

SUPPLEMENTAL MATERIAL

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- Reaction kinetics used for modeling of glucose metabolism shown in Figure 5A.

Supplemental Table 1: ON-TARGETplus SMARTpool siRNA Horizon Discovery Target Sequences.

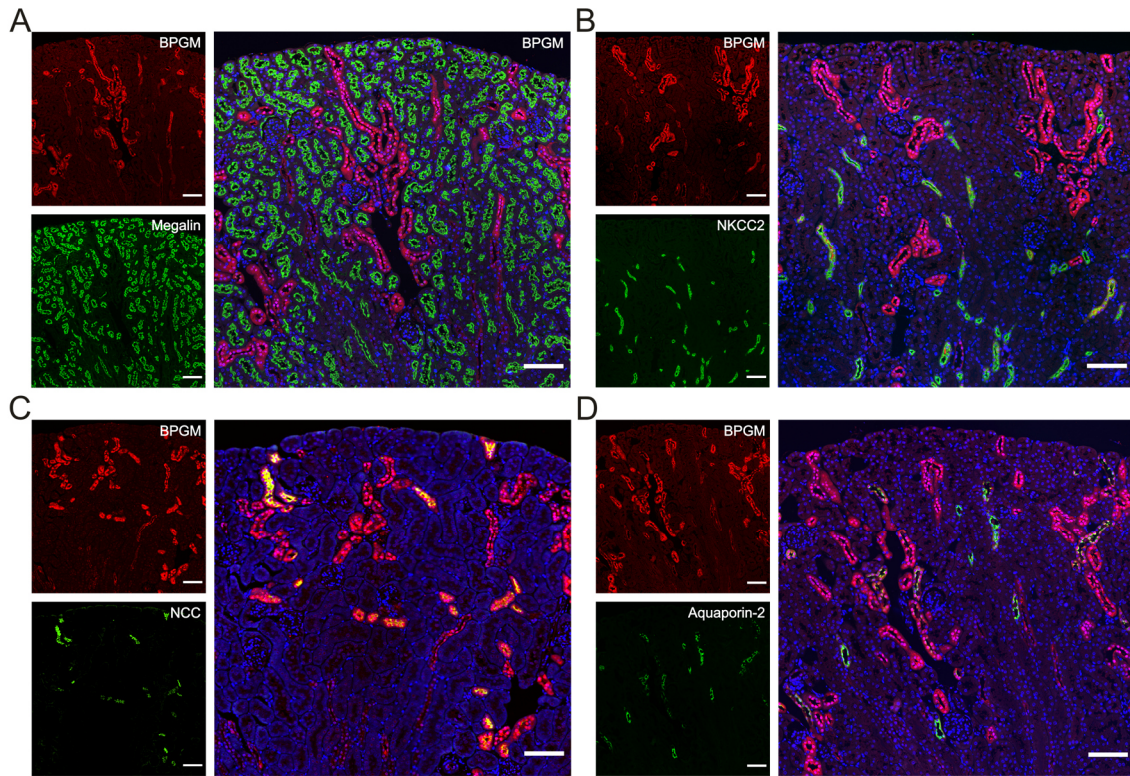
| ON-TARGETplus SMARTpool siRNA | Target Sequences |
|---|-------------------------|
| <i>ON-TARGETplus Mouse BPGM siRNA, Horizon Discovery, Cat. # L-058581-01-0005</i> | GAUCAGAGGCGCAUCGAAU |
| | GAAAGGAUUGCUCGGAAA |
| | AGACAUAGUACUUACGAUA |
| | AAAGCAAGUCCUCGAUAAU |
| <i>ON-TARGETplus Non-targeting Pool, Horizon Discovery, Cat. # D-001810-10-20</i> | UGGUUUACAUGUCGACUAA |
| | UGGUUUACAUGUUGUGUGA |
| | UGGUUUACAUGUUUUCUGA |
| | UGGUUUACAUGUUUCCUA |

Supplemental Table 2: List of primers used for qPCR.

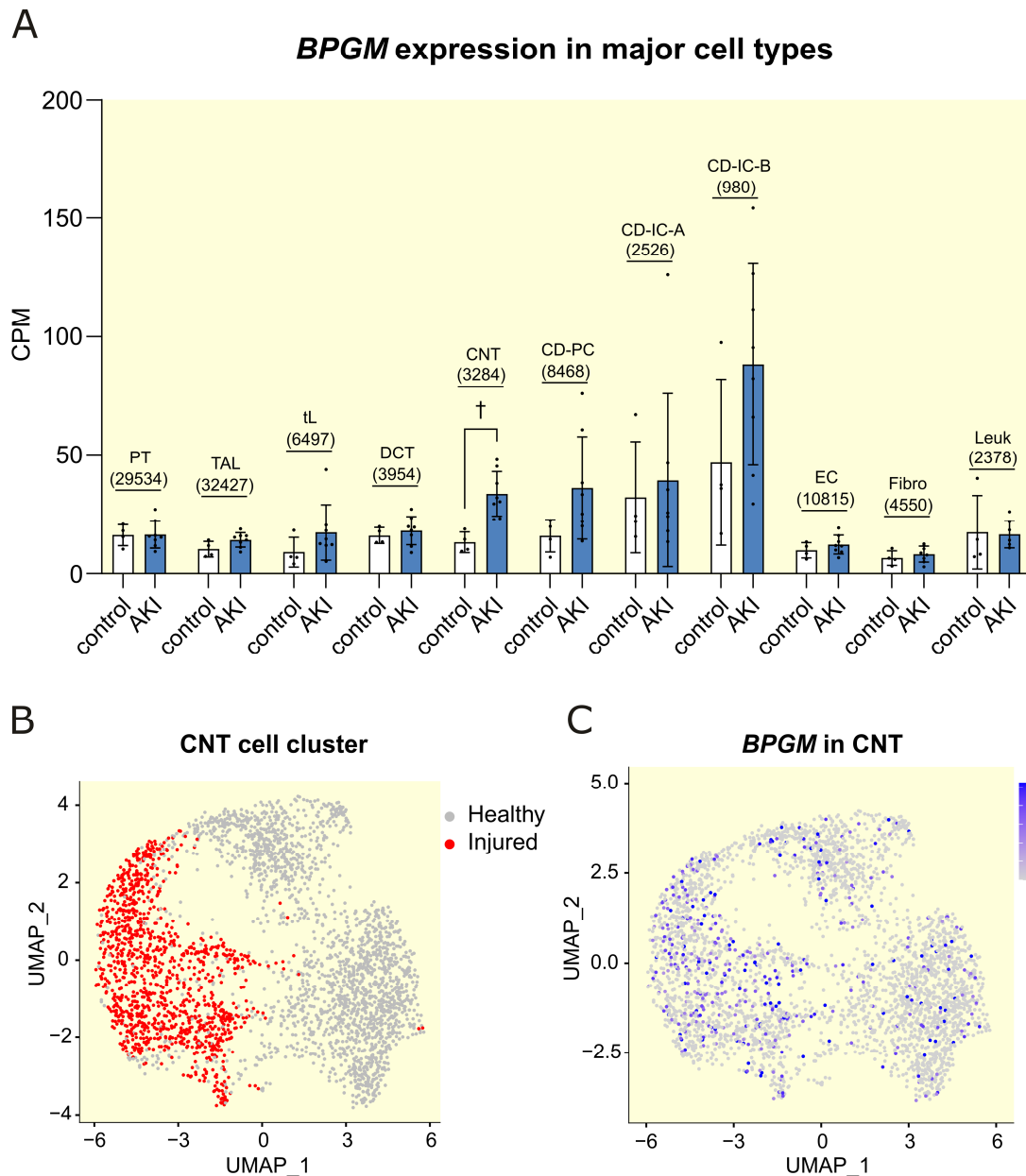
| target gene (mouse) | primer sequences (5' to 3') |
|--------------------------------|-----------------------------------|
| <i>Actb</i> | Forward: 5'-CTGTCGAGTCGCGTCCACC |
| | Reverse: 5'-GGCCTCGTCACCCACATAGG |
| <i>Bpgm</i> | Forward: 5'-TGTGCGATGTGCCCTTGGAT |
| | Reverse: 5'-AACGGCAGCGAGGTTCTCAT |
| <i>Ccl2</i> | Forward: 5'-GCAGTTAACGCCCCACTCAC |
| | Reverse: 5'-CCATTCCTTCTTGGGGTCAGC |
| <i>Tgfb1</i> | Forward: 5'-CGGAGAGCCCTGGATACCAA |
| | Reverse: 5'-TTGCAGGAGCGCACAATCAT |
| <i>Tnf-α</i> | Forward: 5'-TGTAGCCACGTCTAGCAAAA |
| | Reverse: 5'-ACGGCAGAGAGGAGGTTGAC |
| <i>Icam1</i> | Forward: 5'-CCATCCCAAAGCTCGACACC |
| | Reverse: 5'-CTCCCTTCCGAGACCTCCAG |
| <i>Nrf2</i> | Forward: 5'-GTGGATCCGCCAGCTACTCC |
| | Reverse: 5'-GGGATATCCAGGGCAAGCGA |
| <i>Keap1</i> | Forward: 5'-CATGGCTCACAAAGTGGTGC |
| | Reverse: 5'-AAGAACTCCTCCTGCTTGGC |
| <i>Hmox-1</i> | Forward: 5'-AACATCGACAGCCCCACCAA |
| | Reverse: 5'-GCTAGCAGGCCTCTGACGAA |

Supplemental Table 3: List of antibodies used.

