

Cysteamine-bicalutamide combination therapy corrects proximal tubule phenotype in cystinosis

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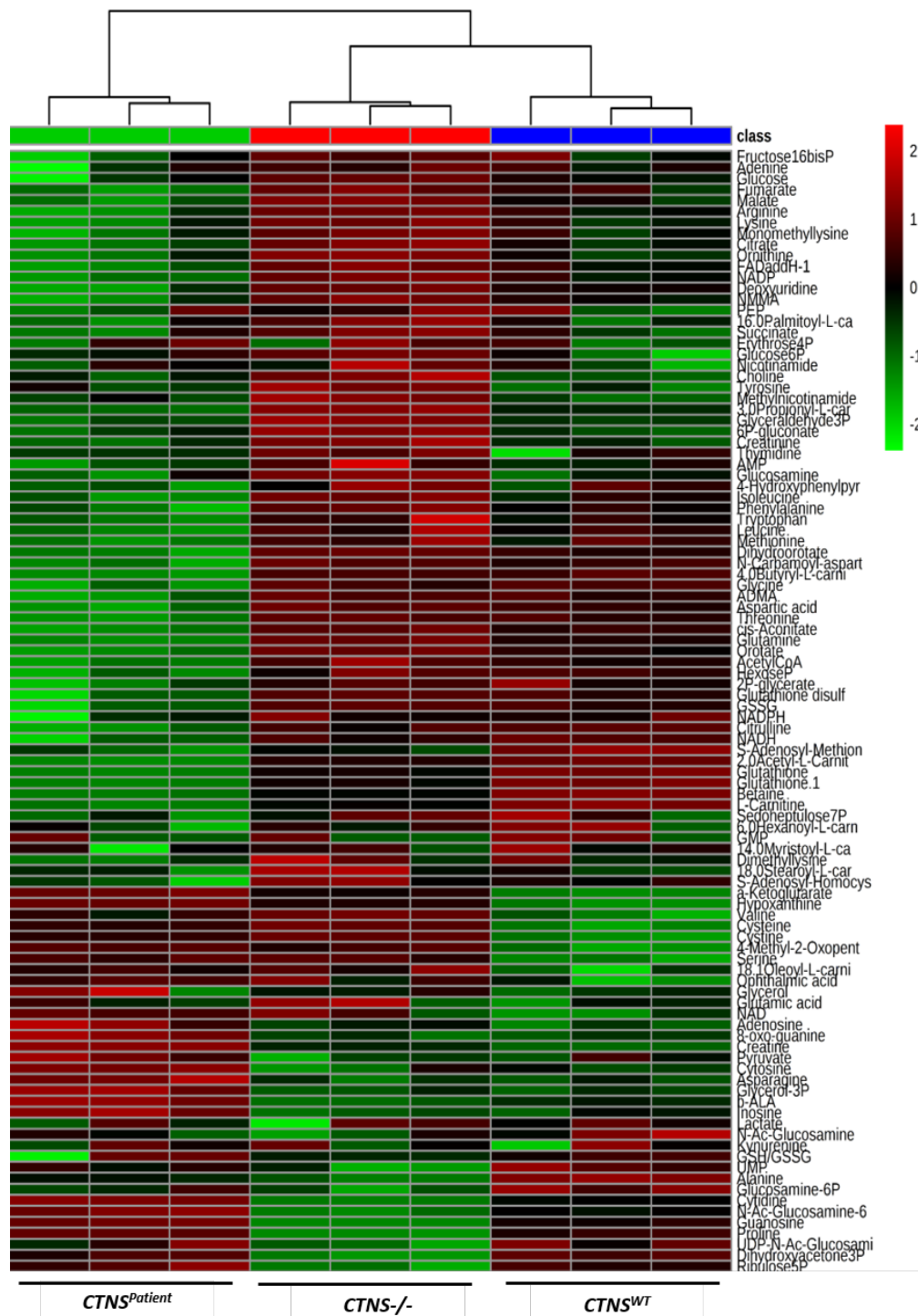
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Running title

