

What is claimed is:

1. Use of an active agent that inhibits PSD-95, cleavable by plasmin, wherein the active agent is a peptide having the amino sequence of SEQ ID NO:3 provided the third amino acid from the C-terminus can be S or T, in the manufacture of a medicament for treating a population of human subjects having or risk of ischemic stroke by a method comprising administering to the human subjects the active agent and reperfusion, wherein the population of subjects includes:

human subjects administered the active agent that inhibits PSD-95 and a tPA thrombolytic agent to effect reperfusion, wherein the active agent that inhibits PSD-95 is administered at least 10 minutes before the tPA thrombolytic agent,

and the population of human subjects lacks:

human subjects in which a thrombolytic agent is administered less than 3 hours before or less than 10 minutes after administering the active agent that inhibits PSD-95;

wherein intervals between administration of the active agent and tPA thrombolytic agent are calculated between the initial points of their administrations.

2. The use of claim 1, wherein the human subjects have ischemic stroke.

3. The use of claim 1 or 2, in which the population lacks human subjects in which the tPA thrombolytic agent is administered less than four hours before the active agent that inhibits PSD-95 or less than 10 minutes after the active agent that inhibits PSD-95.

4. The use of claim 1 or 2, in which the population lacks human subjects in which the tPA thrombolytic agent is administered less than eight hours before the active agent that inhibits PSD-95 and less than 10 minutes after administering the active agent that inhibits PSD-95.

5. The use of claim 1 or 2, in which the population lacks human subjects in which the tPA thrombolytic agent is administered before the active agent that inhibits PSD-95 or less than ten minutes after administering the active agent that inhibits PSD-95.

6. The use of claim 1 or 2, in which the population lacks human subjects in which the tPA thrombolytic agent is administered before the active agent that inhibits PSD-95 or less than 20 minutes after administering the active agent that inhibits PSD-95.

7. The use of claim 1 or 2, in which the population lacks human subjects in which the tPA thrombolytic agent is administered before the active agent that inhibits PSD-95 or less than 30 minutes after administering the active agent that inhibits PSD-95.

8. The use of claim 1 or 2, in which the population lacks human subjects in which the tPA thrombolytic agent is administered before the active agent that inhibits PSD-95 or less than 60 minutes after administering the active agent that inhibits PSD-95.

9. The use of any preceding claim, wherein the population of human subjects includes human subjects administered the active agent that inhibits PSD-95 and mechanical reperfusion without receiving a tPA thrombolytic agent.

10. The use of claim 1 or 2, wherein the population of human subjects consists of:

(a) subjects administered the active agent that inhibits PSD-95 and mechanical reperfusion, a vasodilator agent or a hypertensive agent without a tPA thrombolytic agent; and

(b) subjects administered the active agent that inhibits PSD-95 and a thrombolytic agent, wherein the tPA thrombolytic agent is administered at least 10, 20, 30, 40, 50, 60, or 120 minutes after the active agent that inhibits PSD-95.

11. The use of claim 10, wherein at least some of the human subjects according to item (b) also are administered mechanical reperfusion.

12. The use of claim 1 or 2, wherein the population includes human subjects in which the tPA thrombolytic agent is administered more than 3 or 4.5 hours after onset of stroke when the human subjects were determined to be eligible for treatment with the tPA thrombolytic agent less than 3 hours after onset of stroke.

13. The use of any preceding claim, wherein the population includes human subjects administered the active agent that inhibits PSD-95 intranasally or intrathecally.

14. The use of any preceding claim, wherein the population includes at least 100 human subjects.

15. The use of any preceding claim, wherein the population includes human subjects in which the active agent that inhibits PSD-95 is administered over a ten minute period and the tPA thrombolytic agent is administered at least 20 minutes from the start of administering the active agent.

