METHOD FOR EVALUATING KIDNEY FUNCTION IN A FELINE BY MEASURING GHRELIN HORMONE LEVELS

VERFAHREN ZUR BEWERTUNG DER NIERENFUNKTION EINER KATZE DURCH MESSEN DES GHRELIN-HORMONSPIEGELS

PROCEDE PERMETTANT D’EVALUER LA FONCTION RENALE CHEZ UN FELIN PAR MESURE DE NIVEAU DE L’HORMONE GHRELIN

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BACKGROUND OF THE INVENTION

Field of the Invention

[0001] The present invention relates to methods for evaluating kidney function in felines and methods for diagnosing kidney disease in felines. The invention further relates to kits and communicating means useful in practicing methods of the invention.

Description of the Art

[0002] Feline kidney disease is the second leading cause of feline death. Possible causes of feline kidney disease include congenital disorders (a feline being born with one kidney or an impaired kidney), kidney infection (resulting from an untreated urethra blockage), decreased blood supply to renal arteries (caused by, for example, diabetes, renal blockage, tumors, or arterial collapse), toxic chemicals, glomerulonephritis, interstitial nephritis, feline leukemia virus infection, feline infectious peritonitis, high blood pressure and renal tumors.

[0003] Because the reserve capacity of a kidney is large, kidney disease can progress undetected for a long time, and by the time external signs of the disease are visible, 60% to 75% of the renal mass may already be lost.

[0004] Though feline kidney disease is progressive and fatal, early diagnosis can allow the disease to be effectively managed for some time. Thus, there remains a need for new methods for evaluating kidney function and methods for diagnosing kidney disease in felines.

[0005] Ghrelin is a peptide hormone produced by endocrine cells in the placenta, kidney, pituitary and hypothalamus and by epithelial cells lining the fundus of the stomach. Initially synthesized as a preprohormone, ghrelin is proteolytically processed to a 28-amino acid peptide.

[0006] Ghrelin stimulates growth hormone secretion and regulates energy balance. In rodents and humans, ghrelin increases hunger through activation of hypothalamic feeding centers. Ghrelin secretion is up-regulated under conditions of negative energy balance and down-regulated under conditions of positive energy balance. In humans, dogs and rodents, ghrelin blood levels are reported to increase as kidney function decreases. This is not unexpected as declining kidney function indicates low energy and thus a need for increased food intake. The increase in blood ghrelin levels in these species acts to enhance appetite and in turn, increases food ingestion.

SUMMARY OF THE INVENTION

[0007] Surprisingly, it has now been found that in felines, serum ghrelin levels are directly, as opposed to inversely, correlated with certain indicators of kidney function such as blood urea nitrogen (BUN).

[0008] A method for evaluating feline kidney function is described, comprising determining a ghrelin level in a tissue or biofluid of a feline, and directly correlating the ghrelin level to kidney function.

[0009] Accordingly, the present invention provides a method for diagnosing kidney disease in a feline, comprising determining in vitro an observed ghrelin level in a tissue or biofluid of the feline, and comparing the observed ghrelin level to a reference ghrelin level indicative of normal kidney function, wherein an observed level lower than the reference level is indicative of kidney disease or susceptibility thereto.

[0010] Also described is a method for detecting onset of kidney disease in a feline, comprising monitoring ghrelin level in a tissue or biofluid of the feline over a time period; wherein onset is detected if, at any time point, the ghrelin level exhibits a decrease versus an initial level indicative of healthy kidney function.

[0011] The invention further provides a method for selecting a regimen for a feline, comprising (a) determining in vitro a ghrelin level in a tissue or biofluid of the feline; (b) evaluating kidney function by direct correlation thereof with the ghrelin level; and (c) identifying a regimen appropriate to the kidney function.

[0012] The invention still further provides a method for assessing efficacy of a regimen for managing kidney function in a feline, comprising (a) establishing in vitro a baseline ghrelin level in a tissue or biofluid of the feline prior to initiation of the regimen; (b) monitoring in vitro observed ghrelin level at least at one time point after initiation of the regimen; and (c) comparing the observed level to the baseline level: wherein maintenance or increase in the observed level relative to the baseline level is indicative of efficacy of the regimen.