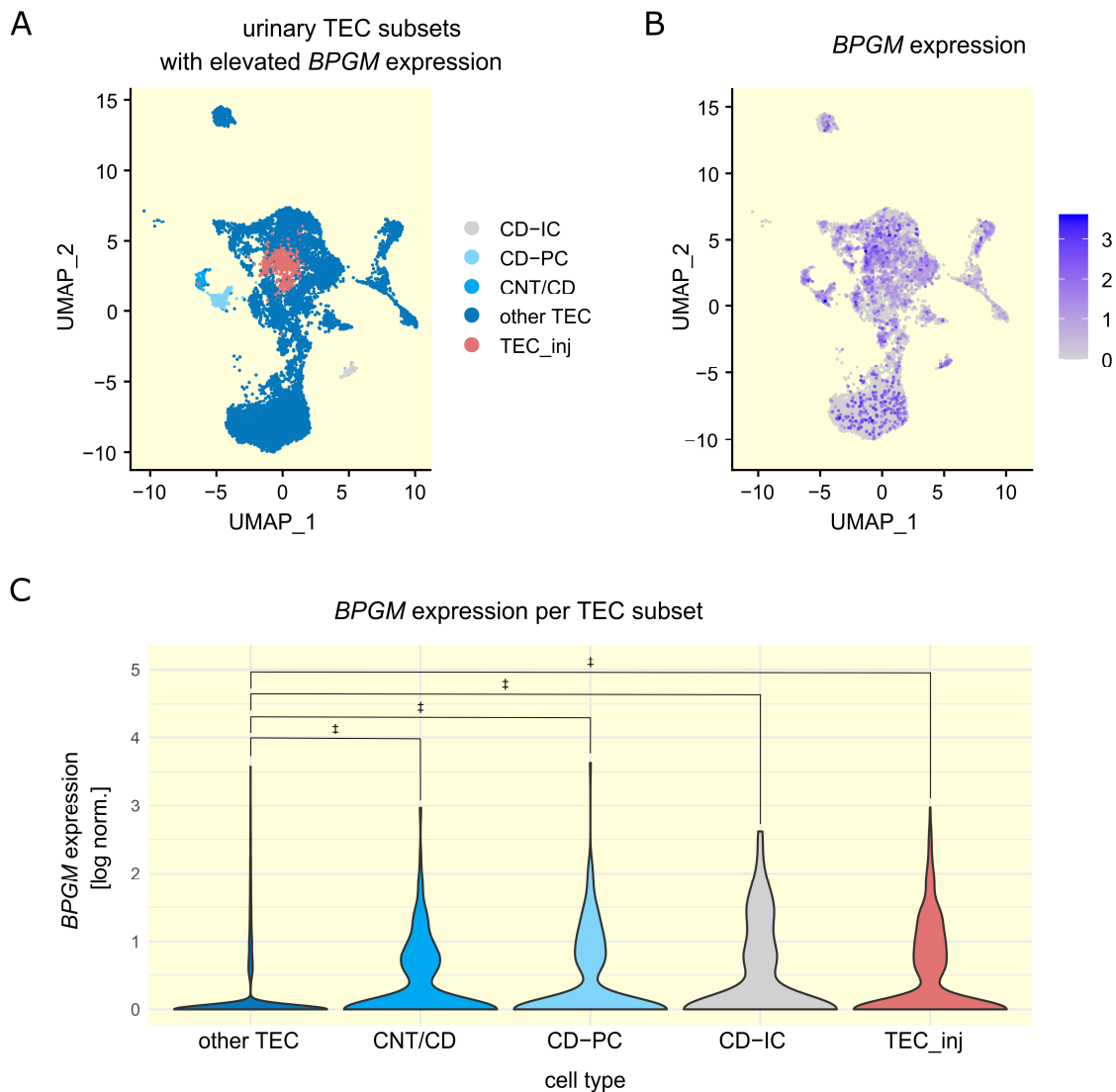
| Antibody target | Host | Supplier/ RRID |
|------------------------------------|-------------------|---|
| <i>primary antibodies</i> | | |
| Aquaporin-2 | polyclonal rat | #20102rs; BiCell Scientific, USA; RRID:AB_2910118 |
| BPGM | polyclonal rabbit | #NBP1-86064, Novus Biologicals, USA; RRID:AB_11013664 |
| Calbindin | monoclonal mouse | #C9848, Sigma-Aldrich, USA; RRID:AB_476894 |
| CD3 | monoclonal rabbit | #ab16669, abcam, UK; RRID:AB_443425 |
| CASP3 | Monoclonal mouse | #AM08377PU-N, Acris Antibodies, USA; RRID:AB_2035249 |
| F4/80 | monoclonal rat | #MCA497GA, Bio-Rad Laboratories, USA; RRID:AB_323806 |
| HO-1 | monoclonal rabbit | #ab68477, abcam, UK; RRID:AB_11156457 |
| KIM-1 | polyclonal goat | #AF1817, R and D Systems, USA; RRID:AB_2116446 |
| LY-6G | polyclonal rat | #127601, BioLegend, USA; RRID:AB_1089180 |
| Megalin | monoclonal mouse | #ab184676, abcam, UK; RRID:AB_2910117 |
| NCC | polyclonal rabbit | #AB3553, Millipore, USA; RRID:AB_571116 |
| NF-kB p65 | monoclonal rabbit | #D14E12, Cell Signaling Technology, USA; RRID:AB_10859369 |
| NGAL | polyclonal goat | #AF1857, R and D Systems, USA; RRID:AB_355022 |
| NKCC2 | polyclonal rabbit | #LS-C313275, Lifespan Biosciences, USA; RRID:AB_2910114 |
| NKCC2 | polyclonal goat | #ab240542, abcam, UK; RRID:AB_2910116 |
| TUBB2B | polyclonal rabbit | #TA337744, OriGene Technologies, USA; RRID:AB_2910113 |
| Vimentin | monoclonal rabbit | #ab92547, abcam, UK; RRID:AB_10562134 |
| α -SMA | polyclonal rabbit | #ab15734, abcam, UK; RRID:AB_443242 |
| <i>secondary antibodies</i> | | |
| anti-goat Alexa Fluor 488 | donkey | #705-545-147; Jackson Immuno Research Labs; RRID:AB_2336933 |
| anti-goat Alexa Fluor 594 | donkey | #705-585-147, Jackson Immuno Research Lab; RRID:AB_2340433 |
| anti-rabbit-HRP | goat | #sc-2030, Santa Cruz Biotechnology, USA; RRID:AB_631747 |
| anti-mouse Cy3 | donkey | #715-165-150, Jackson Immuno Research Labs, RRID:AB_2340813 |
| anti-rabbit Alexa Fluor 488 | donkey | #711-545-152, Jackson Immuno Research Labs; RRID:AB_2313584 |
| anti-rabbit Cy3 | goat | #111-165-003, Jackson Immuno Research Labs, RRID:AB_2338000 |
| anti-rat Cy3 | donkey | #712-165-150, Jackson Immuno Research Labs, RRID:AB_2340666 |



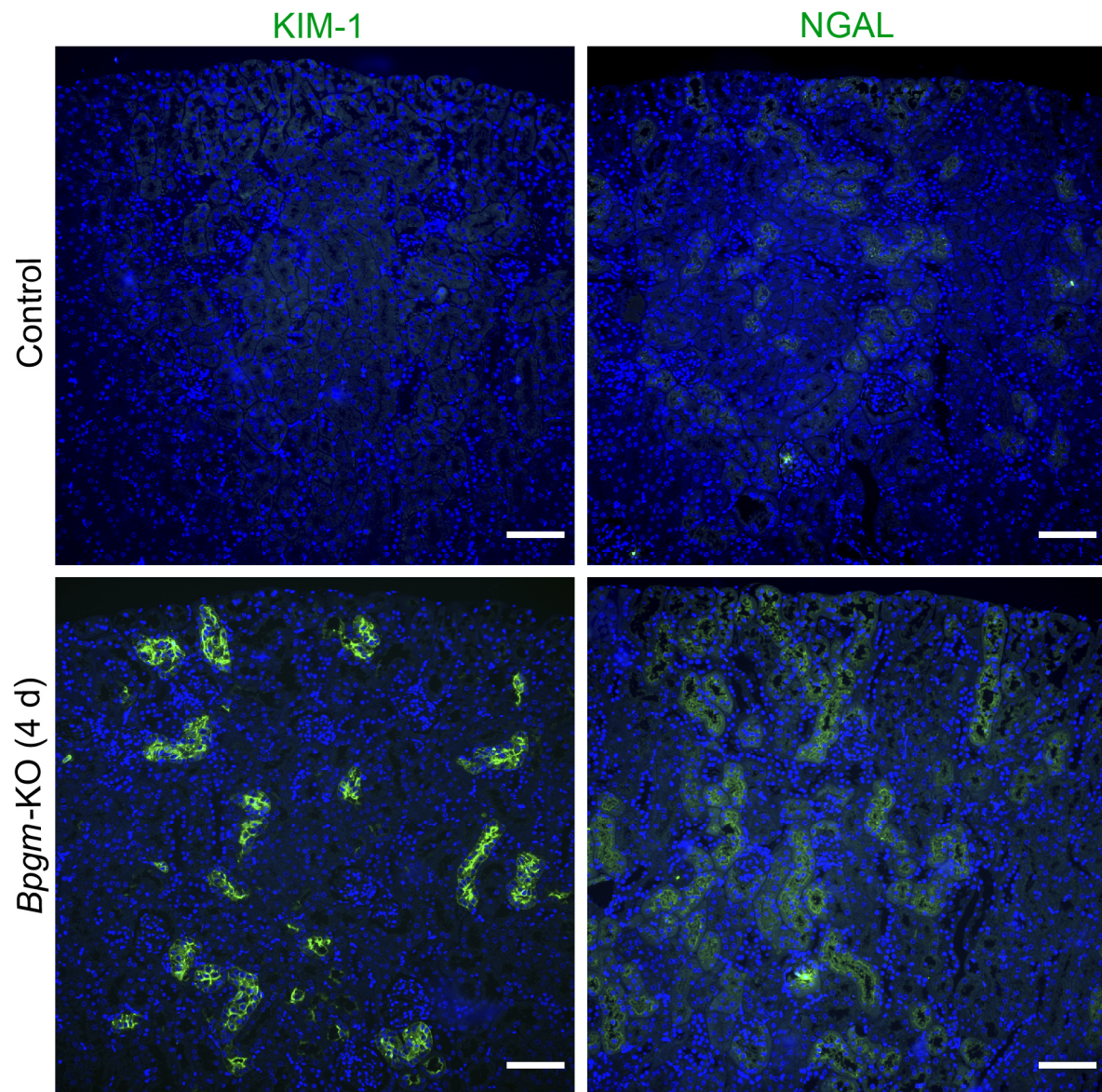
Supplemental Figure 1: BPGM localization in the kidney. (A-D) Immunofluorescence staining of mouse kidney section showing co-localization of BPGM (red) with marker proteins (green): (A) Megalin for PT (proximal tubules), (B) NKCC2 for TAL (thick ascending limb), (C) NCC for DCT (distal convoluted tubule), and (D) Aquaporin-2 for collecting duct. No BPGM expression was found in proximal tubules. Scale bar: 100 μ m. The figure completes data shown in Figure 1B.



