**Assays of human plasma** Plasma samples were analyzed by commercial kits: Glucose (GO) Assay kit (Sigma, St. Louis, MO) for plasma glucose, Human Insulin EIA kit (Mercodia, Uppsala, Sweden) for plasma insulin, Human Corticotropin Releasing Hormone (CRH) EIA kit (Peninsula, San Carlos, CA) for plasma CRH and Cortisol EIA kit (Cayman, Ann Arbor, MI) for plasma cortisol. Homeostasis model assessment of insulin sensitivity (HOMA-IS) was calculated using the following equations: HOMA-IS = 1/ (plasma insulin (mIU/L) × plasma glucose (mM))(1).

**Assays of rat plasma** Plasma glucose was analyzed using Glucose (GO) Assay kit, plasma insulin using Rat Insulin EIA kit (Mercodia, Uppsala, Sweden), plasma CRH using Rat CRH EIA kit (Peninsula, San Carlos, CA) and plasma corticosterone (CORT) using Corticosterone EIA kit (Cayman, Ann Arbor, MI). HOMA-IS was calculated using the following equations: HOMA-IS = 1/ (plasma insulin (ng/mL) × plasma glucose (mM) ×22.5)(1).

**Measurement of metabolites concentration** ATP contents in tissue and cultured islets was determined by using an ATP Luminometric Assay kit (Beyotime, Peking, China) according to the manufacturer’s instructions. ADP content was measured after being converted to ATP by pyruvate kinase (Sigma, St. Louis, MO) with phosphoenolpyruvate (2). AMP content was measured after being converted to ADP by adenylate kinase (Sigma, St. Louis, MO) with deoxycytidine triphosphate and thereby being converted to ATP (3). Lactate and pyruvate was determined with commercial kits (Nanjing Jiancheng Bioengineering Institute, Nanjing, China).

**Drug treatment** In vivo, CRH receptor 1 (CRHR1) antagonist cp-154,526 was suspended in 10% DMSO and 90% saline solution. GR specific antagonist RU486 (Tocris, Bristol, UK) was suspended in 100% DMSO.

For in vitro experiments, cp-154,526 (CRHR1 antagonist), Rp-8-Br-cAMPS (protein kinase A (PKA) antagonist), H89 (PKA antagonist), Go6983 (protein kinase C (PKC) antagonist), U-73122 (phospholipase C (PLC) antagonist), nifedipine (L-type calcium channel inhibitor) and rotenone (inhibitor of mitochondrial respiratory chain complex I) (Sigma, St. Louis, MO) were suspended in DMSO and added from the last 30 min of pre-incubation. CRH (Tocris, Bristol, UK) was suspended in sterile water and presented in testing medium. Dexamethasone (DEX) and forskolin (adenylate cyclase activator, Sigma, St. Louis, MO) were suspended in DMSO and added to testing medium. Final DMSO concentration was less than 0.1% in solution.

**cAMP assay** Islets were washed and pre-incubated for 1 h at 37°C in Krebs-Ringer HEPES buffer (KRBH) containing 2.8 mM glucose. Then 15 size-matched islets per well were used after 1 h incubation in testing KRBH buffer with 5.6 mM glucose and agents as indicated at 37°C. The cAMP within islets was then measured with a cAMP EIA kit (Cayman, Ann Arbor, MI). 1 mM 3-isobutyl-1-methyxanthine (IBMX, Sigma, St. Louis, MO) was added to KRBH for inhibiting cAMP phosphodiesterase activity.

**Quantitative PCR (Q-PCR)** After incubation for 12 h, 30 size-matched islets were patched into lysis buffer. Total RNA was extracted and purified using MicroElute Total RNA kit (Omega bio-tek, Norcross, GA). RNA was converted to cDNA with First-strand cDNA synthesis supermix (Transgen, Beijing, China). Q-PCR was preformed with SYBR premix Ex Taq™ (Takara, Dalian, China) on LightCycler 480II (Roche, Meylan, France). The RNA expression were determined by the ΔΔCt method using 18s ribosome mRNA as endogenous control. Primers are listed below.

SUPPLEMENTARY DATA

**Supplementary Table 1.** Names and sequences of primers

<table>
<thead>
<tr>
<th>Name</th>
<th>Genbank NO.</th>
<th>Primer sequence 5′-3′</th>
<th>Product length</th>
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</thead>
<tbody>
<tr>
<td>Sgk1</td>
<td>NM_019232.3</td>
<td>Sense: GAGCCCGAACTTATGAACGC&lt;br&gt;Antisense: GTCAGAGGGTTTGGCCTGG</td>
<td>99 bp</td>
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<tr>
<td>Glut2</td>
<td>NM_012879.2</td>
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<td>201 bp</td>
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<tr>
<td>Crhr1</td>
<td>NM_030999.3</td>
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<td>271 bp</td>
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<tr>
<td>18s</td>
<td>NR_046237.1</td>
<td>Sense: GTAACCGTGTGAAACGACGACAG&lt;br&gt;Antisense: CCATCCAATCGGTAGTGCG</td>
<td>151 bp</td>
</tr>
</tbody>
</table>

**Immunofluorescence staining** 10 μm frozen sections of pancreas were cut by cryostat microtome (HM505E, Microm, Walldorf, Germany), and employed to immunofluorescence staining as described (4). The primary antibodies were rabbit anti-Serum and glucocorticoid inducible kinase 1 (SGK1) and mouse anti-insulin (1:200, Millipore, Billerica, MA). Secondary antibodies were Alexa Fluor 555 conjugated donkey anti-rabbit and Alexa Fluor 488 conjugated donkey anti-mouse (1:200, Invitrogen, Carlsbad, CA). DAPI was used as a nuclear stain. Imaging was captured and analyzed in confocal microscope and Volocity software (PerkinElmer, Wellesley, MA).

**Rhodiola rosea treatment** *Rhodiola* capsule (Tibet Nuodikang Medicine, Lhasa, China) was dissolved in water (140 mg/mL). The rats received intragastric administration of *Rhodiola rosea* (670 mg/kg) or water daily for 4 days (2 days before hypoxia exposure). Hypoxia group were exposed to hypobaric hypoxia of 5,000 m altitude for 2 days. Normoxia group was placed in an identical chamber at sea level. After hypoxia exposure, rats were sacrificed for collected trunk blood. *Rhodiola rosea* (oral) suppressed the hypoxia-induced high plasma CRH and CORT in rats.
Supplementary Figure 1. *Rhodiola rosea* (oral) suppressed the high plasma CRH and CORT in rats under hypoxia, but did not change plasma CRH and CORT under normoxia. \( n = 7 \). * \( P < 0.05 \), ** \( P < 0.01 \) vs. control group; # \( P < 0.05 \) vs. hypoxia group.

**REFERENCE**