[0013] Also described is a diagnostic kit comprising (a) one or more test materials for determining observed ghrelin levels in a tissue or biofluid of a feline; and (b) one or more user-accessible media carrying information that comprises (i) a reference ghrelin level appropriate to the feline: and (ii) an algorithm that directly correlates an observed ghrelin level, relative to the reference level, to kidney function or that inversely correlates an observed ghrelin level, relative to the reference level, to presence of or susceptibility to kidney disease.
DETAILED DESCRIPTION OF THE INVENTION

[0014] The description also details a means for communicating information about direct correlation of kidney function to ghrelin level in a feline, comprising one or more of a product label, a package insert, a brochure, a handout, an advertisement, a public announcement, an audiotape, a videotape, a DVD, a CD-ROM, a computer readable chip, card or disk, a computer memory or a web page.

[0015] In felines, as in other animals, diminished kidney function is indicated by elevated levels of BUN, creatinine, and BUN to creatinine ratio. It has now been found in domestic cats that increased levels of BUN, or increased BUN to creatinine ratio, correspond to decreased levels of ghrelin. As BUN is a known indicator of diminished kidney function, it can be concluded that ghrelin levels are directly correlated with kidney function in cats. This finding is surprising and contrary to expectations based upon observations of ghrelin levels in other species.

[0016] The methods of the invention are useful for felines, including for example, domesticated cats. Other animals belonging to the family Felidae are also included as “felines” herein, such as lions, tigers, jaguars, and other wild and domestic cats.

[0017] Kidneys have multiple functions including filtering waste products from the body (primarily urea and creatinine), regulating serum electrolyte levels (potassium, calcium, phosphorus and sodium), producing erythropoietin (which stimulates the bone marrow to produce red blood cells), producing renin (an enzyme that controls blood pressure), and producing and concentrating urine. Impaired kidney function can indicate chronic or acute kidney disease. Acute kidney diseases include, but are not limited to, urinary obstruction, infectious disease, physical injury> and poisoning. Chronic kidney diseases include but are not limited to chronic renal failure, chronic tubulo-interstitial nephritis, glomerulonephritis, pyelonephritis, amyloidosis, hydronephrosis, renal lymphoma, polycystic kidney disease, renal aplasia, renal hypoplasia, renal dysplasia and kidney disease caused by congenital disorders.

[0018] The term “kidney disease” herein includes any kidney dysfunction or disorder regardless of whether it is generally recognized as a disease or syndrome.

[0019] A method of the invention for evaluating feline kidney function comprises determining a ghrelin level in a tissue or biofluid of a feline, and directly correlating the ghrelin level to kidney function.

[0020] The step of directly correlating as used herein is characterized as identifying a level of kidney function consistent with the ghrelin level using a direct correlation between ghrelin level and kidney function. For example, high levels of ghrelin can indicate normal kidney function while low levels of ghrelin can indicate impaired kidney function.

[0021] Any tissue or biofluid can be used to determine ghrelin levels. Generally, tissues or biofluids that can be obtained with minimal invasion are more desirable. A biosample, for example, is any sample of a tissue or biofluid used to determine ghrelin levels that is obtained from a live animal. Alternatively, ghrelin levels can be determined in situ without the need to obtain a biosample. Tissues can include but are not limited to bone, muscle, kidney, liver, etc. Biofluids illustratively include whole blood, blood serum, blood plasma, cerebrospinal fluid, crevicular fluid, milk, urine, lymph fluid, intramuscular fluid, nasal secretion and saliva.

[0022] A biosample can be collected, for example, at a point of care facility, i.e., a place where an animal can be seen by a health care practitioner (e.g., veterinarian, veterinary technician, etc.) for evaluation and diagnosis. Alternatively, a biosample can be collected at the animal’s home, farm, stable, kennel or cattery where the animal is kept.

