CLAIMS

~~1. A solubilized human apyrase with at least two modifications selected from the list consisting of: N terminal deletion, C terminal deletion and central modification.~~

~~2. The solubilized human apyrase of claim 1, with N terminal deletion, C terminal deletion and central modification.~~

~~3. The solubilized human apyrase of claim 1 or 2, wherein~~
~~a) the N terminal deletion is between 30 and 50 amino acids long,~~
~~b) the C terminal deletion is between 20 and 40 amino acids long, and~~
~~c) the central modification comprises a deletion and/or a point mutation.~~

~~4. The solubilized human apyrase of any of the preceding claims, wherein the central modification comprises a deletion of 10 to 15 consecutive amino acids.~~

~~5. The solubilized human apyrase of claim 4, wherein the central deletion is a deletion of amino acids number 193 to 204 in relation to the wild type CD39 sequence according to SEQ ID NO: 1.~~

~~6. The solubilized human apyrase of any of the preceding claims, wherein the central modification comprises a point mutation comprising one, two, three, four, or five point mutation(s) in relation to the wild type CD39 sequence according to SEQ ID NO: 1, selected from the group consisting of K71E, N73Q, V95A, G102D, Y104S, T106S, R113M, L149M, V151A, E173D, T229A, L254M, K258R, W263R, E276D, N292Q, R304G, I319T, N327Q, A362N, F365S, N371Q, K405N, Y412F, L424Q, H436D, I437N, F439S, G441D, N457Q, P463S, and S469R.~~

~~7. The solubilized human apyrase of any of the preceding claims, comprising a sequence selected from the group consisting of SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 32, SEQ ID NO: 54, SEQ ID NO: 56, SEQ ID NO: 70, SEQ ID NO: 76, and SEQ ID NO: 78.~~

~~8. The solubilized human apyrase of any of the preceding claims, comprising a sequence selected from the group consisting of SEQ ID NO: 131, SEQ ID NO: 133, SEQ ID NO: 135, SEQ ID NO: 137, SEQ ID NO: 139 and SEQ ID NO: 141.~~

~~9. The solubilized human apyrase of claim 8, comprising or consisting of a sequence selected from the group consisting of SEQ ID NO: 213, SEQ ID NO: 227, SEQ ID NO: 219, SEQ ID NO: 225, SEQ ID NO: 217, SEQ ID NO: 209, SEQ ID NO: 221,~~

SEQ ID NO: 72, SEQ ID NO: 215, SEQ ID NO: 223, SEQ ID NO: 211, SEQ ID NO: 58 and SEQ ID NO: 229.

10. The solubilized human apyrase of claim 9, consisting of a sequence selected from the group consisting of SEQ ID NO: 58, SEQ ID NO: 72 and SEQ ID NO: 229.

11. A pharmaceutical composition comprising a therapeutically effective dose of the apyrase of any of claims 1 to 10 and one or more pharmaceutically acceptable carriers.

12. The pharmaceutical composition of claim 11, further comprising one or more additional active ingredients.

13. An isolated apyrase of claims 1 to 10 for use as a medicament.

14. An isolated apyrase of claims 1 to 10 for use in the treatment of tissue damage.

15. An isolated apyrase for use according to claim 14, wherein the tissue damage is acute brain injury (stroke); acute multi-organ failure; delayed graft function after transplantation of kidney or other solid organs; burn damage; radiation damage; acute damage due to trauma and/or hypoxia, such as acute respiratory distress syndrome (ARDS) or lung injury; acute kidney injury, such as acute kidney injury secondary to thoracic surgery (e.g. aortic valve replacement, coronary artery bypass surgery) or sepsis or rhabdomyolysis or toxic effects of antibiotics or other medication; acute myocardial injury.

16. An isolated apyrase of claims 1-10 for use in the treatment of cardiac surgery associated acute kidney injury.

17. An isolated apyrase of claims 1-10 for use in the treatment of delayed graft function (DGF), acute respiratory distress syndrome (ARDS), acute myocardial infarction (AMI), traumatic brain injury (TBI) / acute ischemic stroke (AIS), ischemia-reperfusion injury (IRI), or combinations thereof often referred to as multi-organ failures (MOF).

18. An isolated apyrase of claims 1-10 for use in the treatment of sepsis associated acute kidney injury.

19. A method of treating tissue damage in a human subject, comprising administering a therapeutically effective dose of solubilized human apyrase to said subject.

~~20. The method of claim 19, wherein the solubilized human apyrase is an apyrase of claims 1 to 10.~~

~~21. The method of claim 19 or 20, wherein the tissue damage is acute brain injury (stroke); acute multi-organ failure; delayed graft function after transplantation of kidney or other solid organs; burn damage; radiation damage; acute damage due to trauma and/or hypoxia, such as acute respiratory distress syndrome (ARDS) or lung injury; acute kidney injury, such as acute kidney injury secondary to thoracic surgery (e.g. aortic valve replacement, coronary artery bypass surgery) or sepsis or rhabdomyolysis or toxic effects of antibiotics or other medication; acute myocardial injury.~~

~~22. A method of treating cardiac surgery associated acute kidney injury comprising administering a therapeutically effective dose of solubilized human apyrase to a subject in need of such treatment.~~