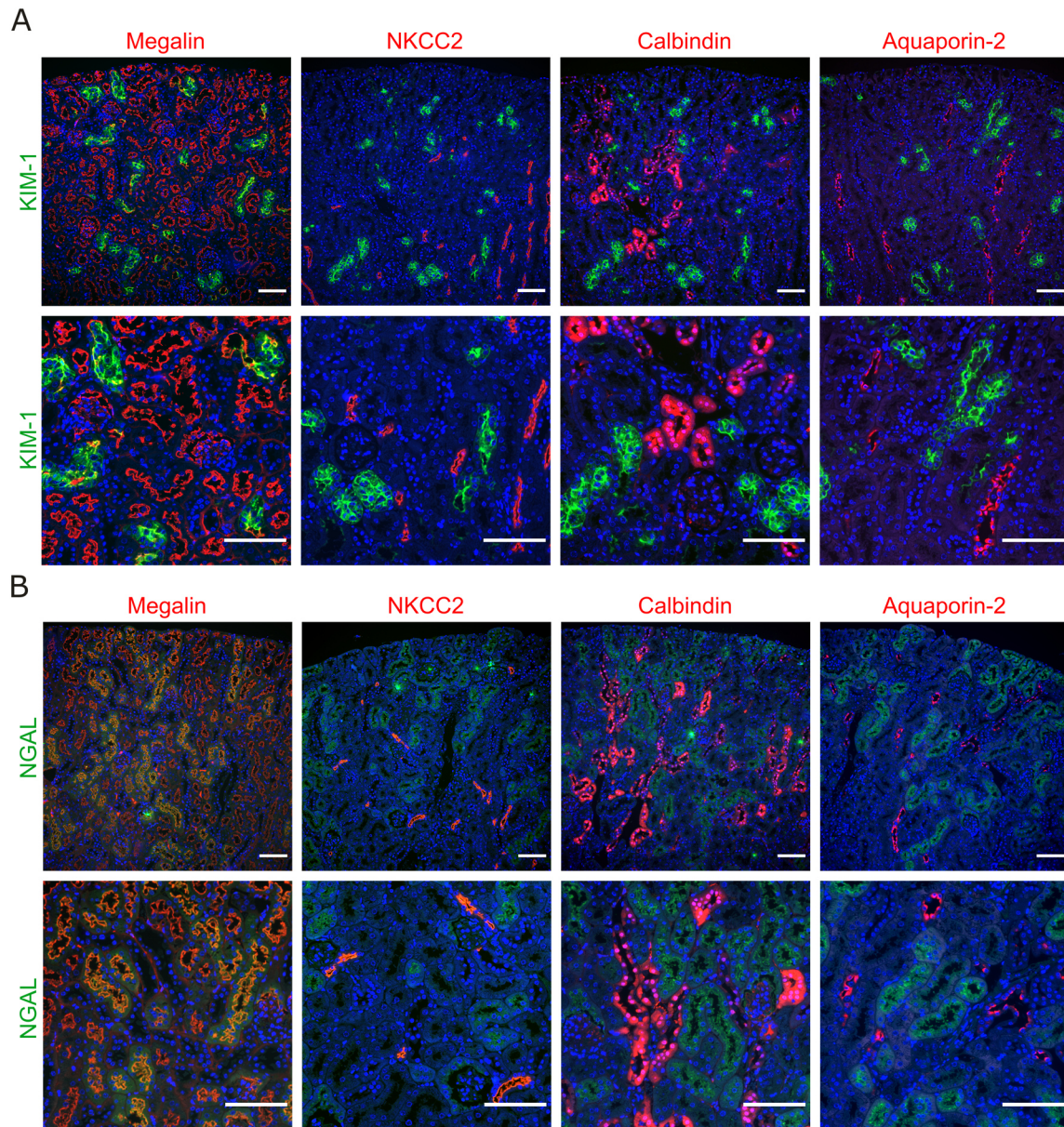
Supplemental Figure 2: Single-cell transcriptomic data from human AKI kidney biopsies. (A-C) Single-cell transcriptomic data from human kidney biopsies as described in Hinze *et al.* (12) (A) Expression values as counts per million (CPM) of *BPGM* mRNA in podocytes (Podo), proximal tubules (PT), thin limb of loop of Henle (tL), thick ascending limb (TAL), distal tubules (DCT), connecting tubules (CNT), collecting duct principal cells (CD-PC), CD intercalated cells type A (CD-IC-A) and type B (CD-IC-B), endothelial cells (EC), leukocytes (Leuko) and fibroblasts (Fibro). Cell numbers of clusters are parenthesized. † $p < 0.01$. (B) Uniform manifold approximation and projection (UMAP) of the sub-clustering for CNT. Cells from AKI-associated potentially injured CNT clusters are highlighted in red. (C) Feature plot of *BPGM* expression on CNT cells from AKI samples and controls. Expression values are log-normalized. Enrichment analysis indicates that *BPGM* is strongly enriched in injured cells ($p < 1e-20$).



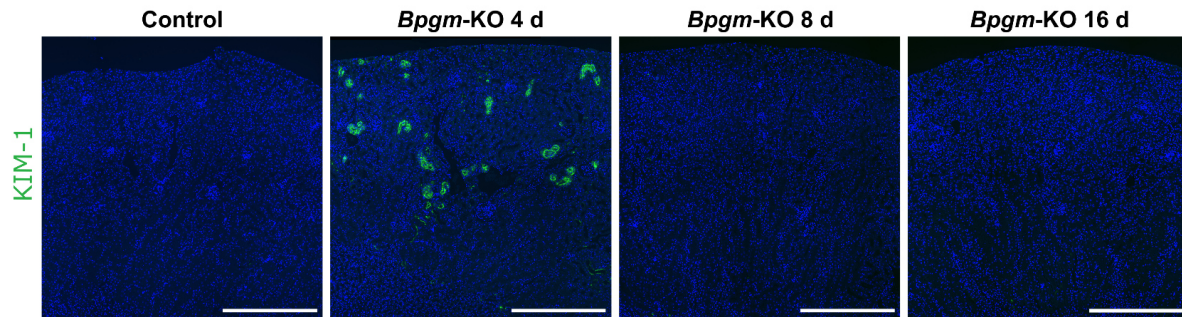
Supplemental Figure 3: Expression of *BPGM* in urine derived human kidney tubular epithelial cells following AKI. UMAP of 12,853 scRNAseq urine transcriptomes of tubular epithelial cells (TEC) from 32 individuals with AKI as described in Klocke *et al.* (13) **(A)** Depiction of TEC subsets with elevated *BPGM* expression in UMAP: *BPGM* expression is elevated in distal parts of the nephron, mostly connecting tubule (CNT), collecting duct principal cells (CD-PC) and intercalated cells (CD-IC) but also in a subset of injured TEC (TEC_inj). For full annotation of TEC subsets see Klocke *et al.* (13) **(B)** The magnitude of log-normalized expression of *BPGM* is depicted by colour code (grey to purple). **(C)** Violin plot of *BPGM* expression in each TEC subset. ‡ $p < 0.001$. CNT/CD p -value $< 3.484e-15$, CD-PC p -value $< 2.2e-16$, CD-IC p -value $< 3.641e-16$, TEC_inj p -value $< 2.2e-16$.



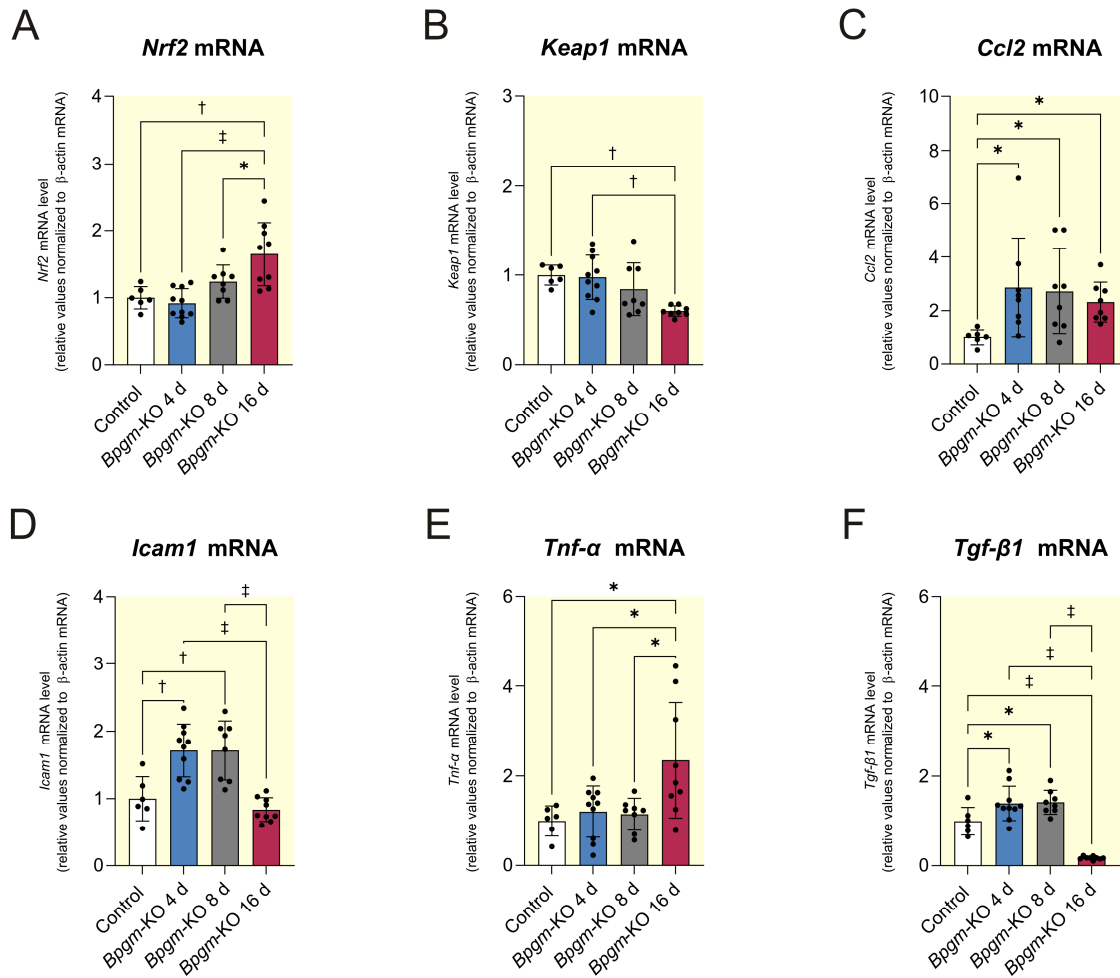
Supplemental Figure 4: Immunofluorescence staining of kidney injury markers KIM-1 and NGAL following 4 days of *Bpgm*-KO. Immunofluorescence staining of kidneys for injury markers KIM-1 and NGAL in control and *Bpgm*-KO mice 4 days after knockout induction. Control mice received doxycycline but were negative for *Cre* expression. KIM-1 and NGAL can only be detected in *Bpgm*-KO animals. Scale bars: 100 μ m.



