

Supplementary Information for:

Human kidney organoids reveal the role of glutathione in Fabry disease

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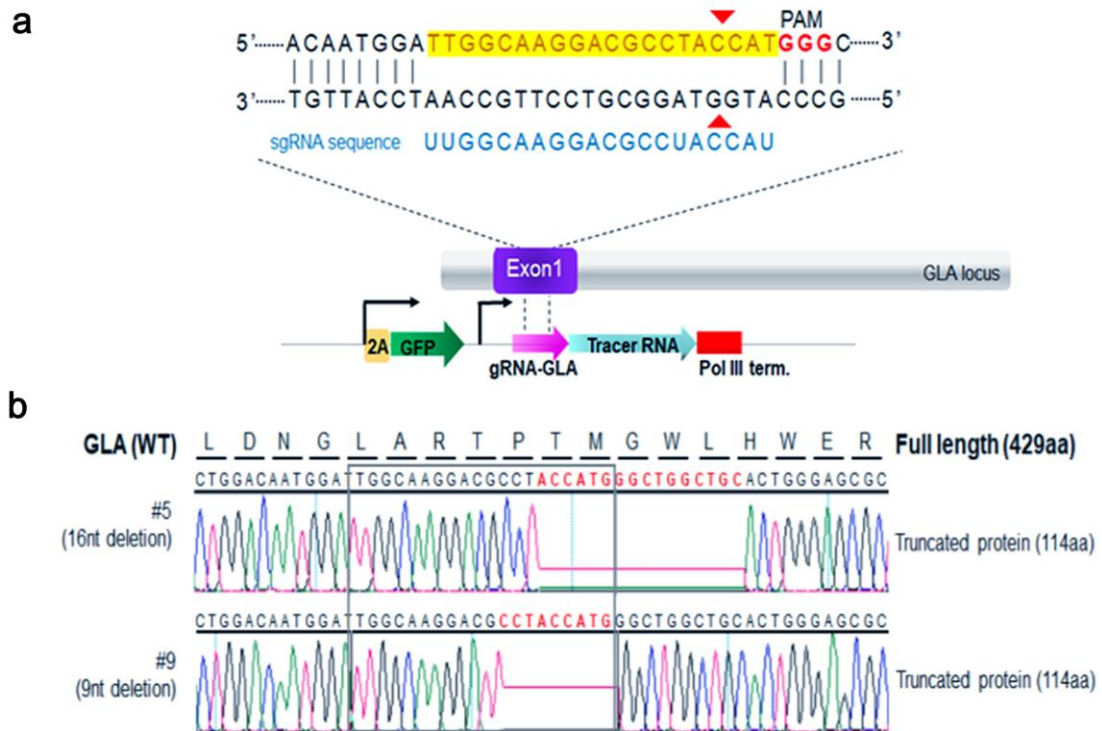
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Supplementary Figures

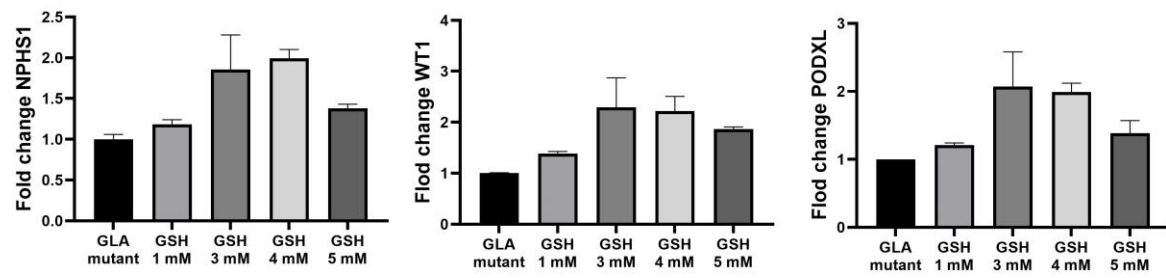
Supplementary Figure 1 GLA knockout human iPSCs generated using CRISPR-Cas9. a Schematic diagram of the single-guide RNA targeting site located exon1 of GLA gene. **b** Clones #5 and #9 Sequence after the knockout GLA target gene

Supplementary Figure 2 Gene expression of podocyte makers of GLA mutant kidney organoids treated with GSH by concentration qRT-PCR analysis of NPHS1, WT1 and PODXL (podocyte markers) at GLA mutant kidney organoids with 1 mM to 5mM GSH.