Combination treatment for cystinosis

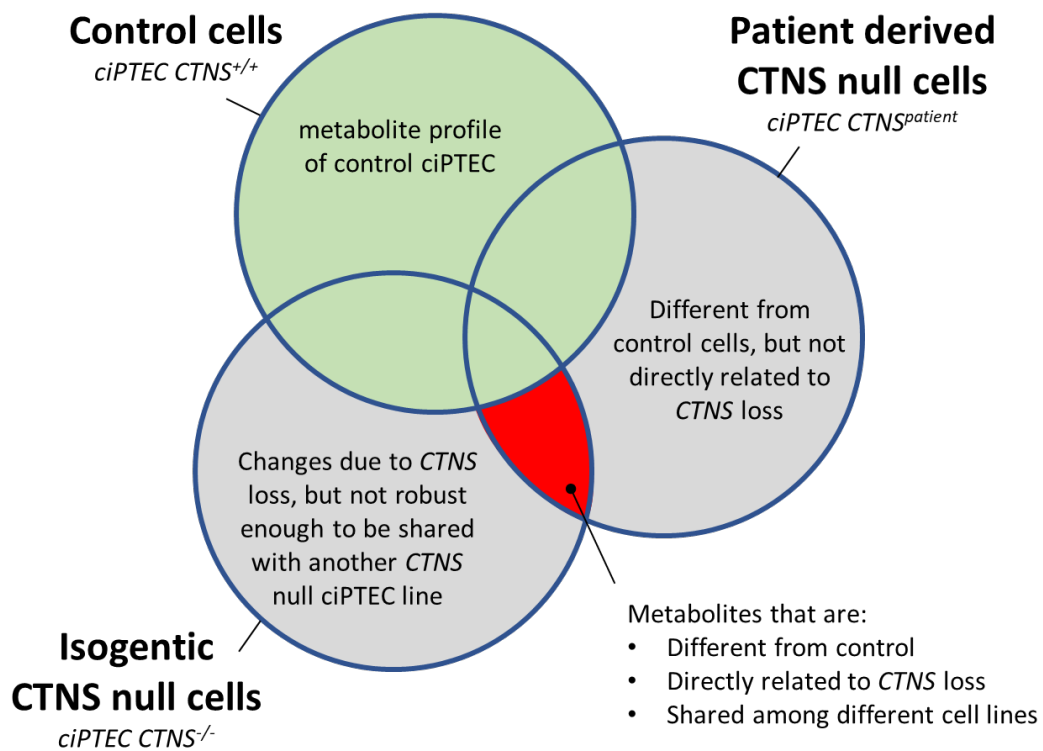
APPENDIX

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Appendix figure S1. Heatmap analysis of metabolites

Heatmap analysis of metabolites distinctively expressed in control (*CTNS*^{WT}), CRISPR-generated cystinotic cells (*CTNS*^{-/-}), and patient-derived cystinotic cells (*CTNS*^{Patient}).



Appendix figure S2. Identification of robustly changed metabolites in *CTNS* null cells

Schematic overview of metabolomic analysis to robustly identify metabolites changed due to *CTNS* loss.

Appendix Table S1. P-values and statistical tests in figures.

