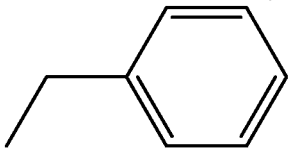
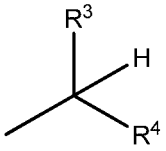
R^{22} is H, CH_3 or CH_2CH_3;

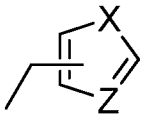
each R is independently C_{1-7} straight-chain alkyl or C_{1-7} branched alkyl;

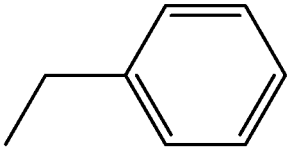
R'' is C_{1-7} straight-chain alkyl or C_{1-7} branched alkyl;

the dashed bonds indicate the presence of an optional ring, which may be saturated or unsaturated;

with the proviso that when R^2 is , , or , R^8 is not ;

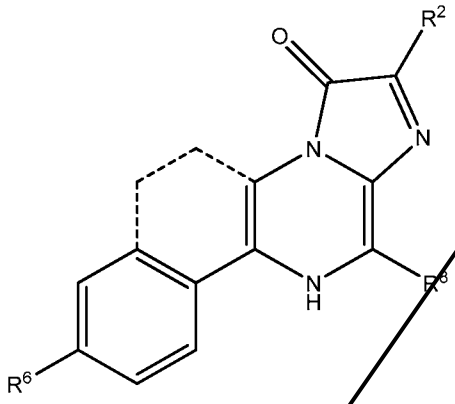
with the proviso that when R^2 is , R^8 is  or lower cycloalkyl; and

with the proviso that when R^6 is NH_2, R^2 is , , or C_{2-5} alkyl;

or R^8 is not .

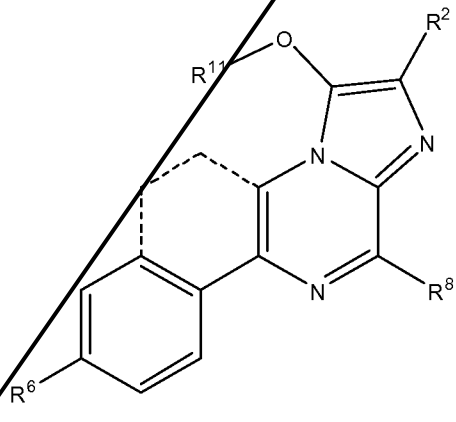
14. The polynucleotide of any one of claims 1-13, wherein the OgLuc variant polypeptide has a change in relative substrate specificity relative to the polypeptide of SEQ ID NO: 3 in the presence of a coelenterazine compared to a different coelenterazine.

15. The polynucleotide of any one of claims 1-14, wherein the OgLuc variant polypeptide has a change in relative substrate specificity relative to the polypeptide of SEQ ID NO: 3 in the presence of a compound of formula (Ia) or (Ib):



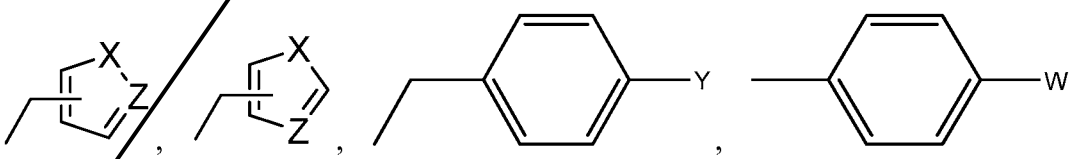
(Ia)

or



(Ib)

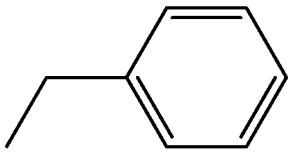
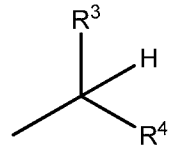
wherein R^2 is selected from the group consisting of



or C_{2-5} straight chain alkyl;

R^6 is selected from the group consisting of -H, -OH, $-NH_2$, -OC(O)R or $-OCH_2OC(O)R$;

R^8 is selected from the group consisting of

, , H or lower cycloalkyl;

wherein R^3 and R^4 are both H or both C_{1-2} alkyl;

W is $-NH_2$, halo, -OH, $-NHC(O)R$, $-CO_2R$;

X is –S-, –O- or $–NR^{22}$-;

Y is –H, -OH, or $–OR^{11}$;

Z is –CH- or –N-;

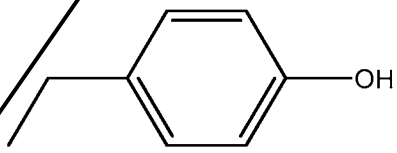
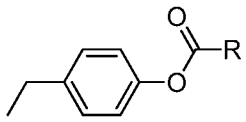
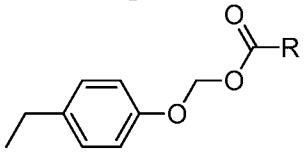
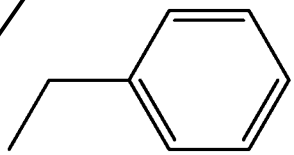
each R^{11} is independently $–C(O)R''$ or $–CH_2OC(O)R''$;

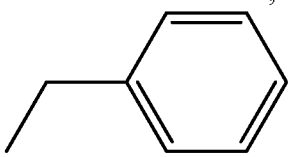
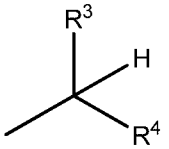
R^{22} is H, CH_3 or CH_2CH_3;

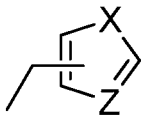
each R is independently C_{1-7} straight-chain alkyl or C_{1-7} branched alkyl;

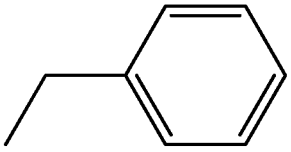
R'' is C_{1-7} straight-chain alkyl or C_{1-7} branched alkyl;

the dashed bonds indicate the presence of an optional ring, which may be saturated or unsaturated;

with the proviso that when R^2 is , , or , R^8 is not ;

with the proviso that when R^2 is , R^8 is  or lower cycloalkyl; and

with the proviso that when R^6 is NH_2, R^2 is , , or C_{2-5} alkyl;

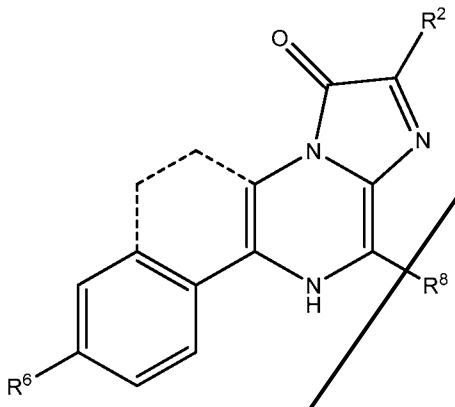
or R^8 is not 

compared to a native or known coelenterazine.

16. The polynucleotide of any one of claims 1-15, wherein the OgLuc variant polypeptide has enhanced biocompatibility relative to the polypeptide of SEQ ID NO: 3.

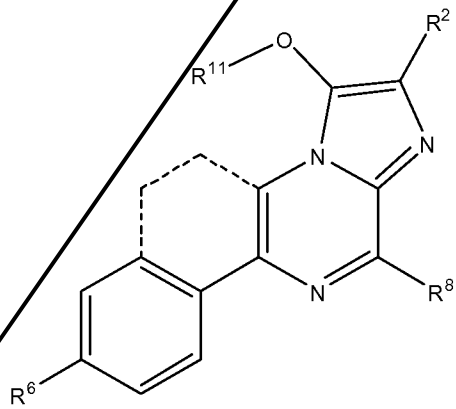
17. The polynucleotide of any one of claims 1-16, wherein the OgLuc variant polypeptide has enhanced luminescence relative to a *Renilla* luciferase in the presence of a coelenterazine.

18. The polynucleotide of any one of claims 1-17, wherein the OgLuc variant polypeptide has enhanced luminescence relative to a *Renilla* luciferase in the presence of a compound of formula (Ia) or (Ib):



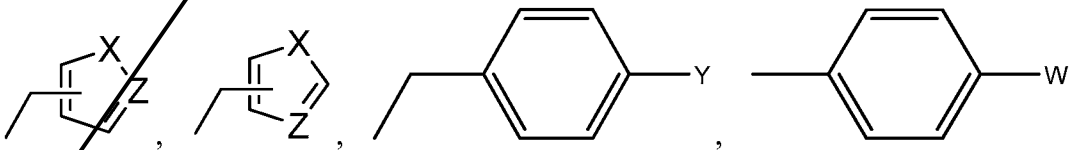
(Ia)

or



(Ib)

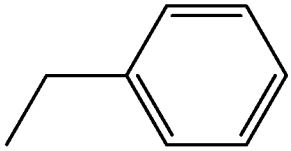
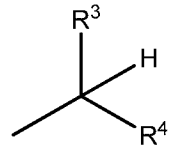
wherein R^2 is selected from the group consisting of



, , , or C_{2-5} straight chain alkyl;

R^6 is selected from the group consisting of -H, -OH, $-NH_2$, -OC(O)R or $-OCH_2OC(O)R$;

R^8 is selected from the group consisting of

, , H or lower cycloalkyl;

wherein R^3 and R^4 are both H or both C_{1-2} alkyl;

W is $-NH_2$, halo, -OH, $-NHC(O)R$, $-CO_2R$;

X is –S-, –O- or $–NR^{22}$-;

Y is –H, -OH, or $–OR^{11}$;

Z is –CH- or –N-;

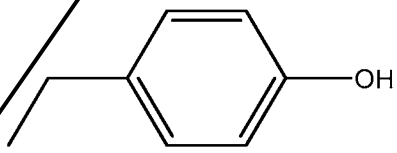
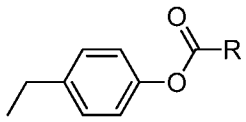
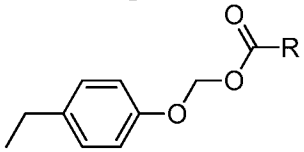
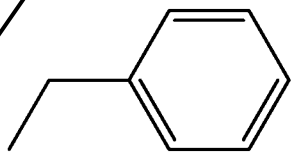
each R^{11} is independently $–C(O)R''$ or $–CH_2OC(O)R''$;

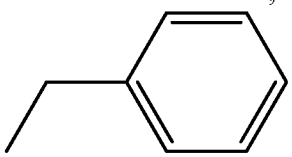
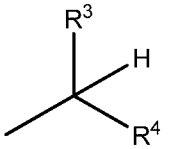
R^{22} is H, CH_3 or CH_2CH_3;

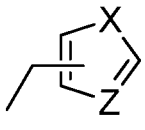
each R is independently C_{1-7} straight-chain alkyl or C_{1-7} branched alkyl;

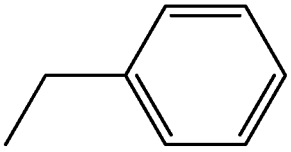
R'' is C_{1-7} straight-chain alkyl or C_{1-7} branched alkyl;

the dashed bonds indicate the presence of an optional ring, which may be saturated or unsaturated;

with the proviso that when R^2 is , , or , R^8 is not ;

with the proviso that when R^2 is , R^8 is  or lower cycloalkyl; and

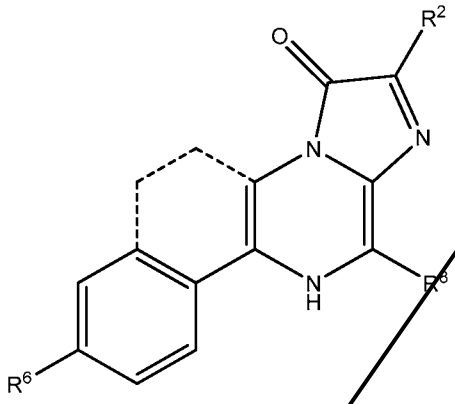
with the proviso that when R^6 is NH_2, R^2 is , , or C_{2-5} alkyl;

or R^8 is not .

.

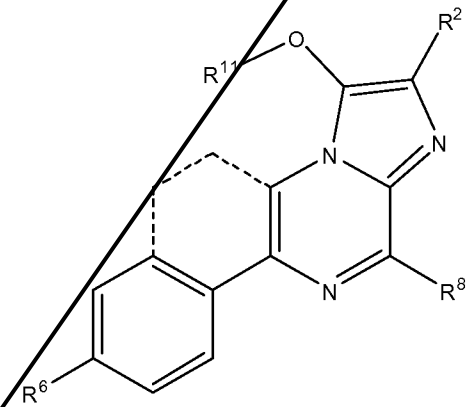
19. The polynucleotide of any one of claims 1-18, wherein the OgLuc variant polypeptide has a change in relative substrate specificity relative to a *Renilla* luciferase in the presence of a coelenterazine compared to a different coelenterazine.