~~23. A method of treating delayed graft function (DGF), acute respiratory distress syndrome (ARDS), acute myocardial infarction (AMI), traumatic brain injury (TBI) / acute ischemic stroke (AIS) ischemia-reperfusion injury (IRI), or combinations thereof often referred to as multi-organ failures (MOF) comprising administering a therapeutically effective dose of solubilized human apyrase to a subject in need of such treatment.~~

~~24. A method of treating sepsis associated acute kidney injury comprising administering a therapeutically effective dose of solubilized human apyrase to a subject in need of such treatment.~~

~~25. An isolated nucleic acid molecule encoding any apyrase of claims 1 to 10.~~

~~26. A cloning or expression vector comprising one or more nucleic acid sequences according to claim 25, wherein the vector is suitable for the recombinant production of isolated apyrase of claims 1 to 10.~~

~~27. A host cell comprising one or more cloning or expression vectors according to claim 26.~~

~~28. A process for the production of an apyrase of any one of claims 1 to 10, comprising culturing a host cell according to claim 27, purifying and recovering said apyrase.~~

1. A solubilized human apyrase with modifications of: N terminal deletion, C terminal deletion and central modification, wherein
a) the N terminal deletion is between 30 and 50 amino acids long,
b) the C terminal deletion is between 20 and 40 amino acids long, and
c) the central modification comprises a deletion of 10 to 15 consecutive amino acids, wherein the deletion is a deletion of amino acids number 193 to 204 in relation to the wild type CD39 sequence according to SEQ ID NO: 1,
and wherein the central modification comprises a point mutation comprising one, two,
three, four, or five point mutation(s) in relation to the wild type CD39 sequence according to SEQ ID NO: 1, selected from the group consisting of K71E, N73Q, V95A,
G102D, Y104S, T106S, R113M, L149M, V151A, E173D, T229A, L254M, K258R, W263R, E276D, N292Q, R304G, I319T, N327Q, A362N, F365S, N371Q, K405N, Y412F, L424Q, H436D, I437N, F439S, G441D, N457Q, P463S, and S469R.

2. The solubilized human apyrase of claim 1, comprising a sequence selected from the group consisting of SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 32, SEQ ID NO: 54, SEQ ID NO: 56, SEQ ID NO: 70, SEQ ID NO: 76, and SEQ ID NO: 78.

3. The solubilized human apyrase of claim 1 or claim 2, comprising a sequence selected from the group consisting of SEQ ID NO: 131, SEQ ID NO: 133, SEQ ID NO: 135, SEQ ID NO: 137, SEQ ID NO: 139 and SEQ ID NO: 141.

4. The solubilized human apyrase of claim 3, comprising or consisting of a sequence selected from the group consisting of SEQ ID NO: 213, SEQ ID NO: 227, SEQ ID NO: 219, SEQ ID NO: 225, SEQ ID NO: 217, SEQ ID NO: 209, SEQ ID NO: 221, SEQ ID NO: 72, SEQ ID NO: 215, SEQ ID NO: 223, SEQ ID NO: 211, SEQ ID NO: 58 and SEQ ID NO: 229.

5. The solubilized human apyrase of claim 4, consisting of a sequence selected from the group consisting of SEQ ID NO: 58, SEQ ID NO: 72 and SEQ ID NO: 229.

6. A pharmaceutical composition comprising a therapeutically effective dose of the apyrase of any one of claims 1 to 5 and one or more pharmaceutically acceptable carriers.

7. The pharmaceutical composition of claim 6, further comprising one or more additional active ingredients.

8. An isolated apyrase of any one of claims 1 to 5 for use as a medicament.

9. Use of an isolated apyrase of any one of claims 1 to 5 in the manufacture of a medicament for the treatment of tissue damage.

10. Use according to claim 9, wherein the tissue damage is acute brain injury (stroke); acute multi-organ failure; delayed graft function after transplantation of kidney or other solid organs; burn damage; radiation damage; acute damage due to trauma and/or hypoxia, such as acute respiratory distress syndrome (ARDS) or lung injury; acute kidney injury, such as acute kidney injury secondary to thoracic surgery (e.g. aortic valve replacement, coronary artery bypass surgery) or sepsis or rhabdomyolysis or toxic effects of antibiotics or other medication; acute myocardial injury.

11. Use of an isolated apyrase of any one of claims 1 to 5 in the manufacture of a medicament for the treatment of cardiac surgery associated acute kidney injury.

12. Use of an isolated apyrase of any one of claims 1 to 5 in the manufacture of a medicament for the treatment of delayed graft function (DGF), acute respiratory distress syndrome (ARDS), acute myocardial infarction (AMI), traumatic brain injury

(TBI) / acute ischemic stroke (AIS), ischemia-reperfusion injury (IRI), or combinations thereof often referred to as multi-organ failures (MOF).

13. Use of an isolated apyrase of any one of claims 1 to 5 in the manufacture of a medicament for the treatment of sepsis associated acute kidney injury.

14. An isolated nucleic acid molecule encoding an apyrase of any one of claims 1 to 5.

15. A cloning or expression vector comprising one or more nucleic acid sequences according to claim 14, wherein the vector is suitable for the recombinant production of isolated apyrase of any one of claims 1 to 5.

16. A host cell comprising one or more cloning or expression vectors according to claim 15.

17. A process for the production of an apyrase of any one of claims 1 to 5, comprising culturing a host cell according to claim 16, purifying and recovering said apyrase.