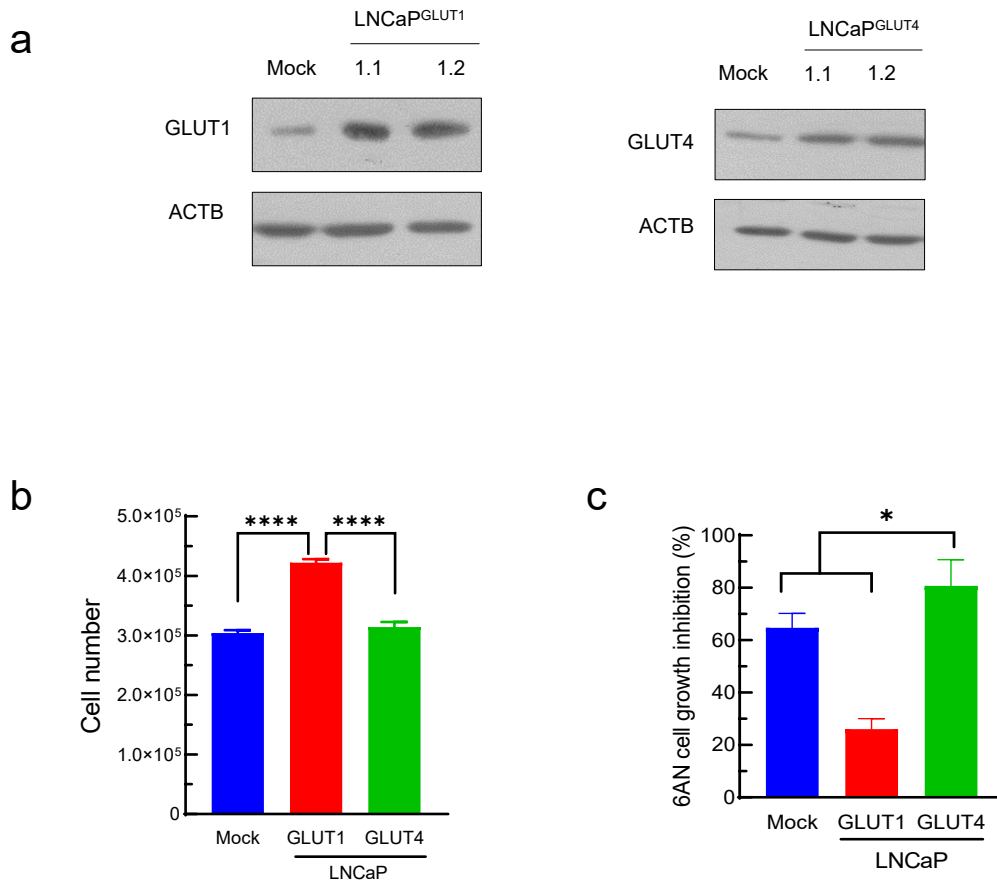


1 **Supplementary data****Supplementary table 1: List of Antibodies/Reagents**

REAGENT or RESOURCE	Ref.	Supplier
Antibodies		
Anti-AKT	05-591 (lot 2838917)	Millipore
Anti-AMPK	07-350 (lot 2626022)	Millipore
Anti-AR	sc-816 (lot H2914)	SantaCruz
Anti-AR	66747-1-Ig	Proteintech
Anti-β actin	sc-69879 (lot G2818)	SantaCruz
Anti-BAX	ABC11 (lot 2646463)	Millipore
Anti-Bcl2	sc-7382 (lot G2915)	SantaCruz
Anti-GLUT1	07-1401 (lot NG1911137)	Millipore
Anti-GLUT3	sc-74499 (lot K1017)	SantaCruz
Anti-GLUT4	07-1404 (lot 2736599)	Millipore
Anti-GLUT4 antiserum	07-1404	Merck Millipore
Anti-GLUT12	ab75441	Abcam
Anti-HDAC2	sc-9959 (lot G0110)	Becton Dickinson
AntiHIF1α	MAB5382	Millipore
Anti-IGFBP3	HPA013357 (lot R05902)	Atlas
Anti-IGF1Rβ	9750 (lot 1)	Cell Signaling
Anti-p21	OP64 (lot D00080461)	Calbiochem
Anti-PCNA	sc-56	SantaCruz
Anti-phosphoAKT ^{Ser473}	05-1003 (lot 2876083)	Millipore
Anti-phosphoAMPK ^{Thr172}	07-626 (lot 2626022)	Millipore
Anti-PSA	MS-260P0	Neomarkers
Anti-TP53	sc-126 (lot I2515)	SantaCruz
Anti-Mouse IgG HRP	sc-2005	SantaCruz
Anti-Rabbit IgG HRP	sc-2004	SantaCruz
anti-Mouse IgG Alexa Fluor 488	A28175	Molecular Probes/Thermofisher
anti-Rabbit IgG Alexa Fluor 488	A27034	Molecular Probes/Thermofisher
anti-rabbit IgG R-Phycoerythrin	711-116-152	Jackson ImmunoResearch
GLUT1 RBD-GFP	GLUT1_G100	Metafora Biosystems
Chemicals		
2-deoxyglucose	L07338	Alfa-Aesar
2-[1,2-3H(N)]-deoxyglucose	NET328001MC	Perkin Elmer
6-aminonicotinamide.	A68203	Sigma-Aldrich
Bicalutamide	B9061	Sigma-Aldrich
Bovine serum albumin	F9665	Sigma-Aldrich
Charcoal activated	102186	Millipore
DAPI	D9542	Sigma-Aldrich
Dehydrotestosterone	A8380	Sigma-Aldrich
D-Glucose	0188	VWR Chemicals
D-Glucose- ¹³ C ₆	389374	Sigma-Aldrich
D-Glucose-6-phosphate	A3789.0001	Panreac
Diaphorase	P5285	Abnova
DMEM-F12	BE12-702F	Lonza
Fugene HD Transfection reagent	E2311	Promega
Glucose-6-phosphate dehydrogenase	P5266	Abnova
