

CLAIMS

1. Use of a CNNM4 inhibitor in the manufacture of a medicament for the treatment of an acute or a chronic disease in a subject, wherein the disease is selected from the group consisting of a liver disease, a kidney disease and a lung disease,
5 wherein said inhibitor is selected from the group consisting of siRNA, shRNA, miRNA, sgRNA, a dicer-substrate 27-mer duplex, an aptamer, a DNAzyme, a ribozyme, a triplex forming oligonucleotide (TFO), an antisense polynucleotide, a phosphorodiamidate morpholino oligomer (PMO) and a non-functional CNNM4 derivative and
10 wherein
- said liver disease is selected from liver fibrosis, veno-occlusive liver disease, drug-induced liver injury (DILI), steatosis, non-alcoholic steatohepatitis (NASH), cirrhosis, hepatocellular carcinoma (HCC), Budd-Chiari syndrome, hepatitis, and alpha1- antitrypsin deficiency;
 - 15 - said kidney disease is selected from acute kidney injury (AKI), chronic kidney disease, nephritis, nephrosis and renal fibrosis;
 - and said lung disease is pulmonary fibrosis.
2. The use according to claim 1, wherein said inhibitor is selected from the group
20 consisting of an antisense polynucleotide, a RNA interference oligonucleotide, a phosphorodiamidate morpholino oligomer (PMO), miRNA, siRNA, shRNA, sgRNA, and combinations thereof.
3. An *in vitro* method for diagnosing liver disease, kidney disease or lung disease
25 in a subject which comprises:
- (a) determining the expression level of CNNM4 in a sample from said subject, and
 - (b) comparing said level with a reference value,
- wherein an increased expression level of CNNM4 in said sample with respect to
30 the reference value is indicative that the patient suffers from a liver disease, a kidney disease or a lung disease,
wherein

- the liver disease is selected from liver fibrosis, veno-occlusive liver disease, drug-induced liver injury (DILI), steatosis, non-alcoholic steatohepatitis (NASH), cirrhosis, hepatocellular carcinoma (HCC), Budd-Chiari syndrome, hepatitis, and alpha1- antitrypsin deficiency;
 - 5 - the kidney disease is selected from acute kidney injury (AKI), chronic kidney disease, nephritis, nephrosis and renal fibrosis and
 - the lung disease is pulmonary fibrosis.
 - 4. The *in vitro* method according to claim 3, wherein the sample is a liver, kidney or lung biopsy.
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5. Use of reagents specific for determining the expression level of CNNM4, for *in vitro* diagnosing a liver disease, a kidney disease or a lung disease in a subject, wherein
 - the liver disease is selected from liver fibrosis, veno-occlusive liver disease, drug-induced liver injury (DILI), steatosis, non-alcoholic steatohepatitis (NASH),
 - 15 cirrhosis, hepatocellular carcinoma (HCC), Budd-Chiari syndrome, hepatitis, and alpha1- antitrypsin deficiency;
 - the kidney disease is selected from acute kidney injury (AKI), chronic kidney disease, nephritis, nephrosis and renal fibrosis and
 - the lung disease is pulmonary fibrosis
 - 20 and wherein the reagents specific for determining the expression level of CNNM4 are selected from the group consisting of a set of probes which specifically hybridize to the mRNA of CNNM4 and a set of primer pairs which are capable of specifically amplifying the mRNAs of CNNM4, or wherein the reagent specific for determining the expression level of CNNM4 is an antibody which specifically binds to the CNNM4
 - 25 polypeptide.
6. An *in vitro* method of reducing an induced disease or condition in a cell, wherein the induced disease or condition is a disease model for the study of DILI, steatosis, NASH, cirrhosis, HCC, liver fibrosis, kidney fibrosis or lung fibrosis, the
 - 30 method comprising contacting the cell with a specific CNNM4 inhibitor in an amount effective to decrease a CNNM4 activity, level or function in the cell, wherein the CNNM4 inhibitor is selected from the group consisting of siRNA, shRNA, miRNA,

sgRNA, a dicer-substrate 27-mer duplex, an aptamer, a DNAzyme, a ribozyme, a triplex forming oligonucleotide (TFO), an antisense polynucleotide, a phosphorodiamidate morpholino oligomer (PMO) and a non-functional CNNM4 derivative.

5 7. An *in vitro* method for identifying a compound potentially useful for reducing an induced CNNM4-mediated disease or condition in a cell, the method comprising contacting the cell with a candidate compound in an amount effective to decrease a CNNM4 activity, level or function in the cell, or in an amount effective to reduce the relative lipid accumulation or to reduce the relative mitochondrial ROS with respect to a reference value, wherein a candidate compound that inhibits CNNM4 activity, reduces the relative lipid accumulation with respect to a reference value or reduces the relative mitochondrial ROS with respect to a reference value in an induced CNNM4-mediated disease or condition in a cell is identified as a compound potentially useful for treating and/or preventing a CNNM4-mediated liver, kidney and/or lung disease, wherein said compound is selected from the group consisting of siRNA, shRNA, miRNA, sgRNA, a dicer-substrate 27-mer duplex, an aptamer, a DNAzyme, a ribozyme, a triplex forming oligonucleotide (TFO), an antisense polynucleotide, a phosphorodiamidate morpholino oligomer (PMO) and a non-functional CNNM4 derivative and wherein the CNNM4-mediated disease or condition is selected from the group consisting of:

- 20 - a liver disease selected from liver fibrosis, veno-occlusive liver disease, drug-induced liver injury (DILI), steatosis, non-alcoholic steatohepatitis (NASH), cirrhosis, hepatocellular carcinoma (HCC), Budd-Chiari syndrome, hepatitis, and alpha1- antitrypsin deficiency;
- a kidney disease selected from acute kidney injury (AKI), chronic kidney disease, nephritis, nephrosis and renal fibrosis; and
- 25 - pulmonary fibrosis.

8. The *in vitro* method according to claim 6 or 7, wherein said inhibitor or said compound is selected from the group consisting of an antisense polynucleotide, a RNA interference oligonucleotide, a phosphorodiamidate morpholino oligomer (PMO), miRNA, siRNA, shRNA, sgRNA and combinations thereof.

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