Figure 1	P-Value	comparison	Statistical test
1A	<0,0001	CTNSWT VS CTNS-/-	One-way ANOVA
	<0,0001	CTNSWT VS CTNSPatient	One-way ANOVA
1B	<0,0001	CTNSWT VS CTNS-/-	One-way ANOVA
	<0,0001	CTNSWT VS CTNSPatient	One-way ANOVA
1C	0,0325	CTNSWT VS CTNS-/-	One-way ANOVA
	0,0463	CTNSWT VS CTNSPatient	One-way ANOVA
1E	0,1185	Untreated CTNSWT VS untreated CTNSPatient	Unpaired t-test
	0,0028	Bafilomycin treated CTNSWT VS Bafilomycin treated CTNSPatient	Unpaired t-test
1G	0,7676	Untreated CTNSWT VS untreated CTNS-/-	Unpaired t-test
	0,3832	Untreated CTNSWT VS untreated CTNSPatient	Unpaired t-test
	0,0174	Bafilomycin treated CTNSWT VS Bafilomycin treated CTNS-/-	Unpaired t-test
	0,0628	Bafilomycin treated CTNSWT VS Bafilomycin treated CTNSPatient	Unpaired t-test
1H	0,1496	Untreated CTNSWT VS untreated CTNS-/-	Unpaired t-test
	0,7092	Untreated CTNSWT VS untreated CTNSPatient	Unpaired t-test
	0,0110	Bafilomycin treated CTNSWT VS Bafilomycin treated CTNS-/-	Unpaired t-test
	0,0003	Bafilomycin treated CTNSWT VS Bafilomycin treated CTNSPatient	Unpaired t-test
1I	0,0025	CTNSWT VS CTNS-/-	One-way ANOVA
	0,0135	CTNSWT VS CTNSPatient	One-way ANOVA
1J	0,5610	CTNSWT VS CTNS-/-	One-way ANOVA
	0,0129	CTNSWT VS CTNSPatient	One-way ANOVA
Figure 2	P-Value	comparison	Statistical test
2D	<0,0001	CTNSWT VS CTNS-/- - Cystine	Unpaired t-test
	<0,0001	CTNSWT VS CTNSPatient- Cystine	Unpaired t-test
	<0,0001	CTNSWT VS CTNS-/- - Cysteine	Unpaired t-test
	<0,0001	CTNSWT VS CTNSPatient- Cysteine	Unpaired t-test
	<0,0001	CTNSWT VS CTNS-/- - AKG	Unpaired t-test
	<0,0001	CTNSWT VS CTNSPatient- AKG	Unpaired t-test
	<0,0001	CTNSWT VS CTNS-/- - Serine	Unpaired t-test
	<0,0001	CTNSWT VS CTNSPatient- Serine	Unpaired t-test
	<0,0001	CTNSWT VS CTNS-/- - Hypoxanthine	Unpaired t-test
	<0,0001	CTNSWT VS CTNSPatient- Hypoxanthine	Unpaired t-test
	0,0019	CTNSWT VS CTNS-/- - Oleoyl-L-carnitine	Unpaired t-test
	0,0008	CTNSWT VS CTNSPatient- Oleoyl-L-carnitine	Unpaired t-test
	<0,0001	CTNSWT VS CTNS-/- - Betaine	Unpaired t-test
	<0,0001	CTNSWT VS CTNSPatient- Betaine	Unpaired t-test
	0,0298	CTNSWT VS CTNS-/- - L-carnitine	Unpaired t-test
	<0,0001	CTNSWT VS CTNSPatient- L-carnitine	Unpaired t-test
	<0,0001	CTNSWT VS CTNS-/- - Glucosamine-6P	Unpaired t-test
	<0,0001	CTNSWT VS CTNSPatient- Glucosamine-6P	Unpaired t-test
2E	0,0095	Control VS Patient	Mann-Whitney test
2I	0,0002	CTNSWT VS CTNS-/- - AKGDH	Unpaired t-test
	<0,0001	CTNSWT VS CTNS-/- - LIPA	Unpaired t-test
	0,0210	CTNSWT VS CTNS-/- - ACP2	Unpaired t-test