Human insulin solution	I9278	Sigma-Aldrich
Humulin 70:30		Lilly

Imalgene		Merial
NADP ⁺	A1394.0250	Applichem
Propidium Iodide	P4170	Sigma-Aldrich
RPMI	12-719F	Lonza
Rompun	572126.2	Bayer
Streptozocin	S0130	Sigma-Aldrich
Testosterone	86500	Sigma-Aldrich
Tri Reagent	T9424	Sigma-Aldrich
Ultima Gold liquid scintillation cocktail	6013329	Perkin Elmer
Commercial assays		
L-lactate assay kit	KC-04-001	Bioquochem
PSA ELISA kit	52030	Human Diagnostics
Rat/Mouse Insulin ELISA kit	EZRMI-13K	Millipore
Testosterone ELISA kit	582701	Cayman
Experimental Models: Cell lines		
LNCaP	89110211	ECACC
PC-3	CRL-1435	ATCC
Experimental Models: Murine models		
C57BL/6J mice	000664	Jackson Labs
C57BL/6-Tg(TRAMP)8247Ng/J	003135	Jackson Labs
Oligonucleotides		
Murine <i>Gapdh</i> forward		2Sigma-Aldrich
5'-GTGCAGTGCCAGCCTCGTCC-3'		
Murine <i>Gapdh</i> reverse		Sigma-Aldrich
5'-GCCACTGCAAATGGCAGCCC-3'		
Murine <i>Psp94</i> forward		Sigma-Aldrich
5'-GTCCTGCTTTGTCACCAT-3'		
Murine <i>Psp94</i> reverse		Sigma-Aldrich
5'-CATCCATGCAGTCATCAGA-3'		
Murine <i>Slc2a1</i> forward		Sigma-Aldrich
5'-GCAGGAGATGAAAGAAGG-3'		
Murine <i>Slc2a1</i> reverse		Sigma-Aldrich
5'-AGAACACAGCATTGATACCC-3'		
Murine <i>Slc2a3</i> forward		Sigma-Aldrich
5'-CCCAGGATGTATCCCAAGAC-3'		
Murine <i>Slc2a3</i> reverse		Sigma-Aldrich
5'-AATAGAACACAGCATTGATCCCAG-3'		
Murine <i>Slc2a4</i> forward		Sigma-Aldrich
5'-ACAGAAGGTGATTGAACAGAG-3'		
Murine <i>Slc2a4</i> reverse		Sigma-Aldrich
5'-GATGCCAATGAGAAAGGAAGAG-3'		
Murine <i>Slc2a12</i> forward		Sigma-Aldrich
5'-GGGTGTCAACCTTCTCATCCT-3'		
Murine <i>Slc2a12</i> reverse		Sigma-Aldrich
5'-CCAAAGAGCATCCCTTAGTCTC-3'		
Plasmids		
pEGFP-C1-AR	28235	Addgene
pcDNA3.2/v5-DEST hGLUT1	18085	Addgene
pcDNA3.2/v5-DEST hGLUT4	18087	Addgene
Software and algorithms		
FlowJo 10.6.2		TreeStar
Kaluza 2.1		Beckman Coulter
Metaboanalyst 4.0		GraphPad
Prism 8.0.2		Agilent Technologies
R 3.4.0		R Development Core Team

