CLAIMS

1. Inhibitor of the activity of DPP3 for use in a method of prevention or treatment of a refractory 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 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, said sample of bodily fluid is selected from the group of whole blood, plasma, and serum.;
   - comparing said level of determined DPP3 to a predetermined threshold that is between 25 and 150 ng/ml for plasma DPP3,

   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 and,

   wherein the inhibitor of the activity of DPP3 is selected from the group comprising anti-DPP3 antibody or anti-DPP3 antibody fragment, and

   wherein said anti-DPP3 antibody or anti-DPP3 antibody fragment is binding to an epitope according to SEQ ID NO.: 2, wherein said epitope is comprised in a DPP3 protein or functional derivative thereof and wherein said anti-DPP3 antibody or anti-DPP3 antibody fragment is a monoclonal antibody or a monoclonal antibody fragment thereof.

2. Inhibitor of the activity of DPP3 for use in a method of prevention or treatment of a refractory shock in a subject that either runs into shock or that has developed shock according to claim 1, wherein said anti-DPP3 antibody or the anti-DPP3 antibody fragment is a human or humanized antibody or derived therefrom or humanized antibody fragment or derived therefrom.

3. Inhibitor of the activity of DPP3 for use in a method of prevention or treatment of a refractory shock in a subject that either runs into shock or that has developed shock according to claim 1 or 2, wherein one or more (murine) CDR's are grafted into a human immunoglobulin backbone.

4. Inhibitor of the activity of DPP3 for use in a method of prevention or treatment of a refractory shock in a subject that either runs into shock or that has developed shock according to any of claims 1 to 3, a humanized monoclonal anti-DPP3 antibody or monoclonal anti-DPP3 antibody fragment thereof that is directed to and binding to an epitope according to SEQ ID NO.: 2, wherein said epitope is comprised in a DPP3 protein or a functional derivative thereof, and wherein the heavy chain comprises at least one CDR of:

   SEQ ID NO.: 6, SEQ ID NO.: 7 or SEQ ID NO.: 8

   and wherein the light chain comprises at least one CDR of:

SEQ ID NO.: 9, KVS or SEQ ID NO.: 10.

5. Inhibitor of the activity of DPP3 for use in a method of prevention or treatment of a refractory shock in a subject that either runs into shock or that has developed shock according to any of claims 1 to 4, wherein said humanized monoclonal anti-DPP3 antibody or monoclonal anti-DPP3 antibody fragment thereof that is directed to and binding to an epitope according to SEQ ID NO.: 2, wherein said epitope is comprised in a DPP3 protein or a functional derivative thereof, a wherein said inhibitor is a monoclonal antibody, wherein the complementarity determining regions (CDR´s) in the heavy chain comprises the sequences: SEQ ID NO.: 6, SEQ ID NO.: 7 and/ or SEQ ID NO.: 8 and the complementarity determining regions (CDR´s) in the light chain comprises the sequences: SEQ ID NO.: 9, KVS and/or SEQ ID NO.: 10.

6. Inhibitor of the activity of DPP3 for use in a method of prevention or treatment of 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 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.

7. Inhibitor of the activity of DPP3 for use in a method of prevention or treatment of a refractory shock in a subject that either runs into shock or that has developed shock according to any of claims 1 to 6, wherein said Inhibitor is administered in combination with an Angiotensin-Receptor-Agonist and/or precursor thereof , and wherein said Angiotensin-Receptor-Agonist and/ or precursor thereof that is selected from the group comprising angiotensin I, angiotensin II, angiotensin III, angiotensin IV, in particular angiotensin II and/or a precursor thereof wherein said precursor is a compound which is able to generate or to release an Angiotensin-Receptor-Agonist peptide under physiological conditions, in particular selected from the group comprising
   - pegylated forms of Angiotensin-Receptor-Agonist peptides
   - larger peptides comprising Angiotensin-Receptor-Agonist peptides, which upon selective cleaving form the Angiotensin-Receptor-Agonist peptide
   - angiotensinogen,
   - angiotensin I or its homologues,
   - peptides with protected amino acids, e.g., having protecting groups at one or more amino groups, more particularly protecting groups selected from the group consisting of benzyloxycarbonyl, t-butyloxycarbonyl (BOC), fluorenylmethyloxycarbonyl (FMOC), formyl, acetyl, and acyl, and/or having protecting groups at one or more carboxylic acid groups, more particularly benzyl esters or t-butyl esters,

- precursor peptides having amino acid substitutions, deletions, additions, the substitutions and additions including the standard D and L amino acids and modified amino acids, such as, for example, amidated and acetylated amino acids, wherein the therapeutic activity of the base peptide sequence is maintained at a pharmacologically useful level.

8. Inhibitor of the activity of DPP3 for use in a method of prevention or treatment of a refractory shock in a subject that either runs into shock or that has developed shock according to claim 7, 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.

9. Inhibitor of the activity of DPP3 for use in a method of prevention or treatment of a refractory shock in a subject that either runs into shock or that has developed shock according to claims 1 to 8, wherein in said therapy a treatment with vasopressors is withheld and/ or terminated if said determined level of DPP3 is above said predetermined threshold.

10. Inhibitor of the activity of DPP3 for use in a method of prevention or treatment of a refractory shock in a subject that either runs into shock or that has developed shock according to claims 1 to 9, wherein in addition in said therapy the level of Pro-adrenomedullin or fragments thereof is determined in a sample of bodily fluid of said subject 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.