Supplementary Information of Model 2

Content

I. TauCl Synthesis

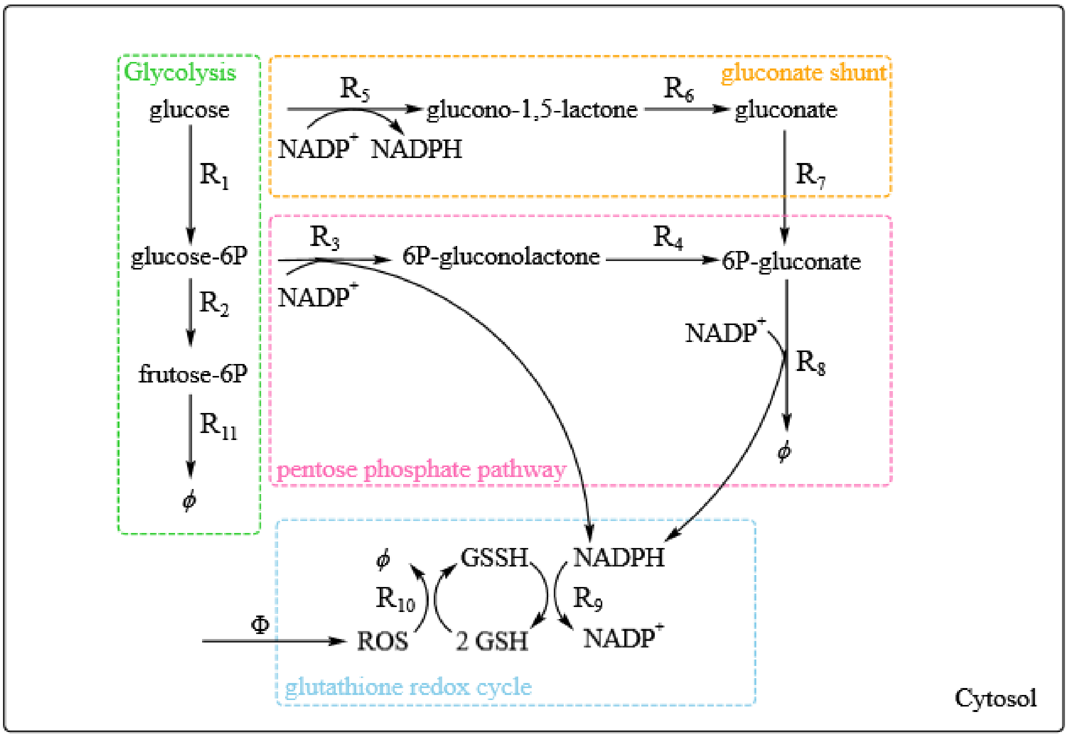
Supplementary Table S1: Rate equations of the kinetic model

Reaction	Equation	Rate equation	Source
MPO	$H2O2 \xrightarrow{MPO} HOCl \xrightarrow{spontaneous} TauCl$	$V_{MPO} = \frac{\frac{k_3 \cdot [E_{MPO}] \cdot [Tau] \cdot [Cl]}{\frac{k_3}{k_2} \cdot [Tau] + [Cl]} \cdot [H_2O_2]}{\frac{\frac{[Cl]}{K+1}}{k_1 \cdot \left(\frac{1}{k_2 \cdot [Cl]} - \frac{1}{k_3 \cdot [Tau]}\right)} + [Cl]}$	[1]

Supplementary Table S2: Parameters of the Rate equations

Reaction	Parameter	Value	Unit	Reference
MPO	k_1	$3.3 \cdot 10^7$	$M^{-1} \cdot s^{-1}$	[1]
	k_2	$2.8 \cdot 10^6$	$M^{-1} \cdot s^{-1}$	[1]
	k_3	$3.3 \cdot 10^7$	$M^{-1} \cdot s^{-1}$	[1]
	K	1.2	mM	[1]
	E_{MPO}	1	mM	[2]
	$[Cl]$	100	mM	[2]
	$[H_2O_2]$	0.1	mM	[2]
	$[Tau]$	25	mM	[1]