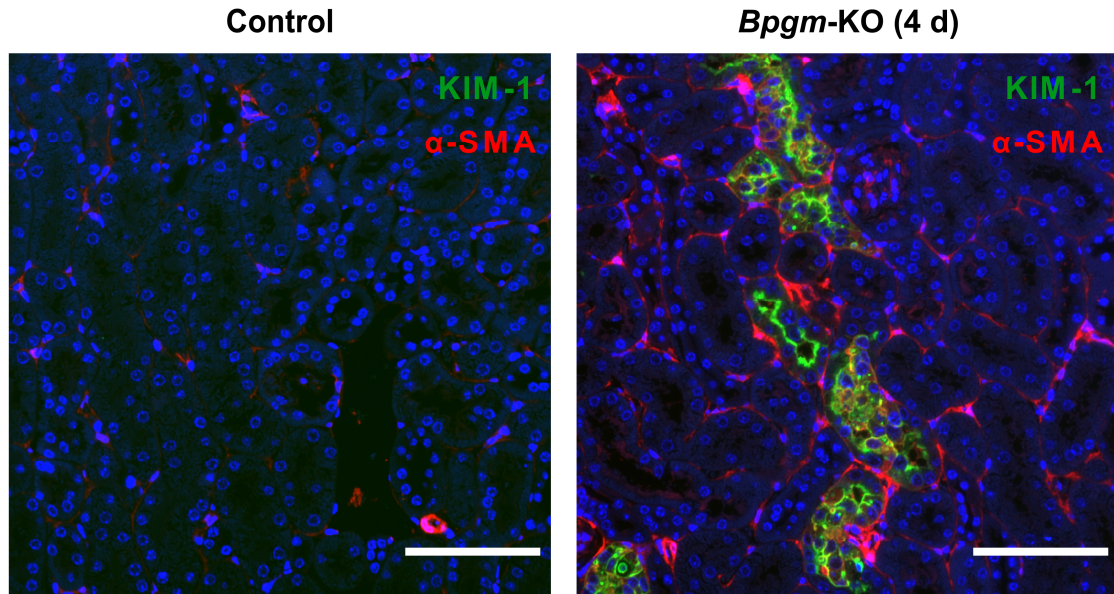
Supplemental Figure 5: Tubular localization of kidney injury markers KIM-1 and NGAL following 4 days of *Bpgm*-KO. A: Immunofluorescence double staining of KIM-1 (A) and NGAL (B) in green with marker proteins (red): Megalin for PT, NKCC2 for TAL, Calbindin for DCT and CNT, and Aquaporin-2 for collecting duct. (A) KIM-1 is co-localized with megalin, indicating damage of PT-cells. (B) NGAL is only co-localized with megalin, indicating damage of PT-cells. Scale bars: 100 μ m.



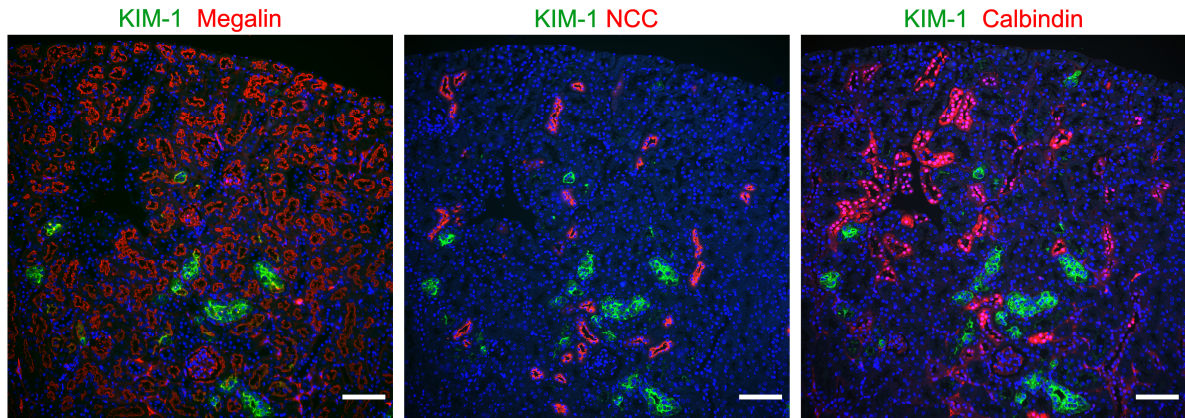
Supplemental Figure 6: Time course of renal KIM-1 expression in *Bpgm*-KO. Immunofluorescence staining for KIM-1 in kidneys of control and *Bpgm*-KO mice 4, 8 and 16 days after knockout induction. Control animals received doxycycline for the respective time point. KIM-1 positive tubules were observed only 4 days after *Bpgm*-KO. Scale bars: 500 μ m.



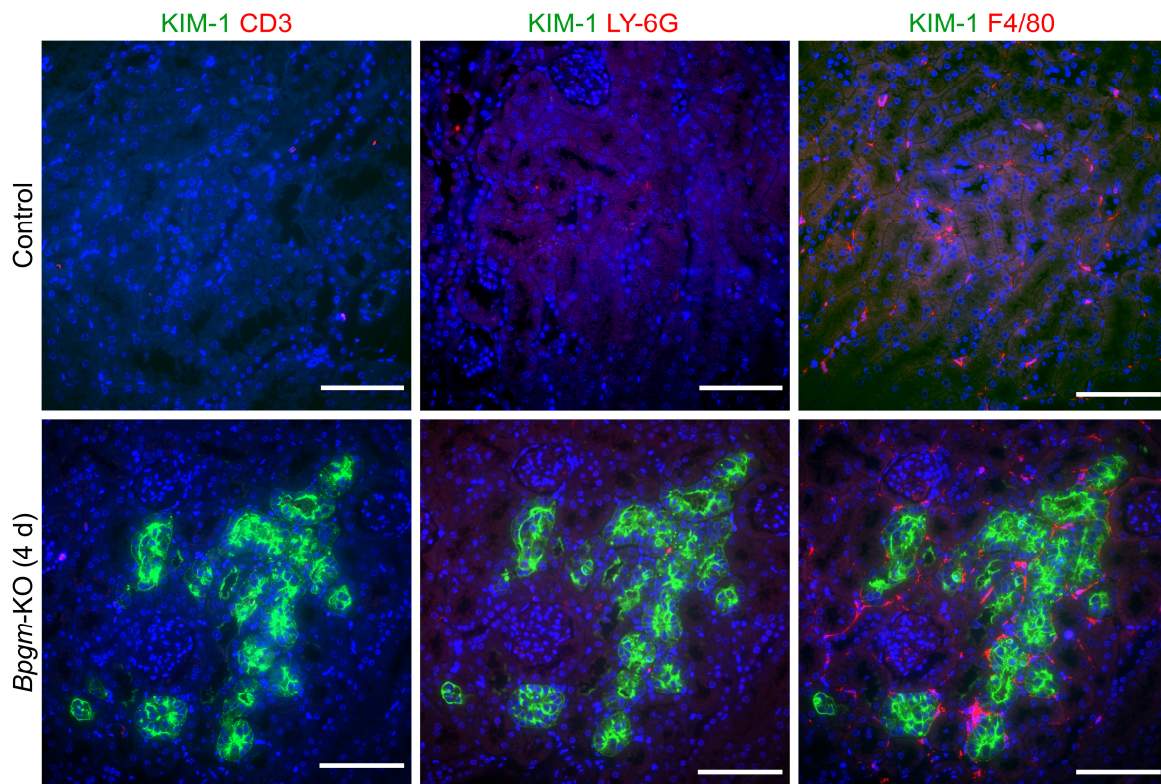
Supplemental Figure 7: *Bpgrm*-KO leads to a marked change in gene expression pattern of key factors involved in ROS metabolism, inflammation and fibrosis. qPCR analyses of candidate genes. **A, B:** The transcription factor *Nrf2* (**A**) shows upregulation after 16 d of *Bpgrm*-KO. In line, *Keap1*, an inhibitor of *Nrf2*, shows downregulation after 16 d (**B**). These data indicate adaptation to oxidative stress. **C-F:** Expression analysis of *Ccl2* (**C**), *Icam1* (**D**), *Tnf-α* (**E**) and *Tgf-β1* (**F**), genes that are associated with inflammation and fibrosis. Box-Plots show the median with lower and upper quartile as box. Whiskers show the minimum and maximum values. Dots represent single values. Statistical analysis was performed using One-Way Anova or Kuskal-Wallis test. * $p < 0.05$; † $p < 0.01$; ‡ $p < 0.001$.



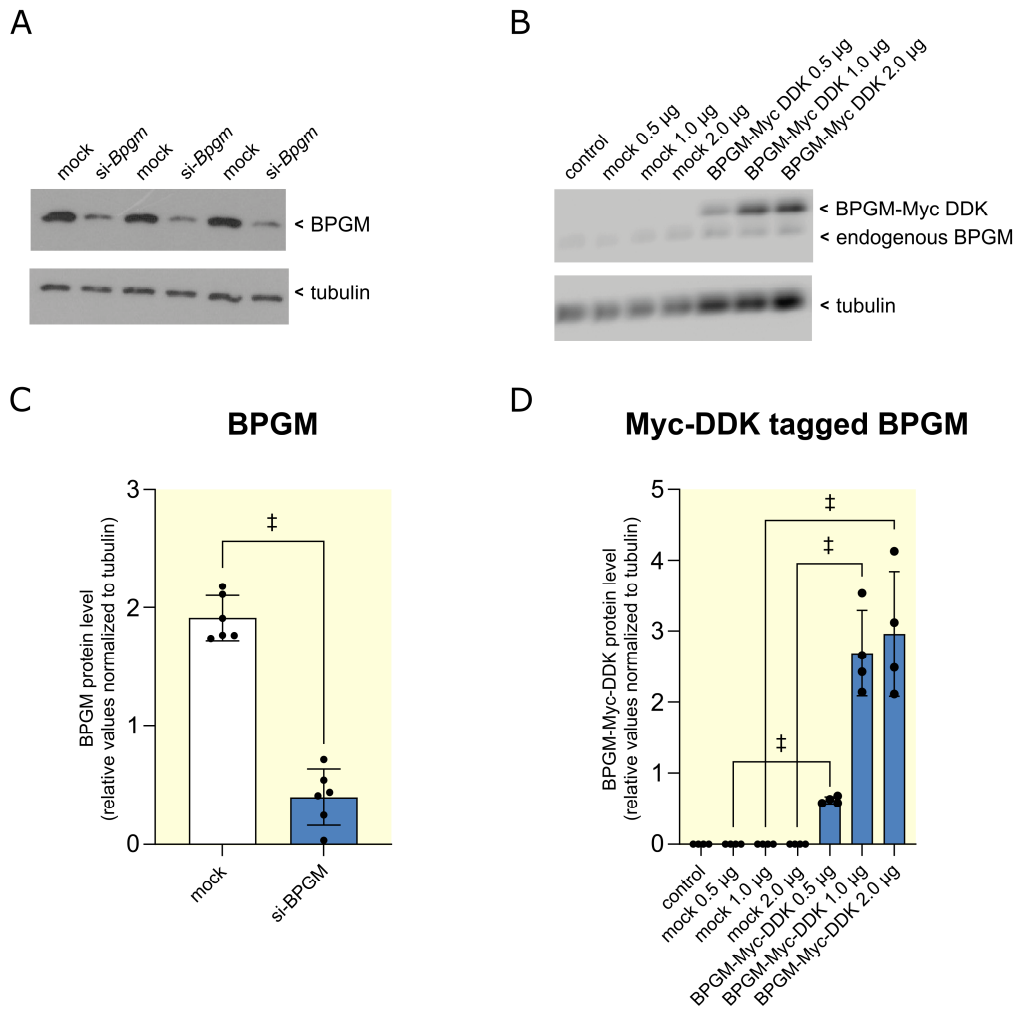
Supplemental Figure 8: *Bpgm*-KO leads to up-regulation of alpha-smooth muscle actin (α -SMA), indicative of cellular de-differentiation. Kidney sections were double stained for the proximal tubular injury marker KIM-1 (green) and the cellular *trans*-differentiation marker α -SMA (red). Expression of α -SMA is strongly enriched in KIM-1 positive cells following *Bpgm*-KO. Scale bars: 100 μ m.