	0,0118	CTNSWT VS CTNS-/- - CTSS	Unpaired t-test
	0,0023	CTNSWT VS CTNS-/- - CTSC	Unpaired t-test
	0,0001	CTNSWT VS CTNS-/- - IGF2R	Unpaired t-test
	0,0094	CTNSWT VS CTNS-/- - SORT1	Unpaired t-test
	0,0005	CTNSWT VS CTNS-/- - CAT	Unpaired t-test
	0,0052	CTNSWT VS CTNS-/- - CTSA	Unpaired t-test
	0,0035	CTNSWT VS CTNS-/- - LDH	Unpaired t-test
	0,0001	CTNSWT VS CTNS-/- - SOD	Unpaired t-test
Figure 3	P-Value	comparison	Statistical test
3A	0,0084	CTNSWT VS CTNS-/-	One-way ANOVA
	0,0049	CTNSWT VS CTNSPatient	One-way ANOVA
3B	<0,0001	CTNSWT FED Condition VS CTNSWT Starvation Condition	One-way ANOVA
	0,0004	CTNSWT FED Condition VS CTNSWT DMKG Treated Condition	One-way ANOVA
	0,0007	CTNSWT Starvation Condition VS CTNSWT DMKG Treated Condition	Unpaired t-test
3C	<0,0001	CTNS-/- FED Condition VS CTNS-/- Starvation Condition	One-way ANOVA
	<0,0001	CTNS-/- FED Condition VS CTNS-/- DMKG Treated Condition	One-way ANOVA
	0,0028	CTNS-/- Starvation Condition VS CTNS-/- DMKG Treated Condition	Unpaired t-test
3D	<0,0001	CTNSPatient FED Condition VS CTNSPatient Starvation Condition	One-way ANOVA
	<0,0001	CTNSPatient FED Condition VS CTNSPatient DMKG treated Condition	One-way ANOVA
	0,0012	CTNSPatient Starvation Condition VS CTNSPatient DMKG treated Condition	Unpaired t-test
3E	<0,0001	CTNSWT VS CTNS-/- (Starvation)	One-way ANOVA
	<0,0001	CTNSWT VS CTNSPatient (Starvation)	One-way ANOVA
	<0,0001	CTNSWT VS CTNS-/- (Starvation + DMKG)	One-way ANOVA
	<0,0001	CTNSWT VS CTNSPatient (Starvation + DMKG)	One-way ANOVA
3G	<0,0001	CTNSWT VS CTNS-/- (Starvation)	One-way ANOVA
	<0,0001	CTNSWT VS CTNSPatient (Starvation)	One-way ANOVA
	<0,0001	CTNSWT VS CTNS-/- (Starvation + DMKG)	One-way ANOVA
	<0,0001	CTNSWT VS CTNSPatient (Starvation + DMKG)	One-way ANOVA
3I	0,0001	CTNSWT FED condition VS CTNSWT BafA1 treated	One-way ANOVA
	0,9517	CTNSWT FED condition VS CTNSWT Starved condition	One-way ANOVA
	0,0998	CTNSWT FED condition VS CTNSWT DMKG treated	One-way ANOVA
	0,0014	CTNS-/- FED condition VS CTNS-/- BafA1 treated	One-way ANOVA
	>0,9999	CTNS-/- FED condition VS CTNS-/- Starved condition	One-way ANOVA
	0,0004	CTNS-/- FED condition VS CTNS-/- DMKG treated	One-way ANOVA
	0,0007	CTNSPatient FED condition VS CTNSPatient BafA1 treated	One-way ANOVA
	0,9694	CTNSPatient FED condition VS CTNSPatient Starved condition	One-way ANOVA
	0,0166	CTNSPatient FED condition VS CTNSPatient DMKG treated	One-way ANOVA
Figure 4	P-Value	comparison	Statistical test
4A			
Glutathione	0,8377	CTNSWT no treatment VS CTNS-/- no treatment	One-way ANOVA
	<0,0001	CTNSWT no treatment VS CTNS-/- cysteamine	One-way ANOVA
	0,0507	CTNSWT no treatment VS CTNS-/- Bicalutamide	One-way ANOVA
	<0,0001	CTNSWT no treatment VS. CTNS-/- Combination	One-way ANOVA
	<0,0001	CTNS-/- Bicalutamide VS CTNS-/- Combination	Unpaired t-test
Cystine	<0,0001	CTNSWT no treatment VS CTNS-/- no treatment	One-way ANOVA