[0023] When a biosample is taken at a single time point, the sample will typically be taken when the feline is in a fasted state, for example, a preprandial (immediately before a meal) time point. However, a biosample can be obtained at any stage of the feline’s feeding cycle, for example preprandial or at a suitable interval after a meal (postprandial). When a biosample is taken at more than one time point, the biosample is typically obtained at a consistent stage of the feeding cycle, most conveniently when the feline is in a fasted state. However, a biosample can be obtained at each of a plurality of time points during a feeding cycle, including at least one preprandial time point and at least one postprandial time point.

[0024] Ghrelin level from a biosample obtained from a feline can be determined at the place, e.g. point of care facility, where the biosample is taken. A kit as described herein can optionally be used in determining the ghrelin level. Alternatively, the biosample can be sent to a secondary facility. The term “secondary facility” herein refers to a laboratory such as a commercial testing laboratory where clinical samples are evaluated, and can be off-site (i.e., at a different location) from a point of care facility.

[0025] In some embodiments, either or both steps of determining a ghrelin level and directly correlating the ghrelin level to kidney function are performed at a point of care facility or a secondary facility.

[0026] Ghrelin levels can be determined using assays known in the art. An assay can include any commercially available or non-commercially available assay. Typically, an assay is chosen based on the type of tissue or biofluid in which the ghrelin level is to be determined. For example, a commercially available monoclonal-based immunoassay utilizing monoclonal antibodies reactive to one or more epitopes on the ghrelin molecule can be used to determine a blood serum level of ghrelin.

[0027] In some embodiments, ghrelin levels are determined using one or more of enzyme immunoassay, enzyme-
linked immunosorbet assay, immunofluorescent assay, radioimmunoassay, western blot assay, biochemical assay, enzymatic assay or colorimetric assay techniques. A variety of labels and conjugation techniques are known by those skilled in the art and can be used in various assays.

0028] Ghrelin level in a sample can be unadjusted, or adjusted for body weight of the feline. An unadjusted level can be expressed in weight/volume concentration units such as mg/l, μg/l or ng/l, or molar concentration units such as μmol/l, nmoll or pmol/l. An adjusted level can be expressed in similar units, but with body weight (BW) as a divisor. e.g., mg/l/kg BW, pmol/l/kg BW, etc.

0029] The invention also provides a method for diagnosing kidney disease in a feline, comprising determining an observed ghrelin level in a tissue or biofluid of the feline, and comparing the observed ghrelin level to a reference ghrelin level indicative of normal kidney function, wherein an observed level lower than the reference level is indicative of kidney disease or susceptibility thereto.

0030] An "observed ghrelin level" herein is the ghrelin level determined from a tissue or biofluid from a feline in which a diagnosis is to be made.

0031] The reference ghrelin level is generally indicative of normal kidney function. The reference level can be established from one or more biosamples obtained from one or more felines with normal kidney function. Typically, reference levels are established for felines of the same breed or breed type. It is further desirable that the reference levels are established for felines of particular age groups and/or for each sex. The reference ghrelin level can also be established from publicly available documentary data, for example a ghrelin value published in the literature or a norm based on documentary data.

0032] In some embodiments, the reference ghrelin level can be obtained from a database accessible to a professional making the diagnosis.

0033] In some embodiments, the observed ghrelin level is determined in a first feline and the reference ghrelin level is determined in a second feline, wherein the second feline has normal kidney function.

0034] In other embodiments, the observed and reference ghrelin levels are determined in the same feline at different time points. For example, the first time point can establish a baseline or reference level for ghrelin. Ghrelin levels determined at one or more subsequent time points can be considered observed ghrelin levels. The observed and reference ghrelin levels are determined in biosamples obtained at time points that are generally at least about 4 hours apart, for example, at least about 8 hours apart, at least about 12 hours apart, at least about 24 hours apart, at least about 3 days apart, at least about 7 days apart, or at least about 1 month apart.