Supplemental Figure 9: KIM-1 positive proximal tubules are in close proximity to distal tubules. Immunofluorescence double staining of the kidney injury marker KIM-1 (green) and nephron segment markers (red): megalin for proximal tubules, NCC for distal convoluted tubules (DCT) and calbindin for the late part of the distal convolute tubule (DCT2) and connecting tubules (CNT). Data suggest that injured (KIM-1 positive) proximal tubules locate within one to three tubular profiles distance from the distal nephron segments affected by the *Bpgm* knockout. Scale bars 100 μ m.



Supplemental Figure 10: Immunofluorescence staining of kidney injury marker KIM-1 along with immune cell markers following 4 days of *Bpgm-KO*. Immunofluorescence staining on parallel sections of kidney slices. The sections were double stained for the specific proximal tubular injury marker KIM-1 (green) and one of three immune cell markers (red), respectively: CD-3 for T-cells, Ly-6G for neutrophils and F4/80 for macrophages. Macrophages, but not neutrophils or T-cells surround the KIM-1 positive tubules. Scale bars: 100 μm.



Supplemental Figure 11: Verification of target specificity of the anti-BPGM antibody used in this study. (A, C) Western blot analysis of siRNA-mediated knockdown of *Bpgm* (24 h). Knockdown lowered the BPGM protein signal intensity to about 20 % of the control value. N=6. **(B, D)** Western blot analysis of BPGM overexpression following transfection using a Myc-DDK tagged BPGM expression vector. The blot shows a dose dependent elevation of the signal intensity of the Myc-DDK tagged BPGM protein (detected at 30 kDa). Endogenous BPGM is detected at 27 kDa. Tubulin served as a loading control. N=4. Box-Plots show the median with lower and upper quartile as a box. Whiskers show the minimum and maximum values. Dots represent single values. Statistical analysis was performed using student's *t*-test. ‡*p* < 0.001.

REACTION KINETICS

Glycoly

ALD (Aldolase)

$$v_{ALD} = v_{max}^{ALD} \cdot \frac{Fru16P_2 - GAP \cdot DHAP / k_{eq}^{ALD}}{\left(1 + \frac{Fru16P_2}{k_m^{Fru16P_2} \cdot \left(1 + \frac{Bpg23}{K_{Bpg23}^i}\right)}\right) + \left(1 + \frac{GAP}{k_m^{GAP}}\right) \left(1 + \frac{DHAP}{k_m^{DHAP}}\right) - 1}$$

$$v_{max}^{ALD} = 7.78 \cdot 10^8 \text{ h}^{-1}$$

$$K_{Bpg23}^i = 1.5 \text{ [1]}$$

$$k_{eq}^{ALD} = 0.099 \text{ mM [2]}$$

$$k_m^{Fru16P_2} = 0.004 \text{ mM [3]}$$

$$k_m^{GAP} = 0.48 \text{ mM [4]}$$

$$K_m^{DHAP} = 0.38 \text{ mM [4]}$$

EN (Enolase)

$$v_{EN} = v_{max}^{EN} \cdot \frac{2PG - PEP / k_{eq}^{EN}}{1 + \frac{2PG}{k_m^{2PG}} + \frac{PEP}{k_m^{PEP}}}$$

$$v_{max}^{EN} = 1.94 \cdot 10^{10} \text{ h}^{-1}$$

$$k_{eq}^{EN} = 1.7 \text{ [5]}$$

$$k_m^{2PG} = 0.14 \text{ mM [6]}$$

$$k_m^{PEP} = 0.31 \text{ mM [6]}$$

FBP1 (Fructose-1,6-bisphosphatase)

$$v_{FBP1} = V_{max}^{FBP1} \cdot \left((1 - \gamma^{FBP1}) * v_{FBP1}^{native} + \gamma^{FBP1} * v_{FBP1}^{phospho} \right)$$

$$V_{max}^{FBP1} = 2.92 \cdot 10^4 \text{ mM} \cdot \text{h}^{-1}$$

$$v_{FBP1}^{native} = \frac{Fru16P_2}{Fru16P_2 + k_m^{Fru16P_2}^{native}} / \left(1 + \frac{Fru26P_2^n}{(K_i^{Fru26P_2})^n}\right) / \left(1 + \left(\frac{AMP}{K_i^{AMP}}\right)^{n_{AMP}}\right)$$

$$k_m^{Fru16P_2} = 0.0029 \text{ mM [7]}$$

$$k_i^{Fru26P_2} = 0.00113 \text{ mM [7]}$$

$$n = 1.26 \text{ [7]}$$

$$n_{AMP} = 2.43 \text{ [7]}$$

$$K_i^{AMP} = 0.023 \text{ mM [7]}$$

$$v_{FBP1}^{phospho} = \frac{Fru16P_2}{Fru16P_2 + k_m^{phospho}} / \left(1 + \frac{Fru26P_2^n}{(k_i^{Fru26P_2})^n} \right) / \left(1 + \left(\frac{AMP}{K_i^{AMP}} \right)^{n_{AMP}} \right)$$

$$k_m^{Fru16P_2} = 0.0019 \text{ mM [7]}$$

$$k_i^{Fru26P_2} = 0.00113 \text{ mM [7]}$$

$$n = 1.26 \text{ [7]}$$

$$K_i^{AMP} = 0.023 \text{ mM [7]}$$

$$n_{AMP} = 2.43 \text{ [7]}$$

GAPDH (Glyceraldehyde 3-phosphate dehydrogenase)

$$v_{GAPDH} = v_{max}^{GAPDH} \cdot \frac{NAD^+ \cdot GAP \cdot P - 13P2G \cdot NADH / k_{eq}^{GAPDH}}{\left(1 + \frac{NAD^+}{k_m^{NAD^+}} \right) \cdot \left(1 + \frac{GAP}{k_m^{GAP}} \right) \cdot \left(1 + \frac{P}{k_m^P} \right) + \left(1 + \frac{NADH}{k_m^{NADH}} \right) \cdot \left(1 + \frac{13P2G}{k_m^{13P2G}} \right) - 1}$$

$$v_{max}^{GAPDH} = 2.92 \cdot 10^8 \text{ h}^{-1} \cdot \text{mM}^{-2}$$

$$k_{eq}^{GAPDH} = 10^{-4} \text{ mM}^{-1} \text{ [8]}$$

$$k_m^{NAD^+} = 0.010 \text{ mM [9]}$$

$$k_m^{GAP} = 0.035 \text{ mM [9]}$$

$$k_m^P = 3.8 \text{ mM [10]}$$

$$k_m^{NADH} = 0.006 \text{ mM [10]}$$

$$k_m^{13P2G} = 0.01 \text{ mM [9]}$$

Hexokinase

$$v_{Hk} = V_{max}^{Hk} \cdot \frac{1}{1 + \frac{Bpg23}{K_{Bpg23}^i}} \cdot \frac{ATP}{ATP + K_m^{ATP}} \cdot \left(1 + \frac{Glc6p}{K_{Glc6p}^{i-ATP}}\right) \cdot \frac{Glc}{Glc + K_m^{Glc}} \cdot \left(1 + \frac{Glc6p}{K_{Glc6p}^{i-Glc}}\right)$$

$$V_{max}^{Hk} = 90$$

$$K_{Bpg23}^i = 4 \text{ [11]}$$

$$K_m^{Glc} = 0.42 \text{ [12]}$$

$$K_m^{ATP} = 2.09 \text{ [12]}$$

$$K_{Glc6p}^{i-ATP} = 0.19 \text{ [12]}$$

$$K_{Glc6p}^{i-Glc} = 0.5 \text{ [12]}$$

Glucokinase

$$v_{GK} = V_{max}^{GK} \cdot \frac{ATP}{ATP + k_m^{ATP}} \cdot \frac{(Glc)^n}{(Glc)^n + (k_m^{Glc})^n}$$

$$V_{max}^{GK} = V_0^{GK} \cdot \frac{(Glc)^{n2}}{(Glc)^{n2} + (k_a^{Glc})^{n2}} \cdot \left(1 - f \cdot \frac{Fru6P}{Fru6P + k_i^{Fru6P}}\right)$$

$$V_0^{GK} = 1.05 \cdot 10^4 \text{ mM h}^{-1}$$

$$n = 1.5 \text{ [13]}$$

$$K_m^{Glc} = 9 \text{ mM [13]}$$

$$k_m^{ATP} = 0.55 \text{ mM [14]}$$

$$k_i^{Fru6P} = 0.005 \text{ mM [15]}$$

$$f = 0.75 \text{ [15]}$$

$$n2 = 3.7 \text{ [16]}$$

$$k_a^{Glc} = 15.9 \text{ mM [16]}$$

GlcT_{ER} (Glucose transport to ER)

$$v_{GlcT_{ER}} = V_{max}^{GlcT_{ER}} \cdot \frac{(Glc - Glc_{ER})}{1 + \frac{Glc}{k_m^{Glc}} + \frac{Glc_{ER}}{k_m^{Glc_{ER}}}}$$

$$V_{max}^{Glc_{ER}} = 1.94 \cdot 10^{10} \text{ h}^{-1}$$

$$k_m^{GlcER} = 1.37 \text{ mM} [17, 18]$$

$$k_m^{Glc} = 1.22 \text{ mM} [17, 18]$$

GLUT2 (Glucose transporter 2)

$$v_{GLUT2} = V_{max}^{GLUT2} \cdot \frac{Glc_{ext} - Glc}{1 + \frac{Glc_{ext}}{k_m^{Glc_{ext}}} + \frac{Glc}{k_m^{Glc}}}$$

$$k_m^{Glc} = 17.3 \text{ mM} [19]$$

$$k_m^{Glc_{ext}} = 17.3 \text{ mM} [19]$$

$$V_{max}^{GLUT2} = 9.09 \cdot 10^1 \text{ h}^{-1}$$

G6P_{ER} (Glucose-6-phosphate phosphatase in the ER) [20, 21]

