WHAT IS CLAIMED IS:

1. A composition comprising a GPCR-fusion partner protein which comprises, from N-terminus to C terminus: (i) a first domain comprising a portion of a G-protein-coupled receptor (GPCR) wherein the first domain comprises the first through fifth transmembrane domains of the GPCR, (ii) a second domain comprising a fusion partner amino acid sequence wherein said sequence is at least 90% homologous to a protein selected from the list consisting of rubredoxin, cytochrome b_{562} RIL (Bril), flavodoxin, xylanase, or a C-terminal fragment of T4lysozyme, and (iii) a third domain comprising a portion of the GPCR wherein the third domain comprises the sixth and seventh transmembrane domains of the GPCR.

2. A composition comprising a GPCR-fusion partner protein which comprises, from N-terminus to C terminus: (i) a first domain comprising a G-protein-coupled receptor (GPCR), and (ii) a second domain comprising a fusion partner amino acid sequence wherein said sequence is at least 90% homologous to a protein selected from the list consisting of rubredoxin, cytochrome b_{562} RIL (Bril), flavodoxin, xylanase, or a C-terminal fragment of T4lysozyme.

3. A composition comprising a GPCR-fusion partner protein which comprises, from N-terminus to C terminus: (i) a first domain comprising a fusion partner amino acid sequence wherein said sequence is at least 90% homologous to a protein selected from the list consisting of rubredoxin, cytochrome b_{562} RIL (Bril), flavodoxin, xylanase, or a C-terminal fragment of T4lysozyme, and (ii) a second domain comprising a GPCR.

4. A composition comprising a GPCR-fusion partner protein which comprises, from N-terminus to C terminus: (i) a first domain comprising a portion of a G-protein-coupled receptor (GPCR) wherein the first domain comprises the first through fifth transmembrane domains of the GPCR, (ii) a second domain comprising a fusion partner amino acid sequence wherein said sequence is at least 90% homologous to a protein selected from the list consisting of 2rhf, 2ehs, 2ip6, 3i7m, 1x3o, 1u84, 1h75, 2huj, 1ysq, 3ls0, 2qr3, 1zuh, 2b8i, 2cgq, 3fxh, 3nph, 2o4d, 1tmy,

1vku, and 2es9, and (iii) a third domain comprising a portion of the GPCR wherein the third domain comprises the sixth and seventh transmembrane domains of the GPCR.

5 A composition comprising a GPCR-fusion partner protein which comprises, from N-terminus to C terminus: (i) a first domain comprising a G-protein-coupled receptor (GPCR), and (ii) a second domain comprising a fusion partner amino acid sequence wherein said sequence is at least 90% homologous to a protein selected from the list consisting of 2rhf, 2ehs, 2ip6, 3i7m, 1x3o, 1u84, 1h75, 2huj, 1ysq, 3ls0, 2qr3, 1zuh, 2b8i, 2cgq, 3fxh, 3nph, 2o4d, 1tmy, 1vku, and 2es9.

6 A composition comprising a GPCR-fusion partner protein which comprises, from N-terminus to C terminus: (i) a first domain comprising a fusion partner amino acid sequence wherein said sequence is at least 90% homologous to a protein selected from the list consisting of 2rhf, 2ehs, 2ip6, 3i7m, 1x3o, 1u84, 1h75, 2huj, 1ysq, 3ls0, 2qr3, 1zuh, 2b8i, 2cgq, 3fxh, 3nph, 2o4d, 1tmy, 1vku, and 2es9, and (ii) a second domain comprising a GPCR.

7. The composition of claims 1-6 wherein the GPCR-fusion partner protein is in crystalline form.

8. The composition of claim 7 wherein the GPCR-fusion partner protein is of sufficient quality to support x-ray crystallographic structure determination for the GPCR at a resolution of at least 3 angstroms.

9. The composition of claim 1 or 4 wherein the fusion partner substantially comprises the domain corresponding to the third intracellular domain of the GPCR between the fifth and sixth transmembrane domains of the GPCR.