20. The polynucleotide of any one of claims 1-19, wherein the OgLuc variant polypeptide has a change in relative substrate specificity relative to a *Renilla* luciferase in the presence of a compound of formula (Ia) or (Ib):



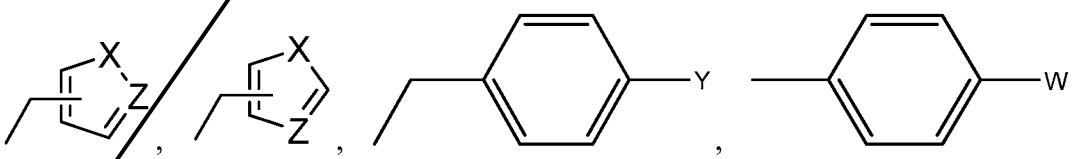
(Ia)

or



(Ib)

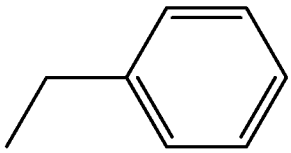
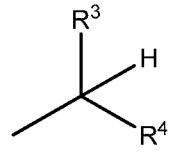
wherein R^2 is selected from the group consisting of



or C_{2-5} straight chain alkyl;

R^6 is selected from the group consisting of -H, -OH, $-NH_2$, -OC(O)R or $-OCH_2OC(O)R$;

R^8 is selected from the group consisting of

, , H or lower cycloalkyl;

wherein R^3 and R^4 are both H or both C_{1-2} alkyl;

W is $-NH_2$, halo, -OH, $-NHC(O)R$, $-CO_2R$;

X is –S-, –O- or $–NR^{22}$-;

Y is –H, -OH, or $–OR^{11}$;

Z is –CH- or –N-;

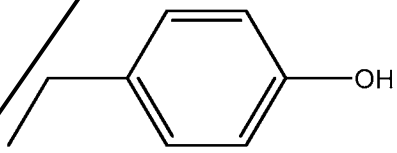
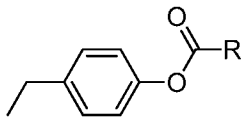
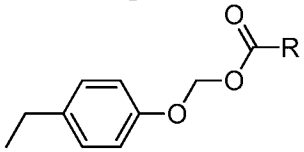
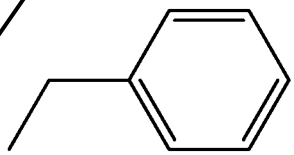
each R^{11} is independently $–C(O)R''$ or $–CH_2OC(O)R''$;

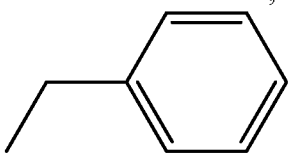
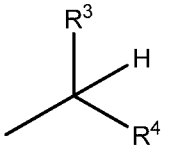
R^{22} is H, CH_3 or CH_2CH_3;

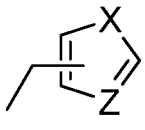
each R is independently C_{1-7} straight-chain alkyl or C_{1-7} branched alkyl;

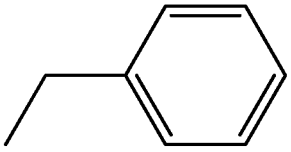
R'' is C_{1-7} straight-chain alkyl or C_{1-7} branched alkyl;

the dashed bonds indicate the presence of an optional ring, which may be saturated or unsaturated;

with the proviso that when R^2 is , , or , R^8 is not ;

with the proviso that when R^2 is , R^8 is  or lower cycloalkyl; and

with the proviso that when R^6 is NH_2, R^2 is , , or C_{2-5} alkyl;

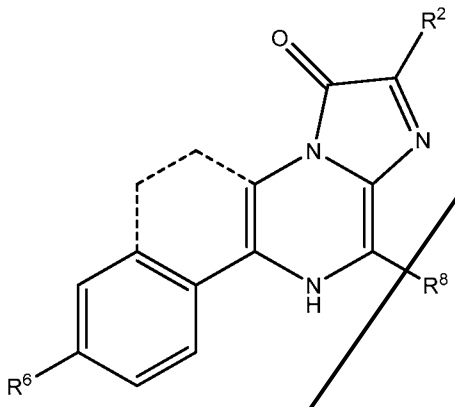
or R^8 is not 

compared to a native or known coelenterazine.

21. The polynucleotide of any one of claims 1-20, wherein the OgLuc variant polypeptide has enhanced biocompatibility relative to a *Renilla* luciferase.

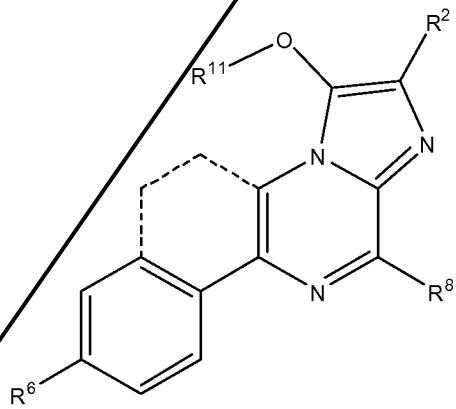
22. The polynucleotide of any one of claims 1-21, wherein the OgLuc variant polypeptide has enhanced luminescence in the presence of a coelenterazine relative to a firefly luciferase in the presence of luciferin.

23. The polynucleotide of any one of claims 1-22, wherein the OgLuc variant polypeptide has enhanced luminescence in the presence of a compound of formula (Ia) or (Ib):



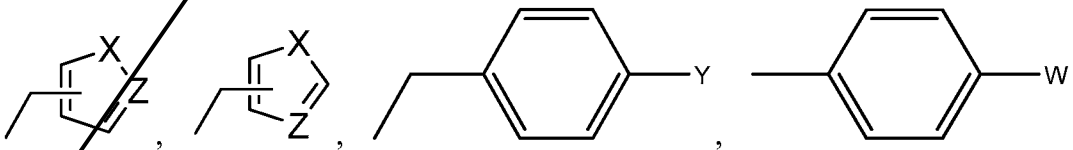
(Ia)

or



(Ib)

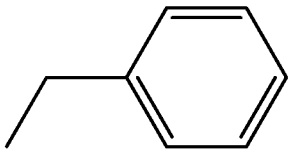
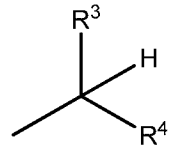
wherein R^2 is selected from the group consisting of



, or C_{2-5} straight chain alkyl;

R^9 is selected from the group consisting of -H, -OH, $-NH_2$, -OC(O)R or $-OCH_2OC(O)R$;

R^8 is selected from the group consisting of

, , H or lower cycloalkyl;

wherein R^3 and R^4 are both H or both C_{1-2} alkyl;

W is $-NH_2$, halo, -OH, -NHC(O)R, $-CO_2R$;

X is –S-, –O- or $–NR^{22}$-;

Y is –H, -OH, or $–OR^{11}$;

Z is –CH- or –N-;

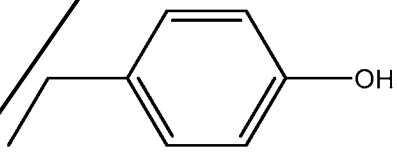
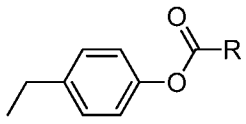
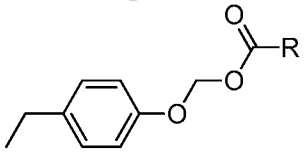
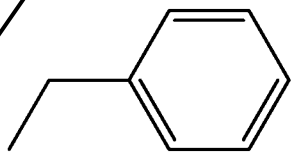
each R^{11} is independently –C(O)R'' or $–CH_2OC(O)R''$;

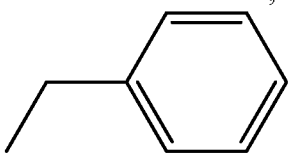
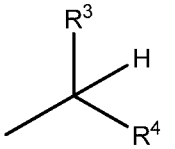
R^{22} is H, CH_3 or CH_2CH_3;

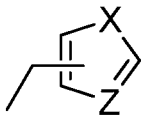
each R is independently C_{1-7} straight-chain alkyl or C_{1-7} branched alkyl;

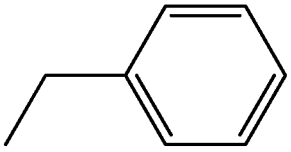
R'' is C_{1-7} straight-chain alkyl or C_{1-7} branched alkyl;

the dashed bonds indicate the presence of an optional ring, which may be saturated or unsaturated;

with the proviso that when R^2 is , , or , R^8 is not ;

with the proviso that when R^2 is , R^8 is  or lower cycloalkyl; and

with the proviso that when R^6 is NH_2, R^2 is , , or C_{2-5} alkyl;

or R^8 is not 

relative to a firefly luciferase in the presence of luciferin.

24. The polynucleotide of any one of claims 1-23, wherein the OgLuc variant polypeptide has enhanced biocompatibility relative to a firefly luciferase.

25. The polynucleotide of any one of claims 1-24, wherein the OgLuc variant polypeptide is from *Oplophorus gracilirostris*, *Oplophorus grimaldii*, *Oplophorus spinicauda*, *Oplophorus foliaceus*, *Oplophorus novaezeelandiae*, *Oplophorus typus*, or *Oplophorus spinosus*.

26. The polynucleotide of any one of claims 1-25, wherein the at least one amino acid substitution is in a position corresponding to positions 1, 4, 6, 10, 11, 14, 15, 16, 18, 19, 20, 21, 22, 23, 24, 25, 27, 28, 31, 32, 33, 34, 36, 38, 39, 40, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 54, 55, 56, 58, 59, 60, 66, 67, 68, 69, 70, 71, 72, 74, 75, 76, 77, 86, 87, 89, 90, 92, 93, 94, 95, 96, 97, 98, 99, 100, 102, 106, 109, 110, 111, 112, 113, 117, 119, 124, 125, 126, 127, 128, 129, 130, 135, 136, 138, 139, 142, 145, 146, 147, 148, 149, 150, 152, 154, 155, 158, 159, 163, 164, 166, 168, or 169, or a combination thereof, of SEQ ID NO: 1.

27. The polynucleotide of any one of claims 1-26, wherein the encoded OgLuc variant polypeptide further comprises a substitution corresponding to at least one of F1I, E4K, F6Y, W10Y, R11Q, A14V/S, G15R, Y16E, Q18D/F/G/H/I/K/L/M/N/P/R/S/V/W/Y, D19N, Q20P/R, V21L/M, L22I/F, E23K, Q24A, G25L, L27M/V/A/D/G/I, S28Y, F31I, Q32H/L/P, A33N/M, L34M, V36E/M, V38F/I, T39I, P40T/I/L/Q, Q42H, K43N/R, I44F, V45E, L46Q, S47P, G48R, E49D/G/K, N50K/S, G51E/R/V, A54I/S, D55E/G, I56V, V58I/L, I59T, I60V, S66T/N, G67D/S, F68L/S/W/Y/D, Q69H, M70V, G71D, L72A/C/F/G/H/I/M/N/P/Q/R/S/T/V/W/Y, E74I/K, M75F/K, I76F/N/V, F77A/C/D/G/M/N/S/T/V/W/Y, H86L/R, H87N/T, K89E, I90D/K/P/Q/R/T/V/Y, L92A/G/H/M/Q/R/S/Y, H93R, Y94F, G95D/S, T96A, L97E, V98F, I99T/V, D100I, V102E/M/T, M106I/K, Y109F, F110I, G111N, R112C, P113H/T/K, I117F, V119M, K124M, I125L, T126R, V127A, T128A/S, G129Q, T130K, N135D/Y, L136M, I138S, D139G, L142V/E/K/W, P145L/Q, D146G, G147N, S148T, L149I/M, L150V, R152H/S/E/T, T154S, I155T, V158I, T159I/S, L163I, C164S, N166I/F/E, L168F, or A169V, or a combination thereof, corresponding to SEQ ID NO: 1.