0035] In some embodiments, an observed ghrelin level lower than the reference level is indicative of kidney disease. In other embodiments, an observed ghrelin level lower than the reference level is indicative of susceptibility to kidney disease. Illustratively, an observed ghrelin level of at least about 10%, at least about 15%, at least about 20%, at least about 25% or at least about 30% lower than the reference ghrelin level is indicative of kidney disease or susceptibility thereto. In general, a greater difference between the reference level and the observed level is indicative of a greater depression of kidney function or a more severe state of kidney disease.

0036] Kidney disease normally progresses over time, initially without detection and/or management by the feline's caregiver. By the time kidney disease is outwardly apparent, kidney function is already greatly diminished. If, however, kidney disease is detected at its onset or a feline is identified as having a predisposition to kidney disease, the animal's health can be managed to minimize the impact of disease.

0037] The invention provides a method for detecting onset of kidney disease in a feline, comprising monitoring ghrelin level in a tissue or biofluid of the feline over a time period; wherein onset is detected if, at any time point, the ghrelin level exhibits a decrease versus an initial level indicative of healthy kidney function.

0038] According to this method, ghrelin levels in a feline are monitored over some period of time, and onset of kidney disease is detected if, at any time point during that period, the ghrelin level decreases relative to the initial ghrelin level. The decrease can be, but is not necessarily, statistically significant.

0039] Monitoring of ghrelin level can be performed at any convenient interval, for example, about hourly, twice daily, daily, twice, weekly, weekly, monthly, bimonthly, twice yearly or yearly intervals.

0040] The invention further provides a method for selecting a regimen for a feline, comprising (a) determining a ghrelin level in a tissue or biofluid of the feline: (b) evaluating kidney function by direct correlation thereof with the ghrelin level; and (c) identifying a regimen appropriate to the kidney function.

0041] One embodiment optionally includes the further step of (d) directing a caregiver of the feline to adopt the regimen so identified. Such an embodiment can be considered a method for prescribing a regimen for a feline.

0042] A regimen appropriate to the kidney function can be selected by the feline's caregiver based on information communicated by any suitable communication means, or can be prescribed or suggested by a health care professional. The regimen can comprise dietary or pharmaceutical intervention or both.

0043] Dietary intervention can be by way of providing a composition for consumption by the feline. The composition has nutrient levels appropriate to the kidney function evaluated. Illustratively, such a composition can be a nutritional composition, such as a food composition, a supplement, a treat or a toy, it being noted that some, but not all, supplements,
treats and toys are themselves food compositions. Food compositions can be, for example, ingested by an animal or administered to an animal by feeding. The composition useful herein is typically one that is nutritionally adapted for feeding to a feline having healthy or impaired kidney function. The food composition can be particularly adapted to the special nutritional needs of felines of particular breeds, ages, sex, etc. The composition can be available with or without a prescription.

Pharmaceutical intervention appropriate to kidney function can comprise administering to the feline at least one renal drug according to a therapeutically effective regimen. For example, such a renal drug can be selected from ACE inhibitors, endothelin inhibitors, vasopptide inhibitors, calcium channel blockers, H2 receptor antagonists, proton pump inhibitors, cytoprotectives, antiemetics, androgens, erythropoietin, phosphate binders, calcitriol, and combinations thereof.

The regimen can be continued at a frequency or for a period of time as is necessary or appropriate for the kidney function, whether healthy or impaired. Illustratively, a regimen can continue for at least about 1 month, at least about 2 months, at least about 6 months, at least about 1 year, or for some other period of time as determined necessary or appropriate by, for example, a veterinarian or other health care professional.

The invention further provides a method for assessing efficacy of a regimen for managing kidney function in a feline, comprising (a) establishing a baseline ghrelin level in a tissue or biofluid of the feline prior to initiation of the regimen; (b) monitoring observed ghrelin level at least at one time point after initiation of the regimen; and (c) comparing the observed level to the baseline level; wherein maintenance or increase in the observed level relative to the baseline level is indicative of efficacy of the regimen.