10. The composition of claims 1-9 wherein the fusion partner amino acid sequence has least 95 % homology with rubredoxin.

11. The composition of claims 1-9 wherein the fusion partner amino acid sequence has at least 95 % homology with cytochrome b_{562} RIL (Bril).

12. The composition of claims 1-9 wherein the fusion partner amino acid sequence has at least 95 % homology with flavodoxin.

13. The composition of claims 1-9 wherein the fusion partner amino acid sequence has at least 95 % homology with xylanase.

14. The composition of claims 1-9 wherein the GPCR is a naturally occurring GPCR.

15. The composition of claims 1-9 wherein the GPCR is a variant of a naturally occurring GPCR.

16. The composition of claims 1-9 wherein the GPCR is a class A GPCR.

17. The composition of claims 1-9 wherein the GPCR is an S1P1 receptor.

18. The composition of claims 1-9 wherein the GPCR is a β2-adrenergic receptor (β2AR).

19. The composition of claim 1-6, wherein the fusion partner is selected from rubredoxin, cytochrome b_{562} RIL (Bril), flavodoxin, or xylanase.

20. The composition of claim 18, wherein the GPCR-fusion partner protein is β2AR-Bril.

21. The composition of claims 1-9 wherein the GPCR is an adenosine A2a receptor

22. The composition of claim 21, wherein the fusion partner is selected from rubredoxin, cytochrome b_{562} RIL (Bril), flavodoxin, or xylanase.

23. The composition of claims 1-9 wherein the GPCR is an NOP1 receptor

24. The composition of claim 23, wherein the fusion partner is selected from rubredoxin, cytochrome b_{562} RIL (Bril), flavodoxin, or xylanase.

25. The composition of claims 1-9 wherein the GPCR is a CCR5 receptor.

26. The composition of claim 25, wherein the fusion partner is selected from rubredoxin, cytochrome b_{562} RIL (Bril), flavodoxin, or xylanase.

27. The composition of claims 1-26 wherein the composition further comprises tri-methyl amine N-oxide as a crystallant additive.

28. A method of using a fusion partner to support crystallization of a protein suitable for crystallographic structural studies of a G-protein-coupled receptor (GPCR) comprising:

(a) incorporating a fusion partner into an intracellular domain of the GPCR to form a GPCR-fusion partner protein, wherein the fusion partner comprises an amino acid sequence which is at least 90% homologous with the amino acid sequence of a protein selected from the group consisting of rubredoxin, cytochrome b_{562} RIL (Bril), flavodoxin, and xylanase;

(b) expressing and purifying the GPCR-fusion partner protein; and

(c) crystallizing the purified GPCR-fusion partner protein.

29. A method of using a fusion partner to support crystallization of a protein suitable for crystallographic structural studies of a G-protein-coupled receptor (GPCR) comprising:

(a) attaching a fusion partner to an N-terminus or C-terminus of the GPCR to form a GPCR-fusion partner protein, wherein the fusion partner comprises an amino acid sequence which is at least 90% homologous with the amino acid sequence of a protein selected from the group consisting of rubredoxin, cytochrome b_{562} RIL (Bril), flavodoxin, and xylanase;

(b) expressing and purifying the GPCR-fusion partner protein; and

(c) crystallizing the purified GPCR-fusion partner protein.

30. The method of claims 28- 29, wherein the GPCR is a class A GPCR.

31. The method of claim 30, wherein the GPCR is selected from a β2-adrenergic receptor (β2AR), an A2A-adenosine receptor, an S1P1 receptor, an OLR1 receptor, or a CCR5 receptor.

32. The method of claims 28-29, wherein the fusion partner comprises the amino acid sequence of rubredoxin.

33. The method of claims 28-29, wherein the fusion partner comprises the amino acid sequence of cytochrome b_{562} RIL (Bril).

34. The method of claims 28-29, wherein the fusion partner comprises the amino acid sequence of T4 lysozyme C-terminal fragment (Cterm-T4L).