28. The polynucleotide of any one of claims 1-27, wherein the polypeptide encoded by the polynucleotide includes at least one of the following amino acids: isoleucine at position 1, lysine at position 4, tyrosine at position 6, tyrosine at position 10, glutamine at position 11, valine or serine at position 14, arginine at position 15, glutamate at position 16, aspartate, phenylalanine, glycine, histidine, isoleucine, lysine, leucine, methionine, asparagine, proline, arginine, serine, valine, tryptophan, or tyrosine at position 18, asparagine at position 19, arginine or proline at position 20, leucine or methionine at position 21, isoleucine or phenylalanine at position 22, lysine at position 23, alanine at position 24, leucine at position 25, valine, methionine, alanine, aspartate, glycine or isoleucine at position 27, tyrosine at position 28, isoleucine at position 31,

proline, histidine, or leucine at position 32, asparagine or methionine at position 33, methionine at position 34, methionine or glutamate at position 36, isoleucine or phenylalanine at position 38, isoleucine at position 39, threonine, isoleucine, leucine or glutamine at position 40, histidine at position 42, asparagine or arginine at position 43, phenylalanine at position 44, glutamate at position 45, glutamine at position 46, proline at position 47, arginine at position 48, aspartate, glycine, or lysine at position 49, lysine or serine at position 50, glutamate, arginine, or valine at position 51, serine or isoleucine at position 54, glycine or glutamate at position 55, valine at position 56, isoleucine or leucine at position 58, threonine at position 59, valine at position 60, threonine or asparagine at position 66, serine or aspartate at position 67, leucine, aspartate, serine, tyrosine or tryptophan at position 68, valine at position 69, valine at position 70, aspartate at position 71, glutamine, alanine, cysteine, phenylalanine, glycine, histidine, isoleucine, methionine, asparagine, proline, arginine, serine, threonine, valine, tryptophan, or tyrosine at position 72, lysine or isoleucine at position 74, lysine or phenylalanine at position 75, asparagine, phenylalanine, or valine at position 76, alanine, cysteine, aspartate, glycine, asparagine, methionine, serine, threonine, valine, tryptophan, or tyrosine at position 77, arginine or leucine at position 86, asparagine or threonine at position 87, glutamate at position 89, aspartate, lysine, proline, glutamine, arginine, threonine, valine, or tyrosine at position 90, alanine, glycine, histidine, methionine, glutamine, arginine, serine, or tyrosine at position 92, arginine at position 93, phenylalanine at position 94, serine or aspartate at position 95, alanine at position 96, glutamate at position 97, phenylalanine at position 98, threonine or valine at position 99, isoleucine at position 100, methionine, glutamate, or threonine at position 102, isoleucine or lysine at position 106, phenylalanine at position 109, isoleucine at position 110, asparagine at position 111, cysteine at position 112, histidine, threonine, or lysine at position 113, phenylalanine at position 117, methionine at position 119, methionine at position 124, leucine at position 125, arginine at position 126, alanine at position 127, alanine or serine at position 128, glutamine at position 129, lysine at position 130, aspartate or tyrosine at position 135, methionine at position 136, serine at position 138, glycine at position 139, valine, glutamate, lysine or tryptophan at position 142, leucine or glutamine at position 145, glycine at position 146, asparagine at position 147, threonine at position 148, isoleucine or methionine at position 149, valine at position 150, histidine, serine, glutamate or threonine at position 152, serine at position 154, threonine at position 155, isoleucine at position 158, serine or isoleucine at position 159, isoleucine at position 163, serine at position 164, phenylalanine at position 168, or valine at position 169, or a combination thereof, corresponding to SEQ ID NO: 1.

29. The polynucleotide of any one of claims 1-28, wherein the OgLuc variant polypeptide comprises the amino acid substitutions A4E, Q11R, A33K, V44I, A54F, P115E, Q124K, Y138I

and N166R corresponding to SEQ ID NO: 1, and at least one additional amino acid substitution at a position corresponding to positions 1, 4, 6, 11, 14, 15, 18, 19, 20, 21, 22, 23, 27, 28, 31, 32, 33, 34, 36, 38, 39, 40, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 54, 55, 56, 58, 59, 60, 66, 67, 68, 69, 70, 71, 72, 74, 75, 76, 77, 86, 89, 90, 92, 93, 94, 95, 96, 98, 99, 102, 106, 109, 110, 112, 113, 117, 119, 124, 126, 127, 128, 135, 136, 138, 139, 142, 145, 148, 149, 152, 154, 155, 158, 159, 163, 164, 168, or 169, or a combination thereof, of SEQ ID NO: 1.

30. The polynucleotide of any one of claims 1-29, wherein the amino acid at position 4 is glutamate, at position 11 is arginine, at position 33 is lysine, at position 44 is isoleucine, at position 54 is phenylalanine, at position 115 is glutamate, at position 124 is lysine, at position 138 is isoleucine, and at position 166 is arginine corresponding to SEQ ID NO: 1, and at least one additional amino acid substitution at a position corresponding to positions 1, 4, 6, 11, 14, 15, 18, 19, 20, 21, 22, 23, 27, 28, 31, 32, 33, 34, 36, 38, 39, 40, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 54, 55, 56, 58, 59, 60, 66, 67, 68, 69, 70, 71, 72, 74, 75, 76, 77, 86, 89, 90, 92, 93, 94, 95, 96, 98, 99, 102, 106, 109, 110, 112, 113, 117, 119, 124, 126, 127, 128, 135, 136, 138, 139, 142, 145, 148, 149, 152, 154, 155, 158, 159, 163, 164, 168, or 169, or a combination thereof, of SEQ ID NO: 1.

31. The polynucleotide of claim 29 or 30, wherein the at least one amino acid substitution corresponds to at least one of F1I, E4K, F6Y, R11Q, A14V, G15R, Q18D/F/G/H/I/K/L/M/N/P/R/S/V/W/Y, D19N, Q20P/R, V21L/M, L22I/F, E23K, L27M/V, S28Y, F31I, Q32H/L/P, A33N/M, L34M, V36E/M, V38F/I, T39I, P40T, Q42H, K43N/R, I44F, V45E, L46Q, S47P, G48R, E49D/G/K, N50K/S, G51E/R/V, A54I/S, D55E/G, I56V, V58I/L, I59T, I60V, S66T/N, G67D/S, F68L/S/W/Y/D, Q69H, M70V, G71D, L72A/C/F/G/H/I/M/N/P/Q/R/S/T/V/W/Y, E74I/K, M75F/K, I76F/N/V, F77A/C/D/G/M/N/S/T/V/W/Y, H86L/R, K89E, I90D/K/P/Q/R/T/V/Y, L92A/G/H/M/Q/R/S/Y, H93R, Y94F, G95D/S, T96A, V98F, I99T/V, V102E/M, M106I/K, Y109F, F110I, R112C, P113H/T, I117F, V119M, K124M, T126R, V127A, T128A/S, N135D/Y, L136M, I138S, D139G, L142V, P145L/Q, S148T, L149I, R152H/S, T154S, I155T, V158I, T159I/S, L163I, C164S, L168F, or A169V, or a combination thereof, corresponding to SEQ ID NO: 1.

32. The polynucleotide of claim 29 or 30, wherein the polypeptide encoded by the polynucleotide includes at least one of the following amino acids: isoleucine at position 1, lysine at position 4, tyrosine at position 6, glutamine at position 11, valine at position 14, arginine at position 15, aspartate, phenylalanine, glycine, histidine, isoleucine, lysine, leucine, methionine, asparagine, proline, arginine, serine, valine, tryptophan, or tyrosine at position 18, asparagine at position 19, arginine or proline at position 20, leucine or methionine at position 21, isoleucine or phenylalanine at position 22, lysine at position 23, valine or methionine at position 27, tyrosine at

position 28, isoleucine at position 31, proline, histidine, or leucine at position 32, asparagine or methionine at position 33, methionine at position 34, methionine or glutamate at position 36, isoleucine or phenylalanine at position 38, isoleucine at position 39, threonine at position 40, histidine at position 42, asparagine or arginine at position 43, phenylalanine at position 44, glutamate at position 45, glutamine at position 46, proline at position 47, arginine at position 48, aspartate, glycine, or lysine at position 49, lysine or serine at position 50, glutamate, arginine, or valine at position 51, serine or isoleucine at position 54, glycine or glutamate at position 55, valine at position 56, isoleucine or leucine at position 58, threonine at position 59, valine at position 60, threonine or asparagine at position 66, serine or aspartate at position 67, aspartate, serine, tyrosine or tryptophan at position 68, histidine at position 69, valine at position 70, aspartate at position 71, glutamine, alanine, cysteine, phenylalanine, glycine, histidine, isoleucine, methionine, asparagine, proline, arginine, serine, threonine, valine, tryptophan, or tyrosine at position 72, lysine or isoleucine at position 74, lysine or phenylalanine at position 75, asparagine, phenylalanine, or valine at position 76, alanine, cysteine, aspartate, glycine, asparagine, methionine, serine, threonine, valine, tryptophan, or tyrosine at position 77, arginine or leucine at position 86, glutamate at position 89, aspartate, lysine, proline, glutamine, arginine, threonine, valine, or tyrosine at position 90, alanine, glycine, histidine, methionine, glutamine, arginine, serine, or tyrosine at position 92, arginine at position 93, phenylalanine at position 94, serine or aspartate at position 95, alanine at position 96, phenylalanine at position 98, threonine or valine at position 99, methionine or glutamate at position 102, isoleucine or lysine at position 106, phenylalanine at position 109, isoleucine at position 110, cysteine at position 112, histidine or threonine at position 113, phenylalanine at position 117, methionine at position 119, methionine at position 124, arginine at position 126, alanine at position 127, alanine or serine at position 128, aspartate or tyrosine at position 135, methionine at position 136, serine at position 138, glycine at position 139, valine at position 142, leucine or glutamine at position 145, threonine at position 148, isoleucine at position 149, histidine or serine at position 152, serine at position 154, threonine at position 155, isoleucine at position 158, serine or isoleucine at position 159, isoleucine at position 163, serine at position 164, phenylalanine at position 168, or valine at position 169, or a combination thereof, corresponding to SEQ ID NO: 1.

33. The polynucleotide of any one of claims 1-26, wherein the OgLuc variant polypeptide comprises the amino acid substitutions A4E, Q11R, A33K, V44I, A54F, P115E, Q124K, Y138I and N166R corresponding to SEQ ID NO: 1, and at least one amino acid at a position corresponding to positions 1, 4, 14, 15, 18, 20, 22, 23, 27, 33, 38, 39, 43, 49, 54, 55, 56, 58, 59, 66, 67, 68, 70, 71, 72, 75, 76, 77, 89, 90, 92, 93, 102, 106, 109, 113, 117, 126, 127, 136, 139, 145, 148, 163, 164, or 169, or a combination thereof, of SEQ ID NO: 1.

34. The polynucleotide of any one of claims 1-26, wherein the amino acid at position 4 is glutamate, at position 11 is arginine, at position 33 is lysine, at position 44 is isoleucine, at position 54 is phenylalanine, at position 115 is glutamate, at position 124 is lysine, at position 138 is isoleucine, and at position 166 is arginine corresponding to SEQ ID NO: 1, and at least one additional amino acid substitution at a position corresponding to positions 1, 4, 14, 15, 18, 20, 22, 23, 27, 33, 38, 39, 43, 49, 54, 55, 56, 58, 59, 66, 67, 68, 70, 71, 72, 75, 76, 77, 89, 90, 92, 93, 102, 106, 109, 113, 117, 126, 127, 136, 139, 145, 148, 163, 164, or 169, or a combination thereof, of SEQ ID NO: 1.

35. The polynucleotide of claim 33 or 34, wherein the encoded OgLuc variant polypeptide further comprises a substitution corresponding to at least one of F1I, E4K, A14V, G15R, Q18D/F/G/H/I/K/L/M/N/P/R/S/W/Y, Q20R, L22I, E23K, L27M/V, A33N, V38I, T39I, K43R, E49K, A54I/S, D55G, I56V, V58I/L, I59T, S66T/N, G67S, F68S/W/Y/D, M70V, G71D, L72A/C/F/G/H/I/M/N/P/Q/R/S/T/V/W/Y, M75F/K, I76N, F77A/C/D/G/M/S/T/V/W/Y, K89E, I90D/K/P/Q/R/T/V/Y, L92A/G/H/M/Q/S/Y, H93R, V102E, M106K, Y109F, P113T, I117F, T126R, V127A, L136M, D139G, P145L, S148T, L163I, C164S, or A169V, or a combination thereof, corresponding to SEQ ID NO: 1.