Supplementary Figure 1



Supplementary Figure 2



Supplementary Tables

Supplementary Table 1 Top 50 Gene list of log₂ Fold change

TYPE	Gene name	log2 Fold change	p-value	TYPE	Gene name	log2 Fold change	p-value
Down regulate	EGR1	-1.004	0.00124	Up regulate	MIR18B	0.842	0.00053
	CHCHD2	-0.878	0.0293		RNU5D-1	0.722	0.00258
	LOC101927372	-0.736	0.00217		LOC105376438	0.707	0.00078
	ZNF585B	-0.582	0.07527		SNORA79	0.698	0.07678
	ZNF229	-0.57	0.00281		LOC105369508	0.687	0.06874
	FOS	-0.556	0.01384		SCARNA15	0.674	0.0276
	LPAL2	-0.541	0.06027		LOC105375032	0.65	0.00657
	BCRP3	-0.539	0.01006		SNORA72	0.641	0.00031
	LBX1	-0.529	0.00227		MIR548F2	0.608	0.0009
	MIR519A1	-0.491	0.04004		SNORD103C	0.592	0.00493
	LOC644919	-0.49	0.00501		LOC105369507	0.582	0.04897
	HIC1	-0.487	0.01558		MIR548H1	0.555	0.11592
	MIR4653	-0.468	0.07066		SCARNA1	0.552	0.00593
	MIR4779	-0.463	0.00458		RNU5E-1	0.541	3.00E-05
	MIR4490	-0.459	0.04868		SNORD90	0.532	0.13779
	MIR221	-0.457	0.00743		SCARNA23	0.521	0.06656
	SNORD124	-0.452	0.12936		TAS2R50	0.516	0.01066
	MIR3926-2	-0.445	0.00361		MIR363	0.514	0.05867
	GSTM5	-0.445	0.153		PMCH	0.5	0.02111
	MIR514B	-0.441	0.12027		SNORD116-25	0.5	0.00042
	CES4A	-0.438	0.00287		SNORD63	0.498	0.01327
	KIAA0895L	-0.43	0.00138		MIR1284	0.492	0.00366
	LOC105369895	-0.426	0.01003		MIR19B2	0.48	0.14025
	CCL23	-0.423	0.01106		LOC101927055	0.473	0.02
	OR4A5	-0.423	0.02728		MIR4802	0.461	0.02749
	MIR3188	-0.42	0.04245		MIR1206	0.459	0.05769
	KRTAP5-4	-0.417	0.01896		RNU5B-1	0.458	0.14358
	AOC2	-0.415	0.00954		EVI2A	0.451	0.00763
	MIR4661	-0.414	0.18795		TAS2R30	0.45	0.00999
	TGFB1I1	-0.412	0.00043		MIR4782	0.44	0.49703
	UBE2Q2P1	-0.411	0.01276		MIR603	0.438	0.05457
	LOC100506470	-0.406	0.01841		SCARNA8	0.436	0.01794
	LOC440300	-0.406	0.26228		PRH2	0.429	0.01097
	MIR4497	-0.4	0.21974		LOC105373257	0.427	0.00072
	RNF208	-0.399	0.02241		SNORA65	0.427	0.00433
	LYZL2	-0.399	0.19027		MIR374A	0.423	0.13185
	FOSB	-0.39	0.10266		UBE2CP5	0.419	0.00145
	LOC100500773	-0.388	0.18784		LOC101927827	0.418	0.02219
	MSTO2P	-0.387	0.00357		MIR4499	0.407	0.04382
	SNORD116-18	-0.386	0.01204		DLEU2L	0.402	0.08457
	CTSG	-0.386	0.04886		C9orf84	0.4	0.01799
	KRTAP5-5	-0.384	0.18508		TRAJ21	0.399	0.13483
	HOXD10	-0.384	0.00345		MIR487A	0.398	0.05652
	MIR520B	-0.382	0.2236		MIR181A1	0.398	0.08131
	SPRY4	-0.38	0.00996		TAS2R20	0.398	0.02409
	LOC105374468	-0.38	0.00284		MIR1278	0.394	0.0005
	LOC440173	-0.378	0.01542		SNORD16	0.394	0.00037
	LOC102723832	-0.374	0.07459		HIF1A-AS2	0.39	0.00697
	TNS2	-0.374	0.0202		LOC105370765	0.389	0.025
	FAM86JP	-0.373	0.045		LRRC19	0.388	0.02835

Supplementary Table 2 Top 10 downregulated and 10 upregulated leading-edge genes in GLA-mutant Fabry kidney organoids compared with WT kidney organoids

TYPE	NAME	ES	NES	p-val	FDR
Downregulated	KEGG_GLUTATHIONE_METABOLISM	-0.44	-1.44	0.032	0.309
	KEGG_JAK_STAT_SIGNALING_PATHWAY	-0.36	-1.36	0.023	0.31
	KEGG_LYSOSOME	-0.39	-1.43	0.005	0.313
	KEGG_ADHERENS_JUNCTION	-0.4	-1.37	0.04	0.316
	KEGG_ETHER_LIPID_METABOLISM	-0.46	-1.37	0.072	0.316
	KEGG_CALCIIUM_SIGNALING_PATHWAY	-0.36	-1.37	0.011	0.318
	KEGG_THYROID_CANCER	-0.5	-1.46	0.049	0.319
	KEGG_GNRH_SIGNALING_PATHWAY	-0.4	-1.42	0.02	0.322
	KEGG_SYSTEMIC_LUPUS_ERYTHEMATOSUS	-0.42	-1.39	0.041	0.322
	KEGG_TOLL_LIKE_RECEPTOR_SIGNALING_PATHWAY	-0.38	-1.38	0.034	0.322
Upregulated	KEGG_PROTEIN_EXPORT	0.49	1.69	0.013	0.153
	KEGG_TASTE_TRANSDUCTION	0.35	1.48	0.016	0.32
	KEGG_ASCORBATE_AND_ALDARATE_METABOLISM	0.46	1.47	0.061	0.225
	KEGG_PENTOSE_AND_GLUCURONATE_INTERCONVERSIONS	0.38	1.28	0.157	0.568
	KEGG_FATTY_ACID_METABOLISM	0.28	1.1	0.273	1
	KEGG_NICOTINATE_AND_NICOTINAMIDE_METABOLISM	0.31	1.1	0.336	1
	KEGG_STARCH_AND_SUCROSE_METABOLISM	0.27	1.08	0.263	0.962
	KEGG_NITROGEN_METABOLISM	0.28	0.94	0.558	1
	KEGG_RETINOL_METABOLISM	0.22	0.94	0.638	1
	KEGG_DRUG_METABOLISM_OTHER_ENZYMES	0.22	0.91	0.636	1