2 Supplementary Figure 1



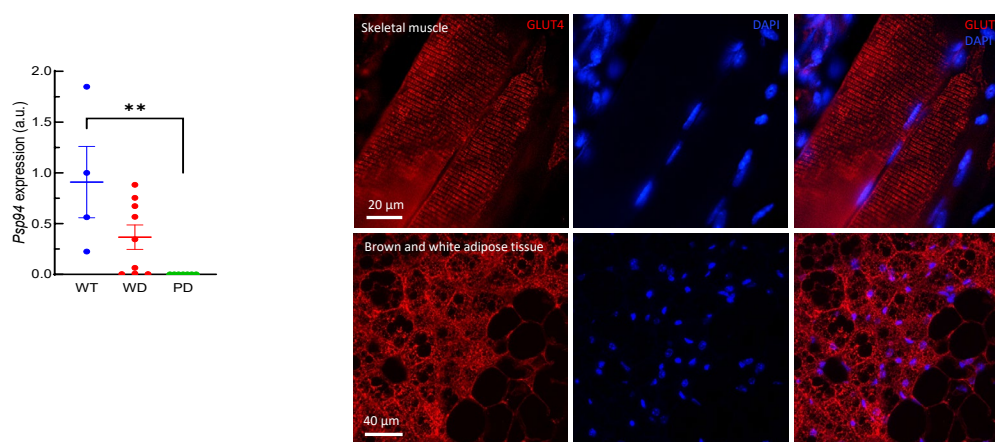
3

4 Supplementary Figure 1: (a) LNCaP^{GLUT1} and LNCaP^{GLUT4} clones were produced. Levels of GLUT1
 5 and GLUT4 were compared to LNCaP cells transfected with an empty vector as control
 6 (LNCaP^{Mock}). Protein levels were determined by western blot. A representative experiment is
 7 shown. ACTB was employed as an internal control. (b) Cell numbers were counted after 72 hours.
 8 Initially, 5×10^4 cells of each clone were seeded in six-well plates. Data are shown as individual
 9 values and mean $\pm$ SEM (n=5). (c) PPP activity (G6PDH and 6GPD activity) was examined by
 10 enzymatic assay. Results are shown as individual values and average $\pm$ SEM. The experiment was
 11 repeated 3 times and a representative experiment is shown. ****p<0.0001