36. The polynucleotide of claim 33 or 34, wherein the polypeptide encoded by the polynucleotide includes at least one of the following amino acids: isoleucine at position 1, lysine at position 4, valine at position 14, arginine at position 15, aspartate, phenylalanine, glycine, histidine, lysine, leucine, methionine, asparagine, proline, arginine, serine, tryptophan, or tyrosine at position 18, arginine at position 20, isoleucine at position 22, lysine at position 23, valine or methionine at position 27, asparagine at position 33, isoleucine at position 38, isoleucine at position 39, arginine at position 43, lysine at position 49, serine or isoleucine at position 54, glycine at position 55, valine at position 56, isoleucine or leucine at position 58, threonine at position 59, threonine or asparagine at position 66, serine at position 67, aspartate, serine, tyrosine or tryptophan at position 68, valine at position 70, aspartate at position 71, glutamine, alanine, cysteine, phenylalanine, glycine, histidine, isoleucine, methionine, asparagine, proline, arginine, serine, threonine, valine, tryptophan, or tyrosine at position 72, lysine or phenylalanine at position 75, asparagine at position 76, tryptophan, tyrosine, serine, threonine, valine, alanine, glycine, cysteine, aspartate or methionine at position 77, glutamate at position 89, aspartate, lysine, proline, glutamine, arginine, threonine, valine, or tyrosine at position 90, alanine, glycine, histidine, methionine, glutamine, serine, or tyrosine at position 92, arginine at position 93, glutamate at position 102, lysine at position 106, phenylalanine at position 109, threonine at position 113, phenylalanine at position 117, arginine at position 126, alanine at position 127, methionine at position 136, glycine at position 139, leucine at position

145, threonine at position 148, isoleucine at position 163, serine at position 164, or valine at position 169, or a combination thereof, corresponding to SEQ ID NO: 1.

37. The polynucleotide of any one of claims 1-26, wherein the OgLuc variant polypeptide comprises the amino acid substitutions A4E, Q11R, A33K, V44I, A54F, P115E, Q124K, Y138I and N166R corresponding to SEQ ID NO: 1, and at least one additional amino acid substitution at a position corresponding to positions 1, 4, 6, 11, 18, 19, 20, 21, 22, 27, 28, 31, 32, 33, 34, 36, 38, 40, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 54, 55, 58, 60, 66, 67, 68, 69, 70, 72, 74, 75, 76, 77, 86, 90, 92, 94, 95, 96, 98, 99, 102, 106, 109, 110, 112, 113, 119, 124, 128, 135, 138, 142, 145, 149, 152, 154, 155, 158, 159, or 168, or a combination thereof, corresponding to SEQ ID NO: 1.

38. The polynucleotide of any one of claims 1-26, wherein the amino acid at position 4 is glutamate, at position 11 is arginine, at position 33 is lysine, at position 44 is isoleucine, at position 54 is phenylalanine, at position 115 is glutamate, at position 124 is lysine, at position 138 is isoleucine, and at position 166 is arginine corresponding to SEQ ID NO: 1, and at least one additional amino acid substitution at a position corresponding to positions 1, 4, 6, 11, 18, 19, 20, 21, 22, 27, 28, 31, 32, 33, 34, 36, 38, 40, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 54, 55, 58, 60, 66, 67, 68, 69, 70, 72, 74, 75, 76, 77, 86, 90, 92, 94, 95, 96, 98, 99, 102, 106, 109, 110, 112, 113, 119, 124, 128, 135, 138, 142, 145, 149, 152, 154, 155, 158, 159, or 168, or a combination thereof, corresponding to SEQ ID NO: 1.

39. The polynucleotide of claim 37 or 38, wherein the encoded OgLuc variant polypeptide further comprises a substitution corresponding to at least one of F1I, E4K, F6Y, R11Q, Q18H/I/LV, D19N, Q20P, V21L/M, L22F, L27V, S28Y, F31I, Q32 H/L/P, A33N/M, L34M, V36E/M, V38F/I, P40T, Q42H, K43N/R, I44F, V45E, L46Q, S47P, G48R, E49D/G, N50K/S, G51E/R/V, A54I, D55E, V58I, I60V, S66N, G67D/S, F68L/Y/D, Q69H, M70V, L72Q, E74I/K, M75K, I76F/N/V, F77N/Y, H86L/R, I90T/V, L92Q/R, Y94F, G95D/S, T96A, V98F, I99T/V, V102E/M, M106I, Y109F, F110I, R112C, P113H, V119M, K124M, T128A/S, N135D/Y, I138S, L142V, P145Q, L149I, R152H/S, T154S, I155T, V158I, T159I/S, or L168F, or a combination thereof, corresponding to SEQ ID NO: 1.

40. The polynucleotide of claim 37 or 38, wherein the polypeptide encoded by the polynucleotide includes at least one of the following amino acids: isoleucine at position 1, lysine at position 4, tyrosine at position 6, glutamine at position 11, histidine, isoleucine, leucine, or valine at position 18, asparagine at position 19, proline at position 20, leucine or methionine at position 21, phenylalanine at position 22, valine at position 27, tyrosine at position 28, isoleucine at position 31, proline, histidine, or leucine at position 32, asparagine or methionine at position 33, methionine at position 34, methionine or glutamate at position 36, isoleucine or phenylalanine at position 38, threonine at position 40, histidine at position 42, asparagine or

arginine at position 43, phenylalanine at position 44, glutamate at position 45, glutamine at position 46, proline at position 47, arginine at position 48, aspartate or glycine at position 49, lysine or serine at position 50, glutamate, arginine, or valine at position 51, isoleucine at position 54, glutamate at position 55, isoleucine at position 58, valine at position 60, asparagine at position 66, serine or aspartate at position 67, aspartate, leucine, or tyrosine at position 68, histidine at position 69, valine at position 70, glutamine at position 72, lysine or isoleucine at position 74, lysine at position 75, asparagine, phenylalanine, or valine at position 76, asparagine or tyrosine at position 77, arginine or leucine at position 86, threonine or valine at position 90, arginine or glutamine at position 92, phenylalanine at position 94, serine or aspartate at position 95, alanine at position 96, phenylalanine at position 98, threonine or valine at position 99, methionine or glutamate at position 102, isoleucine at position 106, phenylalanine at position 109, isoleucine at position 110, cysteine at position 112, histidine at position 113, methionine at position 119, methionine at position 124, alanine or serine at position 128, aspartate or tyrosine at position 135, serine at position 138, valine at position 142, glutamine at position 145, isoleucine at position 149, histidine or serine at position 152, serine at position 154, threonine at position 155, isoleucine at position 158, serine or isoleucine at position 159, or phenylalanine at position 168, or a combination thereof, corresponding to SEQ ID NO: 1.

41. The polynucleotide of any one of claims 1-26, wherein the OgLuc variant polypeptide comprises the amino acid substitutions A4E, Q11R, A33K, V44I, F54I, I90V, P115E, Q124K, Y138I and N166R corresponding to SEQ ID NO: 1, and at least one additional amino acid substitution at a position corresponding to positions 1, 4, 10, 14, 16, 18, 24, 25, 27, 33, 38, 40, 68, 70, 72, 75, 87, 90, 97, 100, 102, 111, 113, 125, 129, 130, 142, 146, 147, 149, 150, 152, or 166, or a combination thereof, of SEQ ID NO: 1.

42. The polynucleotide of any one of claims 1-26, wherein the OgLuc variant polypeptide comprises the amino acid substitutions wherein the amino acid at position 4 is glutamate, at position 11 is arginine, at position 33 is lysine, at position 44 is isoleucine, at position 54 is isoleucine, at position 90 is valine, at position 115 is glutamate, at position 124 is lysine, at position 138 is isoleucine, and at position 166 is arginine corresponding to SEQ ID NO: 1, and at least one additional amino acid substitution at a position corresponding to positions 1, 4, 10, 14, 16, 18, 24, 25, 27, 33, 38, 40, 68, 70, 72, 75, 87, 90, 97, 100, 102, 111, 113, 125, 129, 130, 142, 146, 147, 149, 150, 152, or 166, or a combination thereof, of SEQ ID NO: 1.

43. The polynucleotide of claim 41 or 42, wherein the at least one amino acid substitution corresponds to at least one of F1I, E4K, W10Y, A14S, Y16E, Q18D/F/G/H/K/L/M/N/P/R/S/W/Y, Q24A, G25L, L27M/A/D/G/I, A33N, V38I, P40I/L/Q, F68W/Y, M70V, L72A/C/F/G/H/I/M/N/P/R/S/T/V/W/Y, M75F/K, H87N/T, I90D/K/P/Q/R/Y,

L97E, D100I, V102E/T, G111N, P113K, I125L, G129Q, T130K, L142E/K/W, D146G, G147N, L149M, L150V, R152E/T, or N166I/F/E, or a combination thereof, corresponding to SEQ ID NO: 1.

44. The polynucleotide of claim 41 or 42, wherein the polypeptide encoded by the polynucleotide includes at least one of the following amino acids: isoleucine at position 1, lysine at position 4, tyrosine at position 10, serine at position 14, glutamate at position 16, aspartate, phenylalanine, glycine, histidine, lysine, leucine, methionine, asparagine, proline, arginine, serine, tryptophan, or tyrosine at position 18, alanine at position 24, leucine at position 25, methionine, alanine, aspartate, glycine or isoleucine at position 27, asparagine at position 33, isoleucine at position 38, isoleucine, leucine or glutamine at position 40, tyrosine or tryptophan at position 68, valine at position 70, alanine, cysteine, phenylalanine, glycine, histidine, isoleucine, methionine, asparagine, proline, arginine, serine, threonine, valine, tryptophan, or tyrosine at position 72, lysine or phenylalanine at position 75, asparagine or threonine at position 87, aspartate, lysine, proline, glutamine, arginine, or tyrosine at position 90, glutamate at position 97, isoleucine at position 100, glutamate or threonine at position 102, asparagine at position 111, lysine at position 113, leucine at position 125, glutamine at position 129, lysine at position 130, glutamate, lysine or tryptophan at position 142, glycine at position 146, asparagine at position 147, methionine at position 149, valine at position 150, glutamate or threonine at position 152, or isoleucine, phenylalanine, or glutamate at position 166, or a combination thereof, corresponding to SEQ ID NO: 1.

45. The polynucleotide of any one of claims 1-26, wherein the OgLuc variant polypeptide comprises the amino acid substitutions A4E, Q11R, A33K, V44I, P115E, Q124K, Y138I, N166R, I90V, F54I, Q18L, F68Y, L72Q, and M75K corresponding to SEQ ID NO: 1.

46. The polynucleotide of any one of claims 1-26, wherein the amino acid at position 4 is glutamate, at position 11 is arginine, at position 18 is leucine, at position 33 is lysine, at position 44 is isoleucine, at position 54 is isoleucine, at position 68 is tyrosine, at position 72 is glutamine, at position 75 is lysine, at position 90 is valine, at position 115 is glutamate, at position 124 is lysine, at position 138 is isoleucine, and at position 166 is arginine corresponding to SEQ ID NO: 1.

47. The polynucleotide of claim 45 or 46 wherein the amino acid substitution at a position corresponding to 33 of SEQ ID NO: 1 is asparagine.

48. The polynucleotide of claim 47, wherein position 39 is encoded by codon ACT, the amino acid at position 39 is threonine, at position 43 is arginine, and at position 68 is aspartate corresponding to SEQ ID NO: 1, the OgLuc variant polypeptide having luciferase activity.

49. The polynucleotide of claim 48, wherein the amino acid at position 27 is valine corresponding to SEQ ID NO: 1, the OgLuc variant polypeptide having luciferase activity.

50. The polynucleotide of any one of claims 1-26, comprising the polynucleotide encoding the polypeptide of SEQ ID NO: 19.

51. The polynucleotide of any one of claims 1-26, comprising the polynucleotide of SEQ ID NO: 18, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 42, SEQ ID NO: 88, or SEQ ID NO: 92.

52. The polynucleotide of any one of claims 37-40, wherein the encoded OgLuc variant polypeptide further comprises amino acid substitutions Q18L, F54I, L92H, and Y109F corresponding to SEQ ID NO: 1.

53. The polynucleotide of 52, wherein the encoded OgLuc variant polypeptide further comprises amino acid substitutions V21L, F68Y, L72Q, M75K, H92R and V158I corresponding to SEQ ID NO: 1.

54. The polynucleotide of any one of claims 37-40, wherein the encoded OgLuc variant polypeptide comprises amino acid substitutions F54I, I90V and F77Y corresponding to SEQ ID NO: 1.

55. The polynucleotide of any one of claims 37-40, wherein the amino acid at position 18 is leucine, at position 54 is isoleucine, at position 92 is histidine, and at position 109 is phenylalanine corresponding to SEQ ID NO: 1.