16. The use of any preceding claim, wherein the active agent is a peptide of all L-amino acids.

17. The use of any preceding claim, wherein the active agent is nerinetide.

18. Use of an active agent that inhibits PSD-95, cleavable by plasmin, having the amino acid sequence of SEQ ID NO:3 provided the third amino acid from the C-terminus can be S or T, in the manufacture of a medicament for treating a population of human subjects receiving endovascular thrombectomy for ischemic stroke in a method comprising:

administering both an active agent that inhibits PSD-95, cleavable by plasmin, and a tPA thrombolytic agent to some of the human subjects, wherein the active agent that inhibits PSD-95 is administered at least 10, 20, 30, 40, 50, 60 or 120 minutes before the tPA thrombolytic agent, and

administering the active agent that inhibits PSD-95 or the tPA thrombolytic agent but not both to the other human subjects of the population

wherein intervals between administration of the active agent and tPA thrombolytic agent are calculated between the initial points of their administrations.

19. The use of claim 18, wherein the human subjects receiving the active agent that inhibits PSD-95 and the tPA thrombolytic agent do so before the subjects receive endovascular thrombectomy.

20. The use of claim 18 or 19, wherein the human subjects receiving the active agent that inhibits PSD-95 or the tPA thrombolytic agent but not both do so before the human subjects receive endovascular thrombectomy.

21. The use of any one of claims 18-20, wherein in the human subjects receiving both the active agent that inhibits PSD-95 and the tPA thrombolytic agent, the active agent that inhibits PSD-95 is administered at least 10 minutes before the tPA thrombolytic agent, and the active agent that inhibits PSD-95 or the tPA thrombolytic agent but not both is administered to the other human subjects.

22. Use of an active agent that inhibits PSD-95, cleavable by plasmin, the agent having the amino acid sequence of SEQ ID NO:3 provided the third amino acid from the C-terminus can be S or T, in the manufacture of a medicament for treating a subject suspected of having ischemic stroke, in a method comprising:

determining eligibility of the subject for treatment with a tPA thrombolytic agent;

administering an active agent that inhibits PSD-95, cleavable by plasmin; and thereafter administering the thrombolytic agent wherein the active agent that inhibits PSD-95 is administered over a ten minute period and the thrombolytic agent is administered at least 20 minutes from the start of administering the active agent; wherein intervals between administration of the active agent and thrombolytic agent are calculated between the initial points of their administrations.

23. The use of any preceding claim, wherein the active agent that inhibits PSD-95 is nerinetide.

24. The use of any preceding claim, wherein the tPA thrombolytic agent is alteplase.

25. Use of an active agent that inhibits PSD-95, cleavable by plasmin, the active agent having the amino acid sequence of SEQ ID NO:3 provided the third amino acid from the C-terminus can be S or T, for treating a human subject who has had an ischemic stroke, whereby the active agent is:

administered at least 3 hours after administration of a tPA thrombolytic agent;

wherein intervals between administration of the active agent and the tPA thrombolytic agent are calculated between the initial points of their administrations.

26. The use of claim 25, wherein the active agent that inhibits PSD-95 is administered over a ten minute period and the tPA thrombolytic agent is administered at least 20 minutes from the start of administering the active agent.

27. The use of claim 26, wherein the active agent is nerinetide.

28. Use of an active agent that inhibits PSD-95, cleavable by plasmin, the active agent having the amino acid sequence of SEQ ID NO:3 provided the third amino acid from the C-terminus can be S or T, in the manufacture of a medicament for treating a human patient for ischemic stroke, in a method comprising administering to a subject having ischemic stroke an active agent that inhibits PSD-95, cleavable by plasmin, and 20-40 minutes after initiating administration of the active agent administering a tPA thrombolytic agent, wherein the active agent that inhibits PSD-95 is administered over a period of ten minutes and the tPA thrombolytic agent is administered 20-30 minutes after initiating administration of the active agent, wherein intervals between administration of the active agent and the tPA thrombolytic agent are calculated between the initial points of their administrations.