CLAIMS

1. A method for predicting or diagnosing a refractory shock in a subject that either runs into shock or that has developed shock, wherein said method is comprising the steps:
   - determining the level of DPP3 in a sample of bodily fluid of said subject;
   - comparing said level of determined DPP3 to a predetermined threshold,

   wherein said subject is predicted to run into refractory shock or is diagnosed as having refractory shock if said determined level of DPP3 is above said predetermined threshold.

2. A method for predicting or diagnosing a refractory shock in a subject that either runs into shock or that has developed shock according to claim 1, wherein said shock is selected from the group comprising shock due to hypovolemia, cardiogenic shock, obstructive shock and distributive shock, in particular cardiogenic shock or septic shock.

3. A method for predicting or diagnosing a refractory shock in a subject that either runs into shock or that has developed shock according to claim 1 or 2, wherein said shock is a vasopressor-resistant shock.

4. A method for predicting or diagnosing a refractory shock in a subject that either runs into shock or that has developed shock according to claims 1 to 3, wherein
   - in case of cardiogenic shock said subject may have suffered an acute coronary syndrome (e.g. acute myocardial infarction) or wherein said subject has heart failure (e.g. acute decompensated heart failure), myocarditis, arrhythmia, cardiomyopathy, valvular heart disease, aortic dissection with acute aortic stenosis, traumatic chordal rupture or massive pulmonary embolism, or
   - in case of hypovolemic shock said subject may have suffered a hemorrhagic disease including gastrointestinal bleed, trauma, vascular etiologies (e.g. ruptured abdominal aortic aneurysm, tumor eroding into a major blood vessel) and spontaneous bleeding in the setting of anticoagulant use or a non-hemorrhagic disease including vomiting, diarrhea, renal loss, skin losses/insensible losses (e.g. burns, heat stroke) or third-space loss in the setting of pancreatitis, cirrhosis, intestinal obstruction, trauma, or
   - in case of obstructive shock said patient may have suffered a cardiac tamponade, tension pneumothorax, pulmonary embolism or aortic stenosis, or
   - in case of distributive shock said patient may have septic shock, neurogenic shock, anaphylactic shock or shock due to adrenal crisis.

5. A method for predicting or diagnosing a refractory shock in a subject that either runs into shock or that has developed shock according to claims 1 to 4, wherein said method is used for initiation and/or termination and/ or stratification and/or guidance of treatment.

6. A method for predicting or diagnosing a refractory shock in a subject that either runs into shock or that has developed shock according to any of claims 1 to 5, wherein a treatment is initiated and/or maintained and/or withheld and/ or terminated if said determined level of DPP3 is above said predetermined threshold.

7. A method for predicting or diagnosing a refractory shock in a subject that either runs into shock or that has developed shock according to claim 6, wherein said treatment is selected from the group of vasopressors, Angiotensin-Receptor-Agonists and/or precursors thereof, inhibitors of the DPP3 activity and anti-adrenomedullin antibodies or anti-adrenomedullin antibody fragments.

8. A method for predicting or diagnosing a refractory shock in a subject that either runs into shock or that has developed shock according to any of claims 1 to 7, wherein either the level of DPP3 protein and/or the level of active DPP3 is determined and compared to a predetermined threshold, wherein the level of DPP3 is determined by contacting said sample of bodily fluid with a capture binder that binds specifically to DPP3.

9. A method for predicting or diagnosing a refractory shock in a subject that either runs into shock or that has developed shock according to any of claims 1 to 8, wherein a treatment with Angiotensin-Receptor-Agonists and/ or precursors thereof and/or inhibitors of the DPP3 activity is initiated and/or continued when the level of DPP3 in said sample is above a certain threshold and/or wherein a treatment with vasopressors is withheld and/ or terminated if said determined level of DPP3 is above said predetermined threshold.

10. A method for predicting or diagnosing a refractory shock in a subject that either runs into shock or that has developed shock according to any of claims 1 to 9, wherein a treatment with vasopressors is initiated and/or continued when the level of DPP3 in said sample is below a certain threshold and/or wherein a treatment with Angiotensin-Receptor-Agonists and/ or precursors thereof and/or inhibitors of the DPP3 activity is withheld and/ or terminated if the said determined level of DPP3 is below said predetermined threshold.

11. A method for predicting or diagnosing a refractory shock in a subject that either runs into shock or that has developed shock according to claim 9, wherein in addition the level of Pro-adrenomedullin or fragments thereof is determined and wherein treatment with an anti-ADM antibody or anti-ADM antibody fragment is initiated and/or continued when the level of Pro-adrenomedullin or fragments thereof in said sample is above a certain threshold and/or wherein a treatment with an anti-ADM antibody or anti-ADM antibody fragment is withheld and/ or terminated if the said determined level of Pro-adrenomedullin or fragments thereof is below said predetermined threshold.

12. A method for predicting or diagnosing a refractory shock in a subject that either runs into shock or that has developed shock according to claim 9, wherein treatment with an anti-ADM antibody or anti-ADM antibody fragment and/or Angiotensin-Receptor-Agonists and/ or precursors thereof and/or inhibitors of the DPP3 activity is initiated and/or continued if the level of Pro-adrenomedullin or fragments thereof in said sample is above a certain threshold and said determined level of DPP3 is above said predetermined threshold of DPP3.

13. Vasopressor for use in therapy of shock in a subject that either runs into shock or that has developed shock, wherein said subject has a level of DPP3 in a sample of bodily fluid of said subject that is below a predetermined threshold, when determined by a method according to any of claims 1 – 11.