	0,2649	CTNSWT no treatment VS CTNS-/- cysteamine	One-way ANOVA
	<0,0001	CTNSWT no treatment VS CTNS-/- Bicalutamide	One-way ANOVA
	0,0013	CTNSWT no treatment VS. CTNS-/- Combination	One-way ANOVA
	<0,0001	CTNS-/- Bicalutamide VS CTNS-/- Combination	Unpaired t-test
Cysteine	<0,0001	CTNSWT no treatment VS CTNS-/- no treatment	One-way ANOVA
	0,6000	CTNSWT no treatment VS CTNS-/- cysteamine	One-way ANOVA
	<0,0001	CTNSWT no treatment VS CTNS-/- Bicalutamide	One-way ANOVA
	0,0194	CTNSWT no treatment VS. CTNS-/- Combination	One-way ANOVA
	<0,0001	CTNS-/- Bicalutamide VS CTNS-/- Combination	Unpaired t-test
AKG	0,0015	CTNSWT no treatment VS CTNS-/- no treatment	One-way ANOVA
	0,0226	CTNSWT no treatment VS CTNS-/- cysteamine	One-way ANOVA
	<0,0001	CTNSWT no treatment VS CTNS-/- Bicalutamide	One-way ANOVA
	<0,0001	CTNSWT no treatment VS. CTNS-/- Combination	One-way ANOVA
	0,0467	CTNS-/- Bicalutamide VS CTNS-/- Combination	Unpaired t-test
Serine	<0,0001	CTNSWT no treatment VS CTNS-/- no treatment	One-way ANOVA
	<0,0001	CTNSWT no treatment VS CTNS-/- cysteamine	One-way ANOVA
	0,4286	CTNSWT no treatment VS CTNS-/- Bicalutamide	One-way ANOVA
	0,7028	CTNSWT no treatment VS. CTNS-/- Combination	One-way ANOVA
Betaine	<0,0001	CTNSWT no treatment VS CTNS-/- no treatment	One-way ANOVA
	<0,0001	CTNSWT no treatment VS CTNS-/- cysteamine	One-way ANOVA
	0,0191	CTNSWT no treatment VS CTNS-/- Bicalutamide	One-way ANOVA
	0,0076	CTNSWT no treatment VS. CTNS-/- Combination	One-way ANOVA
Oleoy-L-Carnitine	<0,0001	CTNSWT no treatment VS CTNS-/- no treatment	One-way ANOVA
	<0,0001	CTNSWT no treatment VS CTNS-/- cysteamine	One-way ANOVA
	0,0011	CTNSWT no treatment VS CTNS-/- Bicalutamide	One-way ANOVA
	0,0004	CTNSWT no treatment VS. CTNS-/- Combination	One-way ANOVA
Palmitoyl-L-carnitine	<0,0001	CTNSWT no treatment VS CTNS-/- no treatment	One-way ANOVA
	<0,0001	CTNSWT no treatment VS CTNS-/- cysteamine	One-way ANOVA
	0,0054	CTNSWT no treatment VS CTNS-/- Bicalutamide	One-way ANOVA
	0,0003	CTNSWT no treatment VS. CTNS-/- Combination	One-way ANOVA
Malate	<0,0001	CTNSWT no treatment VS CTNS-/- no treatment	One-way ANOVA
	<0,0001	CTNSWT no treatment VS CTNS-/- cysteamine	One-way ANOVA
	<0,0001	CTNSWT no treatment VS CTNS-/- Bicalutamide	One-way ANOVA
	0,1157	CTNSWT no treatment VS. CTNS-/- Combination	One-way ANOVA
	0,0003	CTNS-/- Bicalutamide VS CTNS-/- Combination	Unpaired t-test
8-oxo-guanine	<0,0001	CTNSWT no treatment VS CTNS-/- no treatment	One-way ANOVA
	<0,0001	CTNSWT no treatment VS CTNS-/- cysteamine	One-way ANOVA
	0,0011	CTNSWT no treatment VS CTNS-/- Bicalutamide	One-way ANOVA
	0,0004	CTNSWT no treatment VS. CTNS-/- Combination	One-way ANOVA
pyruvate	<0,0001	CTNSWT no treatment VS CTNS-/- no treatment	One-way ANOVA
	0,0126	CTNSWT no treatment VS CTNS-/- cysteamine	One-way ANOVA
	<0,0001	CTNSWT no treatment VS CTNS-/- Bicalutamide	One-way ANOVA
	0,0002	CTNSWT no treatment VS. CTNS-/- Combination	One-way ANOVA
	0,0302	CTNS-/- Bicalutamide VS CTNS-/- Combination	Unpaired t-test
Citrate	0,0006	CTNSWT no treatment VS CTNS-/- no treatment	One-way ANOVA
	0,0005	CTNSWT no treatment VS CTNS-/- cysteamine	One-way ANOVA
	0,0003	CTNSWT no treatment VS CTNS-/- Bicalutamide	One-way ANOVA
	0,0744	CTNSWT no treatment VS. CTNS-/- Combination	One-way ANOVA
	0,0063	CTNS-/- Bicalutamide VS CTNS-/- Combination	Unpaired t-test