$$v_{G6P_{ER}} = V_{max}^{G6P_{ER}} \cdot \frac{Glc6P_{ER}}{Glc6P_{ER} + k_m^{Glc6P_{ER}}}$$

$$k_m^{Glc6P_{ER}} = 1.84 \text{ mM} [20]$$

$$V_{max}^{G6P_{ER}} = 4.57 \cdot 10^2 \text{ mM} \cdot \text{h}^{-1}$$

GPI (Glucose-6-phosphate isomerase)

$$v_{GPI} = V_{max}^{GPI} \cdot \frac{Glc6P - Fru6P/k_{eq}^{GPI}}{1 + \frac{Glc6P}{k_m^{Glc6P}} + \frac{Fru6P}{k_m^{Fru6P}}}$$

$$V_{max}^{GPI} = 1.07 \cdot 10^9 \text{ h}^{-1}$$

$$k_{eq}^{GPI} = 0.3 [22]$$

$$k_m^{Glc6P} = 0.055 \text{ mM} [23]$$

$$K_m^{Fru6P_{cyt}} = 0.12 \text{ mM} [23]$$

G6P_{ER} (Glucose-6-phosphate transport to ER)

$$v_{G6P_{T_{ER}}} = V_{max}^{G6P_{T_{ER}}} \cdot \frac{(Glc6P - Glc6P_{ER})}{1 + \frac{Glc6P}{k_m^{Glc6P}} + \frac{Glc6P_{ER}}{k_m^{Glc6P_{ER}}}}$$

$$V_{max}^{G6P_{T_{ER}}} = 1.94 \cdot 10^{10} h^{-1}$$

$$k_m^{Glc6P_{ER}} = 1.12 mM [17]$$

$$k_m^{Glc6P} = 1.12 mM [17]$$

LacT (Lactate transporter)

$$v_{LacT} = v_{max}^{LacT} \cdot \frac{Lac_{ext} - Lac}{1 + \frac{Lac}{k_m^{Lac}} + \frac{Lac_{ext}}{k_m^{Lac_{ext}}}}$$

$$v_{max}^{LacT} = 5.83 \cdot 10^2 h^{-1}$$

$$k_m^{Lac} = 2.42 mM [24]$$

$$k_m^{Lac_{ext}} = 2.42 mM [24]$$

LDH (Lactate dehydrogenase) [25, 26]

$$v_{LDH} = v_{max}^{LDH} * \frac{Pyr \cdot NADH - Lac \cdot NAD^+ / k_{eq}^{LDH}}{\left(1 + \frac{NADH}{k_m^{NADH}}\right) \cdot \left(1 + \frac{Pyr}{k_m^{Pyr}}\right) + \left(1 + \frac{Lac}{k_m^{Lac}}\right) \cdot \left(1 + \frac{NAD^+}{k_m^{NAD^+}}\right) - 1}$$

$$v_{max}^{LDH} = 1.56 \cdot 10^{11} h^{-1} \cdot mM^{-1}$$

$$k_{eq}^{LDH} = 9000 [27]$$

$$k_m^{NADH} = 0.015 mM [26]$$

$$k_m^{Pyr} = 0.15 mM [26]$$

$$k_m^{Lac} = 36 mM [25]$$

$$k_m^{NAD^+} = 0.11 mM [26]$$

MalT (Malate transporter)

$$v_{MalT} = v_{max}^{MalT} \cdot \left(\frac{Mal_{mito} \cdot P - Mal \cdot P_{mito}}{\left(1 + \frac{Mal_{mito}}{K_m^{Mal_{mito}}}\right) \cdot \left(1 + \frac{P}{K_m^P}\right) + \left(1 + \frac{Mal}{K_m^{Mal}}\right) \cdot \left(1 + \frac{P_{mito}}{K_m^{P_{mito}}}\right) - 1} \right)$$

$$v_{max}^{MalT} = 1.94 \cdot 10^3 h^{-1} \cdot mM^{-1}$$

$$k_m^P = 1.41 \text{ mM [28]}$$

$$k_m^{Malmito} = 0.49 \text{ mM [28]}$$

$$k_m^{Pmito} = 1.41 \text{ mM [28]}$$

$$k_m^{Mal} = 0.49 \text{ mM [28]}$$

MDH (Malate dehydrogenase)

$$v_{MDH} = v_{max}^{MDH} \cdot \frac{Mal \cdot NAD^+ - OA \cdot NADH / k_{eq}^{MDH}}{\left(1 + \frac{Mal}{k_m^{Mal}}\right) \cdot \left(1 + \frac{NAD^+}{k_m^{NAD^+}}\right) + \left(1 + \frac{OA}{k_m^{OA}}\right) \cdot \left(1 + \frac{NADH}{k_m^{NADH}}\right) - 1}$$

$$v_{max}^{MDH} = 1.94 \cdot 10^9 h^{-1} \cdot mM^{-1}$$

$$k_{eq}^{MDH} = 3 \cdot 10^{-5} \text{ [29]}$$

$$k_m^{Mal} = 1.1 \text{ mM [30]}$$

$$k_m^{NAD^+} = 0.114 \text{ mM [30]}$$

$$k_m^{OA} = 0.088 \text{ mM [30]}$$

$$k_m^{NADH} = 0.026 \text{ mM [30]}$$

MDH_{mito} (Mitochondrial malate dehydrogenase)

$$v_{MDHmito} = V_{max}^{MDHmito}$$

$$\cdot \left(\frac{Mal_{mito} \cdot NAD_{mito}^+ - 1 / K_{eq}^{MDHmito} \cdot OA_{mito} \cdot NADH_{mito}}{\left(1 + \frac{Mal_{mito}}{K_m^{Malmito}}\right) \cdot \left(1 + \frac{NAD_{mito}}{K_m^{NADmito}}\right) + \left(1 + \frac{OA_{mito}}{K_m^{OAmito}}\right) \cdot \left(1 + \frac{NADH_{mito}}{K_m^{NADHmito}}\right) - 1} \right)$$

$$V_{max}^{MDHmito} = 6.80 \cdot 10^{11} h^{-1} \cdot mM^{-1}$$

$$K_{eq}^{MDHmito} = 3.1 \cdot 10^{-5} \text{ (pH 7.5) [29]}$$

$$K_m^{Malmito} = 0.33 \text{ mM [31]}$$

$$K_m^{NADmito} = 0.06 \text{ mM [32]}$$

$$K_m^{OAmito} = 0.017 \text{ mM [32]}$$

$$K_m^{NADH_{mito}} = 0.044 \text{ mM [32]}$$

PC (Pyruvate carboxylase) [33, 34]

$$v_{PC} = v_{max}^{PC} \cdot \frac{ATP_{mito} \cdot Pyr_{mito} \cdot CO_{2mito} - OA_{mito} \cdot ADP_{mito} \cdot P_{mito} / k_{eq}^{PC}}{(ATP_{mito} + k_m^{ATP_{mito}}) \cdot (Pyr_{mito} + k_m^{Pyr_{mito}}) \cdot (CO_{2mito} + k_m^{CO_{2mito}})}$$

$$v_{max}^{PC} = 3.59 \cdot 10^3 \text{ mM} \cdot \text{h}^{-1}$$

$$k_m^{ATP_{mito}} = 0.14 \text{ mM [33]}$$

$$k_m^{Pyr_{mito}} = 0.33 \text{ mM [33]}$$

$$k_m^{CO_{2mito}} = 4.2 \text{ mM [33]}$$

$$k_{eq}^{PC} = 6.55 \text{ [34]}$$

PEPCK (Phosphoenolpyruvate carboxykinase)

$$v_{PEPCK} = v_{max}^{PEPCK} \cdot \frac{OA \cdot GTP - PEP \cdot GDP \cdot CO_2 / k_{eq}^{PEPCK}}{\left(1 + \frac{OA}{k_m^{OA}}\right) \cdot \left(1 + \frac{GTP}{k_m^{GTP}}\right) + \left(1 + \frac{PEP}{k_m^{PEP}}\right) \cdot \left(1 + \frac{GDP}{k_m^{GDP}}\right) \cdot \left(1 + \frac{CO_2}{k_m^{CO_2}}\right) - 1}$$

$$v_{max}^{PEPCK} = 5.11 \cdot 10^5 \text{ h}^{-1} \cdot \text{mM}^{-1}$$

$$k_{eq}^{PEPCK} = 110 \text{ mM [35]}$$

$$k_m^{OA} = 0.024 \text{ mM [36]}$$

$$k_m^{GTP} = 0.021 \text{ mM [37]}$$

$$k_m^{PEP} = 0.4 \text{ mM [38]}$$

$$k_m^{GDP} = 0.02 \text{ mM [39]}$$

$$k_m^{CO_2} = 1.194 \text{ mM [40]}$$

PEPCK_{mito} (Mitochondrial phosphoenolpyruvate carboxykinase)

$$v_{PEPCK_{mito}}$$

$$= v_{max}^{PEPCK_{mito}}$$

$$\cdot \frac{OA_{mito} \cdot GTP_{mito} - PEP_{mito} \cdot GDP_{mito} \cdot CO_{2mito} / k_{eq}^{PEPCK_{mito}}}{\left(1 + \frac{OA_{mito}}{k_m^{OA_{mito}}}\right) \cdot \left(1 + \frac{GTP_{mito}}{k_m^{GTP_{mito}}}\right) + \left(1 + \frac{PEP_{mito}}{k_m^{PEP_{mito}}}\right) \cdot \left(1 + \frac{GDP_{mito}}{k_m^{GDP_{mito}}}\right) \cdot \left(1 + \frac{CO_{2mito}}{k_m^{CO_{2mito}}}\right) - 1}$$

$$v_{max}^{PEPCK_{mito}} = 1.0 \cdot 10^6 h^{-1} \cdot mM^{-1}$$

$$k_{eq}^{PEPCK_{mito}} = 160 \text{ mM [35]}$$

$$k_m^{OA_{mito}} = 0.0085 \text{ mM [41]}$$

$$k_m^{GTP_{mito}} = 0.022 \text{ mM [39]}$$

$$k_m^{PEP_{mito}} = 0.4 \text{ mM [38]}$$

$$k_m^{GDP_{mito}} = 0.02 \text{ mM [39]}$$

$$k_m^{CO_{2mito}} = 1.06 \text{ mM [42]}$$

PEPT (Phosphoenolpyruvate transporter)

$$v_{PEPT} = v_{max}^{PEPT} \cdot \frac{PEP_{mito} - PEP / k_{eq}^{PEPT}}{1 + \frac{PEP}{k_m^{PEP}} + \frac{PEP_{mito}}{k_m^{PEP_{mito}}}}$$

$$v_{max}^{PEPT} = 1.94 \cdot 10^5 h^{-1}$$

$$k_{eq}^{PEPT} = \exp\left(-\frac{V_{mm} \cdot F}{R \cdot T}\right)$$

$$k_m^{PEP} = 0.1 \text{ mM [43]}$$

$$k_m^{PEP_{mito}} = 0.1 \text{ mM [43]}$$

PFK1 (Phosphofructokinase 1)