II. Innate ROS metabolic pathway



Supplementary Table S3: Differential equations of the kinetic model

Equations[a]
$\frac{d\,[\text{glucose}]}{dt} = 0$
$\frac{d\,[\text{glucose}-6-\text{phosphate}]}{dt} = R_1 \cdot n_{1,3,10,p} - R_2 - R_3 \cdot n_{1,3,10,p}$
$\frac{d\,[\text{fructose}-6-\text{phosphate}]}{dt} = R_2 - n_{i,p} \cdot R_{11}$
$\frac{d\,[\text{6p}-\text{gluconolactone}]}{dt} = R_3 \cdot n_{1,3,10,p} - R_4$
$\frac{d\,[\text{6p}-\text{gluconate}]}{dt} = R_4 + R_7 - R_8$
$\frac{d\,[\text{glucono}-1{,}5-\text{lactone}]}{dt} = R_5 \cdot n_{5,p} - R_6$
$\frac{d\,[\text{NADP+}]}{dt} = 0$
$\frac{d\,[\text{NADPH}]}{dt} = R_3 \cdot n_{1,3,10,p} + R_5 \cdot n_{5,p} + R_8 - R_9$
$\frac{d\,[\text{GSSG}]}{dt} = 0$
$\frac{d\,[\text{GSH}]}{dt} = 2 \cdot R_9 - 2 \cdot R_{10} \cdot n_{1,3,10,p}$
$\frac{d\,[\text{gluconate}]}{dt} = R_6 - R_7$
$\frac{d\,[\text{ROS}]}{dt} = -R_{10} \cdot n_{1,3,10,p} + \Phi$

Supplementary Table S4: Rate equations of the kinetic model

Reaction	Rate equation	Reference
$n_{i,p}$	$\frac{1}{1+[ROS]_p}$	3
$n_{5,p}$	$a_5 \cdot \frac{[ROS]_p - p5^*}{[ROS]_p + kp*,5} + 1$	
$n_{1,3,10,p}$	$a_{1,3,10} \cdot \frac{[ROS]_p - p_{1,3,10}}{[ROS]_p + k_{p_{1,3,10}}} + 1$	
R1	$V_1 = \frac{e_1 \cdot k_{cat\_hex}}{K_{hex\_A} + \left(1 + \frac{[b]}{K_{hex\_Bi}} + \frac{[d]}{K_{hex\_Di}}\right) \cdot a}$	
R2	$V_2 = \frac{e_2 \cdot k_{cat\_GPI\_f} \cdot K_{GPI\_D} \cdot [b] - e_2 \cdot k_{cat\_GPI\_r} \cdot K_{GPI\_B} \cdot [d]}{K_{GPI\_B} \cdot K_{GPI\_D} \cdot \left(1 + \frac{[f]}{K_{GPI\_Gi}}\right) + K_{GPI\_D} \cdot [b] + K_{GPI\_B} \cdot [d]}$	
R3	$V_3 = \frac{e_3 \cdot k_{cat3} \cdot ([NADP]_{tot} - [NADPH]_m) \cdot [b]}{(K_{3\_il} \cdot K_{3\_B} + K_{3\_L} \cdot [b])\left(1 + \frac{[NADPH]_m}{K_{3\_Mi}}\right) + (K_{3\_B} + [b]) \cdot ([NADP]_{tot} - [NADPH]_m)}$	
R4	$V_4 = \frac{e_4 \cdot k_{cat4} \cdot [f]}{K_{4\_F} + [f]}$	
R5	$V_5 = \frac{e_5 \cdot k_{cat5} \cdot ([NADP]_{tot} - [NADPH]_m) \cdot [a]}{(K_{5\_il} \cdot K_{5\_A} + K_{5\_A} + [a]) \cdot ([NADP]_{tot} - [NADPH]_m) + K_{5\_L} \cdot [a]}$	
R6	$V_6 = \frac{e_6 \cdot k_{cat6} \cdot [h]}{K_{6\_H} + [h]}$	
R7	$V_7 = \frac{e_7 \cdot k_{cat7} \cdot K_{GPI\_D} \cdot [gluconate]}{K_{7\_R} + [gluconate] \cdot \left(1 + \frac{[gluconate]}{K_{7\_Ri}} + \frac{[g]}{K_{7\_Gi}}\right)}$	
R8	$V_8 = \frac{e_8 \cdot k_{cat8} \cdot ([NADP]_{tot} - [NADPH]_m) \cdot [g]}{(K_{8\_il} \cdot K_{8\_G} + K_{8\_L} \cdot [g]) \cdot \left(1 + \frac{[NADPH]_m}{K_{8\_Mi}}\right) + ([NADP]_{tot} - [NADPH]_m) \cdot \left(K_{8\_G} \cdot \left(1 + \frac{[d]}{K_{8\_Di}} + \frac{[b]}{K_{7\_Bi}}\right) + [g]\right)}$	
R9	$V_9 = \frac{e_9 \cdot k_{cat9} \cdot ([GSH]_{tot} - [GSH]_o) \cdot [NADPH]_m}{2 \cdot K_{9\_N} \cdot [NADPH]_m + ([GSH]_{tot} - [GSH]_o) \cdot \left([NADPH]_m + K_{9\_M} + \frac{K_{9\_M} \cdot [GSH]_o}{K_{9\_io}}\right)}$	
R10	$V_{10} = \frac{V_{max10} \cdot [GSH]_o \cdot [ROS]_p}{(K_{10\_ip} \cdot K_{10\_o} + 2 \cdot K_{10\_o} \cdot [ROS]_p) + [GSH]_o \cdot (K_{10\_P} + [ROS]_p)}$	
R11	$V_{11} = \frac{e_{11} \cdot k_{cat11} \cdot [d]}{K_{11\_D} + [d]}$	

