CLAIMS

1. A human or humanized CDR-grafted anti-ADM antibody or anti-ADM antibody fragment thereof, wherein said human or humanized CDR-grafted anti-ADM antibody or anti-ADM antibody fragment binds to the N-terminal part, aa 1-21, SEQ ID No. 23, of adrenomedullin.

2. A human or humanized CDR-grafted anti-ADM antibody or anti-ADM antibody fragment thereof according to claim 1, wherein said human or humanized CDR-grafted anti-ADM antibody or anti-ADM antibody fragment binds to the N-terminal end, aa 1-21, SEQ ID No. 23, of adrenomedullin.

3. A human or humanized CDR-grafted anti-ADM antibody or anti-ADM antibody fragment thereof according to claim 1 or 2, wherein said human or humanized CDR-grafted anti-ADM antibody or anti-ADM antibody fragment is an ADM stabilizing human or humanized CDR-grafted anti-ADM antibody or anti-ADM antibody fragment that enhances the half-life ($t_{1/2}$ half retention time) of adrenomedullin in serum, blood, plasma at least 10%, preferably at least 50%, more preferably >50%, most preferably >100%.

4. A human or humanized CDR-grafted anti-ADM antibody or anti-ADM antibody fragment thereof according to any of claims 1-3, wherein said human or humanized CDR-grafted anti-ADM antibody or anti-ADM antibody fragment blocks the bioactivity of ADM to less than 80%, preferably less than 50%.

5. A human or humanized CDR-grafted anti-ADM antibody or anti-ADM antibody fragment thereof according to any of claims 1-4, wherein said human or humanized CDR-grafted anti-ADM antibody or anti-ADM antibody fragment is a monospecific antibody or antibody fragment.

6. A human or humanized CDR-grafted anti-ADM antibody or anti-ADM antibody fragment thereof according to any of claims 1-5, wherein said human or humanized CDR-grafted anti-ADM antibody or anti-ADM antibody fragment is a monoclonal antibody or antibody fragment.

7. A human or humanized CDR-grafted anti-ADM antibody or anti-ADM antibody fragment thereof according to any of claims 1-6, wherein the human or humanized CDR-grafted antibody or antibody fragment thereof comprises an antibody heavy chain (H chain) comprising:

SEQ ID NO:1
GYTFSRYW

SEQ ID NO: 2
ILPGSGST

and/or

SEQ ID NO: 3
TEGYEYDGFDY

and/or further comprises an antibody light chain (L chain) comprising:

SEQ ID NO: 4
QSIVYSNGNTY

SEQ ID NO: 5
RVS

and/or

SEQ ID NO: 6
FQGSHIPYT.

8. A human or humanized CDR-grafted anti-ADM antibody or anti-ADM antibody fragment thereof according to any of claims 1-7, wherein the heavy chain comprises at least one CDR selected from the group comprising:

SEQ ID NO: 1
GYTFSRYW

SEQ ID NO: 2
ILPGSGST

SEQ ID NO: 3
TEGYEYDGFDY

and wherein the light chain comprises at least one CDR selected from the group comprising:

SEQ ID NO: 4
QSIVYSNGNTY

SEQ ID NO: 5
RVS

SEQ ID NO: 6
FQGSHIPYT.

9. A human or humanized CDR-grafted anti-ADM antibody or anti-ADM antibody fragment thereof according to any of claims 1-8, wherein the heavy chain comprises the sequences

SEQ ID NO: 1
GYTFSRYW

SEQ ID NO: 2
ILPGSGST

SEQ ID NO: 3
TEGYEYDGFDY

and wherein the light chain comprises the sequences

SEQ ID NO: 4
QSIVYSNGNTY

SEQ ID NO: 5
RVS

SEQ ID NO: 6
FQGSHIPYT.

10. A human or humanized CDR-grafted anti-ADM antibody or anti-ADM antibody fragment thereof according to any of claims 1-9, wherein said human or humanized CDR-grafted anti-ADM antibody or anti-ADM antibody fragment has a sequence selected from the group comprising: SEQ ID NO 7, 8, 9, 10, 11, 12, 13 and 14.

11. A human or humanized CDR-grafted anti-ADM antibody or anti-ADM antibody fragment thereof according to any of claims 1-10, wherein said human or humanized CDR-grafted anti-ADM antibody or anti-ADM antibody fragment exhibits an affinity towards human ADM in such that affinity constant is greater than 10^{-7} M.

12. Pharmaceutical formulation comprising a human or humanized CDR-grafted anti-ADM antibody or anti-ADM antibody fragment thereof according to any of claims 1-11.