Glutamine	<0,0001	CTNSWT no treatment VS CTNS-/- no treatment	One-way ANOVA
	<0,0001	CTNSWT no treatment VS CTNS-/- cysteamine	One-way ANOVA
	0,5643	CTNSWT no treatment VS CTNS-/- Bicalutamide	One-way ANOVA
	<0,0001	CTNSWT no treatment VS. CTNS-/- Combination	One-way ANOVA
	<0,0001	CTNS-/- Bicalutamide VS CTNS-/- Combination	Unpaired t-test
Guanine	0,0097	CTNSWT no treatment VS CTNS-/- no treatment	One-way ANOVA
	0,0021	CTNSWT no treatment VS CTNS-/- cysteamine	One-way ANOVA
	0,9620	CTNSWT no treatment VS CTNS-/- Bicalutamide	One-way ANOVA
	0,8590	CTNSWT no treatment VS. CTNS-/- Combination	One-way ANOVA
cAMP	0,0055	CTNSWT no treatment VS CTNS-/- no treatment	One-way ANOVA
	0,0010	CTNSWT no treatment VS CTNS-/- cysteamine	One-way ANOVA
	0,9999	CTNSWT no treatment VS CTNS-/- Bicalutamide	One-way ANOVA
	0,0783	CTNSWT no treatment VS. CTNS-/- Combination	One-way ANOVA
	0,0144	CTNS-/- Bicalutamide VS CTNS-/- Combination	Unpaired t-test
4E			
AKGDH	0,0331	CTNSWT no treatment VS CTNS-/- no treatment	One-way ANOVA
	0,0030	CTNSWT no treatment VS CTNS-/- cysteamine	One-way ANOVA
	0,0256	CTNSWT no treatment VS CTNS-/- Bicalutamide	One-way ANOVA
	0,0008	CTNSWT no treatment VS. CTNS-/- Combination	One-way ANOVA
GLUD1;GLUD2	0,0053	CTNSWT no treatment VS CTNS-/- no treatment	One-way ANOVA
	0,0539	CTNSWT no treatment VS CTNS-/- cysteamine	One-way ANOVA
	0,0197	CTNSWT no treatment VS CTNS-/- Bicalutamide	One-way ANOVA
	0,0810	CTNSWT no treatment VS. CTNS-/- Combination	One-way ANOVA
IGF2R	0,0015	CTNSWT no treatment VS CTNS-/- no treatment	One-way ANOVA
	0,0885	CTNSWT no treatment VS CTNS-/- cysteamine	One-way ANOVA
	0,4080	CTNSWT no treatment VS CTNS-/- Bicalutamide	One-way ANOVA
	0,5544	CTNSWT no treatment VS. CTNS-/- Combination	One-way ANOVA
GSTK1	0,0008	CTNSWT no treatment VS CTNS-/- no treatment	One-way ANOVA
	0,3489	CTNSWT no treatment VS CTNS-/- cysteamine	One-way ANOVA
	0,9846	CTNSWT no treatment VS CTNS-/- Bicalutamide	One-way ANOVA
	0,7868	CTNSWT no treatment VS. CTNS-/- Combination	One-way ANOVA
COX6B1	0,0135	CTNSWT no treatment VS CTNS-/- no treatment	One-way ANOVA
	0,9098	CTNSWT no treatment VS CTNS-/- cysteamine	One-way ANOVA
	0,0864	CTNSWT no treatment VS CTNS-/- Bicalutamide	One-way ANOVA
	0,0057	CTNSWT no treatment VS. CTNS-/- Combination	One-way ANOVA
ACACA	0,0005	CTNSWT no treatment VS CTNS-/- no treatment	One-way ANOVA
	<0,0001	CTNSWT no treatment VS CTNS-/- cysteamine	One-way ANOVA
	0,0709	CTNSWT no treatment VS CTNS-/- Bicalutamide	One-way ANOVA
	0,0228	CTNSWT no treatment VS. CTNS-/- Combination	One-way ANOVA
GLS	<0,0001	CTNSWT no treatment VS CTNS-/- no treatment	One-way ANOVA
	<0,0001	CTNSWT no treatment VS CTNS-/- cysteamine	One-way ANOVA
	0,0003	CTNSWT no treatment VS CTNS-/- Bicalutamide	One-way ANOVA
	<0,0001	CTNSWT no treatment VS. CTNS-/- Combination	One-way ANOVA
CASP3	<0,0001	CTNSWT no treatment VS CTNS-/- no treatment	One-way ANOVA
	<0,0001	CTNSWT no treatment VS CTNS-/- cysteamine	One-way ANOVA
	<0,0001	CTNSWT no treatment VS CTNS-/- Bicalutamide	One-way ANOVA
	<0,0001	CTNSWT no treatment VS. CTNS-/- Combination	One-way ANOVA
NPC1	0,0132	CTNSWT no treatment VS CTNS-/- no treatment	One-way ANOVA
	0,0500	CTNSWT no treatment VS CTNS-/- cysteamine	One-way ANOVA
	>0,9999	CTNSWT no treatment VS CTNS-/- Bicalutamide	One-way ANOVA
	0,0490	CTNSWT no treatment VS. CTNS-/- Combination	One-way ANOVA