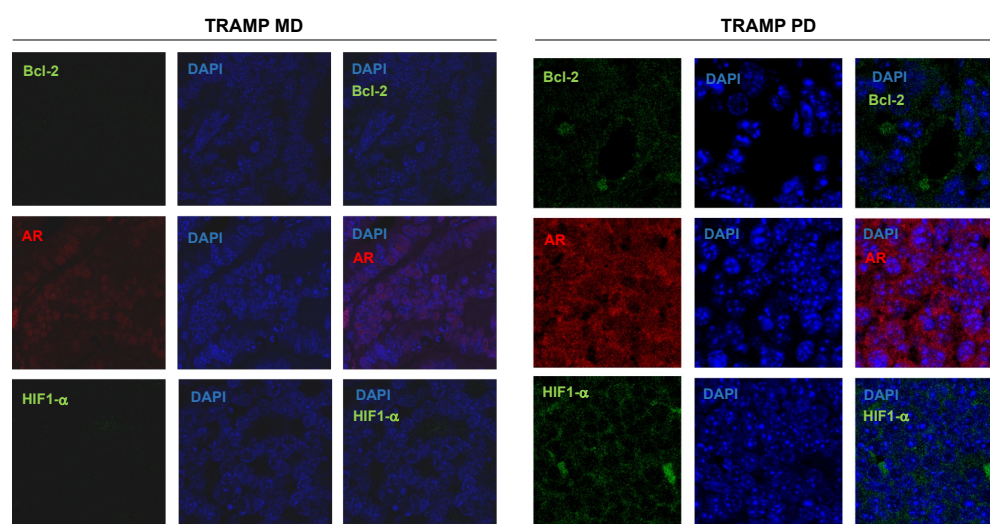
12

13 **Supplementary Figure 2**

a



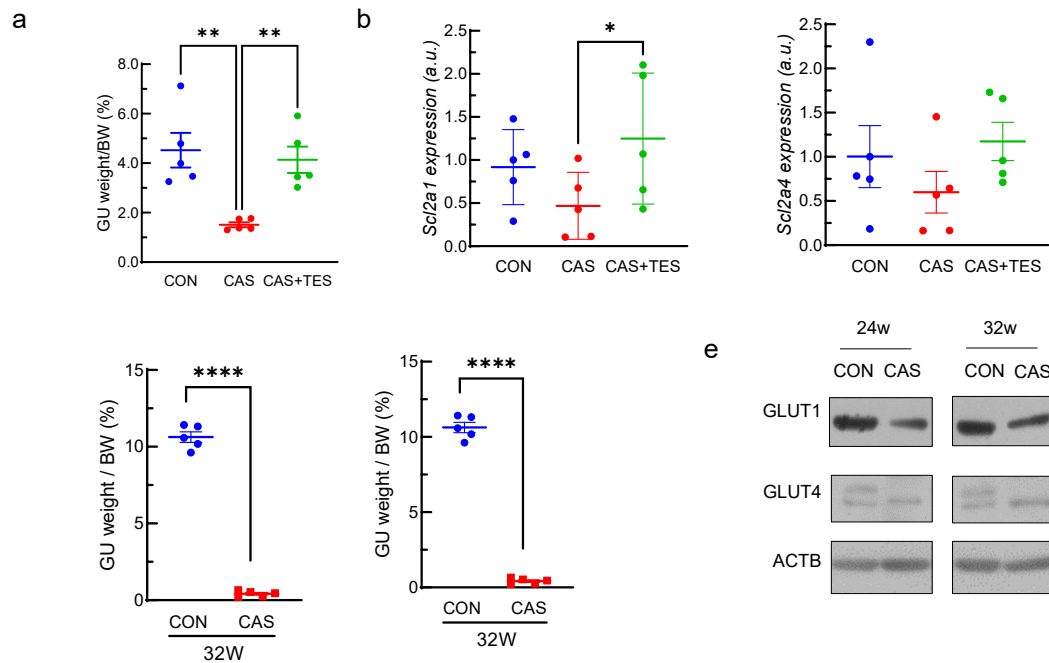
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14

15 Supplementary Figure 2: (a) Prostate tumour tissues of TRAMP mice were classified as well (WD)
 16 and poorly differentiated (PD). Prostate tissues from C57BL/6 mice (WT) were employed as a
 17 control. *Psp94* mRNA levels were determined by qPCR. GAPDH was employed as an internal
 18 control. An arbitrary value of 1.0 was given to one of the replicates of WT mice and results are
 19 shown as individual measurements ± SEM (WT n=4; WD n=9; PD n = 6). (b) anti-GLUT4 was
 20 validates in muscle and adipose tissue. Original magnification 630×. (c) Immunohistochemical
 21 analysis of BCL2, AR and HIF1α was performed in fixed prostatic tissues of MD and PD from 32-
 22 week-old TRAMP mice at 32. Nuclei were counterstained with DAPI. A representative image is
 23 shown for each group. Original magnification 630×.