13. Pharmaceutical formulation comprising a human or humanized CDR-grafted anti-ADM antibody or anti-ADM antibody fragment thereof according to claim 12 wherein said pharmaceutical formulation is a solution.

14. Pharmaceutical formulation comprising a human or humanized CDR-grafted anti-ADM antibody or anti-ADM antibody fragment thereof according to claim 12 wherein said pharmaceutical formulation is in a dried state to be reconstituted before use.

15. Pharmaceutical formulation according to any of claims 12-14, to be used in combination with TNF-alpha antibodies.

16. A human or humanized CDR-grafted anti-ADM antibody or anti-ADM antibody fragment thereof according to claim 11 to be used in combination with TNF-alpha antibodies.

17. A monoclonal antibody or an antibody fragment thereof, wherein the antibody or fragment binds to a region of adrenomedullin (ADM) that is located in the N-terminal part, aa 1-21 of SEQ ID No. 23, wherein the monoclonal antibody is a human or humanized antibody and, wherein the heavy chain (H chain) comprises the sequences

SEQ ID NO: 1

GYTFSRYW

SEQ ID NO: 2

ILPGSGST

SEQ ID NO: 3

TEGYEYDGFDY

and wherein the light chain comprises the sequences

SEQ ID NO: 4

QSIVYSNGNTY

SEQ ID NO: 5

RVS

SEQ ID NO: 6

FQGSHIPYT.

18. The monoclonal antibody or fragment according to claim 17, wherein the antibody or fragment is recombinantly produced.

19. The monoclonal antibody or fragment according to claim 18, wherein the antibody is an IgG.

20. The monoclonal antibody or fragment according to claim 17, wherein the fragment is a Fv fragment, an scFv fragment, a Fab fragment, an scFab fragment, a F(ab)2 fragment or an scFv-Fc Fusion protein.

21. The monoclonal antibody or fragment according to any one of claims 17-20, wherein the antibody or fragment is a human antibody.

22. The monoclonal antibody or fragment according to any one of claims 17-20, wherein the antibody or fragment is a humanized antibody

23. The monoclonal antibody or fragment according to claim 22, wherein the antibody or fragment is produced by humanization of a murine antibody, e.g., by grafting murine CDRs into a human antibody or fragment.

24. The monoclonal antibody or fragment according to claim 23, wherein the process of humanization comprises:

a. Analyzing the antibody sequence of the murine antibody for the structural interaction of framework regions (FR) with the complementary determining regions (CDR) and the antigen;
b. Selecting an appropriate FR of human origin based on structural modelling; and
c. Transplanting the murine CDR sequences into the human FR.

25. The monoclonal antibody or fragment according to any one of claims 17-24, wherein the antibody or fragment is a stabilizing antibody or fragment that enhances the half-life of ADM in serum, blood, plasma at least 10%, preferably at least 50%, more preferably >50%, most preferably >100%.

26. The monoclonal antibody or fragment according to any one of claims 17-25, wherein the antibody or fragment is a non-neutralizing antibody or fragment.

27. The monoclonal antibody or fragment according to any one of claims 17-26, wherein the antibody or fragment blocks the bioactivity of ADM to less than 80 %, preferably less than 50%.

28. The monoclonal antibody or fragment according to any one of claims 17-27, wherein the antibody or fragment exhibits an affinity towards human ADM such that the affinity constant is greater than 10-7 M.

29. Use of the monoclonal antibody or fragment according to any one of claims 17-28 in the manufacture of a medicament for reducing the risk of mortality during a chronic or acute disease or an acute condition.

30. The use according to claim 29, wherein the chronic or acute disease or the acute condition is selected from a severe infection, e.g. meningitis; Systemic inflammatory Response-Syndrome (SIRS); sepsis; diabetes; cancer; acute and chronic vascular diseases, e.g. heart failure, myocardial infarction, stroke, atherosclerosis; shock, e.g.

septic shock; organ dysfunction, e.g. kidney dysfunction, liver dysfunction; burns; surgery; trauma; poisoning; and damage by chemotherapy.

31. The use according to claim 29 or 30, wherein the medicament is to be used in combination with a primary medicament.

32. The use according to claim 31, wherein the chronic or acute disease or the acute condition is an infection and the primary medicament is an antibiotic.

33. A pharmaceutical formulation comprising the monoclonal antibody or fragment of any one of claims 17-32.

34. The pharmaceutical formulation according to claim 33, wherein the pharmaceutical formulation is for administration via infusion.

35. The pharmaceutical formulation according to claim 33 or 34, wherein the pharmaceutical formulation is in a dried state to be reconstituted before use.