35. The method of claims 28-29, wherein the fusion partner comprises the amino acid sequence of flavodoxin.

36. The method of claims 28-29, wherein the fusion partner comprises the amino acid sequence of xylanase.

37. The method of claims 28-29, wherein the fusion partner is incorporated in the intracellular domain between TM5 and TM 6 regions of the GPCR.

38. The method of claims 28-37, wherein the method further comprises the step of crystallizing the purified GPCR-fusion partner protein is performed in the presence of a crystallant additive.

39. The method of claim 38 wherein the crystallant additive is tri-methyl amine N-oxide.

40. A method of selecting a candidate fusion partner for use in a fusion protein of a GPCR protein and such fusion partner where such resulting fusion protein supports formation of diffraction quality crystals comprising the steps of (a) providing one or more databases having information relating to proteins, (b) searching such one or more databases for proteins meeting the following criteria: (i) having N and C termini separated by no more than 15 Å; (ii) having a molecular weight of less than 25kD; (iii) having been demonstrated to be crystallized with a diffraction resolution of at least 3 Å; (iv) having the capacity to form crystals in more than one set of chemical

conditions; and (v) having the capacity to form crystals having more than one space group; and (c) selecting as a candidate fusion partner one or more proteins satisfying criteria (i) –(v).

41. The method of claim 40 wherein in step (b) the one or more databases are searched for proteins which also meet the following criteria: (vi) having at least 50% alpha-helical content; and (vii) having alpha-helical domains at the N-terminus, or the C-terminus or both; and in step (c) candidate fusion partners are selected which satisfy criteria (i) –(vii).

CLAIMS

1. A composition comprising a GPCR-fusion partner protein which comprises, from N-terminus to C terminus: (i) a first domain comprising a portion of a G-protein-coupled receptor (GPCR) wherein the first domain comprises the first through fifth transmembrane domains of the GPCR, (ii) a second domain comprising a fusion partner amino acid sequence wherein said sequence is at least 90% homologous to cytochrome b_{562} RIL (Bril), and (iii) a third domain comprising a portion of the GPCR wherein the third domain comprises the sixth and seventh transmembrane domains of the GPCR, wherein the GPCR is an A2a adenosine receptor and wherein the GPCR-fusion partner protein is of sufficient quality to support x-ray crystallographic structure determination for the GPCR at a resolution of at least 2.4 angstroms.

2. The composition of claim 1, wherein the GPCR-fusion partner protein is in crystalline form.

3. The composition of claim 1 wherein the fusion partner is substituted for some or all of a third intracellular loop of the GPCR between the fifth and sixth transmembrane domains of the GPCR.

4. The composition of claim 1, wherein the fusion partner amino acid sequence has at least 95% homology with cytochrome b_{562} RIL (Bril).

5. The composition of claims 1-3 wherein the GPCR is a variant of a naturally occurring GPCR.

6. A method of using a fusion partner to support crystallization of a protein suitable for crystallographic structural studies of a G-protein-coupled receptor (GPCR) comprising:
(a) incorporating a fusion partner into an intracellular domain of the GPCR to form a GPCR-fusion partner protein, wherein the fusion partner comprises an amino acid sequence which is at least 90% homologous with the amino acid sequence of cytochrome b_{562} RIL (Bril) and , wherein the GPCR is an A2a adenosine receptor;
(b) expressing and purifying the GPCR-fusion partner protein; and

(c) crystallizing the purified GPCR-fusion partner protein, thereby providing crystals of the GPCR-fusion partner protein of sufficient quality to support x-ray crystallographic structure determination for the GPCR at a resolution of at least 2.4 angstroms.

7. The method of claim 6, wherein the fusion partner is incorporated in the intracellular domain between TM5 and TM 6 regions of the GPCR.

8. The method of claim 6, wherein the method further comprises the step of crystallizing the purified GPCR-fusion partner protein is performed in the presence of a crystallant additive.

9. The method of claim 8 wherein the crystallant additive is tri-methyl amine N-oxide.