CLAIMS

1. Use of haptoglobin (Hp) in the preparation of a medicament for treating or preventing an adverse secondary neurological outcome in a subject following a haemorrhagic stroke.

2. The use of claim 1, wherein the Hp is present in an amount of from 2 μM to 20 mM.

3. The use of claim 1 or 2, wherein the Hp is present in an amount of from 2 μM to 300 μM, from 5 μM to 50 μM, or from 10 μM to 30 μM,

4. The use of any one of the preceding claims, wherein the Hp is selected from the group consisting of an Hp1-1 homodimer, an Hp1-2 multimer, an Hp2-2 multimer and a combination of any of the foregoing.

5. The use of claim 4, comprising a Hp2-2 multimer.

6. The use of any one of the preceding claims, wherein the CSF of the subject in need thereof is to be exposed to a therapeutically effective amount of haptoglobin (Hp) for a period of time sufficient to allow the Hp to form a complex with, and thereby neutralise, the cell-free Hb.

7. The use of any one of the preceding claims, wherein the haemorrhagic stroke is a spontaneous haemorrhage or a traumatic haemorrhage.

8. The use of any one of the preceding claims, wherein the haemorrhagic stroke is an intraventricular haemorrhage or a subarachnoid haemorrhage.

9. The use of claim 8, wherein the subarachnoid haemorrhage is an aneurysmal subarachnoid haemorrhage.

10. The use of any one of the preceding claims, wherein the adverse secondary neurological outcome is selected from the group consisting of a delayed ischaemic neurological deficit (DIND), delayed cerebral ischaemia (DCI), neurotoxicity, inflammation, nitric oxide depletion, oxidative tissue injury, cerebral vasospasm, cerebral vasoreactivity and oedema.

11. The use of claim 10, wherein the adverse secondary neurological outcome is a cerebral vasospasm.

12. The use of claim 10, wherein the adverse secondary neurological outcome is a delayed ischaemic neurological deficit.

13. The use of claim 10, wherein the adverse secondary neurological outcome is delayed cerebral ischaemia.

14. The use of any one of the preceding claims, wherein the adverse secondary neurological outcome is an adverse secondary neurological outcome within the brain parenchyma.

15. The use of any one of the preceding claims 6 to 14, wherein the CSF of the subject is to be exposed to the Hp, or the functional analogue thereof, within about 21 days after onset of the haemorrhage.

16. The use of claim 15, wherein the CSF of the subject is to be exposed to the Hp from 2 days to 4 days after onset of the haemorrhage and/or from 5 days to 14 days after onset of the haemorrhage.

17. The use of any one of the preceding claims, wherein the Hp is to be intracranially administered to the subject.

18. The use of any one of claims 1 to 16, wherein the Hp is to be intrathecally administered to the subject.

19. The use of claim 18, wherein the Hp is to be intrathecally administered into the spinal canal.

20. The use of claim 18, wherein the Hp is to be intrathecally administered into the subarachnoid space.

21. The use of any one of claims 1 to 16, wherein the Hp is to be intracerebroventricularly administered to the subject.

22. The use of any one of claims 17 to 21, wherein the period of time to which the CSF is to be exposed to the therapeutically effective amount of Hp is at least 2 minutes.

23. The use of claim 22, wherein the period of time to which the CSF is to be exposed to the therapeutically effective amount of Hp is from 2 minutes to 45 minutes.

24. The use of claim 22, wherein the period of time to which the CSF is to be exposed to the therapeutically effective amount of Hp is from 2 minutes to 20 minutes or from 4 minutes to 10 minutes.

25. The use of any one of claims 6 to 24, wherein the therapeutically effective amount of Hp is at least an equimolar amount to the concentration of cell-free Hb in the CSF of the subject following the haemorrhage.

26. The use of claim 25, wherein the amount of cell-free Hb in an isolated CSF sample following haemorrhage from the subject is measured to determine the at least equimolar amount of Hp based on the concentration of cell-free Hb.

27. The use of any one of claims 7 to 26, further comprising removing Hp:cell-free Hb complexes formed in the CSF.

28. The use of any one of claims 7 to 27, wherein the CSF is to be exposed to the therapeutically effective amount of Hp extracorporeally.

29. The use of claim 28, comprising:
    (i) adding to an isolated CSF sample from the CSG compartment of the subject Hp to obtain an Hp-enriched CSF sample;
    (ii) wherein the Hp-enriched CSF sample is to be administered to the subject, thereby exposing the CSF compartment of the subject to a therapeutically effective amount of Hp for a period of time sufficient to allow the Hp to form a complex with cell-free Hb in the CSF compartment of the subject; and
    (iii) and (ii) and (iii) are to be optionally repeated.