Figure 5	P-Value	comparison	Statistical test
5A	0,0891	CTNS-/- DMKG VS CTNS-/- DMKG and Cysteamine	One-way ANOVA
	0,0002	CTNS-/- DMKG VS CTNS-/- DMKG and Bicalutamide	One-way ANOVA
	0,0013	CTNS-/- DMKG VS CTNS-/- DMKG and Cysteamine and Bicalutamide	One-way ANOVA
5B	0,0002	CTNS-/- fed VS CTNS-/- BafA1	One-way ANOVA
	<0,0001	CTNS-/- fed VS CTNS-/- DMKG	One-way ANOVA
	0,0326	CTNS-/- fed VS CTNS-/- DMKG and Bicalutamide	One-way ANOVA
	<0,0001	CTNS-/- fed VS CTNS-/- DMKG and Cysteamine	One-way ANOVA
	0,5640	CTNS-/- fed VS CTNS-/- DMKG and Cysteamine and Bicalutamide	One-way ANOVA
	0,0005	CTNS-/- DMKG VS CTNS-/- DMKG and Bicalutamide	Unpaired t-test
	0,2782	CTNS-/- DMKG VS CTNS-/- DMKG and Cysteamine	Unpaired t-test
	<0,0001	CTNS-/- DMKG VS CTNS-/- DMKG and Cysteamine and Bicalutamide	Unpaired t-test
	0,0497	CTNS-/- DMKG and Bicalutamide VS CTNS-/- DMKG and Cysteamine and Bicalutamide	Unpaired t-test
5C	<0,0001	CTNS-/- fed VS CTNS-/- starvation	One-way ANOVA
	<0,0001	CTNS-/- fed VS CTNS-/- DMKG	One-way ANOVA
	<0,0001	CTNS-/- fed VS CTNS-/- DMKG and Bicalutamide	One-way ANOVA
	<0,0001	CTNS-/- fed VS CTNS-/- DMKG and Cysteamine	One-way ANOVA
	<0,0001	CTNS-/- fed VS CTNS-/- DMKG and Cysteamine and Bicalutamide	One-way ANOVA
	<0,0001	CTNS-/- starvation VS CTNS-/- DMKG	Unpaired t-test
	<0,0001	CTNS-/- DMKG VS CTNS-/- DMKG and Bicalutamide	Unpaired t-test
	<0,0001	CTNS-/- DMKG VS CTNS-/- DMKG and Cysteamine	Unpaired t-test
	<0,0001	CTNS-/- DMKG VS CTNS-/- DMKG and Cysteamine and Bicalutamide	Unpaired t-test
	0,8017	CTNS-/- DMKG and Bicalutamide VS CTNS-/- DMKG and Cysteamine	Unpaired t-test
	0,0021	CTNS-/- DMKG and Bicalutamide VS CTNS-/- DMKG and Cysteamine and Bicalutamide	Unpaired t-test
	<0,0001	CTNS-/- DMKG and Cysteamine VS CTNS-/- DMKG and Cysteamine and Bicalutamide	Unpaired t-test
5E	0,0007	CTNSWT no Bicalutamide VS CTNSWT with Bicalutamide	One-way ANOVA
	0,0055	CTNSWT no Bicalutamide VS CTNS-/- no Bicalutamide	One-way ANOVA
	0,4194	CTNSWT no Bicalutamide VS CTNS-/- with Bicalutamide	One-way ANOVA
	0,0009	CTNS-/- no Bicalutamide VS CTNS-/- with Bicalutamide	One-way ANOVA
5F	<0,0001	CTNSWT VS CTNS-/- NT	One-way ANOVA
	<0,0001	CTNSWT VS CTNS-/- Bicalutamide	One-way ANOVA
	0,0107	CTNSWT VS CTNS-/- Cysteamine	One-way ANOVA
	0,6945	CTNSWT VS CTNS-/- Combination	One-way ANOVA
	0,0304	CTNS-/- Cysteamine VS CTNS-/- Combination	Unpaired t-test
5G	<0,0001	CTNSWT VS CTNSPatient NT	One-way ANOVA
	<0,0001	CTNSWT VS CTNSPatient Bicalutamide	One-way ANOVA
	0,0097	CTNSWT VS CTNSPatient Cysteamine	One-way ANOVA
	0,9750	CTNSWT VS CTNSPatient Combination	One-way ANOVA
	<0,0001	CTNSPatient Cysteamine VS CTNSPatient Combination	Unpaired t-test
Figure 6	P-Value	comparison	Statistical test
6B	0,9987	CTNSWT-1 VS CTNSWT-2	One-way ANOVA

