

CLAIMS

1. A method for (a) diagnosing or monitoring kidney function in a subject or (b) diagnosing kidney dysfunction in a subject or (c) predicting or monitoring the risk of an adverse event in a diseased subject, wherein said adverse event is selected from the group comprising worsening of kidney function including kidney failure, loss of kidney function and end-stage kidney disease or death due to kidney dysfunction including kidney failure, loss of kidney function and end-stage kidney disease or (d) predicting or monitoring the success of a therapy or intervention comprising:
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- determining the level of Pro-Enkephalin or fragments thereof of at least 5 amino acids in a bodily fluid obtained from said subject; and
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- (a) correlating said level of Pro-Enkephalin or fragments thereof with kidney function in a subject or
- (b) correlating said level of Pro-Enkephalin or fragments thereof with kidney dysfunction, wherein an elevated level above a certain threshold is predictive or diagnostic for kidney dysfunction in said subject or
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- (c) correlating said level of Pro-Enkephalin or fragments thereof with said risk of an adverse event in a diseased subject, wherein an elevated level above a certain threshold is predictive for an enhanced risk of said adverse events or
- (d) correlating said level of Pro-Enkephalin or fragments thereof with success of a therapy or intervention in a diseased subject, wherein a level below a certain threshold is predictive for a success of therapy or intervention, wherein said therapy or intervention may be renal replacement therapy or may be treatment with hyaluronic acid in patients having received renal replacement or predicting or monitoring the success of therapy or intervention may be prediction or monitoring recovery of renal function in patients with impaired renal function prior to and after renal replacement therapy and/or pharmaceutical interventions,
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- wherein said Pro-Enkephalin or fragment is selected from the group comprising SEQ ID No. 1, SEQ ID No. 2, SEQ ID No. 5, SEQ ID No. 6, SEQ ID No. 8, SEQ ID No. 9, SEQ ID No. 10 and SEQ ID No. 11,

wherein said threshold is in the range of 150-1290 pmol/L,
and wherein said subject is a child.

2. A method for diagnosing or monitoring kidney function in a subject comprising:

5 determining the level of Pro-Enkephalin or fragments thereof of at least 5 amino acids in a bodily fluid obtained from said subject; and

wherein during follow-up measurement, a relative change of Pro-Enkephalin and fragments thereof that is lowered correlates with the improvement of the subject's kidney function, or

10 wherein during follow-up measurement, a relative change of Pro-Enkephalin and fragment thereof that is increased correlates with the worsening of the subject's kidney function,

wherein said Pro-Enkephalin or fragment thereof is selected from the group comprising SEQ ID No. 1, SEQ ID No. 2, SEQ ID No. 5, SEQ ID No. 6, SEQ ID No. 8, SEQ ID No. 9, SEQ ID No. 10 and SEQ ID No. 11; and

15 wherein said determination of Pro-Enkephalin or fragments thereof of at least 5 amino acids is performed more than once in one patient,

wherein the subject is a child.

20 3. A method according to claim 1 and 2, wherein said subject is a child at the age of 18 years or below, more preferred at the age of 14 years or below, even more preferred at the age of 12 years or below, even more preferred at the age of 8 years or below, even more preferred at the age of 5 years or below, even more preferred at the age of 2 years or below, most preferred at the age of one year or below.

4. A method according to claims 1 to 3, wherein said child is critically ill.

25 5. A method according to any of claims 1 to 4 comprising

determining the level of immunoreactive analyte by using at least one binder that binds to a region within the amino acid sequence of Pro-Enkephalin (PENK) or fragments thereof in a bodily fluid obtained from said subject; and

- (a) correlating said level of immunoreactive analyte with kidney function in a subject or
- 5 (b) correlating said level of immunoreactive analyte with kidney dysfunction wherein an elevated level above a certain threshold is predictive or diagnostic for kidney dysfunction in said subject or
- (c) correlating said level of immunoreactive analyte with said risk of an adverse event in a diseased subject, wherein an elevated level above a certain threshold is predictive for an
- 10 enhanced risk of said adverse events or
- (d) correlating said level of immunoreactive analyte with success of a therapy or intervention in a diseased subject, wherein a level below a certain threshold is predictive for a success of therapy or intervention.

15 6. A method according to any of claims 1 to 5, wherein said at least one binder binds to a region within the amino acid sequence selected from the group comprising SEQ ID No. 1, 2, 5, 6, 8, 9, 10 and 11, preferably said at least one binder binds to a region with the sequences selected from the group comprising SEQ ID No. 1, 2, 5, 6, 8 and 9, preferably said at least one binder binds to SEQ ID No. 6.

20 7. A method according to any of the preceding claims, wherein the level of Pro-Enkephalin is measured with an immunoassay and said binder is an antibody, or an antibody fragment binding to Pro-Enkephalin or fragments thereof of at least 5 amino acids.

25 8. A method according to any of the claims 1 to 7, wherein an assay is used comprising two binders that bind to two different regions within the region of Pro-Enkephalin that is amino acid 133-140 (LKELLETG, SEQ ID NO. 13) and amino acid 152-159 (SDNEEEVS, SEQ ID No. 14), wherein each of said regions comprises at least 4 or 5 amino acids.

30 9. A method according to any of claims 1 to 8, wherein an assay is used for determining the level of Pro-Enkephalin or fragments thereof of at least 5 amino acids and wherein the assay sensitivity of said assay is able to quantify the Pro-Enkephalin or Pro-Enkephalin fragments of healthy subjects and is < 15pmol/L.

10. A method according to any of claims 1 to 9, wherein said bodily fluid may be selected from the group comprising whole blood, serum, plasma, urine, cerebrospinal liquid (CSF), and saliva.
11. A method according to claims 1 to 10, wherein additionally at least one clinical parameter is determined selected from the group comprising: beta-trace protein (BTP), cystatin C, KIM-1, TIMP-2, IGFBP-7, blood urea nitrogen (BUN), NGAL, Creatinine Clearance, serum Creatinine (SCr), urea, Pediatric Risk of Mortality III [PRISM-III] score, Pediatric Index of Mortality 2 [PIM-II] score and Apache Score.
12. A method according to any of claims 1 to 11, wherein said determination of Pro-Enkephalin or fragments thereof of at least 5 amino acids is performed more than once in one patient.
13. A method according to any of claims 1 to 12, wherein said monitoring is performed in order to evaluate the response of said subject to preventive and/or therapeutic measures taken.
14. A method according to any of claims 1 to 13 in order to stratify said subjects into risk groups.
15. A point-of-care device for performing a method according to any of claims 1 to 14, wherein said point of care device comprises at least two antibodies or antibody fragments directed to amino acid 133-140 (LKELLETG, SEQ ID No. 13) and amino acid 152-159 (SDNEEEVS, SEQ ID No. 14).
16. A kit for performing a method according to any of claims 1 to 15, wherein said kit comprises at least two antibodies or antibody fragments directed to amino acid 133-140 (LKELLETG, SEQ ID No. 13) and amino acid 152-159 (SDNEEEVS, SEQ ID No. 14).