14. Inhibitor of the activity of DPP3 for use in therapy of shock in a subject that either runs into shock or that has developed shock, wherein said subject has a level of DPP3 in a sample of bodily fluid of said subject that is above a predetermined threshold when determined by a method according to any of claims 1 – 11, wherein the inhibitor of the activity of DPP3 is selected from the group comprising anti-DPP3 antibody or anti-DPP3 antibody fragment or anti-DPP3 non-Ig scaffold.

15. Inhibitor of the activity of DPP3 for use in therapy of shock in a subject that either runs into shock or that has developed shock according to claim 14, wherein said inhibitor is administered in combination with an Angiotensin-Receptor-Agonist and/or precursor thereof.

16. Inhibitor of the activity of DPP3 for use in therapy of shock in a subject that either runs into shock or that has developed shock according to claim 15, wherein said Angiotensin-Receptor-Agonist and/ or precursor thereof is selected from the group comprising angiotensin I, angiotensin II, angiotensin III, angiotensin IV, in particular angiotensin II.

17. A method of treatment of shock in a subject that either runs into shock or that has developed shock, the method comprising administering vasopressor to said subject, wherein said subject has a level of DPP3 in a sample of bodily fluid of said subject that is below a predetermined threshold, when determined by a method according to any of claims 1 – 11.

18. Method of treatment of shock in a subject that either runs into shock or that has developed shock, the method comprising administering inhibitor of DPP3 activity to said subject, wherein said subject has a level of DPP3 in a sample of bodily fluid of said subject that is above a predetermined threshold when determined by a method according to any of claims 1 – 11.

19. Method of treatment of shock in a subject that either runs into shock or that has developed shock according to claim 18, the method comprising administering an inhibitor of DPP3 activity to said subject, wherein said inhibitor is administered in combination with an Angiotensin-Receptor-Agonist and/ or a precursor thereof.

20. Method of treatment of shock in a subject that either runs into shock or that has developed shock according to claims 17-18, the method comprising administering Angiotensin-Receptor-Agonists and/ or precursors thereof and/or inhibitor of DPP3 activity to said subject, wherein the treatment with said Angiotensin-Receptor-Agonists and/or inhibitors of the DPP3 activity is initiated and/or continued when the level of DPP3 in a sample of said subject is above a certain threshold and/or wherein a treatment with vasopressors is withheld and/ or terminated if said determined level of DPP3 is above said predetermined threshold.

21. Method of treatment of shock in a subject that either runs into shock or that has developed shock according to claims 17-18, the method comprising administering vasopressor to said subject, wherein the treatment with said vasopressors is initiated and/or continued when the level of DPP3 in a sample of bodily fluid of said subject is below a certain threshold and/or wherein a treatment with Angiotensin-Receptor-Agonists and/ or precursors thereof and/or inhibitors of the DPP3 activity is withheld and/ or terminated if the said determined level of DPP3 is below said predetermined threshold.

22. Method of treatment of shock in a subject that either runs into shock or that has developed shock according to claim 19, the method comprising administering Angiotensin-Receptor-Agonists and/ or precursors thereof and/or inhibitor of DPP3 activity to said subject, and wherein in addition the level of Pro-adrenomedullin or fragments thereof is determined and wherein treatment with said anti-ADM

antibody or anti-ADM antibody fragment is initiated and/or continued when the level of Pro-adrenomedullin or fragments thereof in said sample is above a certain threshold and/or wherein a treatment with an anti-ADM antibody or anti-ADM antibody fragment is withheld and/ or terminated if the said determined level of Pro-adrenomedullin or fragments thereof is below said predetermined threshold.

23. Method of treatment of shock in a subject that either runs into shock or that has developed shock according to claim 20, the method comprising administering vasopressor to said subject, and wherein in addition the level of Pro-adrenomedullin or fragments thereof is determined and wherein treatment with said anti-ADM antibody or anti-ADM antibody fragment is initiated and/or continued when the level of Pro-adrenomedullin or fragments thereof in said sample is above a certain threshold and/or wherein a treatment with an anti-ADM antibody or anti-ADM antibody fragment is withheld and/ or terminated if the said determined level of Pro-adrenomedullin or fragments thereof is below said predetermined threshold.

24. Method of treatment of shock in a subject that either runs into shock or that has developed shock according to claim 21 and 22, the method comprising administering anti-ADM antibody or anti-ADM antibody fragment to said subject, wherein in addition the level of Pro-adrenomedullin or fragments thereof is determined and wherein treatment with said anti-ADM antibody or anti-ADM antibody fragment is initiated and/or continued when the level of Pro-adrenomedullin or fragments thereof in said sample is above a certain threshold and/or wherein a treatment with an anti-ADM antibody or anti-ADM antibody fragment is withheld and/ or terminated if the said determined level of Pro-adrenomedullin or fragments thereof is below said predetermined threshold.

25. A method for prognosing an outcome and/or the risk of an adverse event in a subject that has developed refractory shock, wherein said method is comprising the steps:

- determining the level of DPP3 in a sample of bodily fluid of said subject;
- comparing said level of determined DPP3 to a predetermined threshold,
- correlating said level of DPP3 with said risk of an adverse event in said subject, wherein an elevated level above a certain threshold is predictive for an enhanced risk of said adverse events or,
- correlating said level of DPP3 with success of a therapy or intervention in said subject, wherein a level below a certain threshold is predictive for a success of therapy or intervention.