56. The polynucleotide of 55, wherein the amino acid at position 21 is leucine, at position 68 is tyrosine, at position 72 is glutamine, at position 75 is lysine, at position 92 is arginine, and at position 158 is isoleucine corresponding to SEQ ID NO: 1.

57. The polynucleotide of any one of claims 37-40, wherein the amino acid at position 54 is isoleucine, at position 90 is valine, and at position 77 is tyrosine corresponding to SEQ ID NO: 1.

58. The polynucleotide of any one of claims 52-57, wherein the encoded OgLuc variant polypeptide further comprises a substitution corresponding to at least one of F1I, E4K, F6Y, R11Q, Q18H/I/V, D19N, Q20P, V21M, L22F, L27V, S28Y, F31I, Q32 H/L/P, A33N/M, L34M, V36E/M, V38F/I, P40T, Q42H, K43N/R, I44F, V45E, L46Q, S47P, G48R, E49D/G, N50K/S, G51E/R/V, D55E, V58I, I60V, S66N, G67D/S, F68L/D, Q69H, M70V, E74I/K, I76F/N/V, F77N, H86L/R, I90T, Y94F, G95D/S, T96A, V98F, I99T/V, V102E/M, M106I, F110I, R112C, P113H, V119M, K124M, T128A/S, N135D/Y, I138S, L142V, P145Q, L149I, R152H/S, T154S, I155T, T159I/S, or L168F, or a combination thereof, corresponding to SEQ ID NO: 1.

59. The polynucleotide of any one of claims 52-57, wherein the polypeptide encoded by the polynucleotide includes at least one of the following amino acids: isoleucine amino acid at position 1, lysine at position 4, tyrosine at position 6, glutamine at position 11, histidine,

isoleucine, or valine at position 18, asparagine at position 19, proline at position 20, methionine at position 21, phenylalanine at position 22, valine at position 27, tyrosine at position 28, isoleucine at position 31, proline, histidine, or leucine at position 32, asparagine or methionine at position 33, methionine at position 34, methionine or glutamate at position 36, isoleucine or phenylalanine at position 38, threonine at position 40, histidine at position 42, asparagine or arginine at position 43, phenylalanine at position 44, glutamate at position 45, glutamine at position 46, proline at position 47, arginine at position 48, aspartate or glycine at position 49, lysine or serine at position 50, glutamate, arginine, or valine at position 51, glutamate at position 55, isoleucine at position 58, valine at position 60, asparagine at position 66, serine or aspartate at position 67, leucine or aspartate at position 68, histidine at position 69, valine at position 70, lysine or isoleucine at position 74, asparagine, phenylalanine, or valine at position 76, asparagine at position 77, arginine or leucine at position 86, threonine at position 90, glutamine at position 92, phenylalanine at position 94, serine or aspartate at position 95, alanine at position 96, phenylalanine at position 98, threonine or valine at position 99, methionine or glutamate at position 102, isoleucine at position 106, isoleucine at position 110, cysteine at position 112, histidine at position 113, methionine at position 119, methionine at position 124, alanine or serine at position 128, aspartate or tyrosine, at position 135 is serine at position 138, valine at position 142, glutamine at position 145, isoleucine at position 149, histidine or serine at position 152, serine at position 154, threonine at position 155, serine or isoleucine at position 159, or phenylalanine at position 168, or a combination thereof, corresponding to SEQ ID NO: 1.

60. A polynucleotide encoding an OgLuc variant polypeptide having at least 80% amino acid sequence identity to an OgLuc polypeptide of SEQ ID NO: 1 comprising amino acid substitutions A4E, Q11R, A33K, V44I, P115E, Q124K, Y138I, N166R, I90V, F54I, Q18L, F68Y, L72Q, and M75K corresponding to SEQ ID NO: 1 and the OgLuc variant polypeptide having luciferase activity.

61. A polynucleotide encoding an OgLuc variant polypeptide having at least 80% amino acid sequence identity to an OgLuc polypeptide of SEQ ID NO: 1, wherein the amino acid at position 4 is glutamate, at position 11 is arginine, at position 18 is leucine, at position 33 is lysine, at position 44 is isoleucine, at position 54 is isoleucine, at position 68 is tyrosine, at position 72 is glutamine, at position 75 is lysine, at position 90 is valine, at position 115 is glutamate, at position 124 is lysine, at position 138 is isoleucine, and at position 166 is arginine corresponding to SEQ ID NO: 1 and the OgLuc variant polypeptide having luciferase activity.

62. The polynucleotide of claim 60 or 61 wherein the amino acid substitution at a position corresponding to 33 of SEQ ID NO: 1 is asparagine.

63. The polynucleotide of claim 62, wherein position 39 is encoded by codon ACT, the amino acid at position 39 is threonine, at position 43 is arginine, and at position 68 is aspartate corresponding to SEQ ID NO: 1, the OgLuc variant polypeptide having luciferase activity.

64. The polynucleotide of claim 63, wherein the amino acid at position 27 is valine corresponding to SEQ ID NO: 1, the OgLuc variant polypeptide having luciferase activity.

65. A polynucleotide encoding an OgLuc variant polypeptide having at least 80% amino acid sequence identity to an OgLuc polypeptide of SEQ ID NO: 1 comprising amino acid substitutions A4E, Q11R, A33K, V44I, P115E, Q124K, Y138I, N166R, Q18L, F54I, L92H, and Y109F corresponding to SEQ ID NO: 1 and the OgLuc variant polypeptide having luciferase activity.

66. The polynucleotide of claim 65 further comprising the amino acid substitutions V21L, F68Y, L72Q, M75K, H92R, and V158F corresponding to SEQ ID NO: 1.

67. A polynucleotide encoding an OgLuc variant polypeptide having at least 80% amino acid sequence identity to an OgLuc polypeptide of SEQ ID NO: 1 comprising amino acid substitutions A4E, Q11R, A33K, V44I, A54I, F77Y, I90V, P115E, Q124K, Y138I and N166R corresponding to SEQ ID NO: 1 and the OgLuc variant polypeptide having luciferase activity.

68. A polynucleotide encoding an OgLuc variant polypeptide having at least 80% amino acid sequence identity to an OgLuc polypeptide of SEQ ID NO: 1, wherein the amino acid at position 4 is glutamate, at position 11 is arginine, at position 18 is leucine, at position 33 is lysine, at position 44 is isoleucine, at position 54 is isoleucine, at position 92 is histidine, at position 109 is phenylalanine, at position 115 is glutamate, at position 124 is lysine, at position 138 is isoleucine, and at position 166 is arginine corresponding to SEQ ID NO: 1 and the OgLuc variant polypeptide having luciferase activity.

69. The polynucleotide of claim 68, wherein the amino acid at position 21 is leucine, at position 68 is tyrosine, at position 72 is glutamine, at position 75 is lysine, at position 92 is arginine, and at position 158 is isoleucine corresponding to SEQ ID NO: 1.

70. A polynucleotide encoding an OgLuc variant polypeptide having at least 80% amino acid sequence identity to an OgLuc polypeptide of SEQ ID NO: 1, wherein the amino acid at position 4 is glutamate, at position 11 is arginine, at position 33 is lysine, at position 44 is isoleucine, at position 54 is isoleucine, at position 77 is tyrosine, at position 90 is valine, at position 115 is glutamate, at position 124 is lysine, at position 138 is isoleucine, and at position 166 is arginine corresponding to SEQ ID NO: 1 and the OgLuc variant polypeptide having luciferase activity.

71. A polynucleotide comprising the polynucleotide encoding the polypeptide of SEQ ID NO: 19.

72. A polynucleotide comprising the polynucleotide of SEQ ID NO: 18, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 42, SEQ ID NO: 88, or SEQ ID NO: 92.

73. An isolated polynucleotide encoding a decapod luciferase polypeptide having at least 30% amino acid sequence identity to SEQ ID NO: 1, the polypeptide comprising a sequence pattern corresponding to the sequence pattern of Formula (VII) and including no more than 5 differences, wherein differences include differences from pattern positions 1, 2, 3, 5, 8, 10, 12, 14, 15, 17, or 18 relative to Formula (VII) according to the OgLuc pattern listed in Table 4 as well as gaps or insertions between any of the pattern positions of Formula (VII) according to the OgLuc pattern listed in Table 4, wherein the decapod luciferase produces luminescence in the presence of a coelenterazine.

74. The polynucleotide of claim 73, wherein the decapod luciferase includes no more than 4 differences from the sequence pattern of Formula (VII) according to the OgLuc Pattern listed in Table 4.

75. The polynucleotide of claim 73, wherein the decapod luciferase includes no more than 3 differences from the sequence pattern of Formula (VII) according to the OgLuc pattern listed in Table 4.

76. The polynucleotide of claim 73, wherein the decapod luciferase includes no more than 2 differences from the sequence pattern of Formula (VII) according to the OgLuc pattern listed in Table 4.

77. The polynucleotide of claim 73, wherein the decapod luciferase includes no more than 1 difference from the sequence pattern of Formula (VII) according to the OgLuc pattern listed in Table 4.

78. The polynucleotide of claim 73, wherein the polypeptide comprises a sequence corresponding to Formula (VII) according to the OgLuc pattern listed in Table 4.

79. The polynucleotide of claim 73, wherein the decapod luciferase is from a Aristeidae, Pandalidea, Solenoceridae, Luciferidae, Segestidae, Pasiphaeidae, Oplophoridae, or Thalassocaridae family.

80. The polynucleotide of claim 79, wherein the decapod luciferase is from the Oplophoridae family.

81. The polynucleotide of claim 80, wherein the decapod luciferase is from an Oplophorus species.

82. The polynucleotide of claim 79, wherein the decapod luciferase is a luciferase from *Plesiopenaeus coruscans*, a *Heterocarpus* species, a *Parapandalus* species, *Hymenopenaeus debilis, Mesopenaeus tropicalis*, *Lucifer typus, Sergestes atlanticus, Sergestes arcticus*, *Sergestes armatus*, *Sergestes pediformis, Sergestes cornutus, Sergestes edwardsi, Sergestes henseni,*

Sergestes pectinatus, Sergestes sargassi, Sergestes similis, Sergestes vigilax, Sergia challengeri, Sergia grandis, Sergia lucens, Sergia prehensilis, Sergia potens, Sergia robusta, Sergia scintillans, Sergia splendens, Glyphus marsupialis, Leptochela bermudensis, Parapasiphae sulcatifrons, Pasiphea tarda, Acanthephyra acanthitelsonis, Acanthephyra acutifrons, Acanthephyra brevirostris, Acanthephyra cucullata, Acanthephyra curtirostris, Acanthephyra eximia, Acanthephyra gracilipes, Acanthephyra kingsleyi, Acanthephyra media, Acanthephyra microphthalma, Acanthephyra pelagica, Acanthephyra prionota, Acanthephyra purpurea, Acanthephyra sanguinea, Acanthephyra sibogae, Acanthephyra stylorostratis, Ephyrina bifida, Ephyrina figueirai, Ephyrina koskynii, Ephyrina ombango, Hymenodora glacialis, Hymenodora gracilis, Meningodora miccyla, Meningodora mollis, Meningodora vesca, Notostomus gibbosus, Notostomus auriculatus, Oplophorus gracilirostris, Oplophorus grimaldii, Oplophorus novaezealandiae, Oplophorus spinicauda, Oplophorus foliaceus, Oplophorus spinosus, Oplophorus typus, Systellaspis braueri, Systellaspis cristata, Systellaspis debilis, Systellaspis pellucida, Chlorotocoides spinicauda, Thalassocaris crinita, or *Thalassocaris lucida.*

83. The polynucleotide of claim 73, wherein the sequence pattern of Formula (VII) is aligned with SEQ ID NO: 1 starting at residue 8 of SEQ ID NO: 1

84. The polynucleotide of any one of claims 1-83, wherein the sequence has been codon-optimized.

85. The polynucleotide of claim 84, wherein the polynucleotide comprises SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, or SEQ ID NO: 25.

86. The polynucleotide of any one of claims 1-85, wherein the polynucleotide further encodes a polypeptide of interest linked to the OgLuc variant polypeptide, the polypeptide of interest and the OgLuc variant polypeptide capable of being expressed as a fusion protein.

87. A vector comprising the polynucleotide of any of claims 1-86.

88. The vector of claim 96, wherein the polynucleotide is operably linked to a promoter.

89. A cell comprising the polynucleotide of any one of claims 1-86 or the vector of claim 87 or 88.

90. A non-human transgenic animal comprising the cell of claim 89.

91. A non-human transgenic animal comprising the polynucleotide of any one of claims 1-86 or the vector of claim 87 or 88.