Supplementary Table S5: Parameters of the Rate equations

Reaction	Parameter	Value	Unit	Reference
R1	$e1$	0.0053578	mM	[3]
	k_1,cat	38	s^{-1}	
	K_1,A	0.032	mM	
	K_1,Bi	0.0108	mM	
	K_1,Di	0.160	mM	
R2	e_2	0.0037836	mM	
	k_2,cat,f	1000	s^{-1}	
	k_2,cat,r	115.8	s^{-1}	
	K_2,B	0.03	mM	
	K_2,D	0.01 mM	mM	
	K_2,Gi	0.005 mM	mM	
R3	e_3	4.29×10^{-6} mM	mM	
	k_3,cat	296 s^{-1}	s^{-1}	
	K_3,B	0.040 mM	mM	
	K_3,L	0.020 mM	mM	
	K_3,Mi	0.0171 mM	mM	
	K_3,il	0.009 mM	mM	
R4	e_4	0.0040654 mM	mM	
	k_4,cat	9010 s^{-1}	s^{-1}	
	K_4,F	0.08 mM	mM	
R5	e_5	7.33 × 10–6 mM	mM	
	k_5,cat	41s^{-1}	s^{-1}	
	K_5,A	11 mM	mM	
	K_5,L	0.00812 mM	mM	
	K_5,il	0.00328 mM	mM	
R6	e_6	0.0040008 mM	mM	
	k_6,cat	192 s^{-1}	s^{-1}	
	K_6,H	6.2 mM	mM	
R7	e_7	8.17×10^{-6} mM	mM	
	k_7,cat	9.3 s^{-1}.	s^{-1}	
	K_7,R	0.34 mM	mM	
	K_7,Ri	2.3 mM	mM	
	K_7,Gi	6.9179 mM	mM	