24

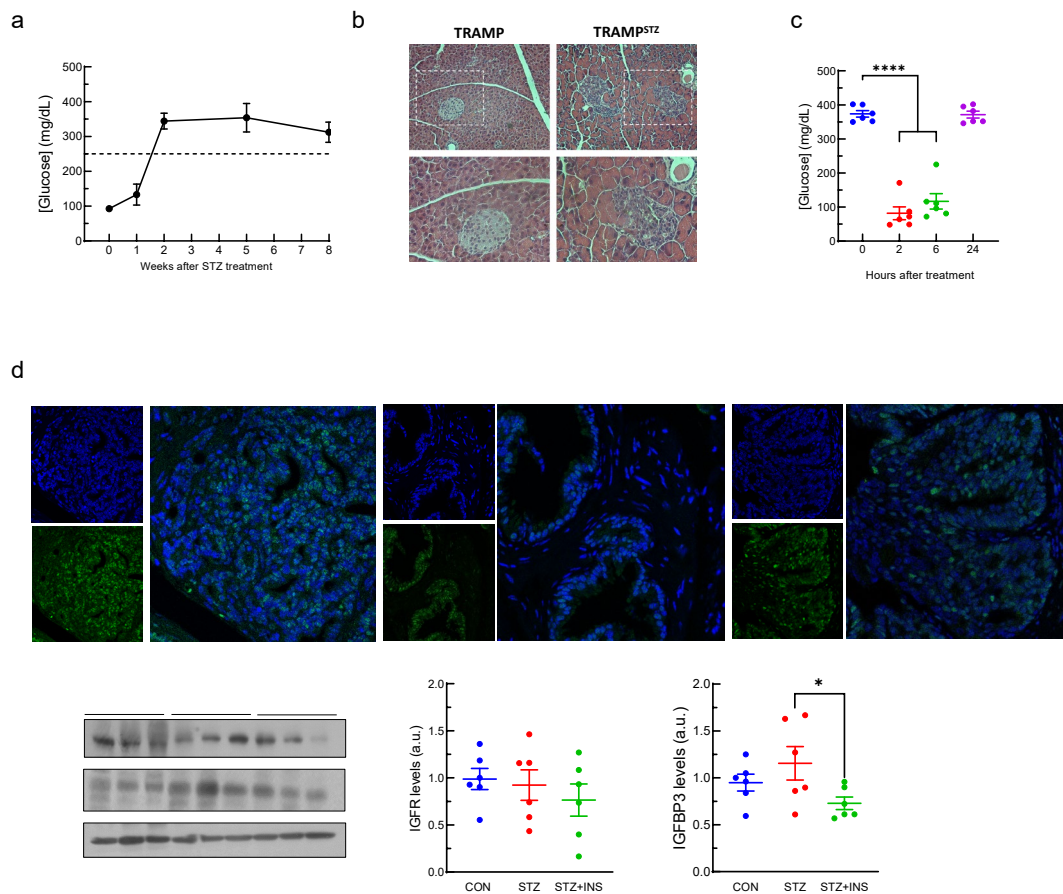
25 **Supplementary Figure 3**

26

27

28 Supplementary Figure 3: (a) Short-term castration in TRAMP mice was performed surgically at
 29 22.5 weeks of age (CAS) and 2.5 mg/kg/day testosterone was administered daily for an additional
 30 5 days after castration (CAS + TEST). Animals were killed at 24 weeks. The GU/body ratio was
 31 calculated, and the results are presented as individual values and mean $\pm$ SEM ($n = 5$). (b) The
 32 *Slc2a1* and (c) *Slc2a4* levels in prostatic tissue were determined by qPCR and normalised to
 33 *GAPDH*. An arbitrary value of 1.0 was given to one of the TRAMP mice samples. Results are shown
 34 as individual values and mean $\pm$ SEM ($n = 5$). (d) Long-term castration was performed surgically in
 35 12-week-old TRAMP mice. Animals were sacrificed at 24 and 32 weeks of age. The GU/body
 36 weight ratio is shown as individual data and mean $\pm$ SEM ($n = 5$). (e) GLUT1 and GLUT4 proteins
 37 were detected in the prostate tissues by western blot. A pool of five samples from each group
 38 was employed. Proteins bands were quantified and normalised to ACTB. * $p < 0.05$; ** $p < 0.01$;
 39 **** $p < 0.0001$