	0,0035	CTNSWT-1 VS CTNSPatient-1	One-way ANOVA
	0,0004	CTNSWT-1 VS CTNSPatient-2	One-way ANOVA
	0,0027	CTNSWT-2 VS CTNSPatient-1	One-way ANOVA
	0,0003	CTNSWT-2 VS CTNSPatient-2	One-way ANOVA
	0,8220	CTNSPatient-1 VS CTNSPatient-2	One-way ANOVA
6C	<0,0001	CTNSPatient-1 NT VS CTNSPatient-1 Bicalutamide	One-way ANOVA
	<0,0001	CTNSPatient-1 NT VS CTNSPatient-1 Cysteamine	One-way ANOVA
	<0,0001	CTNSPatient-1 NT VS CTNSPatient-1 Combination	One-way ANOVA
	0,0218	CTNSPatient-1 Cysteamine VS CTNSPatient-1 Combination	Unpaired t-test
6D	0,1173	CTNSPatient-2 NT VS CTNSPatient-2 Bicalutamide	One-way ANOVA
	<0,0001	CTNSPatient-2 NT VS CTNSPatient-2 Cysteamine	One-way ANOVA
	<0,0001	CTNSPatient-2 NT VS CTNSPatient-2 Combination	One-way ANOVA
	0,0030	CTNSPatient-2 Cysteamine VS CTNSPatient-2 Combination	Unpaired t-test
6E	0,3417	CTNSPatient-1 NT VS CTNSPatient-1 Bicalutamide - AKG level	One-way ANOVA
	0,0671	CTNSPatient-1 NT VS CTNSPatient-1 Cysteamine - AKG level	One-way ANOVA
	0,1765	CTNSPatient-1 NT VS CTNSPatient-1 Combination - AKG level	One-way ANOVA
	0,0033	CTNSPatient-2 NT VS CTNSPatient-2 Bicalutamide - AKG level	One-way ANOVA
	0,5527	CTNSPatient-2 NT VS CTNSPatient-2 Cysteamine - AKG level	One-way ANOVA
	0,0005	CTNSPatient-2 NT VS CTNSPatient-2 Combination - AKG level	One-way ANOVA
6G	0,0040	ctnsWT VS ctns-/-	Unpaired t-test
6H	0,1088	ctns-/- control VS CTNS-/- Bicalutamide	One-way ANOVA
	0,0153	ctns-/- control VS CTNS-/- Cysteamine	One-way ANOVA
	0,0066	ctns-/- control VS CTNS-/- Combination	One-way ANOVA
	0,0888	CTNS-/- Cysteamine VS CTNS-/- Combination	Unpaired t-test
Figure EV1	P-Value	comparison	Statistical test
EV1C	<0,0001	CTNSWT VS colony 3	One-way ANOVA
	<0,0001	CTNSWT VS colony 7	One-way ANOVA
	0,0002	CTNSWT VS colony 35	One-way ANOVA
	<0,0001	CTNSWT VS CTNSPatient	One-way ANOVA
EV1D	<0,0001	Colony 3 VS colony 3 + cysteamine	Unpaired t-test
	<0,0001	Colony 7 VS colony 3 + cysteamine	Unpaired t-test
	<0,0001	Colony 35 VS colony 3 + cysteamine	Unpaired t-test
	<0,0001	CTNSPatient VS CTNSPatient + cysteamine	Unpaired t-test
Figure EV4	P-Value	comparison	Statistical test
EV4E	0,0060	CTNSWT no bicalutamide VS CTNSWT with bicalutamide	Unpaired t-test
	0.0581	CTNSWT no bicalutamide VS CTNS-/- no bicalutamide	Unpaired t-test
	0,6237	CTNS-/- no bicalutamide VS CTNS-/- with bicalutamide	Unpaired t-test
EV4D	0,0002	CTNS-/- control condition VS CTNS-/- bafilomycin treated	One-way ANOVA
	>0,9999	CTNS-/- control condition VS CTNS-/- starvation	One-way ANOVA
	<0,0001	CTNS-/- control condition VS CTNS-/- DMKG treated	One-way ANOVA
	0,9997	CTNS-/- control condition VS CTNS-/- cysteamine treated	One-way ANOVA
	0,9996	CTNS-/- control condition VS CTNS-/- bicalutamide treated	One-way ANOVA
	0,9997	CTNS-/- control condition VS CTNS-/- bicalutamide and cysteamine treated	One-way ANOVA
EV4F	<0,0001	CTNSWT fed VS CTNSWT starvation	One-way ANOVA
	0,0009	CTNSWT fed VS CTNSWT with bicalutamide	One-way ANOVA