The baseline ghrelin level is established before starting the feline on a particular regimen. Then, as described above, the ghrelin level is monitored at one or more time points subsequent to initiation of the regimen. The observed ghrelin level(s) relative to the baseline ghrelin level can be individually or collectively indicative of efficacy of the regimen in managing kidney function. For example, maintenance of or increase in the observed ghrelin level relative to the baseline level is indicative of efficacy of the regimen.

There is also provided a diagnostic kit comprising (a) one or more test materials for determining observed ghrelin levels in a biosample obtained from a feline; and (b) one or more user-accessible media carrying information that comprises (i) a reference ghrelin level appropriate to the feline; and (ii) an algorithm that directly correlates an observed ghrelin level, relative to the reference level, to kidney function or that inversely correlates an observed ghrelin level, relative to the reference level, to presence of or susceptibility to kidney disease. As in previous embodiments, an observed level lower than the reference level is indicative of kidney disease or susceptibility thereto.

"User-accessible" media herein include all media, such as paper, disk, memory chip, card, computer or network, on which instructions, information, an algorithm and/or data can be retrievable contained or stored. The algorithm is typically a software algorithm.

The kit is optionally self-contained so as not to require laboratory equipment. Optionally, the kit further comprises a biosample collection device. The kit can employ one or more of a variety of assays for determining a ghrelin level, including, the assays listed above. Standards and standard additions can be included and used for calibration in quantifying the level of ghrelin in a biosample.

In some embodiments, the one or more test materials can comprise one or more reagents. In other embodiments, the one or more test materials of the kit can comprise at least one antibody, for example a polyclonal or monoclonal antibody against ghrelin. The antibody can be immobilized on a solid support. For example, an ELISA can be utilized to determine a level of ghrelin in a sample. The ELISA can involve coupling an antibody onto a solid support such as a polymer. A sample comprising ghrelin can be introduced and allowed to interact with the antibody, whereupon a signal (e.g., chromogenic signal) generating process can be performed to create an optically detectable signal.

In one embodiment, the kit comprises a first antibody that specifically binds to the ghrelin in the sample, and a second antibody that specifically binds to the resulting complex of the first antibody and the ghrelin. The second antibody can be immobilized to a solid support. For example, upon binding of the second antibody to the first antibody/ghrelin complex, the second antibody can trigger a reaction and, for example, result in a detectable color change.

The diagnostic kit can further comprise a means for communicating information about or instructions for (a) evaluating kidney function or diagnosing kidney disease in a feline or (b) a suggested or prescribed regimen appropriate to the kidney function or disease as discussed above.

The communicating means can be attached to or enclosed in a package containing other elements of the kit. Any suitable form of communicating means can be employed, for example a document such as a label, brochure, advertisement or package insert, a computer-readable digital or optical medium such as a diskette or CD, an audio presentation, for example on an audiotaape or CD, or a visual presentation, for example on a videotape or DVD. The communicating means can refer to further information located elsewhere, such as on a website.

In a still further embodiment, there is provided a means for communicating information about direct correlation of kidney function to ghrelin level in a feline, comprising one or more of a product label, a package insert, a brochure, a handout, an advertisement, a public announcement, an audiotaape, a videotape, a DVD, a CD-ROM, a computer
The invention is not limited to the particular methodology, protocols, and reagents described herein because they may vary. Further, the terminology used herein is for the purpose of describing particular embodiments only and is not intended to limit the scope of the present invention. As used herein and in the appended claims, the singular forms "a," "an," and "the" include plural reference unless the context clearly dictates otherwise. Similarly, the words "comprise", "comprises", and "comprising" are to be interpreted inclusively rather than exclusively.

Unless defined otherwise, all technical and scientific terms and any acronyms used herein have the same meanings as commonly understood by one of ordinary skill in the art in the field of the invention. Although any methods and materials similar or equivalent to those described herein can be used in the practice of the present invention, the preferred methods, devices, and materials are described herein.