92. An OgLuc variant polypeptide encoded by the polynucleotide of any one claims 1-86.

93. A polypeptide encoded by the polynucleotide of any one of claims 1-86.

94. A fusion protein comprising an OgLuc variant polypeptide encoded by the polynucleotide of any one of claims 1-86.

95. A method of producing an OgLuc variant polypeptide comprising growing the cell of claim 89 under conditions that permit expression of the OgLuc variant polypeptide.

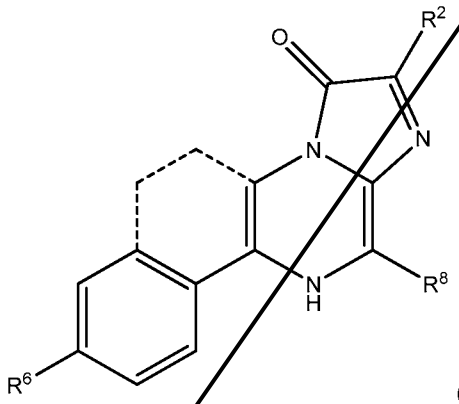
96. A method of producing an OgLuc variant polypeptide comprising introducing the vector of claim 87 or 88 into a cell under conditions which permit expression of the OgLuc variant polypeptide.

97. A kit comprising the polynucleotide of any one of claims 1-86 or the vector of claim 87 or 88.

98. A kit comprising the OgLuc variant polypeptide of claim 92.

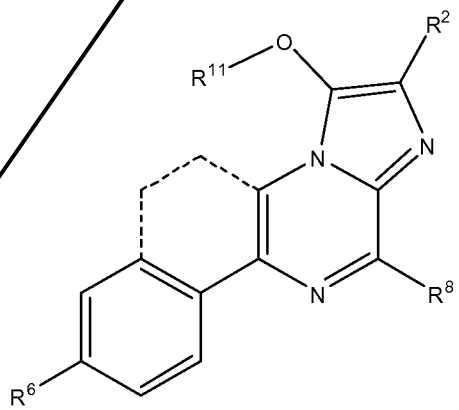
99. The kit of any one of claim 97 or 98, further comprising at least one of:

(a) the compound of formula (Ia) or (Ib):



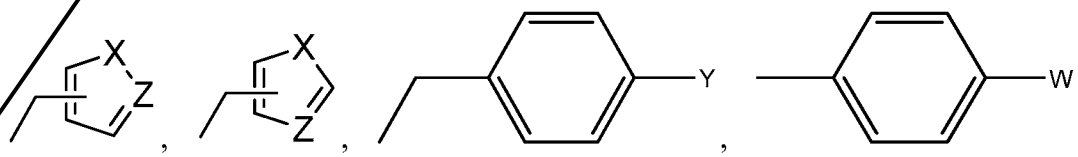
(Ia)

or



(Ib)

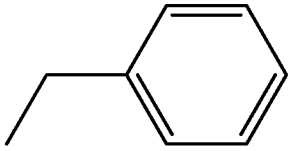
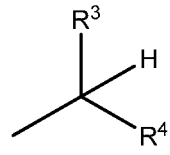
wherein R^2 is selected from the group consisting of



or C_{2-5} straight chain alkyl;

R^6 is selected from the group consisting of -H, -OH, $-NH_2$, -OC(O)R or $-OCH_2OC(O)R$;

R^8 is selected from the group consisting of

, , H or lower cycloalkyl;

wherein R^3 and R^4 are both H or both C_{1-2} alkyl;

W is $-NH_2$, halo, -OH, $-NHC(O)R$, $-CO_2R$;

X is –S-, –O- or $–NR^{22}$-;

Y is –H, -OH, or $–OR^{11}$;

Z is –CH- or –N-;

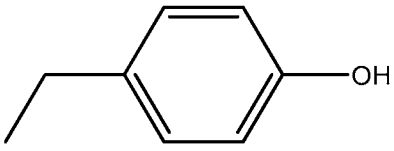
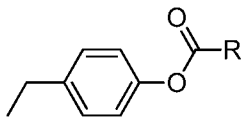
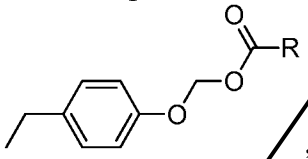
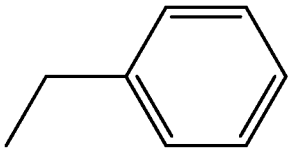
each R^{11} is independently $–C(O)R''$ or $–CH_2OC(O)R''$;

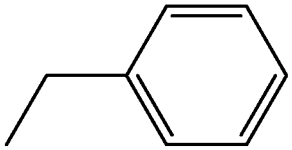
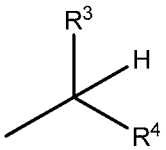
R^{22} is H, CH_3 or CH_2CH_3;

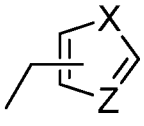
each R is independently C_{1-7} straight-chain alkyl or C_{1-7} branched alkyl;

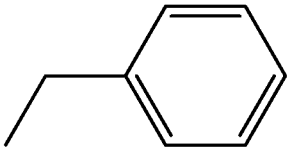
R'' is C_{1-7} straight-chain alkyl or C_{1-7} branched alkyl;

the dashed bonds indicate the presence of an optional ring, which may be saturated or unsaturated;

with the proviso that when R^2 is , , or , R^8 is not ;

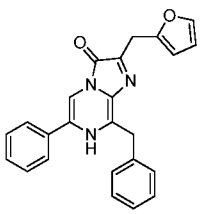
with the proviso that when R^2 is , R^8 is  or lower cycloalkyl; and

with the proviso that when R^6 is NH_2, R^2 is , , or C_{2-5} alkyl;

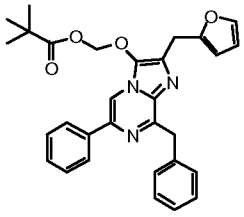
or R^8 is not ; and

(b) a buffer reagent.

100. A kit comprising the compound



or



and the polynucleotide of any one of claims 60-64 or 71-72 or the polypeptide encoded by the polynucleotide of any one of claims 60-64 or 71-72.

101. A method for measuring bioluminescence using at least one of the polynucleotide of any one of claims 1-86; the vector of any one of claims 87 or 88; the cell of claim 89; the animal of any of claims 90-91; the OgLuc variant polypeptide of claim 92; the polypeptide of claim 93; and the fusion protein of claim 94.

102. A synthetic nucleotide sequence encoding an OgLuc variant polypeptide comprising a fragment of at least 100 nucleotides having 80% or less nucleic acid sequence identity to a parent nucleic acid sequence having SEQ ID NO: 2 and having 90% or more nucleic acid sequence identity to SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, or SEQ ID NO: 25 or the complement thereof, wherein the decreased sequence identity is a result of different codons in the synthetic nucleotide sequence relative to the codons in the parent nucleic acid sequence, wherein the synthetic nucleotide sequence encodes a OgLuc variant which has at least 85% amino acid sequence identity to the corresponding luciferase encoded by the parent nucleic acid sequence, and wherein the synthetic nucleotide sequence has a reduced number of regulatory sequences relative to the parent nucleic acid sequence.

103. A synthetic nucleotide sequence encoding an OgLuc variant polypeptide comprising a fragment of at least 300 nucleotides having 80% or less nucleic acid sequence identity to a parent nucleic acid sequence having SEQ ID NO: 14 and having 90% or more nucleic acid sequence identity to SEQ ID NO: 22 or SEQ ID NO: 23 or the complement thereof, wherein the decreased sequence identity is a result of different codons in the synthetic nucleotide sequence relative to the codons in the parent nucleic acid sequence, wherein the synthetic nucleotide sequence encodes a firefly luciferase which has at least 85% amino acid sequence identity to the corresponding luciferase encoded by the parent nucleic acid sequence, and wherein the synthetic nucleotide sequence has a reduced number of regulatory sequences relative to the parent nucleic acid sequence.

104. A synthetic nucleotide sequence encoding an OgLuc variant polypeptide comprising a fragment of at least 100 nucleotides having 80% or less nucleic acid sequence identity to a parent nucleic acid sequence having SEQ ID NO: 18 and having 90% or more nucleic acid sequence identity to SEQ ID NO: 24 or SEQ ID NO: 25 or the complement thereof, wherein the decreased

sequence identity is a result of different codons in the synthetic nucleotide sequence relative to the codons in the parent nucleic acid sequence, wherein the synthetic nucleotide sequence encodes a OgLuc variant which has at least 85% amino acid sequence identity to the corresponding luciferase encoded by the parent nucleic acid sequence, and wherein the synthetic nucleotide sequence has a reduced number of regulatory sequences relative to the parent nucleic acid sequence.

105. The polynucleotide of any one of claims 1-86, wherein the OgLuc variant polypeptide is a soluble monomer.

106. The polynucleotide of claim 86, wherein the fusion protein comprises a signal sequence at the N-terminus of the OgLuc variant polypeptide.

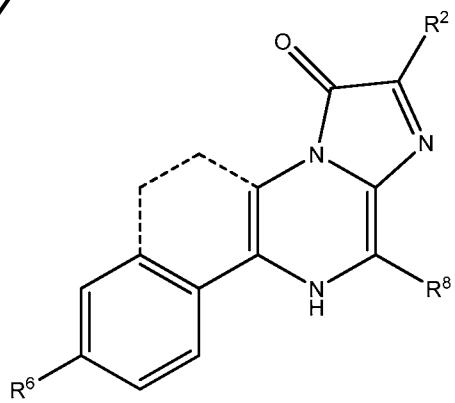
107. The polynucleotide of claim 106, wherein the fusion protein is secreted from a cell.

108. A fusion peptide comprising a signal peptide from *Oplophorus gracilirostris* fused to a heterologous protein, wherein said signal peptide is SEQ ID NO: 54, wherein the fusion peptide is expressed in a cell and secreted from the cell.

109. A bioluminescence resonance energy transfer (BRET) system comprising: a first fusion protein including a first target protein and a bioluminescence donor molecule, wherein the bioluminescence donor molecule is an OgLuc variant encoded by the polynucleotide of any one of claims 10-88; a second fusion protein including a second target protein and a fluorescent acceptor molecule; and an OgLuc substrate.

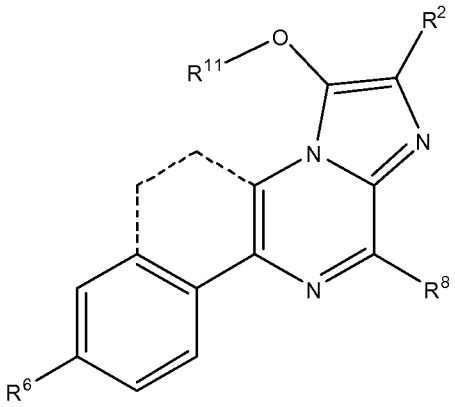
110. The BRET system of claim 109, wherein the OgLuc substrate is a native or known coelenterazine.