Supplementary Table S5:Continue

Reaction	Parameter	Value	Unit	Reference
R8	e_8	2.06775×10^{-4} mM	mM	[3]
	k_8,cat	9 s^{-1}	s^{-1}	
	K_8,G	0.019 mM	mM	
	K_8,L	0.056 mM	mM	
	K_8,Bi	6.85 mM	mM	
	K_8,Di	6.13 mM	mM	
	K_8,Mi	0.041 mM	mM	
	K_8,il	0.0048 mM	mM	
R9	e_9	4.66×10^{-6} mM	mM	
	k_9,cat	210 s^{-1}	s^{-1}	
	K_9,M	0.0085 mM	mM	
	K_9,N	0.065 mM	mM	
	K_9,io	8.5738 mM	mM	
R10	v_{10},max	0.44865 mM/s	mM/s	
	K_{10},O	1.33 mM	mM	
	K_{10},P	0.011 mM	mM	
	K_{10},ip	0.098778 mM	mM	
R11	e_{11}	0.0013059 mM	mM	
	k_{11},cat	110 s^{-1}	s^{-1}	
	K_{11},D	0.047 mM	mM	

Supplementary Table S6:Summary of constants required for enzyme kinetics.

Parameter	Value	Meaning
δ	3000	estimated ratio between extracellular and intracellular volume[a]
Φ	6.6×10^{-3} mM/min	endogenous ROS generation rate[b]
ξ	4.00 mM/min	cellular glucose uptake rate under control conditions[c]
$[NADP]_{tot}$	6.405×10^{-3} mM	total concentration of NADP(H)[d]
$[GSH]_{tot}$	0.15593 mM	total concentration of glutathione[d]
$\alpha_{1,3,10}$	96.962	maximal activation factor of reaction 1, 3 and 10[e]
p∗1,3,10	2.85×10^{-4} mM	ROS activation threshold of reaction 1, 3 and 10[e]
$k_{p*,1,3,10}$	2.29×10^{-3} mM	scaling factor of activation term $\eta_{1,3,10}(p)$[e]
α_5	49.342	maximal activation factor of reaction 5[e]
p∗	2.70×10^{-4} mM	ROS activation threshold of reaction 5[e]
$k_{p*,5}$	45.089 mM	scaling factor of activation term $\eta_5(p)$[e]

III. TauCl Intake System

Supplementary Table S7: Rate equations of the kinetic model

Rate equation	Reference
$Up_{Tau} = [\frac{Up_{max} * T_{ext}}{K_{tau} + C_{tau} + T_{ext}}] + c$	[4]

Supplementary Table S8: Parameters of the rate equations

Parameter	Value	Unit	Description
Up_{TauCl}	Calculation	μmol g^{-1} h^{-1}	Uptake rate of TauCl by intestinal cell
Up_{max}	0.35 ± 0.09	μmol g^{-1} h^{-1}	Maximum uptake rate of TauCl by intestinal epithelial cell
T_{ext}	25	mmol l^{-1}	Extracellular TauCl concentration
C_{tau}	25	mmol l^{-1}	Total TauCl concentration
K_{tau}	35.3 ± 9.6	μmol l^{-1}	TauCl concentration at which transport process is half-maximal
c	90.6 ± 17.4	pmol g^{-1} h^{-1}	Constant

IV. TauCl Induce GSH Production System

Supplementary Table S7: Rate equations of the kinetic model

Formula	Reference
$GSH(\%) = 0.0015\,t^3 - 0.0395t^2 + 0.5277t + 1.002$	Estimated

Supplementary Table S8: Symbols' description

Symbols	Description
$GSH(\%)$	Increase relative amount of GSH produced in intestinal epithelial cell.
$t\ (hr)$	Reaction time

Reference

1. Marquez LA, Dunford HB. Chlorination of taurine by myeloperoxidase. Kinetic evidence for an enzyme-bound intermediate. *Journal of Biological Chemistry*. 1994/03/18/ 1994;269(11):7950-7956. doi:https://doi.org/10.1016/S0021-9258(17)37143-0
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3. Schittenhelm D, Neuss-Radu M, Verma N, Pink M, Schmitz-Spanke S. ROS and pentose phosphate pathway: mathematical modelling of the metabolic regulation in response to xenobiotic-induced oxidative stress and the proposed Impact of the gluconate shunt. *Free Radical Research*. 2019/10/03 2019;53(9-10):979-992. doi:10.1080/10715762.2019.1660777
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