All patents, patent applications, and publications mentioned herein are incorporated herein by reference to the extent allowed by law for the purpose of describing and disclosing the compounds, processes, techniques, procedures, technology, articles, and other compositions and methods disclosed therein that might be used with the present invention. However, nothing herein is to be construed as an admission that the invention is not entitled to antedate such disclosure by virtue of prior invention.

EXAMPLE

The invention can be further illustrated by the following examples of preferred embodiments thereof, although it will be understood that these examples are included merely for purposes of illustration and are not intended to limit the scope of the invention unless otherwise specifically indicated. The example takes the form of a study illustrating that levels of ghrelin, relative to a reference ghrelin level, can be indicative of kidney function and kidney disease, or susceptibility thereto.

Prior to the study, 40 cats are fed the same food containing sufficient nutrients to meet minimum nutritional requirements. The cats show no sign of renal disease. At the start of the study, cats are split into four groups of 10 cats each and each group is assigned one of four commercially available cat foods. The cats are fed their assigned food daily for 30 days. Cats are given fresh food daily and given access to the food for a period of 20 hours.

Blood is drawn and urine collected at day zero and day 30. Ghrelin and BUN levels are determined in serum and microalbuminuria is determined in urine using conventional methods. Microalbuminuria is performed via Heska ERD Kit. Ghrelin analysis utilizes ELISA. Creatinine and BUN are in the routine chemistry screen analysis. Table 1 shows blood metabolites and urine specific gravity measured at day 30.

<table>
<thead>
<tr>
<th>Food 1</th>
<th>Food 2</th>
<th>Food 3</th>
<th>Food 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum ghrelin, ng/ml</td>
<td>1.65</td>
<td>1.66</td>
<td>1.96</td>
</tr>
<tr>
<td>BUN, mg/dl</td>
<td>20.94</td>
<td>22.61</td>
<td>19.86</td>
</tr>
<tr>
<td>Blood creatinine, mg/dl</td>
<td>1.07</td>
<td>1.18</td>
<td>1.08</td>
</tr>
<tr>
<td>BUN to creatinine ratio</td>
<td>19.6</td>
<td>19.18</td>
<td>19.15</td>
</tr>
<tr>
<td>Urine specific gravity</td>
<td>1.041</td>
<td>1.034</td>
<td>1.037</td>
</tr>
<tr>
<td>Microalbuminuria, mg/dl</td>
<td>0.00</td>
<td>0.8</td>
<td>0.4</td>
</tr>
</tbody>
</table>

Each of the four foods contain different concentrations of various nutrients and lead to different outcomes in terms of kidney function as shown at least by BUN levels. The results indicate that low levels of ghrelin are surprisingly associated with high levels of BUN, known to be an indicator of impaired kidney function.

In the specification, there have been disclosed typical preferred embodiments of the invention and, although specific terms are employed, they are used in a generic and descriptive sense only and not for purposes of limitation, the scope of the invention being set forth in the claims. Obviously many modifications and variations of the invention are possible in light of the above teachings. It is therefore to be understood that within the scope of the appended claims the invention may be practiced otherwise than as specifically described.
Claims

1. A method for diagnosing kidney disease or diminished kidney function in a feline comprising determining \textit{in vitro} an observed ghrelin level in a tissue or biofluid of the feline and comparing the observed ghrelin level to a reference ghrelin level indicative of normal kidney function, wherein an observed level lower than the reference level is indicative of kidney disease or diminished kidney function or susceptibility thereto.

2. The method of claim 1 wherein the reference ghrelin level represents a norm based on documentary data, or wherein the observed reference ghrelin level is determined in a first feline and the reference ghrelin level is determined in a second feline having normal kidney function, or wherein an observed ghrelin level at least about 10% lower than the reference ghrelin level is indicative of kidney disease or susceptibility thereto.

3. The method of claim 1 wherein the observed and reference ghrelin levels are determined in the same feline at different time points, or wherein the observed and reference ghrelin levels are determined at time points at least about 4 hours apart, or wherein the observed and reference ghrelin levels are determined at time points at least about 7 days apart.