111. The BRET system of claim 109, wherein the OgLuc substrate is a compound of formula (Ia) or (Ib):



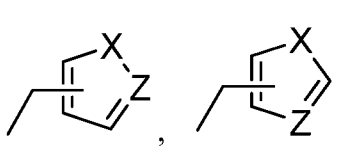
(Ia)

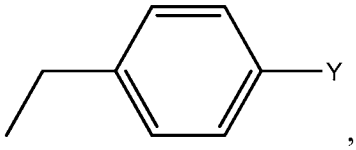
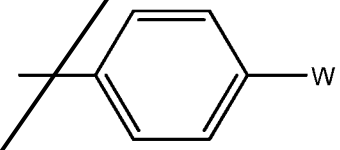
or



(Ib)

wherein R^2 is selected from the group consisting of

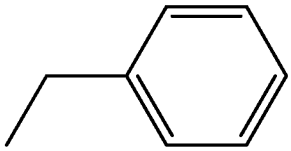
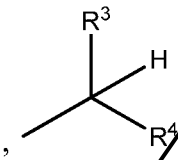


or C_{2-5} straight chain alkyl;

R^6 is selected from the group consisting of -H, -OH, $-NH_2$, -OC(O)R or $-OCH_2OC(O)R$;

R^8 is selected from the group consisting of

, H or lower cycloalkyl;

wherein R^3 and R^4 are both H or both C_{1-2} alkyl;

W is $-NH_2$, halo, -OH, -NHC(O)R, $-CO_2R$;

X is –S-, –O- or $–NR^{22}$-;

Y is –H, -OH, or $–OR^{11}$;

Z is –CH- or –N-;

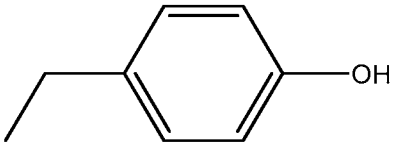
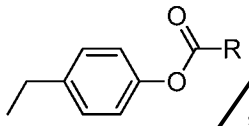
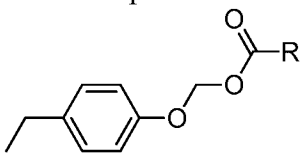
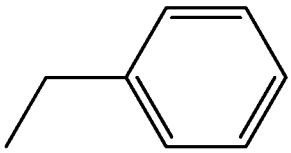
each R^{11} is independently –C(O)R'' or $–CH_2OC(O)R''$;

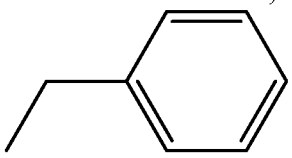
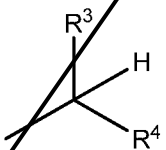
R^{22} is H, CH_3 or CH_2CH_3;

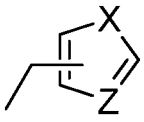
each R is independently C_{1-7} straight-chain alkyl or C_{1-7} branched alkyl;

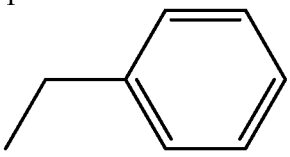
R'' is C_{1-7} straight-chain alkyl or C_{1-7} branched alkyl;

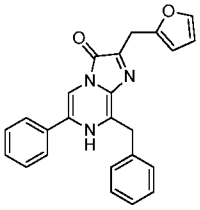
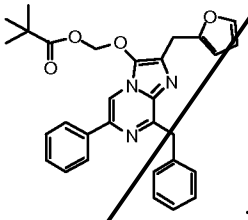
the dashed bonds indicate the presence of an optional ring, which may be saturated or unsaturated;

with the proviso that when R^2 is , , or , R^8 is not ;

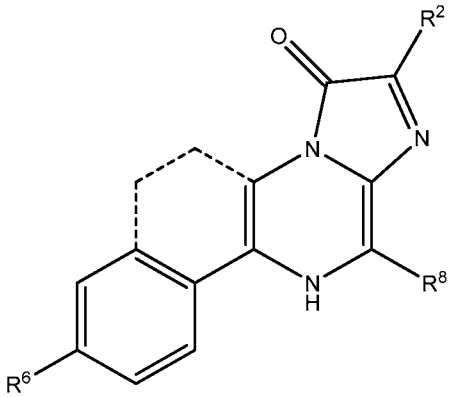
with the proviso that when R^2 is , R^8 is  or lower cycloalkyl; and

with the proviso that when R^6 is NH_2, R^2 is , , or C_{2-5} alkyl;

or R^8 is not .

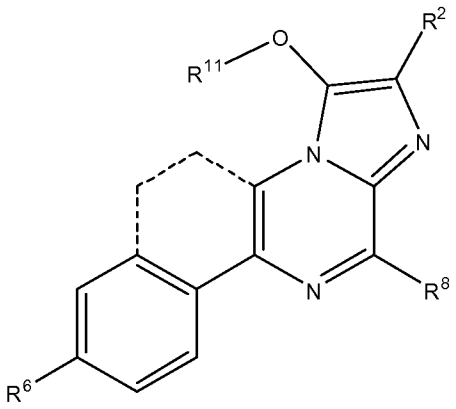
112. The BRET system of claim 109, wherein the OgLuc substrate is the compound  or .

113. A method of measuring the enzymatic activity of a luminogenic protein comprising: contacting a luminogenic protein, a deprotecting enzyme, and a protected luminophore; and detecting light produced from the composition, wherein the luminogenic protein is an OgLuc variant encoded by the polynucleotide of any one of claims 1-86 and the luminophore is a compound of formula (Ia) or (Ib):



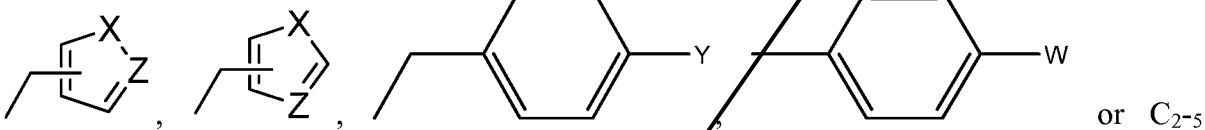
(Ia)

or



(Ib)

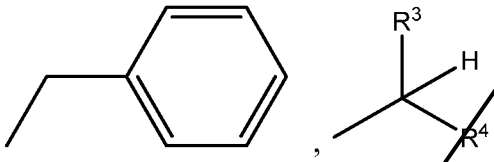
wherein R^2 is selected from the group consisting of



straight chain alkyl;

R^6 is selected from the group consisting of -H, -OH, $-NH_2$, -OC(O)R or $-OCH_2OC(O)R$;

R^8 is selected from the group consisting of



, H or lower cycloalkyl;

wherein R^3 and R^4 are both H or both C_{1-2} alkyl;

W is $-NH_2$, halo, -OH, $-NHC(O)R$, $-CO_2R$;

X is –S-, –O- or $–NR^{22}$;

Y is –H, -OH, or $–OR^{11}$;

Z is –CH- or –N-;

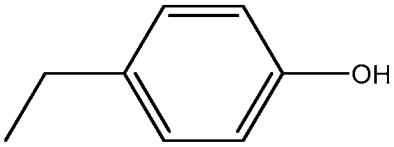
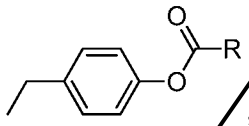
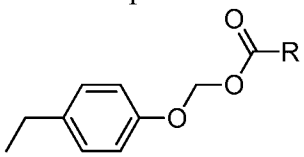
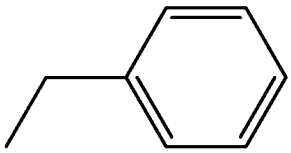
each R^{11} is independently –C(O)R'' or $–CH_2OC(O)R''$;

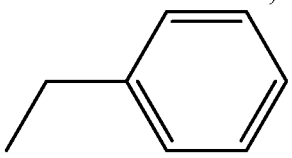
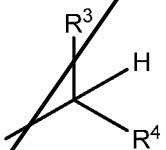
R^{22} is H, CH_3 or CH_2CH_3;

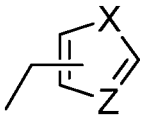
each R is independently C_{1-7} straight-chain alkyl or C_{1-7} branched alkyl;

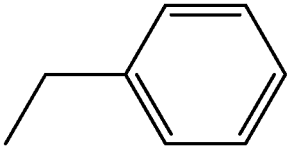
R'' is C_{1-7} straight-chain alkyl or C_{1-7} branched alkyl;

the dashed bonds indicate the presence of an optional ring, which may be saturated or unsaturated;

with the proviso that when R^2 is , , or , R^8 is not ;

with the proviso that when R^2 is , R^8 is  or lower cycloalkyl; and

with the proviso that when R^6 is NH_2, R^2 is , , or C_{2-5} alkyl;

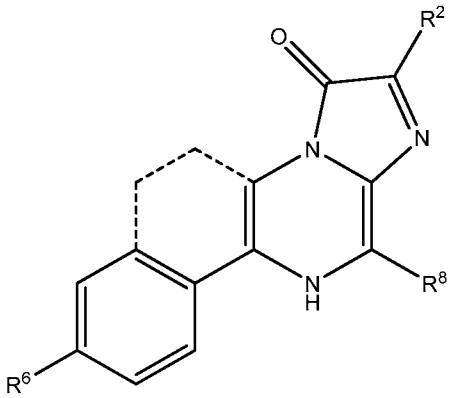
or R^8 is not .

.

114. The method of claim 113 wherein the enzymatic activity is measured in a live, intact non-human animal.

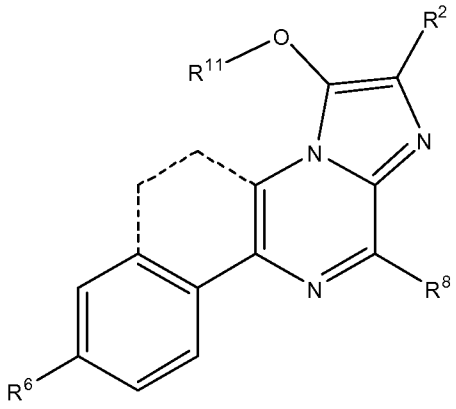
115. A method for measuring the activity of a non-luminescent enzyme of interest comprising: (a) providing a luminogenic molecule wherein the molecule is a substrate for the non-luminescent enzyme of interest and a pro-substrate of an OgLuc variant encoded by the polynucleotide of any one of claims 1-86; (b) contacting the luminogenic molecule with at least one non-luminescent enzyme of interest and at least one OgLuc variant to produce a reaction mixture; and (c) determining activity of the non-luminescent enzyme of interest by measuring luminescence of the reaction mixture.

116. The method of claim 115, wherein the luminogenic molecule is a modification of the compound of formula (Ia) or (Ib):



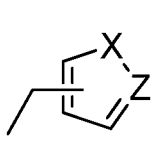
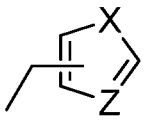
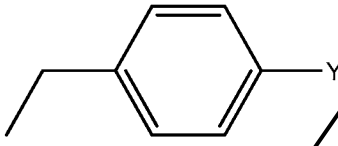
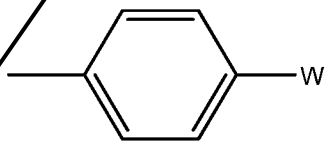
(Ia)

or



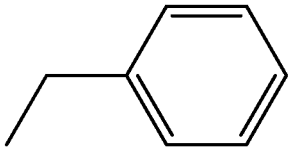
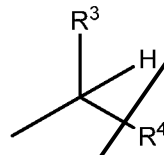
(Ib)

wherein R^2 is selected from the group consisting of

, , ,  or C_{2-5} straight chain alkyl;

R^6 is selected from the group consisting of -H, -OH, $-NH_2$, -OC(O)R or $-OCH_2OC(O)R$;

R^8 is selected from the group consisting of

, , H or lower cycloalkyl;

wherein R^3 and R^4 are both H or both C_{1-2} alkyl;

W is $-NH_2$, halo, -OH, -NHC(O)R, $-CO_2R$;

X is –S-, –O- or $–NR^{22}$-;

Y is –H, -OH, or $–OR^{11}$;

Z is –CH- or –N-;

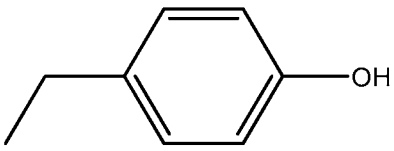
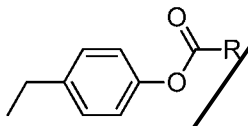
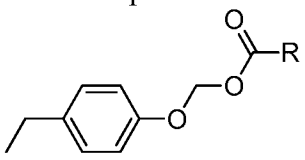
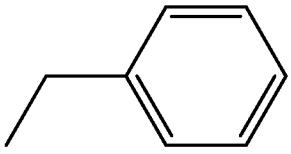
each R^{11} is independently –C(O)R'' or $–CH_2OC(O)R''$;

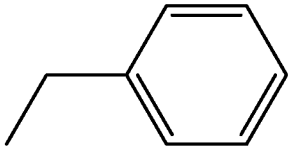
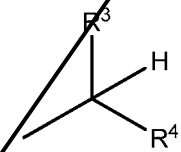
R^{22} is H, CH_3 or CH_2CH_3;

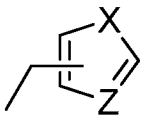
each R is independently C_{1-7} straight-chain alkyl or C_{1-7} branched alkyl;

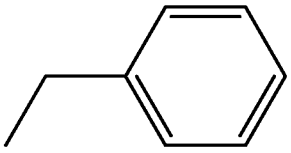
R'' is C_{1-7} straight-chain alkyl or C_{1-7} branched alkyl;

the dashed bonds indicate the presence of an optional ring, which may be saturated or unsaturated;

with the proviso that when R^2 is , , or , R^8 is not ;

with the proviso that when R^2 is , R^8 is  or lower cycloalkyl; and

with the proviso that when R^6 is NH_2, R^2 is , , or C_{2-5} alkyl;

or R^8 is not .

