Claims

1. Composition comprising: (i) a chimeric GPCR having the structure:

[N-terminal sequence]-[TM1]-[IC1]-[TM2]-[EC1]-[TM3]-[IC2]-[TM4]-[EC2]-[TM5]-[IC3]-[TM6]-[EC3]-[TM7]-[C-terminal sequence]

in which TM1, TM2, TM3, TM4, TM5, TM6 and TM6 are extracellular loops; EC1, EC2 and EC3 are extracellular loops; and IC1, IC2 and IC3 are intracellular loops;

in which the extracellular loops and TM's form a functional ligand binding site and the extracellular loops and TM's are derived from a first GPCR and the intracellular loops that are derived from a second GPCR different from the first and (ii) an immunoglobulin single variable domain that can bind to at least one of the intracellular loops that are derived from said second GPCR.

2. Composition according to claim 1, in which the first GPCR and the second GPCR both belong to class A.

3. Composition according to claim 2, in which said immunoglobulin single variable domain is capable of stabilizing and/or inducing a functional and/or active conformational state of the chimeric GPCR upon binding to the chimeric GPCR.

4. Composition according to any of claims 1 to 3, which is a cellular composition.

5. Composition according to any of claims 1 to 4, further comprising a compound or ligand that is capable of binding to an extracellular binding site (as defined herein) on said chimeric GPCR.

6. Method of forming a complex of a chimeric GPCR, an immunoglobulin single variable domain, and a compound or ligand that is capable of binding to an extracellular binding site (as defined herein) on said chimeric GPCR, said method comprising the steps of:

a) providing a composition according to any of claims 1 to 4; and

b) contacting said composition with one or more test compounds or ligands under conditions that (i) allow said immunoglobulin single variable domain to bind to said binding site on the chimeric GPCR that comprises at least one of said intracellular loops; and (ii) allow said test compounds to bind to the extracellular binding site of said chimeric GPCR.

7. Method of identifying and/or generating compounds or ligands that are capable of binding to an extracellular binding site (as defined herein) of a GPCR, said method comprising the steps of:

a) providing a composition according to any of claims 1 to 4;

b) contacting said composition with one or more test compounds or ligands under conditions that (i) allow the immunoglobulin single variable domain to bind to said binding site on the chimeric GPCR that comprises at least one of said intracellular loops; and (ii) allow said test compounds to bind to the extracellular binding site of said chimeric GPCR;

c) evaluating whether each of the test compounds or ligands (and/or which of said test compounds or ligands) binds to the chimeric GPCR; in said composition; and optionally

d) selecting the test compounds or ligands that bind to the chimeric GPCR in said composition.

8. Method of identifying and/or generating compounds or ligands that are capable of binding to an active conformation of a GPCR, said method comprising the steps of:

a) providing a composition according to any of claims 1 to 4, in which the chimeric GPCR comprises at least the extracellular loops and TM's of said GPCR and in which the immunoglobulin single variable domain is ligand is capable of stabilizing and/or inducing an active conformational state of the chimeric GPCR upon binding to the chimeric GPCR.;

b) contacting said composition with one or more test compounds or ligands under conditions that (i) allow said immunoglobulin single variable domain to bind to said binding site on the chimeric GPCR that comprises at least one of said intracellular loops; and (ii) allow said test compounds to bind to the extracellular binding site of said chimeric GPCR;

c) evaluating whether each of the test compounds or ligands (and/or which of said test compounds or ligands) binds to the chimeric GPCR; in said composition; and optionally

d) selecting the test compounds or ligands that bind to the chimeric GPCR in said composition.

9. Method according to claim 7 or 8, in which said immunoglobulin single variable domain is capable of stabilizing and/or inducing a functional and/or active conformational state of the chimeric GPCR upon binding to the chimeric GPCR.

10. Arrangement that comprises at least the following elements:

- a boundary layer that separates a first environment from a second environment;
- a chimeric GPCR having the structure:

[N-terminal sequence]-[TM1]-[IC1]-[TM2]-[EC1]-[TM3]-[IC2]-[TM4]-[EC2]-[TM5]-[IC3]-[TM6]-[EC3]-[TM7]-[C-terminal sequence]

in which TM1, TM2, TM3, TM4, TM5, TM6 and TM6 are extracellular loops; EC1, EC2 and EC3 are extracellular loops; and IC1, IC2 and IC3 are intracellular loops;

in which the extracellular loops and TM's form a functional ligand binding site and the extracellular loops and TM's are derived from a first GPCR and the intracellular loops that are derived from a second GPCR different from the first

- a ligand for the chimeric GPCR that is present in the first environment;
- an immunoglobulin single variable domain that is present in the second environment and that can bind to at least one of the intracellular loops that are derived from said second GPCR; and
- a binding pair that consists of at least a first binding member and a second binding member, which binding pair is capable of generating a detectable signal.

11. Arrangement according to claim 10, in which the chimeric GPCR is fused or linked, either directly or via a suitable spacer or linker, to the first binding member of said binding pair and in which the immunoglobulin single variable domain is fused or linked, either directly or via a suitable spacer or linker, to the first binding member of said binding pair.

12. Arrangement according to claim 10 or 11, in which said immunoglobulin single variable domain is capable of stabilizing and/or inducing a functional and/or active conformational state of the chimeric GPCR upon binding to the chimeric GPCR.

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