4. A method for selecting a regimen for a feline comprising:
   \begin{enumerate}
   \item determining \textit{in vitro} a ghrelin level in a tissue or biofluid of the feline;
   \item evaluating kidney function by comparing the observed ghrelin level to a reference ghrelin level indicative of normal kidney function, wherein an observed level lower than the reference level is indicative of diminished kidney function; and
   \item identifying a regimen appropriate to the kidney function.
   \end{enumerate}

5. The method of claim 4 wherein the regimen comprises dietary or pharmaceutical intervention or both.

6. A method for assessing efficacy of a regimen for managing kidney function in a feline comprising:
   \begin{enumerate}
   \item establishing \textit{in vitro} a baseline ghrelin level in a tissue or biofluid of the feline prior to initiation of the regimen;
   \item monitoring \textit{in vitro} observed ghrelin level at least at one time point after initiation of the regimen; and
   \item comparing the observed level to the baseline level;
   \end{enumerate}
   wherein maintenance or increase in the observed level relative to the baseline level is indicative of efficacy of the regimen.

7. The method of any preceding claim wherein the feline is a cat.

8. The method of any preceding claim wherein the tissue or biofluid comprises a biosample obtained from the feline, and preferably the biosample comprises whole blood, blood plasma, or blood serum.

9. The method of any preceding claim wherein the biosample is obtained when the feline is in a fasted state.

10. The method of any preceding claim wherein the ghrelin level in the biosample is determined using one or more of enzyme immunoassay, enzyme-linked immunosorbent assay, immunofluorescent assay, radioimmunoassay, western blot assay, biochemical assay, enzymatic assay or colorimetric assay techniques.

Patentansprüche


2. Verfahren nach Anspruch 1, bei dem der Vergleichsghrelinspiegel eine auf dokumentierten Daten basierende Norm darstellt, oder bei dem der gemessene Vergleichsghrelinspiegel in einer ersten Katze bestimmt wird und der Ver-
gleichsghrelinspiegel in einer zweiten Katze mit normaler Nierenfunktion bestimmt wird, oder bei dem ein gemessener Ghrelinspiegel um mindestens etwa 10 % niedriger als der Vergleichsghrelinspiegel auf eine Nierenerkranzung oder Prädisposition dafür hinweist.

3. Verfahren nach Anspruch 1, bei dem der gemessene und der Vergleichsghrelinspiegel bei der selben Katze zu unterschiedlichen Zeitpunkten bestimmt werden, oder bei dem der gemessene und der Vergleichsghrelinspiegel zu Zeitpunkten, die mindestens 4 Stunden auseinander liegen, bestimmt werden, oder bei dem der gemessene und der Vergleichsghrelinspiegel zu Zeitpunkten bestimmt werden, die mindestens 7 Tage auseinander liegen.

4. Verfahren zur Auswahl einer Therapie für eine Katze, bei dem:
   (a) in vitro ein Ghrelinspiegel in einem Gewebe oder biologischen Fluid der Katze bestimmt wird,
   (b) die Nierenfunktion bewertet wird, indem der gemessene Ghrelinspiegel mit einem Vergleichsghrelinspiegel, der auf eine normale Nierenfunktion hinweist, verglichen wird, wobei ein gemessener Spiegel, der niedriger liegt als der Vergleichsspiegel, auf eine verminderte Nierenfunktion hinweist, und
   (c) eine Therapie identifiziert wird, die für die Nierenfunktion geeignet ist.

5. Verfahren nach Anspruch 4, bei dem die Therapie einen diätetischen oder medikamentösen Eingriff oder beides umfasst.

6. Verfahren zur Bewertung der Wirksamkeit einer Therapie zum Umgang mit der Nierenfunktion bei einer Katze, bei dem:
   (a) vor Beginn der Therapie in vitro ein Basalghrelinspiegel in einem Gewebe oder biologischen Fluid der Katze ermittelt wird,
   (b) zumindest zu einem Zeitpunkt nach Beginn der Therapie der in vitro gemessene Ghrelinspiegel kontrolliert wird und
   (c) der gemessene Spiegel mit dem Basalghrelinspiegel verglichen wird,
   wobei die Aufrechterhaltung oder Erhöhung des gemessenen Spiegels bezogen auf den Basalghrelinspiegel auf eine Wirksamkeit der Therapie hinweist.