.

117. The method of any one of claims 115 and 116 wherein the non-luminescent enzyme of interest is a protease enzyme, a cytochrome P450 enzyme, a monoamine oxidase enzyme, or a glutathione S-transferase enzyme.

118. The method of any one of claims 115 to 117 wherein the activity of the non-luminescent enzyme is measured in a live, intact animal.

119. A method to detect the presence of at least two molecules in a sample, comprising: contacting the sample with a first reporter molecule comprising an OgLuc variant encoded by the polynucleotide of any one of claims 1-86, wherein the first reporter molecule is operatively linked to a first component of the sample; contacting the sample with a second reporter molecule, wherein the second reporter molecule is operatively linked to a second component of the sample; detecting the presence of the first and second reporter molecules to determine the presence and/or amounts of the first and second components in the sample.

120. A method to detect the presence of at least two molecules in a cell, comprising: contacting the cell with a first reporter molecule comprising an OgLuc variant encoded by the polynucleotide of any one of claims 1-86, wherein the first reporter molecule is operatively linked to a first component of the sample; contacting the sample with a second reporter molecule, wherein the second reporter molecule is operatively linked to a second component of the sample; detecting the presence of the first and second reporter molecules to determine the presence and/or amounts of the first and second components in the sample.

121. A method of generating a polynucleotide encoding a OgLuc variant polypeptide comprising:

(a) using a parental fusion protein construct comprising a parental OgLuc polypeptide and at least one heterologous polypeptide to generate a library of variant fusion proteins; and

(b) screening the library for at least one of enhanced luminescence, enhanced enzyme stability or enhanced biocompatibility relative to the parental fusion protein construct.

122. The method of claim 121, wherein the heterologous polypeptide is C-terminal to the OgLuc polypeptide.

123. The method of claim 121, wherein the heterologous polypeptide is N-terminal to the OgLuc polypeptide.

124. The method of any one of claims 121-123, wherein the heterologous polypeptide is HALOTAG®.

125. The method of claim 121, wherein the fusion protein constructs comprises two heterologous polypeptides.

126. The method of claim 125, wherein the one of the heterologous polypeptide is N-terminal to the OgLuc polypeptide and the other heterologous polypeptide is C-terminal to the OgLuc polypeptide.

127. The method of claim 125 or 126, wherein the heterologous polypeptides are HALOTAG® and Id.

128. A vector comprising the polynucleotide, or a fragment thereof, of any of claims 1-86.

129. A circularly permuted luciferase comprising the polypeptide encoded by the polynucleotide of any of claims 1-86 or a fragment thereof.

130. A method of generating codon-optimized polynucleotides encoding a luciferase for use in an organism, comprising: for each amino acid in the luciferase, randomly selecting a codon from the two most commonly used codons used in the organism to encode for the amino acid to produce a first codon-optimized polynucleotide.

131. The method of optimizing codons of claim 130, further comprising selecting the other of the two most commonly used codons used in the organism to encode for the amino acid to produce a second codon-optimized polynucleotide.

CLAIMS

1. An isolated polynucleotide encoding variant a polypeptide having at least 80% sequence identity to SEQ ID NO: 1 comprising one or more amino acid substitutions relative to SEQ ID NO: 3, wherein at least one amino acid substitution is at a position corresponding to position 18 of SEQ ID NO: 1, wherein the polypeptide has enhanced luminescence relative to SEQ ID NO: 3.

2. The polynucleotide of claim 1, wherein the at least one amino acid substitution corresponds to an aspartate, phenylalanine, glycine, histidine, isoleucine, lysine, leucine, methionine, asparagine, proline, arginine, serine, valine, tryptophan, or tyrosine at a position corresponding to position 18 of SEQ ID NO: 1.

3. The polynucleotide of claim 1, wherein the polypeptide comprises an amino acid substitution at one or more positions corresponding to positions 27, 43, 38, 109, 15, 19, 21, 22, 36, 40, 56, 58, 70, 93, 95, 102, 110, 112, 119, 127, 128, 149, 152, 155, 158, 159, 1, 6, 10, 14, 16, 24, 25, 31, 32, 39, 42, 46, 47, 48, 49, 50, 55, 59, 60, 66, 67, 69, 71, 74, 86, 87, 94, 96, 97, 98, 100, 106, 111, 113, 117, 125, 126, 129, 130, 136, 142, 145, 146, 147, 148, 150, 154, 163, and 168 of SEQ ID NO: 1.

4. The polynucleotide of claim 3, wherein the polypeptide comprises amino acid substitutions at position 54 and at position 90.

5. The polynucleotide of claim 4, wherein the amino acid at position 54 is isoleucine or alanine and at position 90 is valine.

6. The polynucleotide of claim 5, wherein the polypeptide further comprises an amino acid substitution at positions corresponding to positions 68, 72 and 75 of SEQ ID NO: 1.

7. The polynucleotide of claim 6, wherein the amino acid at position 18 is leucine, at position 68 is tyrosine, at position 72 is glutamine and at position 75 is lysine.

8. The polypeptide of claim 7, wherein the polypeptide comprises SEQ ID NO: 19.

9. The polynucleotide of claim 6, wherein the polypeptide further comprises an amino acid substitution at positions corresponding to positions 33, 27, and 43 of to SEQ ID NO: 1.

10. The polynucleotide of claim 9, wherein the amino acid at position 33 is asparagine, at position 27 is valine, at position 43 is arginine and at position 68 is aspartate.

11. The polynucleotide of claim 10, wherein the polypeptide comprises SEQ ID NO: 89.

12. The polynucleotide of claim 9, wherein the polypeptide further comprises at least one amino acid substitution at a position corresponding to positions 11, 44, 115, 124, or 138 of SEQ ID NO: 1.

13. The polynucleotide of claim 12 wherein the at least one amino acid substitution corresponds to at least one of glutamine at position 11, valine at position 44, proline at position 115, glutamine at position 124, or tyrosine at position 138 corresponding to SEQ ID NO: 1.

14. The polynucleotide of claim 9, comprising an amino acid substitution selected from the following group: the amino acid at position [[4]] 27 is glycine or isoleucine, the amino acid at position 33 is lysine or alanine, and the amino acid at position 43 is lysine.

15. The polynucleotide of claim 1, wherein the sequence has been codon-optimized for a host cell.

16. A polynucleotide encoding a fusion protein comprising the polynucleotide of claim 1 and a nucleic acid encoding a polypeptide of interest.

17. A vector comprising the polynucleotide, or a fragment thereof, of claim 1.

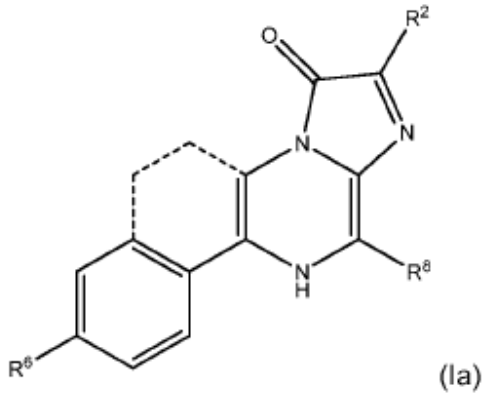
18. The vector of claim 17, wherein the polynucleotide is operably linked to a promoter.

19. An isolated cell comprising the polynucleotide of claim 1.

20. A non-human cell comprising the polynucleotide of claim 1.

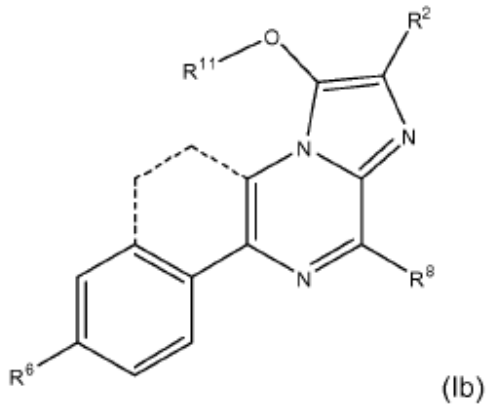
21. A kit comprising the polynucleotide of claim 1.

22. The kit of claim 21, further comprising at least one of: (a) the compound of formula (Ia) or (Ib):



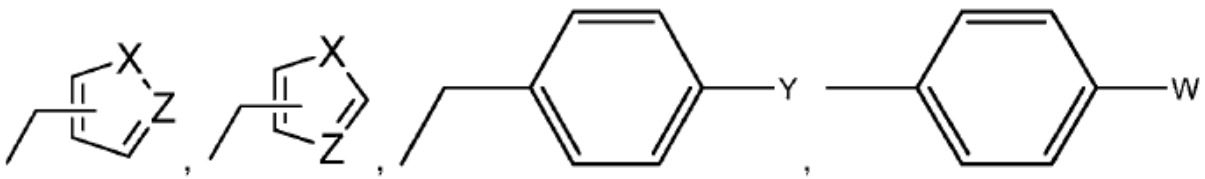
(Ia)

or



(Ib)

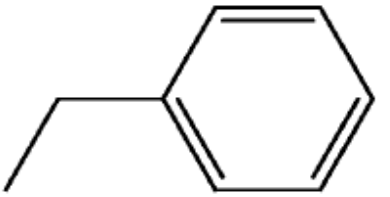
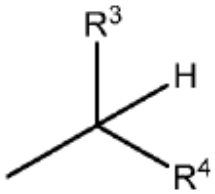
wherein R^2 is selected from the group consisting of



or C_{2-5} straight chain alkyl;

R^6 is selected from the group consisting of --H, --OH, --NH_2, --OC(O)R or --$OCH_2OC(O)R$;

R^8 is selected from the group consisting of


, 

, H or lower cycloalkyl;

wherein R^3 and R^4 are both H or both C_{1-2} alkyl;

W is --NH_2, halo, --OH, --NHC(O)R, --CO_2R;

X is --S--, --O-- or --NR^{22}--;

Y is --H, --OH, or --OR^{11};

Z is --CH-- or --N--;

each $R^{11}$is independently --C(O)R" or --$CH_2OC(O)R$";

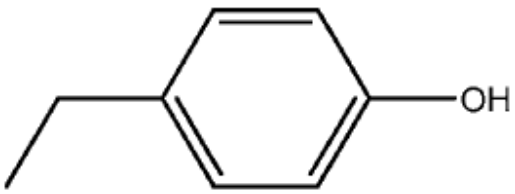
R^{22} is H, CH_3 or CH_2CH_3;

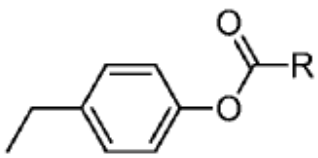
each R is independently C_{1-7} straight-chain alkyl or C_{1-7} branched alkyl;

R" is C_{1-7} straight-chain alkyl or C_{1-7} branched alkyl;

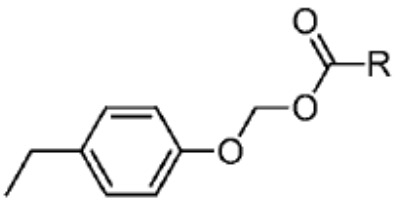
the dashed bonds indicate the presence of an optional ring, which may be saturated or unsaturated;

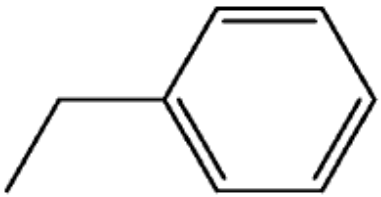
with the proviso that when R^2 is



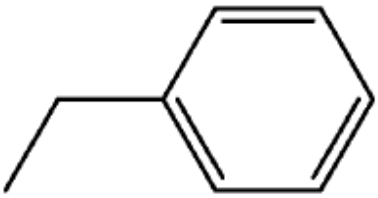
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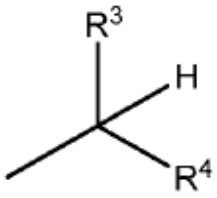
, or

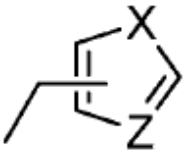


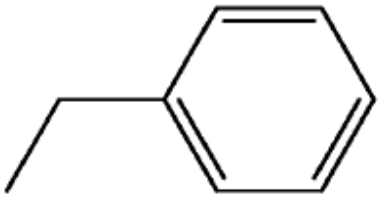
, R^8 is not 
;

°

with the proviso that when R^2 is ,

R^8 is  or lower cycloalkyl;

and with the proviso that when R^6 is NH_2, R^2 is,  or C_{2-5} alkyl;

or R^8 is not  ; and

(b) a buffer reagent.