GLP-1 receptor signalling promotes β-cell glucose metabolism *via* mTOR-dependent HIF-1α activation

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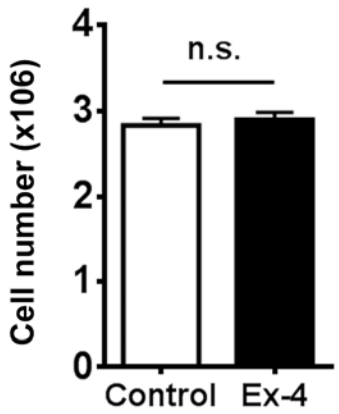
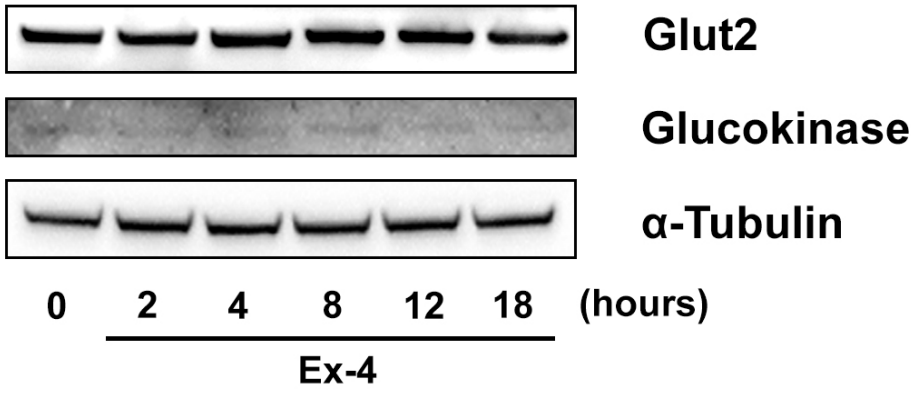
Supplementary Information

Supplementary Table 1. List of genes assessed by qRT-PCR and respective RT² qPCR Primer Assay catalogue numbers.

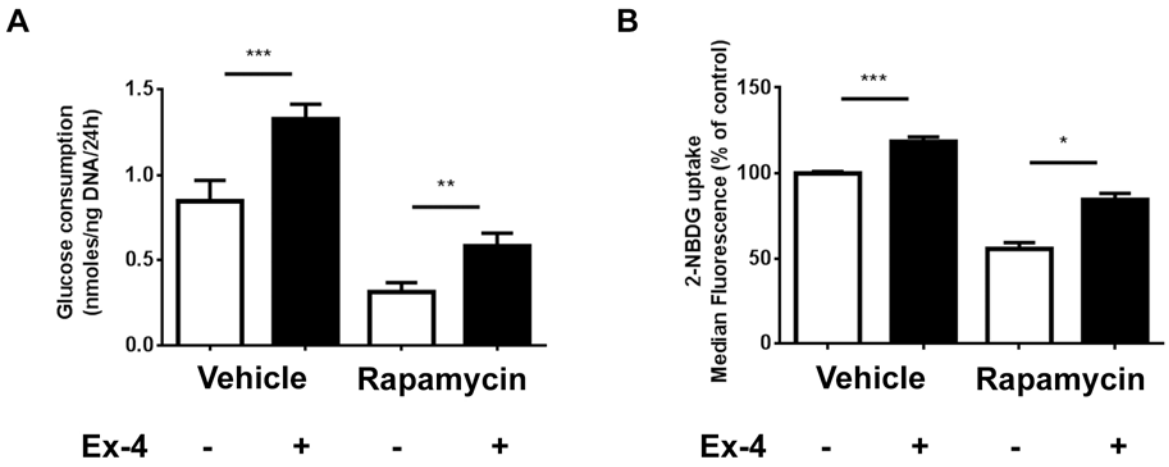
Gene Symbol	Refseq #	Qiagen Catalogue Number
Pklr	NM_012624	PPR50315
Pgam2	NM_017328	PPR44447
Gpi	NM_207592	PPR52501
Pfkp	NM_206847	PPR59714
Aldoa	NM_012495	PPR42582
Ldha	NM_017025	PPR56603
Actb	NM_031144	PPR06570



S1. **18h of Ex-4 treatment does not induce BRIN-BD11 cell proliferation.** BRIN-BD11 cells were seeded in 6 well plates at a density of 10^6 cells per well and allowed to grow overnight. Cells were then treated in the presence or absence of 50 nM Exendin-4 for additional 18h in media containing 20 mM of glucose. At the end of incubation time cells were manually counted using a Neubauer chamber. Data are mean ± SEM, n = 6; n.s. = non-significant.

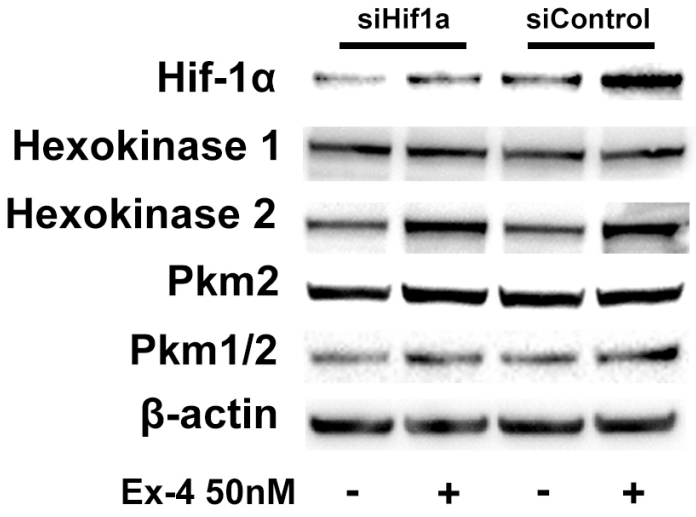


S2. Protein levels of Glut2 and Glucokinase are unaffected by prolonged exposure to Exendin-4. BRIN-BD11 cells were treated with 50 nM Exendin-4 for 2, 4, 8, 12 and 18 hours followed by immunoblot analysis of Glut2 and Glucokinase. Results are representative of at least three independent experiments.



S3. **Exendin-4 conserves stimulatory activity in the presence of mTORC1 inhibitor, Rapamycin.** (A) BRIN-BD11 cells were pre-incubated with either vehicle or 100 nM Rapamycin for 30 min, followed by addition (or not) of 50 nM Exendin-4 for 18 hours, as indicated. Then, media was changed to RPMI containing 20 mM of glucose for additional 24 hours in the absence of Exendin-4 and glucose consumption was determined. (B) Cells were treated similarly to (A), but instead of the additional 24 hours incubation time, 2-NBDG

uptake was performed immediately following the 18 hours incubation period as described in Methods. Data represent mean ± SEM, n = 3; *P < 0.05; **P < 0.01; ***P < 0.001.



S4. **There is no evidence of an effect on protein levels of Hexokinase 1, Hexokinase 2, Pyruvate Kinase M 1 and M2 in response to HIF-1α knockdown by siRNA transfection.** BRIN-BD11 cells were transfected with either HIF-1α specific siRNAs (*siHIF1a*) or non-targeting siRNAs (*siControl*) for 24h, and subsequently exposed to 50 nM Exendin-4 (or not) for 18h. Results are representative of at least three independent experiments.