40

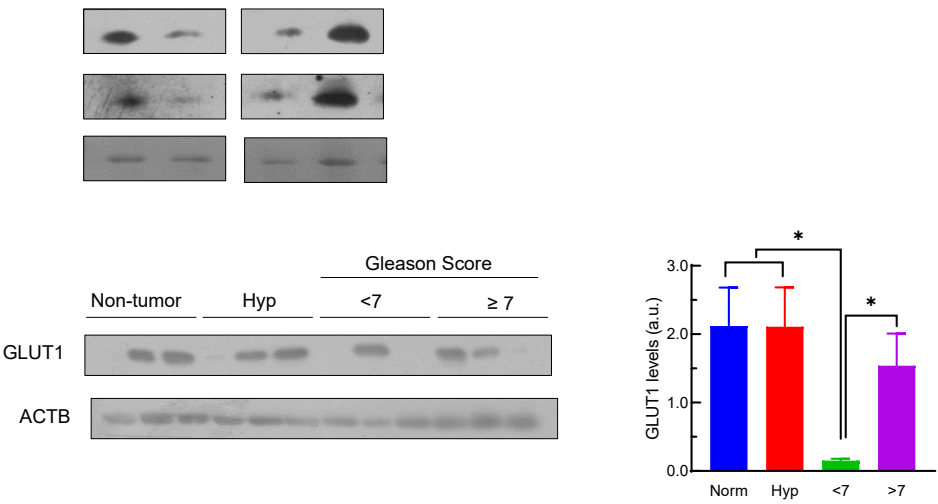
41 **Supplementary Figure 4**

42

43 Supplementary Figure 4: (a) Fasting blood glucose levels in 16-week-old mice treated with 50 mg
 44 streptozotocin (STZ)/kg body weight for 5 days (week 0). Mice were sacrificed at 24 weeks old.
 45 Results are expressed as mean $\pm$ SEM ($n = 6$). (b) Haematoxylin–eosin staining in fixed pancreas
 46 from 24-week-old non-treated (left) and STZ-treated (right) TRAMP mice, with the islets of
 47 Langerhans shown at a higher magnification. Original magnification 200 $\times$ (top) and 400 $\times$
 48 (bottom). A representative sample from each group is shown (c) Blood glucose levels in STZ-
 49 treated 20-week-old TRAMP mice after 0.6 U Humulin 70:30 s.c. injection. Results are presented
 50 as individual values $\pm$ SEM ($n = 6$). (d) Immunohistochemical analysis of AR (green fluorescence)
 51 in fixed the prostates of 24-week-old non-diabetic TRAMP mice (CON) and diabetic TRAMP mice
 52 (STZ) treated or not with Humulin 70:30. Samples were counterstained with DAPI. Control
 53 prostates of different pathology are shown. Original magnification 630 $\times$. (f) IGF-1R and IGFBP3
 54 protein quantification was performed by western-blot. A representative analysis is shown.
 55 Quantification is represented as individual values $\pm$ SEM ($n=6$). An arbitrary value of 1.0 was given
 56 to one control sample. * $p < 0.05$; **** $p < 0.0001$.

57

58 **Supplementary Figure 5**



59

60 Supplementary Figure 5: (a) Levels of PSA and BLC-2 were determined in prostate tumours of
61 patients by western-blot. Non tumour tissues, hyperplasia (Hyp) and tumour tissues classified in
62 Gleason score < 7 or ≥7 were analysed. Prostates of 5 to 10 patients were pull and one analysis was
63 performed. (b) GLUT1 protein quantification was performed by western blot. A representative
64 analysis is shown. Quantification is represented as SEM (n=6). *p<0.05