$$v_{PFK1} = v_{max}^{PFK1} \cdot \frac{1}{1 + \frac{Bpg23_{cyt}}{K_{Bpg23}^i}} \cdot \frac{ATP}{ATP + K_m^{ATP}} \cdot \left(1 - \frac{ATP^{n_i}}{ATP^{n_i} + (K_i^{ATP})^{n_i}}\right) \cdot \frac{(Fru6P)^{n_{Fru6P}}}{(Fru6P)^{n_{Fru6P}} + (k_m^{Fru6P})^{n_{Fru6P}}}$$

$$v_{max}^{PFK1} = 7.68 \cdot 10^4 \text{ mM} \cdot \text{h}^{-1}$$

$$K_{Bpg23}^i = 1 \text{ [11]}$$

$$K_m^{ATP} = K_0^{ATP} \cdot \left(1 - \frac{Fru26P_2}{Fru26P_2 + K_a^{Fru26P_2}} \right)$$

$$K_0^{ATP} = 0.2 \text{ mM [44, 45]}$$

$$K_a^{Fru26P_2} = 0.0027 \text{ mM [44, 45]}$$

$$K_i^{ATP} = K_{i0}^{ATP} \cdot \left(1 + f_{Fru26P_2} \frac{Fru26P_2}{Fru26P_2 + K_{a2}^{Fru26P_2}} \right)$$

$$K_{i0}^{ATP} = 0.7 \text{ mM [44, 45]}$$

$$f_{Fru26P_2} = 9 \text{ [44, 45]}$$

$$K_{a2}^{Fru26P_2} = 0.54 \text{ mM [44, 45]}$$

$$n_i = 4 \text{ [44, 45]}$$

$$k_m^{Fru6P} = K_0^{Fru6P} \cdot \left(1 + \frac{ATP}{k_i^{ATP}} \right) \cdot \left(1 + \frac{Cit}{k_i^{Cit}} \right) \cdot \left(1 - f_{AMP} \frac{AMP^{n_{AMP}}}{AMP^{n_{AMP}} + (K_a^{AMP})^{n_{AMP}}} \right) \\ \cdot \left(1 - f_P \frac{P}{P + K_a^P} \right) \cdot \left(1 - f_{Fru26P_2} \frac{Fru26P_2^{n_{Fru26P_2}}}{Fru26P_2^{n_{Fru26P_2}} + (K_a^{Fru26P_2})^{n_{Fru26P_2}}} \right)$$

$$K_0^{Fru6P} = 1.14 \text{ mM [46]}$$

$$k_i^{ATP} = 0.6 \text{ mM [46]}$$

$$k_i^{Cit} = 3.27 \text{ mM [46]}$$

$$f_{AMP} = 0.77 \text{ [46]}$$

$$K_a^{AMP} = 0.1 \text{ mM [46]}$$

$$n_{AMP} = 1.84 \text{ [46]}$$

$$f_P = 0.85 \text{ [46]}$$

$$K_a^P = 0.69 \text{ mM [46]}$$

$$f_{Fru26P_2} = 0.92 \text{ [44]}$$

$$K_a^{Fru26P_2} = 0.0045 \text{ mM [44]}$$

$$n_{Fru26P_2} = 1.2 \text{ [44]}$$

$$n^{Fru6P} = \left(n_0 + \frac{ATP^{n_{ATP}}}{ATP^{n_{ATP}} + (K_i^{ATP})^{n_{ATP}}} \right) \cdot \left(1 - f_{AMP} \frac{AMP^{n_{AMP}}}{AMP^{n_{AMP}} + (K_a^{AMP})^{n_{AMP}}} \right) \\ \cdot \left(1 + f_{Cit} \frac{Cit^{n_{Cit}}}{Cit^{n_{Cit}} + (K_i^{Cit})^{n_{Cit}}} \right) \cdot \left(1 - f_P \frac{P^{n_P}}{P^{n_P} + (K_a^P)^{n_P}} \right) \cdot \\ \cdot \left(1 - f_{Fru26P_2} \frac{Fru26P_2^{n_{Fru26P_2}}}{Fru26P_2^{n_{Fru26P_2}} + (K_a^{Fru26P_2})^{n_{Fru26P_2}}} \right)$$

$$n_0 = 3.67 [46]$$

$$K_i^{ATP} = 0.13 \text{ mM} [46]$$

$$n_{ATP} = 1.59 [46]$$

$$f_{AMP} = 0.4 [46]$$

$$K_a^{AMP} = 0.086 \text{ mM} [46]$$

$$n_{AMP} = 2.22 [46]$$

$$f_{Cit} = 0.1 [46]$$

$$K_i^{Cit} = 0.18 \text{ mM} [46]$$

$$n_{Cit} = 4 [46]$$

$$f_P = 0.28 [46]$$

$$K_a^P = 0.53 \text{ mM} [46]$$

$$n_P = 4 [46]$$

$$f_{Fru26P_2} = 0.37 [44]$$

$$K_a^{Fru26P_2} = 0.0021 \text{ mM} [44]$$

$$n^{Fru26P_2} = 4 [44]$$

PFK2/FBP2 (Phosphofruktokinase 2/Fruktose-2,6-bisphosphatase)

$$v_{PFK2} = (1 - \gamma^{PFK2}) \cdot v_{PFK2}^{native} + \gamma^{PFK2} \cdot v_{PFK2}^{phospho}$$

$$v_{PFK2}^{native} = V_{max}^{PFK2} \frac{Fru6P^n}{Fru6P^n + (k_m^{Fru6P})^n} \cdot \frac{ATP}{ATP + k_m^{ATP}} \cdot \left(1 - n_0 \cdot \frac{PEP}{PEP + k_i^{PEP}} \right)$$

$$V_{max}^{PFK2} = 1.51 \cdot 10^2 \text{ mM} \cdot \text{h}^{-1}$$

$$k_m^{Fru6P} = 0.015 \text{ mM [47]}$$

$$n = 1.3 \text{ [47]}$$

$$k_m^{ATP} = 0.25 \text{ mM [47]}$$

$$k_i^{PEP} = 0.25 \text{ mM [45]}$$

$$n_0 = 0.85 \text{ [45]}$$

$$v_{PFK2}^{phospho} = V_{max}^{PFK2} \frac{Fru6P^n}{Fru6P^n + k_m^{Fru6P}^n} \cdot \frac{ATP}{ATP + k_m^{ATP}} \cdot \left(1 - n_0 \cdot \frac{PEP}{PEP + k_i^{PEP}}\right)$$

$$k_m^{Fru6P} = 0.05 \text{ mM [47]}$$

$$n = 2 \text{ [47]}$$

$$k_m^{ATP} = 0.5 \text{ mM [47]}$$

$$k_i^{PEP} = 0.25 \text{ mM [45]}$$

$$n_0 = 0.85 \text{ [45]}$$

$$v_{FBP2} = V_{max}^{FBP2} * \left((1 - \gamma^{FBP2}) \cdot v_{FBP2}^{native} + \gamma^{FBP2} \cdot v_{FBP2}^{phospho} \right)$$

$$V_{max}^{FBP2} = 5.49 \cdot 10^2 \text{ mM} \cdot \text{h}^{-1}$$

$$v_{FBP2}^{native} = \frac{Fru26P_2}{Fru26P_2 + k_m^{Fru26P_2}} / \left(1 + \frac{Fru6P}{k_i^{Fru6P}}\right)$$

$$k_m^{Fru26P_2} = 0.01 \text{ mM [48]}$$

$$k_i^{Fru6P} = 0.0035 \text{ mM [47]}$$

$$v_{FBP2}^{phospho} = \frac{Fru26P_2}{Fru26P_2 + k_m^{Fru26P_2}} / \left(1 + \frac{Fru6P}{k_i^{Fru6P}}\right)$$

$$k_m^{Fru26P_2} = 0.0005 \text{ mM [47]}$$

$$k_i^{Fru6P} = 0.01 \text{ mM [47]}$$

PGK (Phosphoglycerate kinase)

$$v_{PGK} = v_{max}^{PGK} * \frac{ADP \cdot 13P2G - ATP \cdot 3PG / k_{eq}^{PGK}}{\left(1 + \frac{ADP}{k_m^{ADP}}\right) \cdot \left(1 + \frac{13P2G}{k_m^{13P2G}}\right) + \left(1 + \frac{ATP}{k_m^{ATP}}\right) \cdot \left(1 + \frac{3PG}{k_m^{3PG}}\right) - 1}$$

$$v_{max}^{PGK} = 1.94 \cdot 10^{10} \text{ h}^{-1} \cdot \text{mM}^{-1}$$

$$k_{eq}^{PGK} = 1830 [49]$$

$$k_m^{ADP} = 0.35 \text{ mM} [50]$$

$$k_m^{13P2G} = 0.0022 \text{ mM} [50]$$

$$k_m^{ATP} = 0.24 \text{ mM} [51]$$

$$k_m^{3PG} = 1.65 \text{ mM} [51]$$

BPGP (Bisphosphoglycerate Phosphatase)

$$v_{BPGP} = V_{max}^{BPGP} \cdot \frac{BPG23_{cyt}}{BPG23_{cyt} + K_m^{BPG23_{cyt}}}$$

$$K_m^{BPG23_{cyt}} = 0.0051 [52]$$

$$V_{max}^{BPGP} = 5.832 \text{ mM} \cdot h^{-1}$$

BPGM (Bisphosphoglycerate Phosphatase)

$$v_{BPGM} = V_{max}^{BPGM} \cdot \frac{BPG13_{cyt}}{BPG213_{cyt} + K_m^{BPG13_{cyt}} \cdot \left(1 + \frac{BPG23_{cyt}}{K_i^{BPG13_{cyt}}} \right)}$$

$$V_{max}^{BPGM} = 583.2 \text{ mM} \cdot h^{-1}$$

$$K_m^{BPG23_{cyt}} = 0.004 [53]$$

$$K_i^{BPG13_{cyt}} = 0.11 [53]$$

PGM (Phosphoglycerate mutase)

$$v_{PGM} = v_{max}^{PGM} \cdot \frac{3PG - 2PG/k_{eq}^{PGM}}{1 + \frac{3PG}{k_m^{3PG}} + \frac{2PG}{K_m^{2PG}}}$$

$$v_{max}^{PGM} = 1.94 \cdot 10^{10} h^{-1}$$

$$k_{eq}^{PGM} = 0.096 [54]$$

$$k_m^{3PG} = 0.52 \text{ mM} [55]$$

$$K_m^{2PG} = 0.24 \text{ mM} [55]$$

PK (Pyruvate kinase)

$$v_{PK} = v_{max}^{PK} \cdot \left((1 - \gamma^{PK}) \cdot v_{PK}^{native} + \gamma^{PK} \cdot v_{PK}^{phospho} \right)$$

