Claims

1. Use of at least one bioactive molecule upregulating GLP-1r in the manufacture of a medicament for treating insulin resistance and/or restoring glucose homeostasis wherein said at least one bioactive molecule is to be locally administered by local administration to the peri-portal region of the portal vein.

2. The use according to claim 1, wherein administration is via a trans-gastric route, a trans-vena cava route, or by direct laparoscopic access, preferably via a trans-gastric route.

3. The use according to claim 1 wherein administration to the peri-portal region of the portal vein is at least partially in the wall of the portal vein and/or in the connective tissue surrounding the portal vein.

4. The use according to any one of claims 1 to 3, wherein the bioactive molecule is a steroid, preferably androgen, and more preferably dihydrotestosterone.

5. The use according to any one of claims 1 to 4, wherein the bioactive molecule is to be administered at a dose that is at least about 10-fold inferior to the ED_{50} of the molecule, preferably at a dose that is about 100-fold inferior to the ED_{50} of the molecule, more preferably at a dose that is from about 10-fold inferior to about 100-fold inferior to the ED_{50} of the molecule, yet more preferably at a dose that is from 10-fold inferior to 100-fold inferior to the ED_{50} of the molecule.

6. The use according to any one of claims 1 to 5, wherein the bioactive molecule is to be administered at a dose that is equal or superior to 100 µg/24h for dihydrotestosterone, more preferably at a dose that is from about 100 µg/24h to about 1000 µg/24h, yet more preferably at a dose that is from 100 µg/24h to 1000 µg/24h.

7. The use according to any one of claims 1 to 6, wherein the bioactive molecule is to be administered in a volume that is equal or inferior to 1 mL per 24h period.

8. The use according to any one of claims 1 to 7, wherein the bioactive molecule is to be administered to a subject that is obese, has type 2 diabetes, has metabolic syndrome, has portal hypertension, pre diabetes, or any combination of two or more thereof.

9. The use according to any one of claims 1 to 8, wherein GLP-1r is detected in the peri-portal region of a subject.

10. The use according to any one of claims 1 to 9, wherein a reduction of the density of GLP-1r in the peri-portal region of a subject as compared to the density of GLP-1r in a healthy subject is detected.

11. The use according to claim 9 or 10, wherein the presence and/or reduction in the density of GLP-1r is determined via positron emission tomography (PET) using a GLP-1r positron emitting ligand, preferably in combination with radio-opaque marker enhanced computed tomography (CT).

12. The use according to any one of claims 1 to 11, wherein the bioactive molecule is to be administered by means of a device in the portal vein comprising an effective amount of the bioactive molecule.

13. Use of at least one bioactive molecule upregulating GLP-1r in the manufacture of a medicament for treating insulin resistance and/or restoring glucose homeostasis, wherein said at least one bioactive molecule is to be administered in the peri-portal region, at a dose that is at least about 10-fold inferior to the ED_{50} of said bioactive molecule, preferably at a dose that is from 10-fold inferior to 100-fold inferior to the ED_{50} of the molecule.

14. The use according to claim 13, wherein the bioactive molecule is to be administered in the peri-portal region, at a dose that is equal or superior to 100 µg/24h for dihydrotestosterone, preferably at a dose that is from about 100 µg/24h to about 1000 µg/24h, more preferably at a dose that is from 100 µg/24h to 1000 µg/24h.