7. Verfahren nach einem der vorhergehenden Ansprüche, bei dem die Katze eine Haustatze ist.

8. Verfahren nach einem der vorhergehenden Ansprüche, bei dem das Gewebe oder biologischen Fluid eine von der Katze erhaltene biologische Probe umfasst, und die biologische Probe vorzugsweise vollständiges Blut, Blutplasma oder Blutserum umfasst.

9. Verfahren nach einem der vorhergehenden Ansprüche, bei dem die biologische Probe erhalten wird, während sich die Katze im nüchternen Zustand befindet.


Revendications

1. Procédé pour diagnostiquer une maladie rénale ou une fonction rénale réduite chez un félin, comprenant la détermination in vitro d’un taux de ghélrate observé dans un tissu ou dans un fluide biologique du félin et la comparaison du taux de ghélrate observé avec un taux de ghélrate de référence indicateur d’une fonction rénale normale, dans lequel un taux observé inférieur au taux de référence est indicateur d’une maladie rénale ou d’une fonction rénale réduite ou d’une susceptibilité d’un tel état.

2. Procédé selon la revendication 1, dans lequel le taux de ghélrate de référence représente une norme basée sur des données de documentation, ou dans lequel le taux de ghélrate de référence observé est déterminé chez un premier félin et le taux de ghélrate de référence est déterminé chez un second félin présentant une fonction rénale
normale, ou dans lequel un taux de ghréline observé qui est au moins environ 10 % inférieur au taux de ghréline de référence est indicator d’une maladie rénale ou d’une susceptibilité de maladie rénale.

3. Procédé selon la revendication 1, dans lequel les taux de ghréline observé et de ghréline de référence sont déterminés chez le même félin à divers moments dans le temps, ou dans lequel les taux de ghréline observé et de ghréline de référence sont déterminés à des moments séparés dans le temps par au moins environ 4 heures, ou dans lequel les taux de ghréline observé et de ghréline de référence sont déterminés à des moments séparés dans le temps par au moins environ 7 jours.

4. Procédé de sélection d’un traitement pour un félin comprenant les étapes consistant à :

   (a) déterminer in vitro un taux de ghréline dans un tissu ou dans un fluide biologique du félin ;
   (b) évaluer la fonction rénale en comparant le taux de ghréline observé à un taux de ghréline de référence indicateur d’une fonction rénale normale, dans lequel un taux observé inférieur au taux de référence est indicateur d’une fonction rénale réduite ; et
   (c) identifier un traitement approprié à la fonction rénale.

5. Procédé selon la revendication 4, dans lequel le traitement comprend une intervention au plan alimentaire ou pharmaceutique ou les deux.

6. Procédé pour évaluer l’efficacité d’un traitement destiné à gérer la fonction rénale d’un félin, comprenant les étapes consistant à :

   (a) établir in vitro un taux de ghréline basal dans un tissu ou dans un fluide biologique du félin avant de commencer le traitement ;
   (b) surveiller in vitro le taux de ghréline observé au moins à un moment dans le temps situé après le début du traitement ; et
   (c) comparer le taux observé au taux basal ;

dans lequel le maintien ou l’augmentation du taux observé par rapport au taux basal est un indicateur de l’efficacité du traitement.

7. Procédé selon l’une quelconque des revendications précédentes, dans lequel le félin est un chat.

8. Procédé selon l’une quelconque des revendications précédentes, dans lequel le tissu ou le fluide biologique comprend un échantillon biologique prélevé chez le félin et, de préférence, l’échantillon biologique comprend le sang entier, le plasma sanguin ou le sérum sanguin.

9. Procédé selon l’une quelconque des revendications précédentes, dans lequel l’échantillon biologique est prélevé lorsque le félin est à l’état de jeûne.