$$v_{PK}^{native} = \frac{PEP}{PEP + k_m^{PEP} \cdot \left(1 + \frac{ATP}{k_i^{ATP}} \right) \cdot \left(1 - \frac{Fru16P_2}{Fru16P_2 + k_a^{Fru16P_2}} \right)} \cdot \frac{ADP}{ADP + k_m^{ADP}}$$

$$v_{max}^{PK} = 1.28 \cdot 10^4 \text{ mM} \cdot \text{h}^{-1}$$

$$k_m^{PEP} = 0.13 \text{ mM} [56]$$

$$k_i^{ATP} = 1 \text{ mM} [56]$$

$$k_a^{Fru16P_2} = 0.0078 \text{ mM} [57]$$

$$k_m^{ADP} = 0.25 \text{ mM} [58]$$

$$v_{PK}^{phospho} = \frac{PEP^n}{PEP^n + \left(k_m^{PEP} \cdot \left(1 + \frac{ATP}{k_i^{ATP}} \right) \cdot \left(1 - \frac{Fru16P_2}{Fru16P_2 + k_a^{Fru16P_2}} \right) \right)^n} \cdot \frac{ADP}{ADP + k_m^{ADP}}$$

$$k_m^{PEP} = 5.8 \text{ mM} [56]$$

$$n = 2.9 [56]$$

$$k_a^{Fru16P_2} = 0.0095 \text{ mM} [57]$$

$$k_i^{ATP} = 0.32 \text{ mM} [59]$$

$$k_m^{ADP} = 0.33 \text{ mM} [58]$$

PyrMalT (Pyruvate/malate antiporter)

$$v_{PyrMalT} = v_{max}^{PyrMalT} \cdot \left(\frac{Mal_{mito} \cdot Pyr - Mal \cdot Pyr_{mito}}{\left(1 + \frac{Mal_{mito}}{K_m^{Mal_{mito}}} \right) \cdot \left(1 + \frac{Pyr}{K_m^{Pyr}} \right) + \left(1 + \frac{Mal}{K_m^{Mal}} \right) \cdot \left(1 + \frac{Pyr_{mito}}{K_m^{Pyr_{mito}}} \right) - 1} \right)$$

$$v_{max}^{PyrMalT} = 1.94 \cdot 10^4 \text{ h}^{-1} \cdot \text{mM}^{-1}$$

$$k_m^{Pyr} = 0.84 \text{ mM} [60]$$

$$k_m^{Mal} = 0.7 \text{ mM} [43]$$

$$k_m^{Pyr_{mito}} = 0.84 \text{ mM [60]}$$

$$k_m^{Mal_{mito}} = 0.7 \text{ mM [43]}$$

PyrT (Pyruvate transporter)

$$v_{PyrT} = v_{max}^{PyrT} \cdot \frac{Pyr \cdot H^+ - Pyr_{mito} \cdot H_{mito}^+}{1 + \frac{Pyr}{k_m^{Pyr}} + \frac{Pyr_{mito}}{k_m^{Pyr_{mito}}}}$$

$$v_{max}^{PyrT} = 1.94 \cdot 10^8 \text{ h}^{-1} \cdot \text{mM}^{-1}$$

$$k_m^{Pyr} = 0.15 \text{ mM [61]}$$

$$k_m^{Pyr_{mito}} = 0.15 \text{ mM [61]}$$

TPI (Triosephosphate isomerase)

$$v_{TPI} = v_{max}^{TPI} \cdot \frac{DHAP - GAP/k_{eq}^{TPI}}{1 + \frac{DHAP}{k_m^{DHAP}} + \frac{GAP}{k_m^{GAP}}}$$

$$v_{max}^{TPI} = 1.94 \cdot 10^8 \text{ h}^{-1}$$

$$k_{eq}^{TPI} = 0.04545 \text{ [2]}$$

$$k_m^{DHAP} = 0.59 \text{ mM [62]}$$

$$k_m^{GAP} = 0.415 \text{ mM [62]}$$

Polyol pathway

Aldose reductase

$$v_{aldr} = V_{max}^{aldr} \cdot \left(\frac{Glc_{cyt}}{Glc_{cyt} + K_m^{glc_{cyt}}} \right) \cdot \left(\frac{Nadh_{cyt}}{Nadh_{cyt} + K_m^{nadh_{cyt}}} \right)$$

$$V_{max}^{aldr} = 2.16$$

$$K_m^{glc_{cyt}} = 155 \text{ [63]}$$

$$K_m^{nadh_{cyt}} = 0.01 \text{ [63]}$$

Sorbital dehydrogenase

$$v_{sordh} = V_{max}^{sordh} \cdot \frac{\left(Fru_{cyt} \cdot Nadh_{cyt} - 1/K_{eq}^{sordh} \cdot Sorb_{cyt} \cdot Nad_{cyt} \right)}{\left(1 + \frac{Fru_{cyt}}{K_m^{fru_{cyt}}} \right) \cdot \left(1 + \frac{Nadh_{cyt}}{K_m^{nadh_{cyt}}} \right) + \left(1 + \frac{Sorb_{cyt}}{K_m^{sorb_{cyt}}} \right) \cdot \left(1 + \frac{Nad_{cyt}}{K_m^{nad_{cyt}}} \right) - 1}$$

$$V_{max}^{sordh} = 3.6 [2]$$

$$K_m^{fru_{cyt}} = 136 [64]$$

$$K_m^{nadh_{cyt}} = 0.067 [64]$$

$$K_m^{sorb_{cyt}} = 0.38 [64]$$

$$K_m^{nad_{cyt}} = 0.082 [64]$$

Fructokinase

$$v_{fruk} = V_{max}^{fruk} \cdot \left(\frac{Fru_{cyt}}{Fru_{cyt} + K_m^{fru_{cyt}}} \right) \cdot \left(\frac{ATP_{cyt}}{ATP_{cyt} + K_m^{atp_{cyt}}} \right) \cdot \left(1 - \frac{ADP_{cyt}^n}{ADP_{cyt}^n + (K_i^{adp_{cyt}})^n} \right)$$

$$V_{max}^{fruk} = 3.6$$

$$K_m^{fru_{cyt}} = 0.4 [38]$$

$$K_m^{atp_{cyt}} = 1.5 [38]$$

$$n = 1.5 [65]$$

$$K_i^{adp_{cyt}} = 3.06 [65]$$

Aldolase B

$$v_{aldB} = V_{max}^{aldB} \cdot \frac{\left(Fru1p_{cyt} - 1/K_{eq}^{aldB} \cdot Gra_{cyt} \cdot Dhap_{cyt} \right)}{\left(1 + \frac{Fru1p_{cyt}}{K_m^{fru1p_{cyt}}} \right) + \left(1 + \frac{Gra_{cyt}}{K_m^{gra_{cyt}}} \right) \cdot \left(1 + \frac{Dhap_{cyt}}{K_m^{dhap_{cyt}}} \right) - 1}$$

$$V_{max}^{aldB} = 3.6$$

$$K_{eq}^{aldB} = 0.0028 [66]$$

$$K_m^{fru1p_{cyt}} = 4.5 [67]$$

$$K_m^{gra_{cyt}} = 0.48 [4]$$

$$K_m^{dhap_{cyt}} = 0.016 [68]$$

Triokinase

$$v_{triok} = V_{max}^{triok} \cdot \left(\frac{Gra_{cyt}}{Gra_{cyt} + K_m^{gra_{cyt}}} \right) \cdot \left(\frac{ATP_{cyt}}{ATP_{cyt} + K_m^{atp_{cyt}}} \right)$$

$$V_{max}^{triok} = 180$$

$$K_m^{gra_{cyt}} = 0.03 \text{ [69]}$$

$$K_m^{atp_{cyt}} = 0.2 \text{ [69]}$$

STOICHIOMETRIC MATRIX

$$\frac{d}{dt} DHAP = v_{ALD} - v_{TPI} + v_{aldB}$$

$$\frac{d}{dt} Fru_{cyt} = +v_{sordh} - v_{fruk}$$

$$\frac{d}{dt} Fru1p_{cyt} = +v_{fruk} - v_{aldB}$$

$$\frac{d}{dt} Fru16P_2 = v_{PFK1} - v_{FBP1} - v_{ALD}$$

$$\frac{d}{dt} Fru26P_2 = v_{PFK2} - v_{FBP2}$$

$$\frac{d}{dt} Fru6P = v_{GPI} - v_{PFK1} - v_{PFK2} + v_{FBP1} + v_{FBP2}$$

$$\frac{d}{dt} GAP = v_{ALD} + v_{TPI} - v_{GAPDH} + v_{triok}$$

$$\frac{d}{dt} Glc = v_{GLUT2} - v_{GK} + v_{GlcTER} - v_{aldr}$$

$$\frac{d}{dt} Glc_{ER} = v_{G6PER} - v_{GlcTER}$$

$$\frac{d}{dt} Glc1P = v_{GP} - v_{G1PI} - v_{UGT}$$

$$\frac{d}{dt} Glc6P = v_{GK} + v_{G6PTER} - v_{GPI} + v_{G1PI}$$

$$\frac{d}{dt} Glc6P_{ER} = -v_{G6PER} - v_{Glc6PTER}$$

$$\frac{d}{dt} Gra_{cyt} = +v_{aldB} - v_{triok}$$

$$\frac{d}{dt}Lac = v_{LacT} + v_{LDH}$$

$$\frac{d}{dt}Mal = v_{MalT} - v_{MDH} + v_{PyrMalT}$$

$$\frac{d}{dt}Mal_{mito} = -v_{MalT} - v_{MDH_{mito}} - v_{PyrMalT}$$

$$\frac{d}{dt}OA = v_{MDH} - v_{PEPCK}$$

$$\frac{d}{dt}OA_{mito} = v_{PC} - v_{PEPCK_{mito}} + v_{MDH_{mito}}$$

$$\frac{d}{dt}PEP = v_{EN} - v_{PK} + v_{PEPCK} - v_{PEPT}$$

$$\frac{d}{dt}PEP_{mito} = v_{PEPCK_{mito}} + v_{PEPT}$$

$$\frac{d}{dt}13P2G = v_{GAPDH} - v_{PGK}$$

$$\frac{d}{dt}23P2G = v_{BPGM} - v_{BPGP}$$

$$\frac{d}{dt}2PG = v_{PGM} - v_{EN}$$

$$\frac{d}{dt}3PG = v_{PGK} - v_{PGM}$$

$$\frac{d}{dt}Pyr = v_{PK} - v_{LDH} - v_{PyrT} - v_{PyrMalT}$$

$$\frac{d}{dt}Pyr_{mito} = v_{PyrT} - v_{PC} + v_{PyrMalT}$$

$$\frac{d}{dt}Sorb_{cyt} = +v_{aldr} + v_{sordh}$$

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