30. The use of claim 28, wherein
    (i) an artificial CSF comprising Hp is to be administered to replace a volume of CSF of the subject following haemorrhage, thereby exposing the CSF compartment of the subject to a therapeutically effective amount of Hp for a period of time sufficient

to allow the Hp to form a complex with cell-free Hb in the CSF compartment of the subject; and

(ii) (i) is optionally to be repeated.

31. The use of claim 28, comprising:

(i) exposing isolated CSF sample following haemorrhage from the subject to Hp under conditions to allow the Hp, or the functional analogue thereof, to form a complex with cell-free Hb in the CSF;

(ii) extracting the Hp:cell-free Hb complexes from the CSF following step (ii) to obtain an Hb-diminished CSF that has a lower amount of cell-free Hb when compared to the CSF from step (i);

(iii) optionally repeating steps (i) and (ii) to obtain an Hb-diminished CSF that is substantially free of cell-free Hb; and wherein

(iv) the Hb-diminished CSF from (ii) or (iii) is to be administered to the CSF compartment of the subject.

32. The use of claim 31, further comprising adding to the Hb-diminished CSF prior to step (vi) a therapeutically effective amount of Hp.

33. The use of claim 31 or claim 32, wherein the Hp is immobilised on a substrate.

34. The use of claim 33, wherein the substrate is an affinity chromatography resin.

35. The use of claim 34, wherein step (ii) comprises passing the CSF from step (i) through an affinity chromatography resin under conditions that allow the cell-free Hb in the CSF to bind to the resin; wherein step (iii) comprises eluting the CSF from the resin following step (ii); and wherein step (iv) comprising recovering the eluted CSF.

36. The use of any one of claims 31 to 35, optionally comprising washing the CSF compartment following step (i) with a wash solution.

37. The use of claim 36, wherein the wash solution is an artificial CSF.

38. The use of claim 30 or claim 37, wherein the artificial CSF comprises NaCl, KCl, KH_2PO_4, $NaHCO_3$, $MgCl_6H_20$, $CaCl_2H_2O$ and glucose.

39. The use of any one of claims 37 to 39, wherein the wash solution comprises Hp.

40. The use of claim 39, wherein the wash solution comprises from 2 μM to 20 mM Hp or from 2 μM to 300 μM Hp.

41. The use of any one of claims 6 to 40, wherein:
    (i) the CSF is to be removed from the subject following the haemorrhage;
    (ii) the CSF compartment of the subject following is to be rinsed with a wash solution comprising a therapeutically effective amount of Hp;
    (iii) optionally repeating (ii); and
    (iv) an artificial CSF is to be administered to the CSF compartment of the subject, following (ii) or (iii).

42. The use of claim 41, wherein the artificial CSF comprises NaCl, KCl, KH_2PO_4, $NaHCO_3$, $MgCl_6H_20$, $CaCl_2H_2O$ and glucose.

43. The use of claim 41 or claim 42, wherein the artificial CSF comprises Hp.

44. The use of claim 43, wherein the artificial CSF comprises from 2 μM to 20 mM Hp or from 2 μM to 300 μM Hp.

45. The use of any one of claims 1 to 44, wherein the Hp is selected from the group consisting of an Hp1-1 homodimer, an Hp1-2 multimer, an Hp2-2 multimer and a combination of any of the foregoing.

46. The use of claim 45, wherein the Hp comprises an Hp2-2 multimer.

47. The use of any one of claims 1 to 46, wherein the Hp is a recombinant protein.

48. The use of any one of claims 1 to 46, wherein the Hp is plasma derived.

49. The use of any one of claims 1 to 48, further comprising a second agent for treating or preventing an adverse secondary neurological outcome following an intraventricular haemorrhage to be administered to the subject.

50. The use of claim 49, wherein the second agent is a vasodilator.

51. The use of claim 49 or claim 50, wherein the second agent is selected from the group consisting of a sydnone and sodium nitroprusside.

52. An artificial cerebral spinal fluid (CSF) comprising Hp.

53. The artificial CSF of claim 52, wherein the Hp is present in an amount of from 2 μM to 20 mM, from 5 μM to 300 μM, from 5 μM to 50 μM or from 10 μM to 30 μM.

54. The artificial CSF of 52 or 53, wherein the Hp is selected from the group consisting of an Hp1-1 homodimer, an Hp1-2 multimer, an Hp2-2 multimer and a combination of any of the foregoing.

55. The artificial CSF of claim 54, wherein the Hp comprises an Hp2-2 multimer.

56. The artificial CSF of any one of claims 52 to 55, wherein the Hp is a recombinant protein.

57. The artificial CSF of any one of claims 52 to 56, wherein the Hp is plasma derived.

58. A kit comprising the artificial CSF of any one of claims 52 to 57